POLYURETHANE INTERPENETRATING POLYMER NETWORKS FOR BIOMEDICAL APPLICATIONS

A THESIS PRESENTED

BY

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CERTIFICATE

I, Prabha D. Nair , hereby certify that I had personally carried out the work depicted in the thesis entitled " POLYURETHANE INTERPENETRATING POLYMER NETWORKS FOR BIOMEDICAL APPLICATIONS ", expect where external help sought are acknowledged.

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entitled

POLYURETHANE INTERPENETRATING POLYMER NETWORKS FOR BIOMEDICAL APPLICATIONS

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TO

MY BELOVED PARENTS

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SYNOPSIS

Polyurethane materials are extensively used in blood contacting applications and organ reconstruction due to the wide range of excellent physical and mechanical properties and relatively good biocompatibility. Surface modifications of polyurethanes, however, have been attempted to increase the biocompatibility which in turn is dependent on several factors such as surface, topography, energy etc. A balance of hydrophobic-hydrophilic sites is found to be beneficial for enhancing blood compatibility. However modifications produce alterations in the physical and mechanical properties of polyurethanes and make it more susceptible to degradation. Surface cracking, biodegradation and calcification are other problems associated with polyurethane materials. Better compatibility, enhancement of mechanical properties and resistance to degradation may be achieved with interpenetrating polymer networks.

Interpenetrating polymer networks (IPNs) are a new class of materials formed by interlocking of two or more polymer networks. Used widely in the new generation of plastics, IPN synthesis aims at enhancing the compatibility of thermodynamically incompatible polymers. The use of IPNs as biomaterials is, however, not extensively explored. This thesis projects the author's efforts to synthesise and evaluate polyurethane based IPNs for biomedical applications. The introductory chapter

reviews the background literature on IPNs and factors influencing the biocompatibility of implant materials. The objectives and scope of the work is also outlined in this chapter.

Chapter II deals with the experimental procedures utilized during the course of the work and also the synthetic route employed for IPN synthesis. The IPNs synthesised are mainly of polyurethane, (PU), as polymer I and vinyl polymers as the second polymer, such as polyurethane-polyacrylamide, (PU-PAM), polyurethane-polyvinylpyrrolidone, (PU-PVP), polyurethane-poly 2-hydroxyethylmethacrylate, (PU-PHEMA), and polyurethane-polymethylmethacrylate, (PU-PMMA). The polyurethanes are based on two aromatic diisocyanates, namely, toluene-2,4 diisocyanate,(TDI), and 4,4' diphenyl methane diisocyanate,(MDI). Polyol nature, molecular weight and crosslinking were varied for an indepth study of the characteristics of PU-PAM IPNs. A polyurethane composition based on the polyol, polytetramethylene glycol, (PTMG 1010), was used to study the effect of varying the vinyl polymer, on IPN properties. The IPNs were characterised for their mechanical, thermal, dynamical mechanical, surface and morphological properties. In vitro biocompatibility and stability of IPNs were studied. In vivo biocompatibility and biostability of candidate IPNs were also assessed.

Chapter III comprises the results and discussion of the characterisation of the synthesised IPNs. Mechanical properties of the IPNs studied demonstrated the IPN's elastomeric nature. Tensile stress and percent elongation at break of PU-PAM IPNs

were observed to be influenced by the factors such as crosslinking of polyurethane, the type of isocyanate or polyol used and composition of the IPN. The 90/10 IPN was selected for further evaluations and comparisons owing to its superior properties. The dynamic mechanical analyses (DMA) of IPNs served to indicate IPN formation. Thermal properties such as glass transition were evaluated to support the conclusions obtained by DMA studies. Thermogravimetric analyses of the IPNs were carried out. The IPNs were found to have a 50% thermal decomposition temperature around 400 degree Centigrade. The polymer-water-air contact angle of the surface of the IPNs showed that PU-PAM IPN, PU-PHEMA IPN and PU-PVP IPN have a relatively more hydrophilic surface than the polyurethane and PU-PMMA IPN has a relatively more hydrophobic surface. Crosslink density was found to increase on IPN formation. Scanning electron microscope studies were carried out to have an insight of phase morphology. The microphotographs revealed the semicompatible nature of the IPNs.

Chapter IV discusses the results of in-vitro procedures on the IPNs. Recalcification time, platelet aggregation and haemolysis of the IPNs were evaluated in addition to its stability evaluation in phosphate-buffered saline. The recalcification time of the IPNs showed that all the 90/10 IPNs had a comparitively prolonged recalcification time compared to the polyurethanes, demonstrating the nonthrombogenic nature of the IPNs. ADP induced platelet aggregation of calf plasma exposed to the IPNs was comparable to that observed for a biomedical grade

polyurethane with slight variations. Haemolysis studies demonstrated the nonhaemolytic nature of the IPNs. Stability of IPNs stored in phosphate-buffered saline showed that the IPNs were quite stable in the aqueous environment.

Chapter V discusses the results of the in-vivo implantation of the IPNs. The IPNs were implanted in the subcutaneous of wistar rats to assess their biostability. The changes in mechanical property with post-implantation were followed upto 3 months. It was observed that the IPNs have less degradation compared to a commercially available polyurethane. The TDI based IPNs were found to be superior to the MDI based IPNs.

Toxicological analysis of the materials showed that the materials are nontoxic. Histopathological studies of IPNs implanted in the intramuscular region of rabbits for a post-implantation period of 3 months showed that the IPNs are relatively inert materials. However the TDI based IPNs were found to elicit less inflammatory host response than MDI based IPNs at the end of one month. Implantation of TDI based IPNs for a post-implantation period of 3 months could serve to highlight a slight difference in host response due to different IPNs. It was observed that the more hydrophilic PU-PVP IPN and more hydrophobic PU-PMMA IPN performed better i.e. elicited minimal reactions of host tissue in the hostile physiological environment. Intermediate hydrophobic or hydrophilic surfaces elicited moderate tissue response. The tissue reactions in all IPNs were comparable to that of control biomedical grade polyurethane.

Chapter VI, the final chapter, summarises the conclusions and the future prospects of the investigation.

INTRODUCTION

INTRODUCTION

CHAPTER I

Development of new polymeric materials by the synthesis of unique monomers is at a technological plateau in the plastics industry. Multicomponent polymer systems obtained by blending or alloying two or more polymers with different chemical structures and physical properties have recently created considerable interest and they represent a new and important challenge for research. Blending of polymers is significant because it is often the easiest and most economical method for improving rheological, mechanical, degradative and other performance properties.

Normal blending or mixing of polymers results in a multiphase morphology due to the well known thermodynamic incompatibility of polymers. However, if mixing is accomplished simultaneously with crosslinking, phase separation may be kinetically controlled by permanent interlocking of entangled chains. Thus blending by cosynthesis of two different polymer networks provide promising tool for achieving mutual improvement in physical properties. This technique is called interpenetrating and the polymer network then prepared is called interpenetrating polymer network (IPN). With this increased synthetic capacity to tailor polymer properties, new and important applications can emerge. This is achieved by selecting the proper component of the polymer system and arriving at actual reaction conditions.

Incorporation of a compatible elastomeric component in to a plastic network is shown to improve the toughness and impact resistance of the plastic component. Similarly interpenetration of a plastic network into an elastomeric network increases the strength of the material, often retaining the elastic properties to a great extent. An IPN of hydrophobic and hydrophilic monomers would be expected to have enhanced biocompatibility while retaining its superior mechanical properties and also possess greater stability in the invivo environment.

An'IPN'is defined as a combination of two polymers in network form, atleast one of which is synthesised and/or crosslinked in the immediate presence of the other (1) Fig. 1.1 illustrates some IPN structures (2). Structure (a) illustrates an IPN formed when only one of the polymers is crosslinked and structure (b) illustrates an IPN with both polymer crosslinked. While grafts between networks I and II may occur to a greater or lesser extent, the IPN topology may be said to exist if the deliberately introduced crosslink sites outnumber the accidently introduced graft sites.When this condition prevails, the crosslinks dominate and control the morphology and hence most of the physical and mechanical behaviour.

The term IPN implies an interpenetration of two polymer networks of some kind and was coined before the full sequences of phase separation were realised. Molecular interpenetration occurs only in the case of total mutual solubility. However, IPN synthesis to date exhibit varying degrees of phase separation, depe-

ndent principally on the compatibility of the polymers. With highly incompatible polymers, the thermodynamic forces leading to phase separation are so powerful that it occurs substantially before the kinetic ramification can prevent it. In these cases only small gains in phase mixing occur and in cases where the polymers are more compatible, phase separation can be almost completely circumvented. Complete compatibility is not necessary to achieve complete phase mixing, since the permanent entanglements (catenation) can effectively prevent phase separation.With intermediate situations of incompatibility, intermediate and complex phase behaviour results. Thus IPNs with dispersed phase domains ranging from a few micrometers (incompatible) to a few tens of nanometers (intermediate) (3) and finally to those with no resolvable domain structure (complete phase mixing) have been reported (4,5). If the polymers are chemically identical the product is called a Miller IPN (6). In this case, true compatibility is achieved and the network chains are believed to actually interpenetrate at the molecular level.

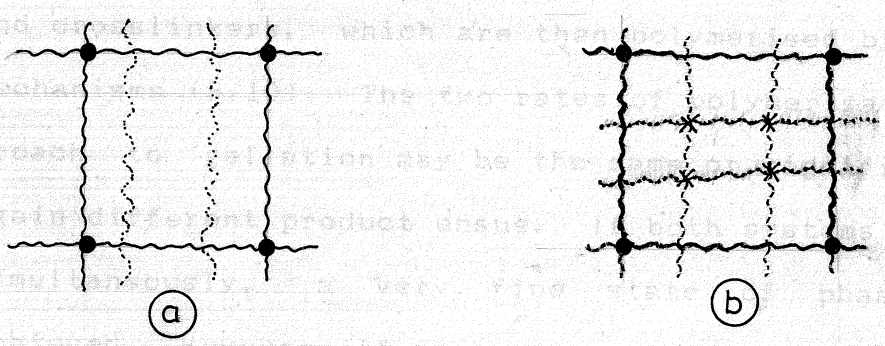


Fig.1.1 Schematic diagram of some IPNs :(a) semi IPN , (b) an IPN

1.1 Classification and nomenclature of IPNs:

Several types of IPNs have been described. They are sequential IPNs, simultaneous IPNs, semi IPNs, interpenetrating elastomeric networks, thermoplastic IPNs and gradient IPNs.

In the sequential type, crosslinked polymer I is first synthesised and is then swollen with monomer II plus it own crosslinker and initiator and polymerised in situ. This type of IPN may be written as Polymer I/Polymer II where I and II are polymers synthesised in that order. An inverse IPN (7,8) can also be formed by polymerising the above polymer II network first followed by polymer I. The inverse IPNs will in general exhibit far different behaviour than the normal synthesis.

Instead of sequential synthesis, both networks can be synthesised simultaneously. From a practical viewpoint, the most vital chemical requirement involves finding independent, noninterfering polymer reactions that can be run simultaneously under the same overall conditions. A general solution to this requirement entails the use of condensation and addition reactions. Thus, simultaneous IPNs (SINs) begin with a solution of both monomers and crosslinkers, which are then polymerised by non-interfering mechanisms (9,10). The two rates of polymerisation and their approach to gellation may be the same or significantly different, again different product ensue. If both systems reach gelpoint simultaneously, a very fine state of phase dispersion is achieved. However, if one monomer reacts faster, a larger domain size is obtained.

When one of the polymers is crosslinked and the other is linear, the product is called a semi-IPN or pseudo IPN (11). If the polymerisation are sequential in time, four semi IPNs may be distinguished. When the polymers are synthesised simultaneously in a semi IPN it is known as semi SIN. Allen et al (12) has used the term "interstitial composites" to describe the semi SINs. Another mode of IPN synthesis takes two latexes of linear polymers, mixes and coagulates them and crosslinks both components simultaneously, the product is called an IEN (13).

The bulk synthesised interpenetrating polymer and interpenetrating elastomer networks once prepared are thermoset in nature and cannot be reformed. This is a natural consequence of macroscopic network formation. Thermoplastic IPNs can be produced, however, through the art of emulsion polymerisation. One starts with a crosslinked seed latex I, adds monomer II plus crosslinker but no new soap, and polymerises monomer II in the presence of I. Ideally no new particles are formed and each finished particle contains both networks in miniform (14,15). Latex semi IPNs can also be synthesised (16). Whereas the simultaneous IPNs could be processed upto the gelation stage, the thermoplastic IPNs can be processed or reprocessed at any time.

There is yet another class of IPNs known as the 'gradient' IPNs. In gradient IPNs, the composition is varied within the sample at the macroscopic level (17,18). This is conveniently carried out by soaking a sheet of network I in monomer II for a limited period of time and then polymerising II rapidly, before

diffusion equilibrium can occur.

1.2 General properties of IPNs:

An IPN can be distinguished from simple polymer blends, blocks and grafts in two ways. 1) An IPN swells, but does not dissolve in solvents and 2) creep and flow are suppressed.

Most IPNs and related materials investigated show phase separation. The phases however vary in amount, size, shape sharpness of their interfaces and degree of continuity. These aspects together constitute the morphology of the material and the multitude of possible variations controls many of the material properties. The properties of IPNs depend on 1) the property of the component polymers 2) the phase morphology and 3) interactions between the phases. As with other two component materials, some properties of IPNs are approximately simple averages of the properties of the component polymers but synergistic behaviour is observed. For example, optical transparency is one property which departs completely from simple averaging. The IPNs of two amorphous, transparent polymers such as polyethyl acrylate (PEA) and polystyrene (PS) are hazy and transclucent in thin sheets because the phase domains have different refractive indices and scatter light. Phase separation in less compatible IPNs such as SBR-PS results in white opaque materials because of increased scattering as the size of the domain approaches the wavelength of light.

When two polymers form a phase separated mixture, each retains its glass transition. In general the transitions may be

broadened or shifted inward by mixing, and in the limit of mutual solubility only one transition is observed. Klempner et al (19) remark that depending on thermal history sometimes an intermediate glass transition was observed for full IPNs, indicating the presence of a possible third phase.

Thermogravimetric properties of polyurethane, polymethyl methacrylate IPNs (20) and polyurethane/polystyrene SINs (5) reported by Kim et al, exhibit unusual synergism with certain compositions showing significantlyy greater temperature resistance than the homopolymers. A number of IPN compositions (21,22) exhibit considerable toughness as measured by stress strain curves or impact strength.

1.3 Brief historical aspects.

As in many other areas of scientific and engineering endeavours it is difficult to pinpoint an exact time origin for the ideas leading to interpenetrating polymer networks. The first IPN, however was invented by Aylsworth (23). This was a mixture of natural rubber, sulphur and partly reacted phenol formaldehyde resins. On curing an IPN was formed, the patent does not use the word "polymer" or any modern concepts. The first use of the term "interpenetrating polymer network" was by Millar in 1960 (6). Employing suspension polymerisation techniques, Millar prepared interpenetrating polymer networks with both network I and network II being composed of identical styrene-divinyl benzene combinations.

In 1969, Frisch and Sperling independently arrived at the

IPN topology through different thought processes. Frisch's appr-oach arose through the concept of macromolecular topological isomers (24) and catenanes (25).

Sperling originally synthesised his materials in an effort to develop a poorman's polymer blend where the phases would be finely divided without the need for mechanical mixing (26-28), Network I of the interpenetrating polymer networks is continuous and after swelling with II remains so. At low concentration of polymer network II, a cellular structure is formed with I con-stituting the cell walls and II constituting the honey. At higher concenterations of II the cell interiors become connected to form two continuous phases.

Yu Lipatov (29) also studied IPNs and was the first to consider the IPNs as polymer/polymer composites, where the second network constituted a filler in the first formed network. Yu et al (30) also considered the IPNs to have interfacial regions giving rise to heterogenous morphology.

The research in the field of IPN synthesis has been reviewed by several authors (22,31-35).

The physicomechanical properties of IPNs depend on their chemical composition and morphology. Recent reports in the field of IPNs have emphasised the relationship between morphology and mechanical behaviour of IPNs (36,37). The fine structure and domain size of an IPN depend on several factors. Differences be-tween the solubility parameters of both polymers, crosslink den-sity of the matrix networks, relative polymerisation rates of

both components (in the case of SINS), component I-component II ratios and content of grafting or intercrosslinking bonds (if any) play an important role. Sperling et al (38) studied the effect of crosslink density in the IPNs and semi IPNs on morphology and mechanical properties. In another study Touhsaent et al (39) investigated the morphology and mechanical behaviour of SINs. When simultaneous gelation of both networks was achieved, a minimum in gel size was obtained. The gel size obtained was too small for optimum toughness and less simultaneously reacted compositions were tougher than the more simultaneous ones.

Studies on the thermal behaviour and glass transition temperature of IPNs are mentioned in several reports (40,41). While simple homopolymers and random copolymers exhibited single sharp glass transitions, polymer blends in general and IPN in particular showed two such transitions, one for each phase. A third intermediate transition has also been observed and attributed (42) to an interfacial region contribution. The intensity of each transition was clearly related to the overall composition and phase continuity while shifts and broadenings of the transition indicated the extent of molecular mixing. For simultaneous IPNs, Frisch et al (43) have a single Tg intermediate in temperature to the Tg's of the component networks. They also found that the measured Tgs were lower than the computed arithmetic means of the Tgs of the components. The amount of lowering has been related to the extent of interpenetration.

The permeability behaviour of a polyurethane-epoxy SIN type

material was found to be dependent upon composition in a non-linear fashion, probably due to phase inversion and dual phase continuity (44).

Neubauer et al (45) studied semi IPNs synthesis from polyethyl acrylate (PEA) and polystyrene (PS).The crosslinker for the PEA was composed of various ratios of diethylene glycol dimethacrylate (DEGDM), a permanent type of crosslinker and acrylic acid anhydride (AAA) a hydrolysable crosslinker. As the quantity of (AAA) increased from 0 to 100%, the modulus change on annealing increased very significantly, suggesting morphological changes. The decrosslinking of an IPN or semi-1-composition results in a chemically induced blend. Systematic and controlled decrosslinking offers a new mode of morphological control through which new or improved physical and mechanical behaviour pattern can be achieved.

A large variety of polymer networks were used for IPN synthesis. But major fraction of IPN studies concenterates on IPNs where one component is a polyurethane network. The work by Cassidy et al (46), on 2 component polyurethane-epoxy IPNs describes the effect of charge groups on the properties and morphology. Detailed study on PU-PMMA IPNs has been conducted by Xiao et al (47). Semi and full IPNs based on polyurethanes and polyacrylates were also investigated (48,49). It was found that in these IPNs introduction of charged groups increase phase miscibility and decreased the extent of phase separation (50). Kim et al (5) has related phase separation occurring in PS-PU IPNs to the

incompatibility of the 2 networks. Simultaneous IPNs based on polybutadiene based PU/Poly (styrene co divinyl benzene) has been also investigated (51).

Recently 3 component IPNs were reported (52,53,54). These IPNs were prepared from PU epoxy resins and acrylic polymers using the simultaneous technique. The IPNs exhibited a variety of morphologies and their properties depended on the type of polymer, prepolymer molecular weight, presence of charge groups and the presence of intentional grafts.

With the fast increasing price of petroleum products, researchers on the renewable sources for products of plastic, elastomer and other materials had gained momentum and this trend had its impact on IPN synthesis also. Thus, naturally ocurring triglyceride oils were made use of in IPN synthesis. Simultaneous IPNs containing crosslinked polystyrene and elastomeric components based on trimer acid, crosslinked epoxidised linseed, crambe, lunaria and lesquerella oils were prepared (55). Another triglyceride oil used in IPN synthesis is Lesquerella palmeri oil which has a structure similar to castor oil. The oil could be reacted with sebacic acid or 2,4 TDI to form polyesters or polyurethanes. Several IPNs and simultaneous IPNs with divinyl benzene were made and both were found to be tough leathery material (56). In another study, the IPNs of sebacic acid-veronia oil copolymer with styrene divinylbenzene copolymer exhibited a continuous veronia oil elastomeric phase with a binodal distributed polystyrene domain phase (57).

Castor oil with its unique nature among other naturally occurring triglyceride oils of having functionality as double bonds and hydroxyl groups is capable of substituting some of the polymer and other high value products which are currently based on petroleum derivatives. Considerable work was done using castor oil for constructing the PU network in IPN synthesis (58,59). The investigation on castor oil based IPNs allowed better understanding of the effect of chemical composition and the structure of IPNs consisting of a high elastic network and a glassy network on their mechanical behaviour.

Before proceeding to a significance of IPNs in biomedical applications, an introduction to biomaterials and aspects of biocompatibility would be appropriate.

1.4 Biomaterials :

A biomaterial can be defined (60) as any nonviable material used in a medical device and intended to interact with the biological system. Biomedical materials include metals, ceramics, natural or synthetic polymers and combinations and composites of these materials. The major properties of a biomaterial that need consideration are its material characterstics, mechanical behaviour and processability and its interaction with the biological environment (61).

1.5 Biomedical polymers :

Large number of polymers have been used in biomedical applications. These polymers range from naturally occurring materials such as natural rubber, cellulose to synthetic elastom-

ers (including silicone rubber), the polyurethanes and hydrogels. The most widely used synthetic polymer is medical grade silicone rubber (62) which is composed of about 65% polydimethyl siloxane and 35% silica filler. Other widely used polymers include plasticized polyvinylchloride (PVC), polyethylene, Teflon (R) polytetrafluroethylene, Dacron (R) polyester, and nylon. PVC is probably the most widely used polymer in disposable devices (63).

Among the remaining polymers, the polyurethanes are an interesting family of materials. They are a unique class of polymers because their reactions are quantitative and complete and a large variety of polyurethanes with widely varying physical and chemical properties can be synthesized(64). The polyurethanes as a class have been found to be relatively biocompatible materials and it is this property, together with the broad possibilities for the design and synthesis of different polyurethanes with superior physical and mechanical properties that have made the polyurethanes so appealing for biomedical applications.

1.6 Aspects of Biocompatibility:

Biocompatibility can be defined (60) as the ability of a material to perform with an appropriate host response in a specific application. Biocompatibility of a material is a two fold process, one which is concerned with compatibility with the tissues and the other more rigid one being compatibility with blood.

While coming to the latter, the compatibility of a material

with blood appears to be influenced by a number of different properties, most of which relates to the surface of the material which contacts blood (65-67). Surface free energy, surface molecular motions, surface topography, critical surface tension, electrical conductivity and water content are determining factors of blood compatibility (68,69). Andrade (70) put forward the hypothesis that material surfaces with an interfacial energy of 0 would be expected to be highly nonthrombogenic. Hydrogels possessing minimum interfacial energy (71) attract lower thrombus adherence and validate the hypothesis. Surface free energy is also believed to have an important role in blood material interactions. Baier (72) hypothesizes a zone of critical surface tension of 20 to 30 dyne/cm as ideal for blood compatible surfaces. However exceptions have been reported in the case of LTI carbon with γ_c =50 dyne/cm (73). Kaelble and Moacanin (74) have indicated that dispersive and polar components of polymer surfaces play an important role in interfacial interactions. Several of these theories are however in conflict with one another.

Other properties of the surface which seem to affect blood material interactions, especially in the case of polymeric materials is the chemical nature of the surface. Distribution of chemical groups on the suface could affect interactions such as thrombus formation, emboliformation, haemolysis of red cells and distribution of proteins. The surface concentration and type of hard segment (75) and relative concentration of the hard segment (75,76) are seen to be of importance in the determination of the

blood responses of polyurethanes. Even the method of fabrication was seen to affect the surface properties of polyurethane block copolymer (77,78). In a study of polyurethanes with varying polyol molecular weight of 710 and 1025 (79), it was concluded that polyurethane urea (PEUU) 1025 had relatively better blood compatibility.

The ratio of hydrophilic to hydrophobic area is also believed to have an important influence on blood compatibility. Protein adsorption (80) and platelet adhesion (81) vary with changes in hydrophilicity and hydrophobicity of the polymer surface.

A dependance of platelet adhesion on crystalline and amorphous domains in polypropylene oxide segmented polyamides have been observed by Yui et al (82). The morphology and texture of the blood contact surface hence appears to play a role in blood material interactions.

In polyether urethanes an increasing polyether content has been shown (83) to result in a reduction of platelet adhesion. Polyols seem to actively suppress platelet adhesion in a trend of PEO > PPO > PTMO (84). The surface is also dynamic with chain segments or pendant functional groups either migrating to or from the surface and influencing blood material interactions. Lyman (85) observed the surface of polyether polyurethanes to be richer in polyether content while Refojo (71) has shown that the molecular motions of a surface of polyHEMA could result in polyHEMA appearing more hydrophobic than a polymethyl methacrylate surface under the same conditions. Further, even casting

solvent (75) or the mold facing side or air facing side (85) of polymers appear to have some role in determining blood material interactions. The initial effect of molecular molecular motions on the thrombogenesis is believed (86) to occur independent of morphological order/disorder, crystallinity and/or associated water (at 0.01 mg bound water/mg polymer level).

1.7 Protein adsorption and platelet adhesion:

One of the first events to take place when an artificial surface contacts blood is the adsorption of proteins (87). Protein adsorption is a competitive process in which all the plasma proteins may be involved to some extent. Serum proteins including albumin, globulin, fibrinogen, fibrinoectin (Fn), coagulation factors (Fg G) etc have been found adsorbed to various artificial surfaces in vitro (88-90). The adsorption of proteins is influenced by a number of factors such as material properties, enzymatic influences and blood flow patterns (91,92). In general, proteins interact more strongly with hydrophobic surfaces than with hydrophilic ones (89,93). Hydrophilic surfaces also seem to adsorb less protein than hydrophobic surfaces (94). Polymers would thus seem to selectively adsorb protein from a bulk concentration. Studies done so far are not conclusive for the complicated process of protein adsorption on to various surfaces.

Initial protein adsorption brings about changes in platelets which may trigger blood coagulation. Platelets are complex structural elements of the blood which circulate in disc

form averaging 3 μm in diameter and 1 μm in thickness and have a volume of ~6 μm^3. The adhesion of platelet to artificial surfaces involves the interaction of platelets with a layer of plasma adsorbed (95,96) to the surface. It has been suggested that the carbohydrate component of adsorbed proteins are involved in the reaction with platelet receptors (97,98) and probably also with the surface charged groups such as Nacetyl neuroamino acid (99). Following the exposure of a surface to blood, platelets are seen to adhere rapidly either as a monolayer or as aggregates and they also may have an associated fibrin network (100,101) Platelets can adhere to a surface and via different mechanisms can adhere to each other (102,103). In addition to becoming adherent to a surface, the platelets (104,105) may undergo shape change or extend pseudopods or release their granular contents to the surrounding medium resulting in platelet aggregation.

Materials vary in their thrombogenicity which in turn is dependent on platelet release reaction and aggregation. Several surface parameters have been seen to influence platelet attachment, spreading and also correlated with blood compatibility. Baier et al (106) has correlated surface energetics of substrates towards platelet attachment. Bubbles and gas nucleii at solid/liquid interface has been seen to enhance platelet adhesion (107).Several authors have attempted to correlate surface hydrophilicity or hydrophobicity and smoothness or roughness to its platelet adhering capacity (107-110).

The flow rate of blood or plasma medium has been corre-

lated with adhesion of platelets (111). Thus, surface topography, chemistry, energy, haemodynamic parameters are all highly interrelated to the thrombus formation at the blood material interface.

1.8 Tissue responses to implant materials (Biocompatibility):

Biocompatibility of an implant material as differentiated from blood compatibility can be divided into two parts: The effects of the implant on the host and the effect of the host on the implant. The effect of the implant on the host can be subdivided into local and systemic responses. Local tissue responses or histocompatibility are those which elicit effects in the immediate tissue area around the implant such as inflammation, neoplasm, necrosis and immune responses. Systemic responses are those which affect tissues in other parts of the body and are usually due to implant degradation. These include toxic responses, carcinogenic responses and allergic responses. The responses of the body on the implant include degradation, corrosion and phagocytosis.

The tissue responses to implants can be better understood with reference to the normal wound healing (112-114) and associated cellular responses.

1.8.1 Cellular response to foreign materials.

Any foreign material present in the wound area will affect the tissue changes associated with the healing process, although the extent of its influence is quite variable. There is usually an accumulation of polymorphonuclear leucocytes in the vicinity

of the foreign body at first, this soon being followed by an invasion of macrophages. They sometimes develop into cells known as foreign body giant cells which are extremely large cells often with a diameter of the order of several hundred microns. They contain large numbers of nucleii which tend to be localized, and often the cytoplasm can be seen containing particles of the foreign material. These foreign body giant cells often arrange themselves so as to have intimate contact with the foreign material. At the same time as this formation of giant cells, there is fibroblastic reaction, such that the foreign material becomes enclosed in fibrous tissue.

Under some conditions, when the material can be considered chemically and physically inert, the responses of the tissues to the implant may be only slightly different from that involved in normal post operative healing. The macrophages which may be initially present may not lead to foreign body giant cells formation, and the end result is only a slight thickening of the fibrous scar tissue that would otherwise have been formed, perhaps being somewhat less vascular and less cellular. This type of response which leads to the foreign body being completely covered by a fibrous tissue capsule is considered by some (113) to be the most favourable response clinically, for the material is then virtually extracorporeal and is effectively ignored by the body.

If the material is less 'inert' or more 'irritant' then the foreign body giant cells are produced. It has been suggested(115)

that the presence of giant cells in the surrounding tissue is a clinically undesirable feature indicating basic tissue instability. This is not an universally accepted conclusion being challenged by Charnley amongst others (116). Their argument being that the fibrous tissue lining of polymethacrylate used in orthopaedic procedures is "histologically indeterminate" with occassional phagocytes and giant cell collection even after nine years.

Inflammation describes the vascular and cellular reaction of the tissues to harmful stimuli.These are acute or chronic inflammations,the former involving an exudation of fluid (117) and cells into the tissue in response to an irritant and the latter involving a local cellular proliferation in the absence of a fluid exudate.Such a cellular proliferation,involving polymorphonuclear leucocytes, macrophages,fibroblasts and others give rise to granulation tissue,which by virtue of the cells that it contains,combines the functions of phagocytosis and organisation (that is revascularisation and eventually fibrosis).Granulation occurs under the stimulus of either infection or irritant foreign bodies.Healing is delayed when this is present and the eventual scar or fibrous tissue layer is usually much thicker than in its absence.

A final type of response is death of the adjacent tissue or necrosis.The implant has to be active chemically,mechanically or possibly thermally for this to happen.The presence of an implanted foreign body could thus be categorised into a scale,one

end of which shows little more than normal postoperative fibrosis,at the other end,granulation or even necrosis and in between,changes involving varying amounts of macrophages and foreign body giant cells.

1.9 Factors influencing foreign body reactions to implants

There are three types of foreign body reactions to implants (1)reactions due to the physical characteristics of the implant. (2)reactions due directly to the chemical properties of the implant. (3)immune reactions.

1.9.1 Reactions due to physical characteristics of implant:

These deal chiefly with the size,shape,porosity of the implant and also the site of implantation.It has been observed(118)that materials may be compatible in one tissue, location or application but not in another. The physical form of the implant causes responses ranging from simple capsule thickening, epithelial encapsulation of the plastic, epithelial keratinization in cutaneous implants, formation of ground substance and presence of giant cells due to the mechanical trauma to local tissues to tumour formation induced by a large impervious solid. Implant shape (sharp corners or edges), implant rigidity (particularly in soft tissues) and surface roughness can cause increase in encapsulation. Paradoxically capsule thickening reduces the trauma and can lead to a well tolerated implant. The significance of implant shape has been examined by Wood et al (119) who implanted disc and rod shaped polymers in mandible, calvarium and muscular sites of rabbit. They observed the grea-

test reaction in the muscular sites with discs showing microareas of tissue reactions randomly across the periphery.The rod shaped samples in muscle showed greater reaction at ends rather than in the midportion of the shaft . B.F.Matlaga et al (120) has observed that a triangular shaped implant showed highest enzyme activity in gluteal muscle of rat with the enzyme activity around pentagonal shaped and circular shape successively decreasing.

Another factor related to the physical characteristics of an implant is its porosity. Large pores in an implant facilitate normal tissue growth. However, an implant with pore sizes approaching that of ingrowing cell causes problems with the outer part of the implant becoming choked with cells and newly synthesised connective tissue. As it becomes increasingly difficult to maintain a normal cellular environment for those cells that have penetrated most deeply into the body of the implant, the result is often cell death, vacuolation and calcification with the consequent hardenening of what might originally have been intended a soft prosthesis. An optimum pore size for polymers for biomedical applications has been suggested (121) to be (1-200 μm). While porosity is a bulk property, its effect could be felt on the surface with the surface suffering undulations due to open pores. This could affect thrombogenesis (122) through nucleation of micron sized bubbles at the surface.

1.9.2 Reactions due to the chemical properties of the implant:

Residual monomers, leachants, additives, surfactants etc. and other inadvertent contaminants may be responsible for the

toxicity of the implant and produce adverse reactions. It was noted (123) that responses of increased severity were associated with the following: polyelectrolyte coated implants, epoxy resins, epoxy resin with a hydrophobic diluent which did not bind permanently to the resin, and experimental adhesives caused in vivo growth of keratotic cysts and accelerated growth of epithelium occurred contiguous with polyelectrolyte coated material. Mild irritants have been shown (122) to stimulate epithelial growth. An acute response with secretions of mucoid substances around the surface of a resin containing a hydrophobic diluent and presence of large spaces and abundant extracellular amorphous material in inflammatory tissue around a toxic adhesive cured in vivo has been observed (123). No fibrous capsule was found around the implant and the capsule, when present, was outside the necrotic regions, the mucoid substance and the inflammatory cells.

1.9.3 Reactions based on immunologic response:

A third group of reactions is attributed to infection based on direct observation and histological data. Implants with shafts or conduits projecting through the skin showed (123) gross signs of infection in dogs and pigs: purulent weeping, edema, chronic scabs at the interface between the skin and conduit. Histological evidence of infection was the presence of numerous plasma cells and other round cells in proliferating inflammation tissue. Plasma cells are invariably present in chronic infection and are believed to produce antibodies to foreign bodies (124).

A few investigators have postulated that toxic plastic materials may denature host proteins which may then become antigenic (125). Physical features of plastic implants are related in an indirect way to infection. Surfaces with many interstices tend to trap bacteria and stimulate the immune response.

1.10. Modifications to increase blood compatibility:

With a view of selecting a suitable polymer for particular blood contacting applications, various attempts have been made to understand the relationship between blood compatibility and the surface properties of polymers. Surface modification of polymeric materials have been attempted (126-128) to avoid adverse reactions with blood components. One such modification(129 to increase nonthrombogenicity is to maintain a negative charge on the surface from -40 to -120 mV zeta potential. Several of the modifications involve fixation and immobilization of albumin coatings on polymeric substrates (130,131). Further hydrogels which adsorb and retain more than 20% water within their structures are also grafted on polymeric materials for decreasing the interfacial free energy. HEMA (132), acrylamide (133) vinyl alcohol or N-vinyl pyrrolidone (134) have been grafted for enhancing blood compatibility. While hydrophilic surfaces are found to reduce platelet adhesion (135) and protein adsorption, an optimisation of hydrophobic/hydrophilic ratio is believed to be more beneficial (136) for enhancing blood compatibility. Other modifications include covalent binding of C18 alkyl residues (137) to selectively enhance albumin binding and reduce fibrinog-

en adsorption or (138) mimicking phospholipid components. Selective bonding of phosphorylcholine to substrates has been attempted (139) for inhibiting platelet adhesion.

Prostaglandins which play a key role in thrombosis have been immobilized to polyetherurethane urea surface to inhibit platelet adhesion (140). However, the presence of prostaglandins in a polymer matrix affects the mechanical properties of the polymer (141) in addition to having reduced biological activity. Albumin-heparin conjugates (142,143) and high AT-III affinity form part of modifications using drug complexes intended to induce nonthrombogenity. Heparin bonded (144) and heparin releasing polymers (145) have been prepared for enhancing clotting time. Enzymes have been immobilized on surfaces (146) and polyelectrolytes similar to heparin have been grafted (147) to enhance nonthrombogenicity. Attempts have also been made to induce the growth of endothelial cells on the surface of devices (148). The disadvantage to biological modification of polymers is the short lifetime of the biological entity on the surface due to leaching or diffusion from the surface. Stronger binding agents when used have tended to reduce or destroy the functionality of the biological moiety.

However, inspite of the intensive efforts to the understanding of blood compatibility, the small diameter vascular graft still eludes investigators and no single substitute material is still perfect for such applications. Modifications to increase the tissue compatibility of materials also seem to be scarce.

1.11. Applications of IPNs:

Increasing number of commercial products were developed utilizing the concept of IPNs, to date there are some hundred patents which explore the application of IPNs and closely related materials. The following (Table 1.1) gives an abbreviated list of IPN related patents indicating their applications.

Mode of combination	Actual or anticipated use of IPNs Application	Ref
Natural leather rubber	Improved leather	149
Anionic-catonic	Ion exhange resins	150
Plastic rubber	Noise damping	151
Rubber -plastic semi IPN	Impact resistant plastic	152
Plastic - plastic	Optically smoth surfaces	153
Rubber - Rubber	Pressure sensitive adhesive	154
Plastic-plastic	Compression molding composition	155
Plastic rubber	Tough plastic	156
Rubber-Plastic	impact modifier	157
Plastic-plastic SINs	sheet molding compounds	158

Rubber-crystaliine plastic	thermoplastic elastomer	159
Block copolymer-crystalline plastic	high temperature elastomer	160
unsaturated polyester-styrene crosslinked suspension	low polypropylene	161
Water swellable non water swellable	soft contact lenses	162

Besides the above patent specifications, there is a growing number of suggested uses, in the scientific literature.

Semi compatible IPNs of low and high Tg polymers damp noise and vibrations over the intervening transition range. Thus, the most promising uses of IPNs are noise and vibration damping systems in the form of films, constrained layers and so called silent parts (163-164).

A broad range of applications can result from the improved mechanical properties of IPNs consisting of glassy network I and high elastic network II. Tough plastics with elevated tensile stress and elongation as well as high impact resistance are seen to be the most important group of future applications (165).

Another anticipated use of polyurethane base semi IPNs is in the field of modified PU foam (166). Reaction injection molding materials of PU IPNs are also under development utilising the second component to increase the thermal stability of the polyur-

ethane. Epoxy PU and PU unsaturated polyester systems were also reported (166).

Synthetic substituted leather lacks uniformity and is the subject of chemical deterioration, water penetration and abrasion damage even though it is already a versatile material. To improve the structure and elastic properties as well as fill in the open areas, eliminate defects and control water permeation, a series of vinyl acrylic and styrene type monomers were incorporated via an emulsion technique (167). After polymerisation a semi IPN is formed if the vinyl monomer mixture contains no crosslinker and a full IPN is formed if a crosslinker is incorporated.

Polyester-polyurethane IPN based adhesive was found to have better adhesive strength than that of either components (168). Uses of IPNs in adhesives have also been discussed by Wake (169). Novel adhesive and casting resins have been made by the use of unsaturated polyester-styrene/epoxy resins imparting flexibility, improved low temperature properties and underwater use (170).

Semi SINs using amine cured epoxides and butadiene acrylonitrile rubber (171) were found to yield adhesives with extremely high bonding strength to metals. A curable epoxy resin containing a crosslinked elastomeric latex (172) yields a special type of sequential IPN. Mendoyanis (173) revealed an epoxy/liquid rubber. SIN, where the final products could be extended upto 400% at 0 °F.

Coating compostions were also developed based on acrylic

polyurethane IPNs (174). The performance of these coatings viz hardness, lap shear strength on steel and tensile strength were superior to the polyurethane and acrylic separately.

Among the biomedical applications, Predecki (175) has mentioned the use of IPNs as arteriovenous shunts and in their SIN method, Touhsaent et al (176), suggest uses as casting syrups. IPN modified polymer beads have been found useful for the release of water soluble drug from hydrogel beads to an aqueous environment (177).

Semipermeable membranes consisting of IPNs from -NCO terminated polyethers, vinylpyridine or N-vinyl pyrrolidone polymers as porous supports were reported to be useful in reverse osmosis, ultrafiltration, gas separation etc (178). Haemodialysis membranes of cellulose or colloidion (179)was made hemocompatible by interpenetrating with coatings of NVP, polyacrylamide and polyHEMA.

Kronick (180) prepared IPNs of polyacrylamide on polyether polyurethane by introducing monomers in 50% solution in glycolmethoxy ethanol onto a substratum of polyether urethane block copolymer which it penetrated. After the volatile glycolmethoxy ethanol evaporated the polymerisation was intiated by atomic hydrogen. Inextricable IPNs were reported to be formed but the mechanical properties were very much reduced. Dror M. et al (181,182) synthesised semi IPNs of a polyether urethane urea with acrylamide, NVP, HEMA. Loss of 30% of the mechanical properties as compared to that of polyurethane was reported.

Collagen/HEMA/N,N'Dimethacrylamide IPN and HEMA/PDMS IPNs have been developed (183)for use as contact lenses. HEMA/polyurethane gradient IPN has been developed for controlled drug delivery systems(184). An ethylene copolymer ionomer /PVC IPN has been developed (185) for use as medical tubing.

Other IPNs developed are an IPN of silicone rubber, HEMA, PVP by Vale et al (186) and commercially available Rimplast by Petrarch systems Inc.(187) that consist of silicone-polyurethane IPNs. Another commercial IPN for medical uses is the acrylic based trubyte bioform IPN and De trey bio stabil artificial teeth material (165).

1.12 Significance of the need for IPNs in biomedical application:

Polyurethane materials are extensively used in blood contacting applications and organ reconstruction. Thermoplastic polyurethane elastomers are the largest group of biomedical polymers. Biomer (R), Cardiothane, Avcothane, Cardiomat, Tecoflex, Pellathane etc are commercially available polyurethanes(64). The polyurethanes are based on aromatic and aliphatic diisocyanates. Several investigators surface modify the above or other synthesised polymers for better blood compatibility. The modifications may alter the physical, mechanical properities of the substrate polyurethane and may also make it more susceptible to degradation.

A number of investigators (188,189) used polyurethane elastomer foams as blood vessel grafts with failures due to thrombosis and inflammation. Early polyurethane elastomers made from

polyester polyols possess poor hydrolytic stability and can degrade in the biological environment (190). This problem has been overcome by incorporation of stable polyether soft segments in the biomedical polyurethanes used today. However still some problems remain.

Aromatic polyurethanes are reported to produce toxic (191) carcinogenic (192) mutagenic (193) and teratogenic (194), 4,4'-diamino diphenyl methane (MDA), as a degradation product of diphenyl methane diisocyanate (MDI). MDA has been found in trace quantities on storage (195), as a result of processing (196) and on steam sterilization (197). The aromatic polyurethanes are also unstable on exposure to sunlight (198) resulting in loss of mechanical properties and discolouration. Use of the aliphatic analog of MDI ie methylene bis cyclohexyl diisocyanate, gave better stability on exposure to light,and mechanical properties did not deteriorate (199). However,the polyurethane has poorer physical properties and also produced the aliphatic analog of (MDA) on storing which may be toxic. Pellathane is another commercial polyurethane used widely in heart pacemaker connectors (200) heart pacemaker lead tubing (201), blood bag and other devices. Surface cracking of Pellathane pacemaker wire coatings (202) has been a major problem (203,204). Another problem on using polyurethanes for long term applications is calcification (205). Environmental stress cracking and calcification are enhanced by ion complexation (206). Polyetherurethane urea elastomers are also known to undergo biodegradation (207,208) in physiological

solution or bile or subcutaneous implantation.

Hydrolytic instability and oxidative degradation of polyurethanes have been reported (209,210). Previous studies on some polyurethanes have indicated the possibility of an inflammation reaction at the surface (211) .

There thus exists a need for improving the physical and chemical properties of the bulk polyurethane itself to render it more resistant to degradation. The surface of this polyurethane could be structured to achieve biocompatibility and thus avoid a two layered structure as is obtained during most modifications.

The development of materials that can remain in contact with human tissues and fluids for extended time periods without evoking adverse biological reactions is a great challenge. The applications of IPNs reported (section 1.11) do not seem to address the problem of biodegration which is also a challenge to biomedical scientists. There also do not seem to be any studies on the tissue reactions of any of the IPN materials reported so far.

1.13 Aims and objectives of the work:

The main objective of the present study was to synthesise and evaluate interpenetrating polymer networks (IPNS) of polyurethane with hydrophilic vinyl monomers for biomedical applications. The distribution of hydrophobic and hydrophilic groups on the surface of the IPNs would provide the necessary impetus for biocompatibility. The IPNs when formed would be expected to possess synergistic properties of polyurethane and the

vinyl polymer in addition to being resistant to chemical and hydrolytic degradation. It was also planned to study the stability and tissue compatibility of the synthesised IPNs, and to assess the suitability of the IPNs as biomaterials.

EXPERIMENTAL

CHAPTER II

2.1. Materials and their purification:

Isocyanates: Toluene -2,4- diisocyanate (TDI), (Fluka, AG) 99% pure) and 4,4' diphenyl methane diisocyanate (MDI), (Polysciences Inc., USA 99.9% pure) were used as such.

Polyols:Polytetramethylene glycol (PTMG), Molecular weight 1010 and 2000,(Quaker Oats, USA),

Polypropylene glycol (PPG), Molecular weight 2000, (Fluka, AG) and trimethylol propane (TMP), (Merck-Schuchardt) were dried at 50 degree C in vacuum for 5 hour.

Monomers: 2-hydroxy ethyl methacrylate (HEMA) (Fluka, AG) and N-vinyl pyrrolidone (NVP) (Fluka, AG)

Ethyleneglycol dimethacrylate (EGDMA) (Fluka, AG)

Methylmethacrylate (MMA): (Fluka, AG) were vacuum distilled over cuprous chloride. Middle fraction was collected and used.

Acrylamide (AM) : (Sisco Laboratories, India) was recrystalized from chloroform-methanol (1:1)

N.N' methylene bisacrylamide (MBA) (Sisco, India) used as such.

Initiators: Azobisisobutyronitrile (AIBN): (Sisco, India) and N,N' dimethyl toluidene: (Fluka, AG) used as such.

Benzoyl peroxide (BOP): (BDH, India) recrystallised from chloroform-methanol (1:1).

Dibutyl tin dilaurate (DBTL),(Fluka, AG) was used as such. Dimethyl acetamide (DMAC) (S.D. chemicals, India) HPLC grade was dried over alumina and used.

Tecoflex SG-60D of Thermedics Inc. was cast from a dimethylacetamide solution, extracted using water-ethanol (8:2)and hexane. The sheets were then cleaned using an ultrasonic cleaner and used as control for invitro and in-vivo tests.

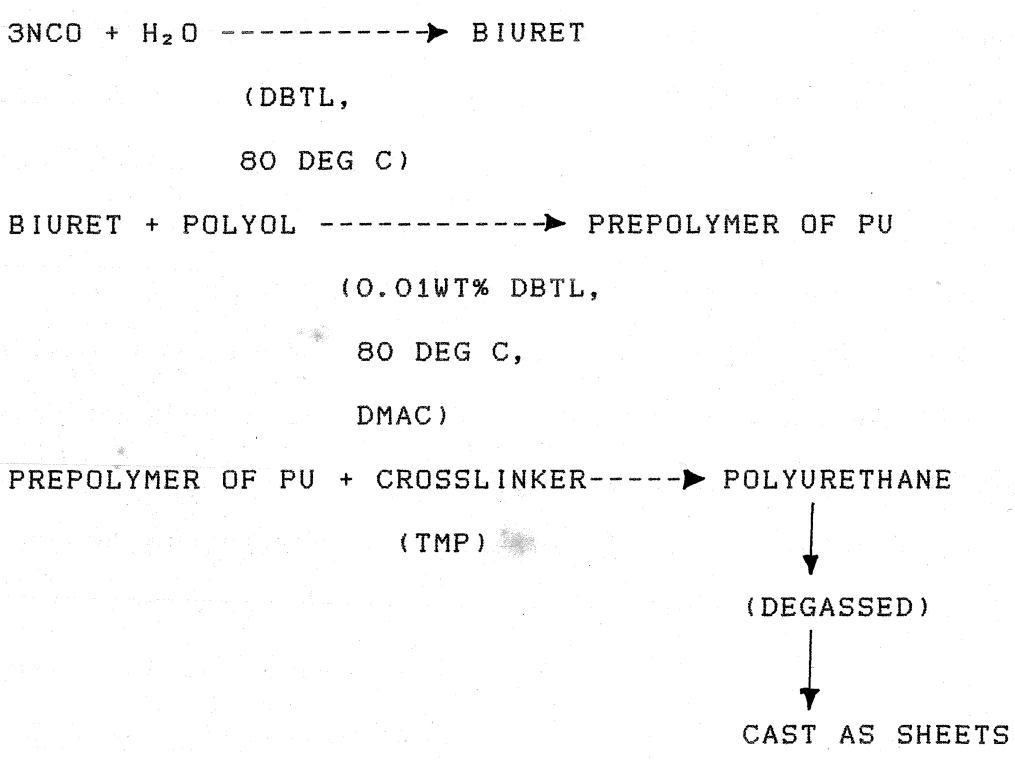
2.2. Synthesis:

Synthesis of the homopolymers:-

2.2.1. Polyurethane:

The synthesis of the polyurethane has been reported (212). Biurets of toluene-2,4-diisocyanate (TDI) and 4,4'diphenylmethane diisocyanate (MDI) were prepared by reacting three moles of the diisocyanate with one mole of water at 80 degree C in a nitrogen atmosphere. 0.01 wt % dibutyltindilaurate was used as a catalyst. The biuret of the respective isocyanate was solution polymerised in dimethylacetamide (DMAC) with an equivalent amount of polyol at 80 degree C for one hour in case of TDI and for one and half hour in the case of MDI. After cooling the prepolymer, trimethylol propane dissolved in DMAC, was added with high torque mixing. The mixture was degassed by applying vacuum at room temperature for 10 minutes, and cast on silicone oil-coated glass molds. Curing was carried out at 60 degree C for 3 hours followed by 80 degree C for 24 hours. Post curing was at 60 degree C for 24 hours. The polyurethane was then extracted with distilled

water-ethanol (8:2) and hexane before properties were evaluated. The water-ethanol and hexane were removed by subjecting to vacuum at 50 degree C. The NCO/OH of the polyurethane was varied from 1.09 to 2.01 to get different polyurethanes. The scheme of the synthesis is depicted in the Fig.2.1.



CURING---

60 DEG C - 3 HOURS

80 DEG C - 24 HOURS

60 DEG C - 24 HOURS POST CURING

EXTRACTION--- WATER-ETHANOL, HEXANE.

Fig 2.1 : Flow chart of the synthesis of the polyurethane

2.2.2. Polyacrylamide:

Acrylamide monomer was dissolved in dimethylacetamide (DMAC), to get a 10 wt% solution.1 wt% benzoyl peroxide was added as initiator. 2 wt% N,N'methylenebisacrylamide was added as the crosslinker. The mixture was heated with stirring in a nitrogen atmosphere at 80 degree C until a viscous prepolymer solution was obtained. The prepolymer solution was poured into a closed glass mold with silicone rubber gasket and cured at 80 degree C for 3 hours and 60 degree C for 24 hours.

2.2.3. Polyvinylpyrrolidone:

N-vinyl pyrrolidone monomer was polymerised by initiating it with 1 wt % of azobisisobutyronitrile (AIBN). The crosslinker, 2 wt% ethyleneglycoldimethacrylate (EGDMA) was added. Polymerisation was carried out at 60 degree C in a nitrogen atmosphere until a viscous prepolymer was obtained. The prepolymer was poured into a closed glass mold sealed by silicone rubber and cured at 60 degree C for 24 hours.

2.2.4. Polymethylmethacrylate:

Methylmethacrylate monomer was polymerised by adding the mixture of 0.5 wt% benzoyl peroxide and 0.5 wt% N,N' dimethyl p-toluidene as initiator, crosslinker EGDMA was added and the polymerisation was carried out directly in the sealed glass mold at room temperature. Curing was at 60 degree for 24 hours.

2.2.5.Poly 2-hydroxyethyl methacrylate:

Polymerisation of 2-hydroxyethylmethacrylate monomer was initiated by 1 wt% of AIBN.2 wt% of EGDMA was added as crosslink-

er and polymerisation was carried out at 60 degree C in a nitrogen atmosphere until a syrupy prepolymer was obtained. This prepolymer was poured into a sealed glass mold and cured at 60 degree C for 24 hours.

Synthesis of the IPNs:-

2.2.6. Polyurethane-Polyacrylamide (PU-PAM) IPNs:

In general, for all IPNs synthesised, the condensation polymerisation of polyurethane was allowed to proceed simultaneously with the addition polymerisation of the vinyl polymers.

Prepolymer of polyurethane was prepared as mentioned above. The synthesis of the PU-PAM IPNs have been reported (212). After cooling the prepolymer to 0 degree C, calculated weight percentage amounts of acrylamide monomer dissolved in dimethyl acetamide (DMAC) and 1 wt% benzoyl peroxide was added to the prepolymer with stirring. An equivalent amount of trimethylolpropane with respect to the corresponding polyurethane, was dissolved in DMAC and added with high torque mixing along with 2 wt% N,N' methylene bisacrylamide which is the crosslinker for polyacrylamide. After degassing, the mixture was cast and cured. The cured polyurethane was extracted as mentioned above. The IPNs prepared were varied with ratios of NCO/OH, weight percent of polyacrylamide and type of isocyanate as indicated in Table 2.I. The scheme of synthesis is depicted in Fig.2.2.

PU-PAM IPNS---

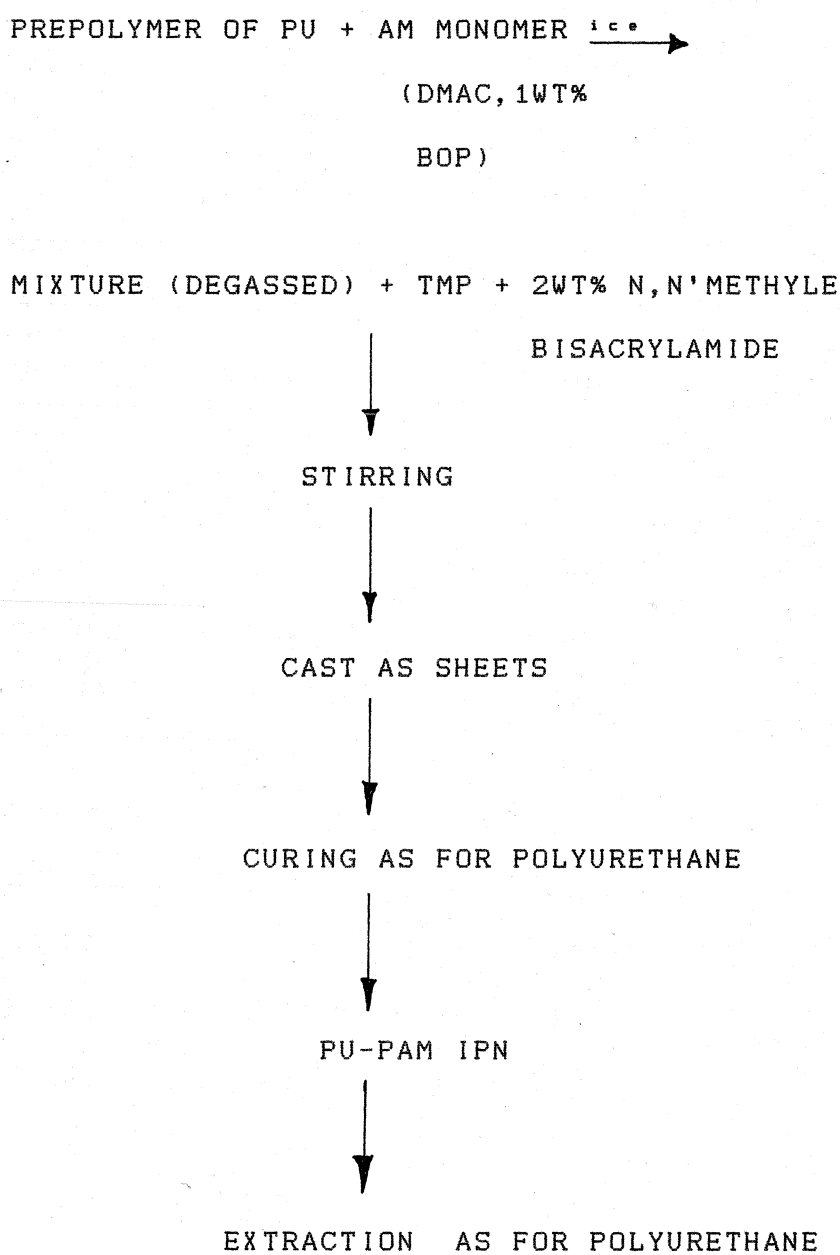


Fig 2.2 Flow chart of the synthesis of PU-PAM IPNs

TABLE-2.I

COMPOSITION OF THE PU-PAM IPNS

Polymer code	NCO/OH ratio	Polyurethane content (wt%)	Acrylamide content (wt%)
PU1A[a]	1.09	100	-
PU1A-PAM 90/10	1.09	90	10
PU1A-PAM 80/20	1.09	80	20
PU1A-PAM 70/30	1.09	70	30
PU1A-PAM 50/50	1.09	50	50
PU1B[a]	2.01	100	-
PU1B-PAM 90/10	2.01	90	10
PU1B-PAM 80/20	2.01	80	20
PU1B-PAM 70/30	2.01	70	30
PU2A[b]	1.09	100	-
PU2A-PAM 90/10	1.09	90	10
PU2A-PAM 80/20	1.09	80	20
PU2A-PAM 70/30	1.09	70	30
PU2A-PAM 50/50	1.09	50	50
PU2B[b]	2.01	100	-
PU2B-PAM 90/10	2.01	90	10
PU2B-PAM 80/20	2.01	80	20
PU2B-PAM 70/30	2.01	70	30
PU3A[c]	1.09	100	-
PU3A-PAM 90/10	1.09	90	10

TABLE-2.I(contd.)

PU3A-PAM 80/20	1.09	80	20
PU3A-PAM 70/30	1.09	70	30
PU3A-PAM 50/50	1.09	50	50
PU3B[c]	1.68	100	-
PU3B-PAM 90/10	1.68	90	10
PU3B-PAM 80/20	1.68	80	20
PU3B-PAM 70/30	1.68	70	30
PU3B-PAM 50/50	1.68	50	50
PU4A[d]	1.09	100	-
PU4A-PAM 90/10	1.09	90	10
PU4A-PAM 80/20	1.09	80	20
PU4A-PAM 70/30	1.09	70	30
PU4A-PAM 50/50	1.09	50	50

---

a) Series PU1A and IPNS,PU1B and IPNS are based on PTMG molecular weight = 1010,Isocyanate = TDI.

b) Series PU2A and IPNS,PU2B and IPNS are based on PTMG molecular weight = 2000,Isocyanate = TDI.

c) Series PU3A and IPNS, PU3B and IPNS are based on PPG molecular weight = 2000,Isocyanate = TDI.

d) Series PU4A and IPNS are based on PTMG molecular weight = 1010,Isocyanate = MDI.

2.2.7. Polyurethane - polyvinylpyrrolidone (PU-PVP) IPNs:

Prepolymer of polyurethane was prepared as mentioned above After cooling the prepolymer to 0 degree C, calculated weight percentages of N-vinylpyrrolidone monomer and 1 wt% of azoisobutyronitrile (AIBN) was added to the prepolymer with stirring. An equivalent amount of trimethylol propane with respect to the corresponding polyurethane was dissolved in DMAC and added with high torque mixing along with 2 wt% ethylene glycol dimethacrylate (EGDMA). After degassing, the mixture was cast, cured and extracted as mentioned in section 2.2.1. PU-PVP IPNs were prepared by varying the type of isocyanate and weight per cent of polyvinyl pyrrolidone as in Table 2.II. Flow chart of the synthesis is depicted in Fig.2.3.

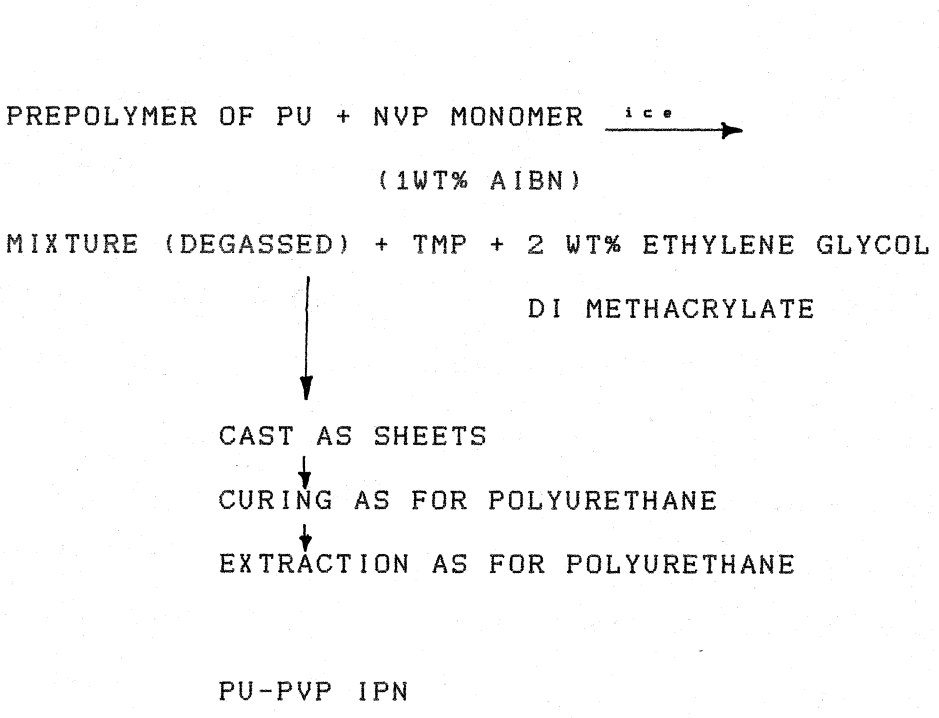


Fig 2.3:Flow chart of the synthesis of PU-PVP IPNs

TABLE-2.II

COMPOSITION OF PU-PVP IPNS

Polymer code	NCO/OH ratio	Polyurethane content(wt%)	N-vinyl pyrrolidone content(wt%)
PU1A-PVP 90/10[a]	1.09	90	10
PU1A-PVP 80/20	1.09	80	20
PU1A-PVP 70/30	1.09	70	30
PU4A-PVP 90/10[b]	1.09	90	10
PU4A-PVP 80/20	1.09	80	20
PU4A-PVP 70/30	1.09	70	30

a) Polyol = PTMG molecular weight = 1010; Isocyanate = TDI.

b) Polyol = PTMG molecular weight = 1010; Isocyanate = MDI.

2.2.8. Polyurethane-polymethyl methacrylate (PU-PMMA) IPNs:

Prepolymer of polyurethane was prepared as mentioned above. After cooling the prepolymer to 0 degree C, calculated weight percentages of methyl methacrylate monomer was added. A mixture of 0.5 wt% of benzoyl peroxide, 0.5 wt% N,N' dimethyl p-toluidene was added to initiate methylmethacrylate polymerisation at room temperature with a view to avoid monomer loss at the higher temperature of curing.2 wt% ethylene glycol dimethacrylate

(EGDMA) and trimethylol propane were added with high torque mixing. The mixture was cast on silicone oil coated glass mold and the curing was carried out at room temperature for 3 hours, followed by 80 degree C for 24 hours. Extraction was carried out as mentioned in section 2.2.1, the weight percent of PMMA and type of isocyanate were varied for the PU-PMMA IPNs as indicated in Table 2.III. Flow chart of the synthesis is given in Fig 2.4.

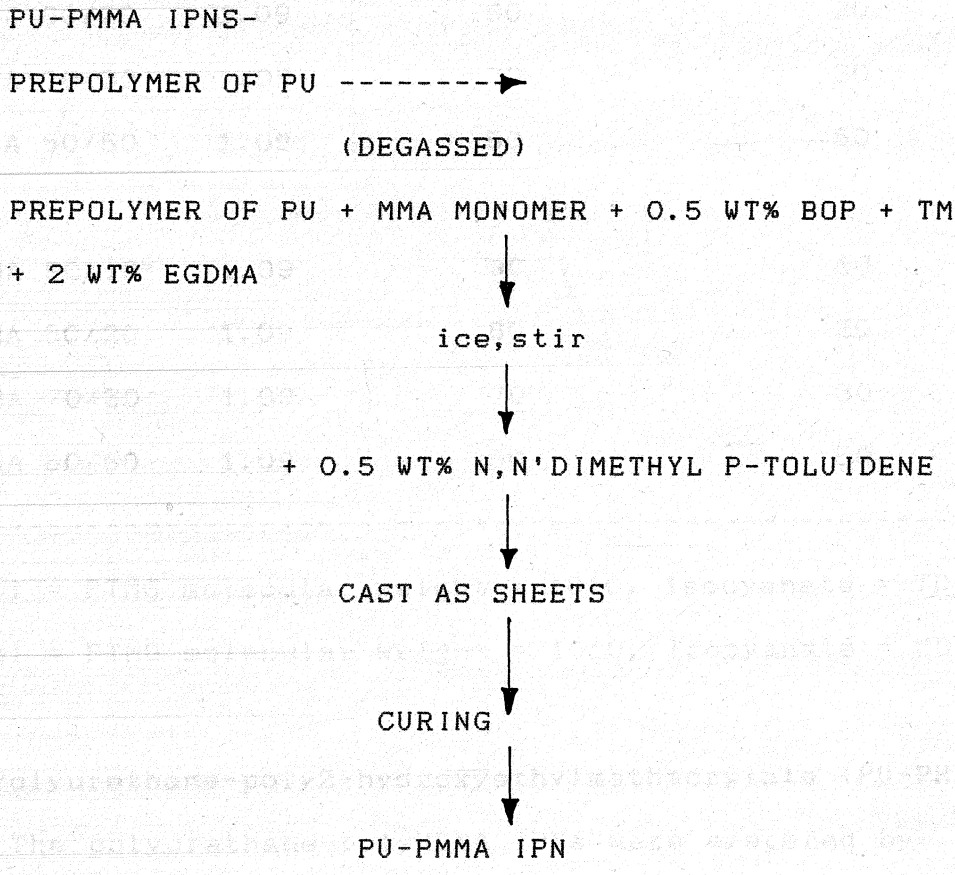


Fig 2.4 :Flow chart of the synthesis of PU-PMMA IPNs

TABLE-2.III

COMPOSITION OF PU-PMMA IPNS

Polymer code	NCO/OH ratio	Polyurethane content(wt%)	Methyl methacrylate content(wt%)
PU1A-PMMA 90/10[a]	1.09	90	10
PU1A-PMMA 80/20	1.09	80	20
PU1A-PMMA 70/30	1.09	70	30
PU1A-PMMA 50/50	1.09	50	50
PU4A-PMMA 90/10[b]	1.09	90	10
PU4A-PMMA 80/20	1.09	80	20
PU4A-PMMA 70/30	1.09	70	30
PU4A-PMMA 50/50	1.09	50	50

a) Polyol = PTMG molecular weight = 1010, Isocyanate = TDI.

b) Polyol = PTMG molecular weight = 1010, Isocyanate = MDI.

2.2.9. Polyurethane-poly2-hydroxyethylmethacrylate (PU-PHEMA) IPN

The polyurethane-polyHEMA IPNs were prepared by swelling the cured polyurethane films in a mixture containing HEMA monomer, 1 wt% AIBN and 2 wt% EGDMA. The swelling was allowed until the required weight % uptake of HEMA was obtained. Polymerisation of the swollen films was initiated by suspending the swollen films in a vapour of hexane at 80 degree C for 24

hours. This method was adopted to avoid the grafting reaction of the -OH group of HEMA and the -NCO group of the prepolymer of polyurethane. After the HEMA was polymerised, the IPNs formed were extracted as mentioned above. Different PU-PHEMA IPNs were prepared by varying weight percent of HEMA and type of isocyanate as in Table 2.IV.Flow chart of the synthesis is given in Fig.2.5.

TABLE-2.IV

COMPOSITION OF PU-PHEMA IPNS

Polymer code	NCO/OH ratio	Polyurethane content (wt%)	2-Hydroxyethyl methacrylate content (wt%)
PU1A-PHEMA 90/10[a]	1.09	90	10
PU1A-PHEMA 80/20	1.09	80	20
PU1A-PHEMA 70/30	1.09	70	30
PU1A-PHEMA 50/50	1.09	50	50
PU4A-PHEMA 90/10[b]	1.09	90	10
PU4A-PHEMA 80/20	1.09	80	20
PU4A-PHEMA 70/30	1.09	70	30
PU4A-PHEMA 50/50	1.09	50	50

a) Polyol = PTMG molecular weight = 1010, Isocyanate = TDI.

b) Polyol = PTMG molecular weight = 1010, Isocyanate = MDI.

PU-PHEMA IPNS

CURED POLYURETHANE SHEETS

↓

SWELLING IN

↓

HEMA MONOMER + 1 WT% AIBN + 2 WT% EGDMA

↓

POLYMERISATION OF SWOLLEN STRIPS IN HEXANE VAPOUR

60 - 80 DEG C

↓

EXTRACTION AS FOR POLYURETHANE.

Fig 2.5 : Flow chart of the synthesis of PU-PHEMA IPNs

2.3. Physicochemical characterisation:

2.3.1. Infrared spectroscopy:

Infrared spectra of thin films of prepolymers cast and cured on the NaCl windows was recorded on a Perkin Elmer 597 IR spectrophotometer in the range of 4000 cm-1 to 200 cm-1. ATR-IR spectra of cured polyurethane and IPN films were also recorded using an ATR accessory. The reflecting crystal used was KRS-5 in the 45 degree position. The results are discussed in section.3.2

2.3.2.Solvent Resistance:

Solvent resistance of the IPNs were evaluated using the solvents of different polarity such as n-hexane, carbon tetrachloride, toluene, methanol, distilled water, dioxan, 3% NaCl, 10% HCl, 10% NaOH, 25% acetic acid as per ASTM D543 (1978) procedure (213). (5x10x10mm) samples were immersed in the reagents for 7 days. After a week, they were removed and solvents evaporated . The samples were checked for loss in weight, gloss or other changes. The results are discussed in section 3.3.

2.3.3.Mechanical Properties:

The mechanical properties were measured using an Instron Universal Testing Machine 1193 as per the ASTM method D882 (1981) for thin plastic sheeting (214). (10X1X0.1 CM) wide strips were cut from the sheets and conditioned over anhydrous calcium chloride for 24 hours before testing. The strips were pulled using a crosshead speed of 100 mm/min. At least 6 samples were tested in each case and standard deviation of the values estimated. From the load vs extention graph and the thickness of the

strips, the ultimate tensile stress, elongation at break and modulus at 100% elongationwere determined using the following equations.

$$\text{Ultimate tensile stress} = \frac{\text{Load at break}}{\text{Crossectional area}} \quad (2.1)$$

$$\%\ \text{Elongation at break} = \frac{\text{Change in length}}{\text{Original length}} \times 100 \quad (2.2)$$

$$\text{Modulus at 100\% elongation} = \frac{\text{Load at 100\% elongation}}{\text{Crossectional area}} \quad (2.3)$$

The results of these experiments are discussed in section 3.4.

2.3.4. Dynamic mechanical properties:

Dynamic mechanical tests measure the response of a material to sinusoidal stress. The dynamic mechanical properties were determined using Rheovibron viscoelastometer DDV-III-C. The instrument utilizes the forced vibration method and covers the range 1 Hz to 110 Hz. It also covers a wide temperature range (-150 degree to 300 degree C) suitable to all types of polymeric materials.

Molded samples measuring 70 mm x 10 mm x 5 mm were used for testing. Samples were tested at a frequency of 35 Hz using a strain amplitude of 2.5 x 10^{-4} mm. The heating rate used was 1 degree C /min. The instrument directly provides the loss tangent ($\tan \delta$) whereas the complex modulus (E*), storage modulus (E') and loss modulus (E") are calculated using the following equation.

$$E^* = \frac{L}{\delta \times A \times S \times (D-K)} \times 10^{11}\ N/m^2 \quad \ldots\ldots\ldots 2.4$$

Storage modulus $E' = E^* \cos \delta$ 2.5

Loss modulus $E'' = E \sin \delta$ 2.6

where L = Length of sample between clamps

A = amplitude factor

D = dynamic force reading

S = crossectional area of the sample

K = instrument error constant

δ = phase difference.

A computer programm was devised to computate E*, E' and E" using equation 2.4 to 2.6 respectively. The computation was carried out on a CDC cyber 1730 computer. The results are discussed in section 3.5.

2.3.5. Thermal analysis;

The glass transition temperature was evaluated using a DuPont 990 Thermal analyser with 900 differential scanning calorimeter (DSC). 2 to 5 mgs of the sample was heated in non-hermetically sealed aluminium pans using a heating rate of 10 degree C/ min in a nitrogen atmosphere. The samples were heated upto 100 degree C, cooled, and reheated. The glass transition temperature is observed as a shift in baseline of the second scan. Thermogravimetric analyses were carry out in a 951 Thermo-

gravimetric accessory of the DuPont 990 system. Heating rate utilized was 10 degree C/ min and all analyses carried out in an atmosphere of nitrogen. The initial decomposition temperature, 50% decomposition temperature, final decomposition temperature were evaluated from the thermogram. The results of the thermal analysis are discussed in section 3.6.

2.3.6. Contact angles:

A measure of the surface free energy and/or surface wettability of solid materials is most readily and simply obtained by measuring the contact angle of a diagnostic liquid on the solid surface. Under water solid-air contact angle and solid-octane coantact angles were measured by the captive air bubble technique of Hamilton (215,216) using a Ramie'and Hart goniometer. Samples in the form of thin films (5x20x0.5 mm) were equilibrated in distilled water for a week before the contact angles were measured. The films were firmly fixed onto glass slides and immersed in a perspex trough containing water. The microbubble of air or octane was introduced on the surface of the film using a hypodermic syringe. The interfacial free energy of the surface, were calculated from the air and octane contact angles using the equations and assumptions of Andrade et al (132). The results of this investigation are discussed in section 3.7.

2.3.7. Density Determination:

Densities of the materials were determined by water, displacement method according to the ASTM procedure No.D.792 (217). The samples were first weighed in air (a), weight of the sample

and sinker and wire in water (w). Weight of wire and sinker in water (b)

$$\text{The specific gravity} = \frac{a}{(a+w-b)} \quad \ldots\ldots 2.7$$

$$\text{Density} = \text{Specific gravity} \times 0.9975 \quad \ldots\ldots 2.8$$

The results are discussed in section 3.8

2.3.8. Determination of swelling ratio and crosslink density:

Swelling ratio of the IPN materials in toluene were determined from the weight of the materials before and after swelling to equilibrium. The materials were immersed in the respective solvents and weight of sample was periodically recorded after blotting out the excess solvent. The equilibrium swelling ratio Q was determined from a plot of W vs time of swelling where

$$W = \frac{W_1 - Wo}{Wo} \quad \ldots\ldots\ldots 2.9$$

W_1 = weight of sample after swelling, Wo = initial dry weight of the sample.

$$Q = W \times dr/ds \quad \ldots\ldots\ldots 2.10$$

Crosslink density of the IPN materials was calculated from swelling ratio Q in toluene using Flory Rehner equation (218).

$$\nu_c = -\frac{Vr + X\,Vr^2 + \ln(1-Vr)}{dr\,Vo\,(Vr^{1/3} - Vr/2)} = \frac{1}{\overline{Mc}} \quad \ldots\ldots 2.11$$

where ν_c = effective number of moles of crosslinked units per gram of rubber; $\overline{Mc}$ = molecular weight between crosslinks; Vr = volume fraction of rubber in the swollen vulcanizate; X = polymer-solve-

nt interaction parameter; dr = density of polymer;

Vo = molar volume of the solvent; X=0.35 for polyurethane (219)

The volume fraction $Vr = \frac{1}{1+Q}$ 2.12

The results of the investigations of the crosslink density and molecular weight between crosslinks are discussed in section 3.8.

2.3.9 Scanning electron microscopy (SEM):

Scanning electron microscopy (SEM) studies of IPN materials were carried out to determine phase separations or phase mixing in the IPNs. The samples were fixed on aluminium stubs with silver adhesive paste and coated with a thin film of gold in a vacuum coating system. SEM photomicrographs of the gold coated samples were obtained using a Cambridge instruments S-1600 scanning electromicroscope with stereoscan 250-MK-3 attachment. The results are discussed in section 3.9.

2.3.10 Radiation stability:

The changes in the mechanical properties of the IPN materials which were exposed to γ-irradiation of 2.5 M.rads were evaluated to determine the radiation stability of the IPNs. The samples were cut into strips as for ASTM procedure D-882,(214) sealed in glass containers in the presence of nitrogen gas . γ Irradiation was carried out in a Panbit Co-60 source batch irradiator with a dose rate of 0.2 Mrads/hour upto a total dose of 2.5 M.rads. Determination of the mechanical properties before and after γ irradiation were carried out as per the procedure in section 2.3.3. The results are discussed in section 3.10.

2.3.11 ^{13}C Solid state NMR studies:

^{13}C Solid state NMR studies were carried on a Bruker NMR 220 MHz spectrometer. The samples were cut into very small pieces or powdered and packed in the tubes. Technique used was CP-MAS. Spectra were recorded at 3.07 KHz.

2.4. Invitro studies:

2.4.1. Haemolysis:

Red cell lysis in the presence of the IPN materials were tested by treating 20 mgs of the materials with 2 ml of ACD anticoagulated(Appendix A.1) calf blood at 37 degree C for 1 hour. Blood was centrifuged twice at 150 g for 15 mins for the complete removal of red blood cells,(RBC). The control was untreated blood. 3.6 ml of distilled water and 0.4 ml of plasma were mixed and the absorbance units were measured at 429 nm, 414 nm and 398 nm. The haemoglobin released was assayed according to the method of Raphael (220) as follows.

$$\frac{\text{Mg of plasma haemoglobin released}}{\text{100 ml of plasma}} = [A414-(\frac{A429 + A398}{2})] \times 266.$$

The results are discussed in Chapter IV.

2.4.2. Recalcification time test (RCT):

In this test platelet thromboplastic function is estimated. The method followed is that of Austen and Rhymes (221). In this test, citrated plasma is recalcified and clotting takes place via the intrinsic pathway, being initiated by the surface activity of the material of the clotting tube. Variations between glass tubes and variation of phospholipid content of plasma are reported (221) to have significant effect on the results.

Preparation of platelet rich plasma (PRP): 9 vols of whole blood was placed in a disposable polystyrene tube containing one volume of ACD anticoagulant(AppendixA.1).After mixing by inversion seve-

al times, the tube is immediately centrifuged at 100 g for 10 minutes. The plasma is carefully pipetted from the tube using a disposable plastic pipette.

RCT test: 0.1 millilitre of plasma (PRP) is placed in a 12 x 75 mm glass tube which was coated with the polyurethane or IPN material. 0.1 ml of 0.85% sodium chloride is added and the mixture incubated at 37 degree for 1 minute. The mixture is then recalcified by the addition of 0.1 ml of 0.025 M calcium chloride warmed to 37 degree C. A stopwatch is started when the calcium solution is added. The tube is incubated at 37 degree C for 60 to 80 seconds. The reaction mix is then examined at intervals of 1 or 2 second for clotting by tilting the tube slowly so that the reaction mix runs about half way up the side of the tube. The clotting time is recorded as the interval from the addition of calcium to the appearance of the first detectable fibrin threads in the mixture. The results are discussed in Chapter IV.

2.4.3. Platelet Aggregability:

Aggregation of platelets which had been exposed to the polymer films was determined by the method (222). This method is a modification of the photometric platelet aggregation assay of Born (223) and is concerned mainly with the changes in light transmission through a stirred concenterated suspension of platelets when an agonist is added. 1 x 1 sq.cm polymer films of uniform thickness were stored in 5 ml of PRP for one hour. After one hour, the PRP was diluted with TRIS buffer (1:2),(Appendix A.2). Platelet aggregation was assayed using a Shimadzu UV-240

microprocessor controlled spectrophometer, equipped with thermostated cuvette holders maintained at constant temperature (usually 31±1 degree C).

The diluted PRP were taken in each of a pair of rectangular polystyrene, or siliconized glass, cuvettes (pathlength 10 mm) and placed in the sample and reference positions. The instrument was set to read zero at 540 nm. After temperature equilibration, agonist- Adenosine diphosphate(ADP) of different concentration (< 10 µl in volume) were added to the sample cuvette and mixed by quickly inverting it, covered with parafilm three times. The ensuring changes in absorbance (turbidity) were recorded as a function of time after appropriate choice of the absorbance scale expansion and chart speed. A tangent was drawn to the initial steady, linear, downward pen deflection, by visual inspection. Its slope expressed in (A) min-1 was taken as the initial rate of aggregation (ro). The results are discussed in Chapter IV.

2.4.4. Phosphate buffer stability:

The changes in the mechanical properties of the IPN materials which were stored in phosphate buffered saline were evaluated. Samples were cut in strips as for ASTM D-882 (214)and stored in 0.15 M phosphate buffered saline, (Appendix A.3) at 37 degree C for one month. The mechanical properties such as ultimate tensile strength, percent elongation at break and the weight loss were estimated for the samples, both before and after storing in the saline. Determination of the mechanical properties

were as per the procedure in section 2.3.3. The results are discussed in Chapter IV.

2.5. In vivo tests:

2.5.1. Preparation of samples for in vivo tests.

All samples which were earlier extracted with hexane and water-ethanol 8:2 were used. The samples were all precut according to the specifications of each in vivo test before the cleaning procedures were undertaken. The samples were cleaned using a 0.1 wt% benzalkonium chloride solution which acts as a disinfectant. Further the samples were ultrasonically cleaned several times with distilled water. The samples were then dried at 40 degree C in a hot oven, packed in double layers of polyethylene packing and sterilized using γ irradiation of 2.5 Mrads.

2.5.2. Systemic Injection Test:

The test was carried out according to the protocol adopted in the Canadian Standards (224). Extract of the test material was prepared as follows: 4 g of the material was cut into strips of approximately 0.3 cm width and 5 cm length. Sodium chloride injection (1.P. 0.9 % w/v) and cotton seed oil (refined) were used as extraction media. The materials were extracted by 25 ml of the extraction media at 70 degree C for 24 hours. Samples were prepared in duplicate. The extracting medium alone served as control. The extracts prepared were used for the test within 24 hours of extraction.

Albino mice of either sex weighing between 17 and 30 g were used for this test. Two groups of five mice each were injected

intravenously/intraperitoneally (50 ml/kg) with the extract from each of the two tubes of the same sample. Thus a total of 10 mice received the injection of each type of extract. 10 mice were also injected with control portion of each type of extract. Therefore a total of 20 mice were used for testing a single material in one extracting medium. The animals were observed immediately and thereafter for a period of 72 hours after injection. If during the observation period none of the animals treated with the test extract show a significant greater reaction than the animals treated with the control extract, the test sample meets the requirements of the test. On the other hand, if some of the animals showed signs of toxicity, the test was repeated to confirm the same. The results of this investigation are discussed in Chapter V.

2.5.3. Intracutaneous irritation test:

Extracts of the test material were prepared as described for the systemic injection test.

Albino rabbits of either sex weighing 1.5 to 2.0 kg were selected for the test. The fur on the rabbits back, on both sides of the spinal column, was clipped over a sufficiently large area. One rabbit received 10 intracutaneous injections of 0.2 ml extract from one tube on one side and 10 similar injections on the contralateral side, using the control saline extract. A second rabbit was similarly treated with the control and test portion of the extracting medium. Thus a total of two rabbits received intracutaneous injections for a single material in one

extracting medium. The injection sites were observed at 24, 48 and 72 hours after injection for gross evidence of tissue reaction such as erythema, oedema and necrosis. The sample meets the requirements of the test if the response of the sample is not significantly greater than that of control.

2.5.4. Determination of biostability:

Biostability was determined by evaluation of change of mechanical properties of the materials which were implanted in rats.

0.5 cm x 0.5 cm x 4 cm strips of the test materials were implanted in the subcutaneous pouches of wistar rats. 2 pieces were implanted on each side of the spinal column. Each material was implanted in triplicate. After periods of 1 month and 3 months the animals were sacrificed by an overdose of anaesthesia and the materials were retrieved and placed in saline. Only a thin layer of skin covered the materials which was removed manually. The materials were then dried in a vacuum oven at 50 degree C until constant weight was obtained. The mechanical properties of the materials were determined on an Instron Universal Testing Machine Model No.1193. The distance between the grips was fixed at 2 cm. Chart speed and crosshead speed were maintained at 100 mm/min. The results are discussed in Chapter V.

2.5.5. Intramuscular Implantation Test:

The samples, IPNs which were of 90/10 composition and a negative control which was a biomedical grade polyurethane Tecoflex 60D.supplied by Thermomedics Inc. Woburn, MA, U.S.A.,

were prepared for implantation in the form of strips (10x1x1 mm.) Protocol adopted was the Canadian Standard (224). Healthy rabbits of either sex weighing between 1.5 kg and 2.00 kg with well developed paravertebral muscles were chosen. The fur on both sides of the spinal column was clipped closely and shaven on the day of the experiment.

The animals were anaesthetised with 45 mg/kg sodiumpentobarbitone intravenously. The skin was scrubbed with 70% ethyl alcohol. Three strips of the test samples were implanted into the paravertebral muscle on the side of the spine of each of two rabbits. Simultaneously three strips of the negative control sample were implanted in the opposite muscle of each animal. The test and negative control strips were inserted into Klima bone marrow puncture needles and implantation was made by introducing the needle perpendicular to the longitudinal axis of the spinal column at such an angle to place the strip as nearly in the centre of the muscle bundle as practicable. Then a stile was used to hold the strip in place while the needle was withdrawn.

The animals were maintained under observation for a period of 3 months. At the end of the observation period and at periods of 1 week and 4 weeks the rabbits were sacrificed with an overdose of anaesthetic agent. The tissue surrounding the middle portion of each implant was examined macroscopically. The parameters used in evaluating the severity of the tissue reactions were necrosis, haemorrhage, encapsulation etc. The scoring of the histological responses was carried out by Turner's method (225).

RESULTS AND DISCUSSION

CHARACTERISATION

CHAPTER III

3.1 Synthesis of IPNs:

The IPNs used in the present study comprise of polyurethane as polymer 1 and vinyl polymers such as polymethylmethacrylate, PMMA; poly2,hydroxyethylmethacrylate,PHEMA; polyvinylpyrrolidone PVP; and polyacrylamide, PAM; as polymer 2. The synthesis is of simultaneous type for PU-PMMA, PU-PAM and PU-PVP IPNs and of sequential type for the PU-PHEMA IPN. In both cases, the polymerisation of the two polymers in the IPN takes place by non-interfering reaction modes, namely, condensation polymerisation in case of the polyurethane and addition polymerisation in case of the vinyl polymers. The detailed procedure of the synthesis is dealt with in the experimental section.

The primary reaction of the polyurethane comprises of the reaction between -OH group of the polyol and -NCO group of the isocyanate to form the urethane group. Reaction scheme is shown in Fig.3.1. The reaction is catalysed by dibutyl tin dilaurate. Crosslinking takes place mainly by reaction of the free -NCO groups in the urethane prepolymer with the -OH group of the crosslinker trimethylol propane. Excess -NCO present in the higher NCO/OH ratio prepolymers also crosslink by allophanate formation.

The addition polymerisation of the vinyl polymer involves

following reactions, given in Fig.3.2. The first reaction is the formation of free radical of the initiator molecule by application of heat or irradiation. The radical formed reacts with the double bond of the monomer to form the initiated chain. The initiated chains collide with other monomer molecules to form a growing chain. The reaction finally ends by combination or coupling of two macroradicals or disproportionation where chain transfer of a hydrogen atom from one chain end to the free radical chain end of another growing chain takes place. Crosslinking takes place by similar free radical reactions, where the crosslinker molecules are multifunctional vinyl monomers.

SCHEME - I

Formation of biuret:

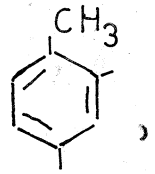
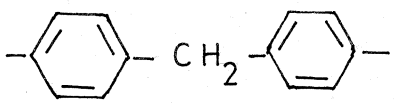
i. $OCN-R-NCO + H_2O \longrightarrow OCN-R-NHCOOH \xrightarrow{-CO_2} OCN-R-NH_2$

ii. $OCN-R-NH_2 + OCN-R-NCO \longrightarrow OCN-R-NH-CO-NH-R-NCO$

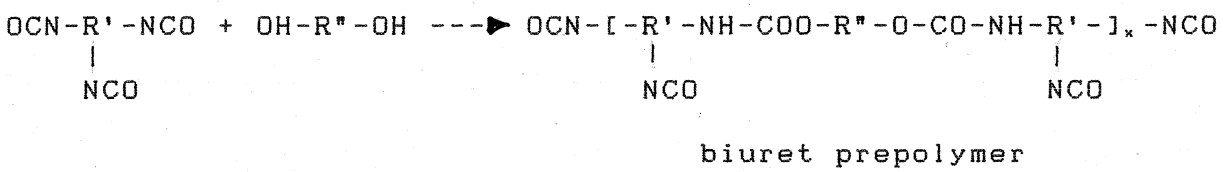
(UREA)

iii. $UREA + OCN-R-NCO \longrightarrow OCN-R-N(-CO-NH-R-NCO)-CONH-R-NCO$

(BIURET)

R=  , 

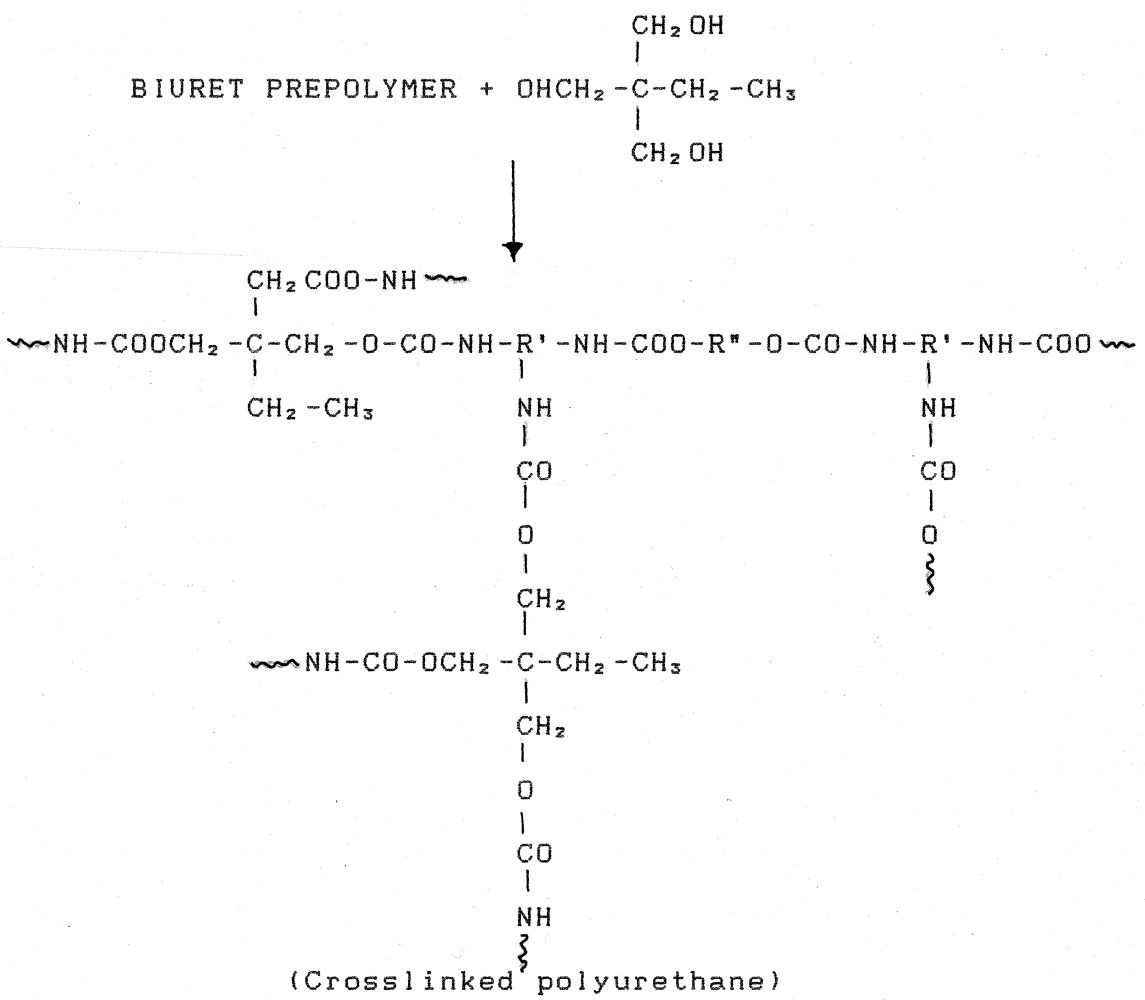
Formation of biuret prepolymer:



biuret prepolymer

R'= BIURET R" = -[CH2-CH2-CH2-CH2-]n

Formation of crosslinked polyurethane



(Crosslinked polyurethane)

Fig.3.1: Scheme of the synthesis of crosslinked polyurethane

SCHEME - II

Addition reactions:

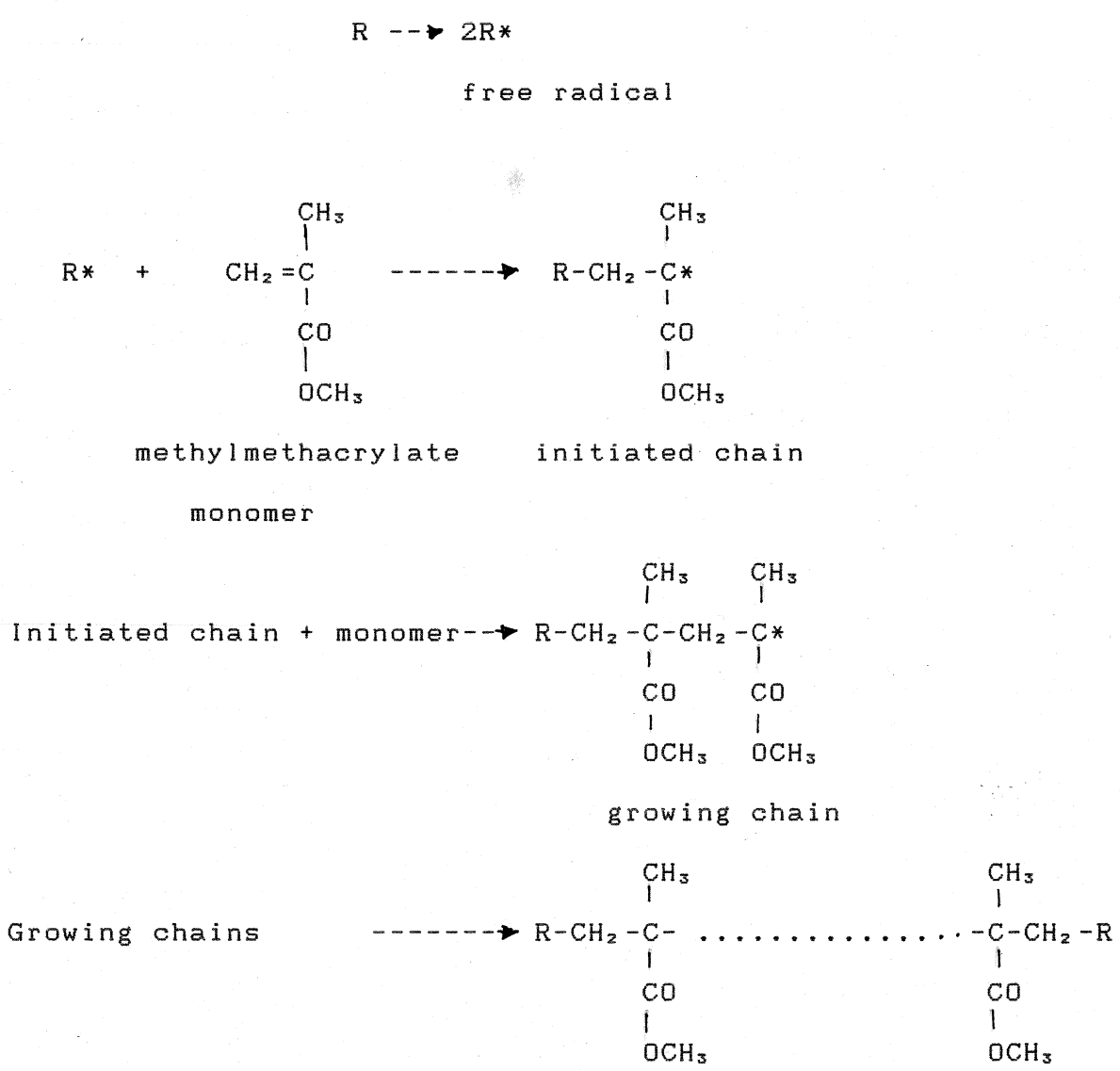


Fig.3.2 : Typical polymerisation of a vinyl polymer

3.2. Infrared spectroscopy :

Typical Infrared spectra of TDI based polyurethane PU1A and MDI based polyurethane PU4A are given in Fig.3.3A and Fig.3.4A. The spectra show minor differences of peak shape at 1550 cm^{-1}, due to amide band and in the doublet due to the aromatic structure. The main difference in the two polyurethane spectra, is the increased intensity of the peak at 2270 cm^{-1} due to the NCO group, seen in the case of MDI polyurethane PU4A. Increased intensity of the NCO peak at 2270 cm^{-1} has been reported for MDI foams(226). Another difference observed is the intensity of peaks at 3100cm^{-1} and 3150 cm^{-1} in PU4A. The increased intensity of these peaks may be due to the more number of aromatic protons in the MDI polyurethane. The general band analysis and assignments of the various peaks of polyurethane are given in Table 3.I. The IR band obtained and their respective assignments for the vinyl polymers PAM, PVP, PMMA, PHEMA are given in Table3.II-3.V. A comparis on of the peaks for the polyurethane and vinyl polymers reveal overlapping of peaks. New peaks may not be therefore expected for the IPNs. Fig 3.3B and 3.4B which are representative IR spectra of a TDI based IPN and an MDI based IPN show that the IPNs do not have any new peaks in comparision to the polyurethane. The minor peak broadening of the C=O peak at 1600 cm^{-1} of PU1A-PVP IPN, Fig.3.3B, is due to the overlapping of individual C=O peaks of polyurethane and PVP. The absences of major spectral differences in the IPN and polyurethane spectra, indicates that there may be no chemical interaction between the constituent polymers

in the IPN. Similar spectral features for polyurethane and PU--PMMA IPNs have also been reported by Frisch et al (227).

TABLE-3.I

PEAK ASSIGNMENT OF POLYURETHANE

PEAK CM^{-1}	ASSIGNMENT	PEAK CM^{-1}	ASSIGNMENT
3300	NHstr	1379	$C-CH_3$, sym def.
2941	CH_2, CH_3 str	1600	PHENYL
1724	AMIDE I, C=Ostr	1227	-C-O, POLYETHER
1538	AMIDE II, NH def	1150-1160	POLYETHER, C-O-C str.

-

TABLE-3.II

PEAK ASSIGNMENTS OF POLYVINYLPYRROLIDONE

PEAK CM^{-1}	ASSIGNMENT	PEAK CM^{-1}	ASSIGNMENT
2925	C-H, str	1290	C-O, acrylate
2850	"	1170	C-C, str.
1670	AMIDE, C=O str.	740	CH_2, rock
1465	C-H, bend		

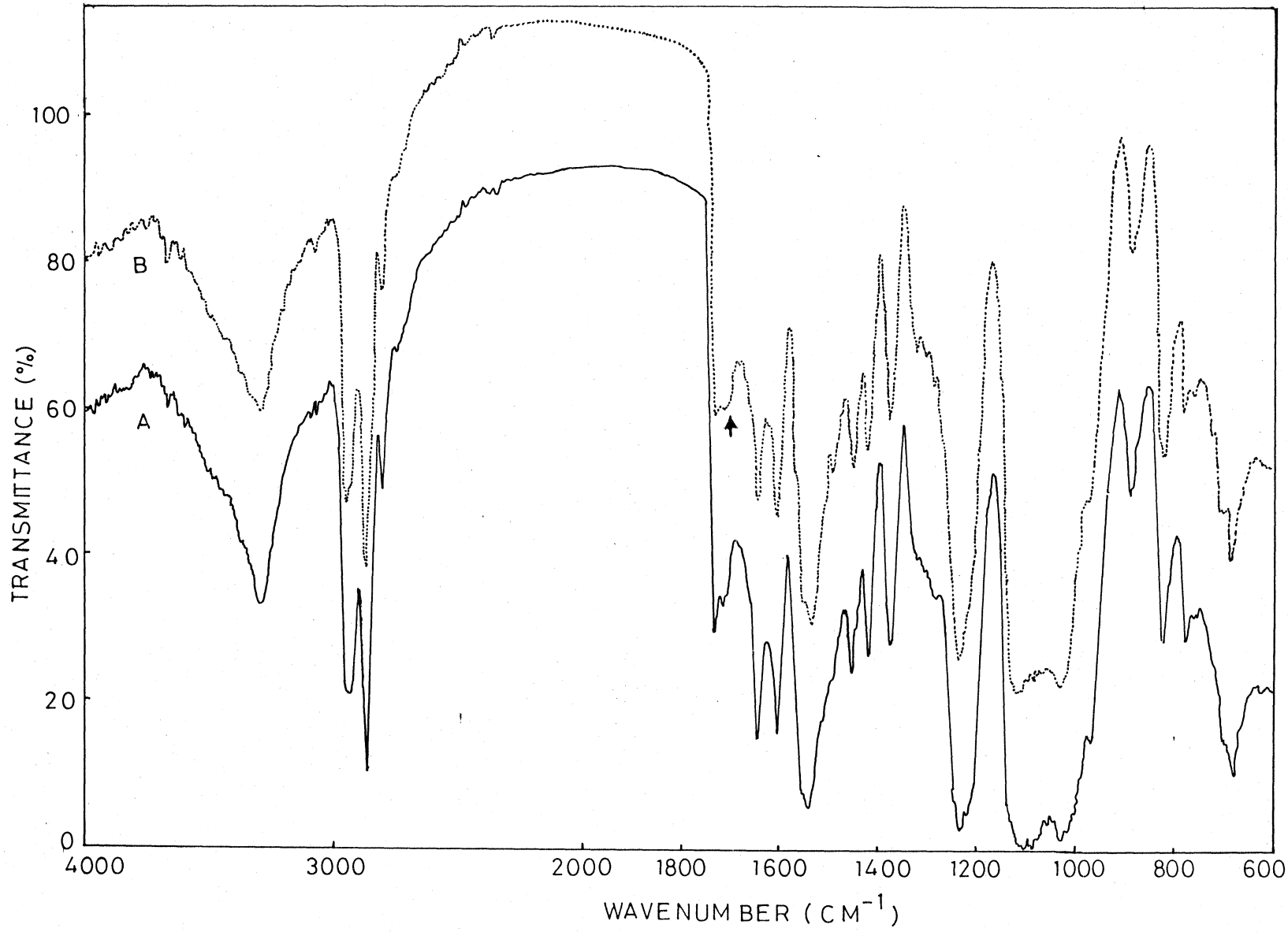


Fig. 3.3. Infrared spectra of TDI based polyurethane and IPN. A=PUIA, B=PUIA-PVP 80/20

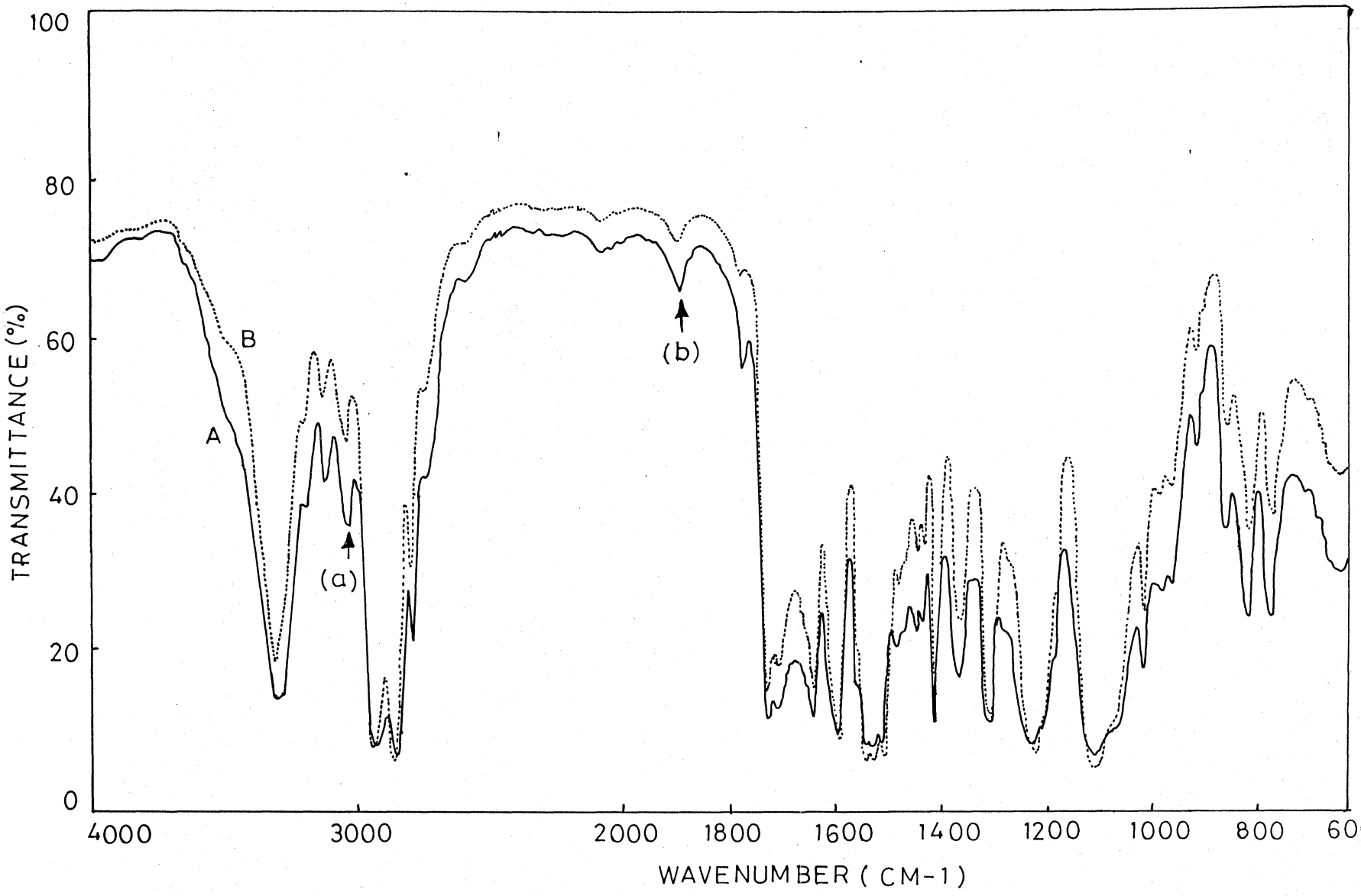


Fig. 3.4. Infrared spectra of MDI based polyurethane and IPN A= PU4A, B= PU4A-PAM80/20

TABLE-3.III

PEAK ASSIGNMENTS OF POLYACRYLAMIDE

PEAK CM^{-1}	ASSIGNMENT	PEAK CM^{-1}	ASSIGNMENT
3400	NH_2, assym str.	1280	C-N,str
3175	NH_2,sym str	1138	NH_2, rock
2940	CH_2,sym str	1050	CH_2, rock
1650	AMIDE I, C=O str.	984	C-C, str
1380	C-H, def.	888	NH_2, wag

TABLE-3.IV

PEAK ASSIGNMENTS OF POLYMETHYLMETHACRYLATE

PEAK CM^{-1}	ASSIGNMENT	PEAK CM^{-1}	ASSIGNMENT
3000-2960	CH_3,str.	1234	C-O, ACRYLATE
2925	CH_2, str.	1190	C-O, ACRYLATE
2850	CH_2,str.		
1730	C=O str.	1149	C-O, ACRYLATE
1266	C-O, ACRYLATE	746	C-O, ACRYLATE

TABLE-3.V

PEAK ASSIGNMENTS OF POLY HYDROXYETHYL METHACRYLATE

PEAK CM-1	ASSIGNMENT	PEAK CM-1	ASSIGNMENT
3448	O-H str.	1266	C-O , ACRYLATE
3000-2960	CH_3 str.	1234	C-O , ACRYLATE
2925	CH_2 str.	1190	C-O , ACRYLATE
2850	CH_2 str.	1149	C-O , ACRYLATE
1730	C=O,str.	746	C-O , ACRYLATE

3.3. Solvent Resistance:

One of the most simplest way to ascertain the formation of an IPN is to determine the solvent resistance.Sperling(22)report that an IPN can be distinguished from simple polymer blends, blocks and grafts because (1) an IPN swells, but does not dissolve in simple solvents and (2) creep and flow are suppressed. Solvents of polar, and non polar types as mentioned in the experimental section, Chapter II,were used to determine the solvent resistance. After exposure to the chemicals, each of the IPN samples were examined on the basis of physical appearance such as discolouration, loss of gloss and change in weight.Table3.VI gives the weight loss of the TDI based IPNs of 90 wt% composition of polyurethane PU1A. It is observed that less than 5 wt % loss is obtained for the IPNs in all the solvents studied. The weight

TABLE 3.VI

PERCENTAGE WEIGHT LOSS OF TDI BASED IPNS

SOLVENTS	POLYMERS				
	PU1A	PU1A-PMMA 90/10	PU1A-PAM 90/10	PU1A-PHEMA 90/10	PU1A-PVP 90/10
Hexane	4.05	0.93	1.65	1.02	2.05
Toluene	7.25	3.09	1.96	2.49	3.56
Dioxan	15.56	4.78	3.73	3.86	5.03
Methanol	8.89	4.41	1.56	2.68	3.24
CCl_4	4.52	2.57	1.05	2.46	2.76
10% HCl	2.53	-	0.95	1.15	1.26
3% H_2O_2	2.58	0.73	1.00	0.78	0.96
10% NaOH	1.26	-	0.50	1.10	0.64
H_2O	1.33	-	-	0.50	-
25% CH_3COOH	2.51	0.54	-	0.78	1.10

TABLE 3.VII

PERCENTAGE WEIGHT LOSS OF MDI BASED IPNS

SOLVENTS	POLYMERS				
	PU4A	PU4A-PMMA 90/10	PU4A-PAM 90/10	PU4A-PHEMA 90/10	PU4A-PVP 90/10
Hexane	3.06	0.85	1.15	1.12	1.67
Toluene	6.35	2.57	1.73	1.98	2.48
Dioxan	11.0	3.64	2.98	2.57	4.58
Methanol	5.78	3.20	1.18	1.76	2.28
CCl_4	3.24	1.95	1.00	1.37	2.01
10% HCl	1.98	0.67	0.85	0.97	1.34
3% H_2O_2	1.86	-	1.00	0.98	1.28
10% NaCl	0.95	-	0.25	0.65	0.88
10% NaOH	1.05	-	0.39	0.96	0.50
H_2O	0.78	-	-	-	-
25% CH_3COOH	1.46	0.20	-	0.35	0.98

loss in each IPN is maximum in dioxane which is a strong solvent for the polyurethane, which forms the major continuous phase. The polyurethane homopolymer, PU1A, even though crosslinked shows a weight loss of 15.56% in dioxan and leading to brittleness. In the IPNs, however no such changes are observed. Table 3.VII gives the weight loss of the MDI based IPNs of 90 wt% composition of polyurethane PU4A. Similar weight loss of less than 5 % is obtained for the MDI IPNs. The MDI polyurethane, PU 4A, with weight loss of 11 % is more stable than the TDI polyurethane, PU 1A.

3.4. Mechanical properties:

Mechanical properties are the totality of properties determining the response of materials to external mechanical influences, manifested in the ability of the materials to develop reversible and irreversible deformations and to resist failure. It has been shown (34,228,229) that an enhancement of polymer properties may be brought about by the formation of heterogeneous systems in which one polymer exists with its glass transition temperature Tg above room temperature, whilst the other exists with its Tg below room temperature. This situation results in a composite, having one component being glassy whilst the other remains rubbery, at room temperature. By varying the relative amounts of each polymer in the IPN, the properties may be altered very often resulting in a synergistic behaviour (230) but these are mainly dependent upon which of the two materials forms the continuous phase. Thus, the produced material can range from a reinforced rubber to a high impact plastic. Synergistic behaviour

implies that the specific interactions could lead to the properties of the whole material to be greater than the arithmetic average of its part. However, it has been reported (22) that properties of some materials will be average and other will have even below average behaviour.

3.4.1. Polyurethane - Polyacrylamide (PU-PAM) IPNs:

Nominal stress-strain dependencies under conditions of isothermal extension were evaluated for the polyurethanes and IPNs. The stress-strain dependence curve, Fig 3.5 ,of the polyurethane PU1A (TDI-PTMG 1010-TMP) and PU1A-PAM IPNs showed the typical viscoelastic behaviour of an amorphous polymer in its rubbery state (231). Fig 3.5a and Table 3.VIII. indicates that the ultimate tensile stress of the PU 1A is less than that for the corresponding IPNs of PU1A-PAM series,Fig 3.5b-e. The IPNs could thus be behaving as a reinforced rubber. Tables 3.IX-3.XI also indicate that in each case the homopolymer polyurethane, exhibits less ultimate tensile stress than the corresponding IPNs in which the polyurethane forms the continuous phase. The tensile stress of most of the polyurethane-polyacrylamide IPNs with the exception of some (PPG 2000-TDI) IPNs are also higher than the tensile stress of polyacrylamide PAM shown in Table 3.XII. The synergism of the tensile properties observed for the polyurethane-polyacrylamide IPNs could thus be due to the interpenetrated structure.

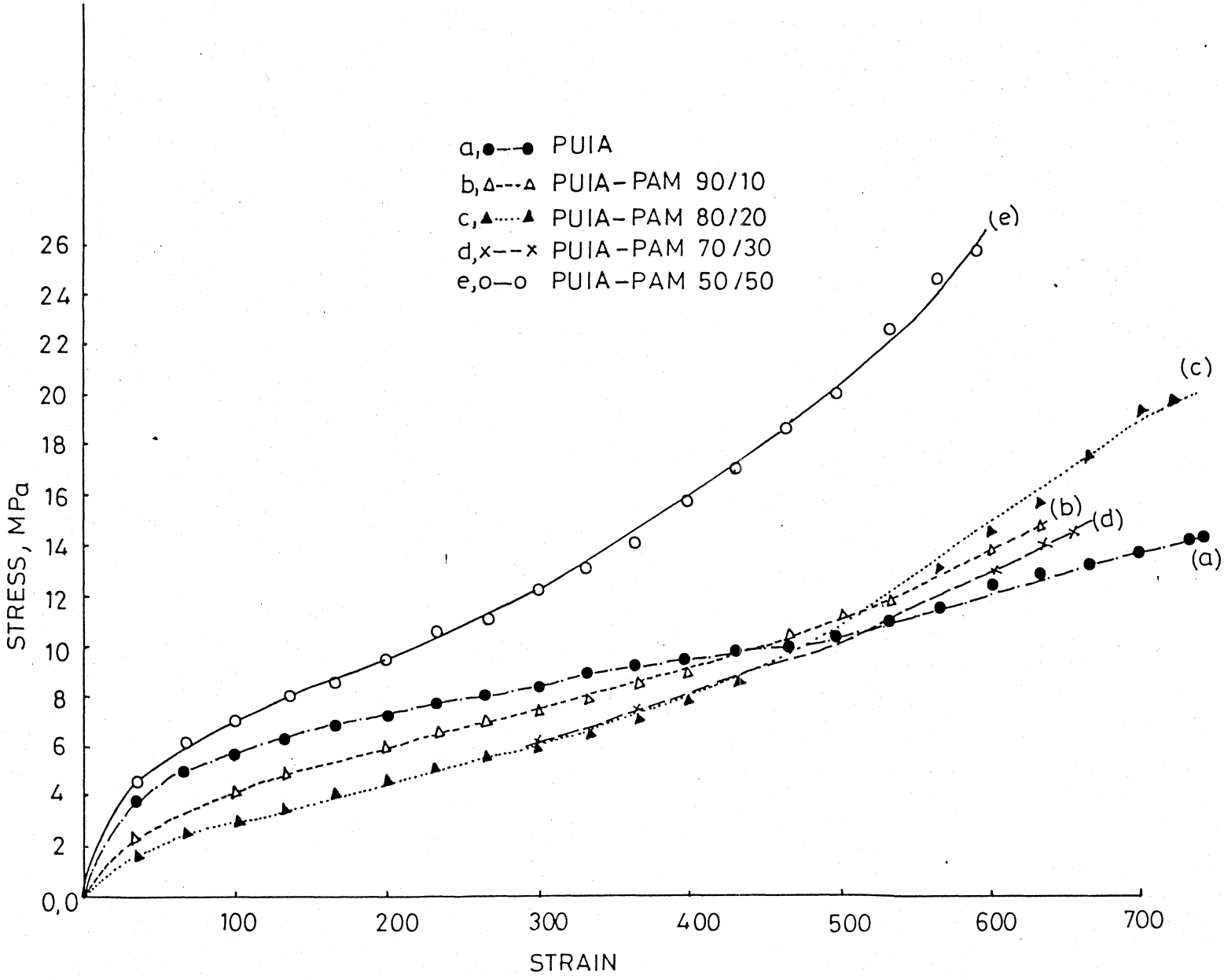


Fig.3.5 Stress VS strain curves for TDI based polyurethane PUIA and PUIA–PAM

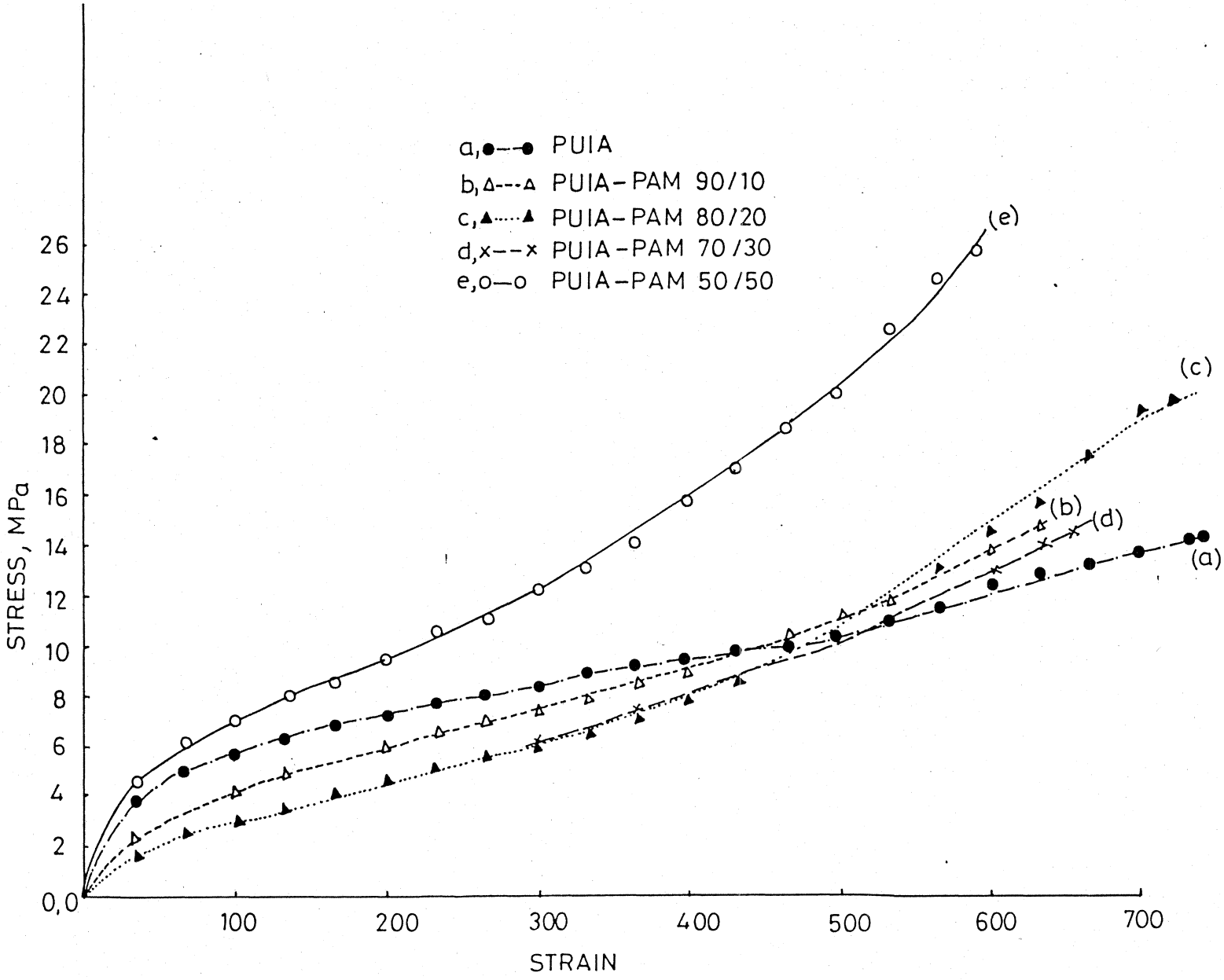


Fig.3.5 Stress VS strain curves for TDI based polyurethane PUIA and PUIA-PAM

3.4.1.1 Effect of the second monomer composition on the mechanical properties of PU-PAM IPNs

Tables 3.VIII-3.XI give the values of ultimate tensile stress, elongation at break and modulus at 100% elongation for the different PU-PAM IPNs. It can be observed that in almost all cases, an initial substantial increase in tensile stress over that of the corresponding PU, can be obtained on incorporating even 10 wt % of PAM. A gradual increase of tensile stress is observed for all the PU-PAM IPNs on subsequent increase of weight fraction of PAM. However, in some of the compositions ie. PU2A-PAM 70/30, (Table 3.IX), PU1A-PAM 70/30,and PU1B-PAM 70/30,(Table 3.VIII),a decrease of tensile stress is observed in comparison to the 80/20 compositions of the same series . This could be due to an onset of a phase inversion process. Similar phase inversion at approximately 60 to 70% of polyurethane in other polyurethane -polymethylmethacrylate IPNs has also been observed (19,232). The PU1A-PAM 50/50 IPN (Table 3.VIII) and PU3A-PAM 50/50 IPN (Table 3.X) exhibit increased tensile stress in comparision to that of corresponding with PU1A-PAM IPN with 70/30 ratio. This behaviour, could be attributed to the formation of heterogenous interphase structures when the polyacrylamide tends to form a continuous phase. Such complex behaviour of IPNs have also been observed for polyurethane-polystyrene (PU-PS) IPNs (42) especially in regions where the two polymers tend to coexist as co-continuous phases. Maxima and minima obtained in the tensile stress of IPNs with lower NCO/OH ratio (Table 3.VIII-3.XI) could

also be attributed to decreases in hydrogen bonding within the polyurethane with polyacrylamide acting as plasticizer. Similar behaviour has already been reported (233) for polyurethane-urea polyacrylate IPNs.

3.4.1.2 Effect of crosslinking of polyurethane on the mechanical properties of PU-PAM IPNs:

The crosslinking of the first formed polymer network is reported (234) to exert a dominant controlling effect on the morphology of the IPNs, while the crosslinking of the second polymer does not seem to have much influence on the properties. In the present study, the crosslinking of the polyurethane, which is the first formed network, was varied to understand the effect on the mechanical properties of the PU-PAM IPNs. Generally, the crosslink density of the polyurethane is increased by varying the NCO/OH ratio . In the present case, the NCO/OH ratio has been varied from 1.09 to 2.01.

By increasing the NCO/OH ratio, the first formed urethane reacts with excess NCO to form allophanates. Excess -NCO could also form some hydrogen bonding (235). The formation of allophanates and hydrogen bonding contributes towards an enhancement of tensile stress of crosslinked polyurethanes of higher isocyanate index eg PU1B. One of the physical consequences of crosslinking is a reduction in volume (236) partly because creation of a network leads to an increase in internal pressure, changes in the local molecular packing resulting in a reduction occupied and free volume. Another consequence of crosslinking is

the reported (237) increase of tensile stress upto a crosslink density of $5x10^{-5}$ mole crosslinks per gram of rubber followed by the decrease with increasing density of crosslinks. It is inherently difficult to obtain reliable structure-property relationships for crosslinked elastomers. The situation is further complicated owing to the presence of distributions of average molecular weight, $\overline{Mc}$ between crosslinks, imperfections in network structure eg. number and average lengths of dangling chains (238).

The nominal stress-strain plots for a polyurethane of higher crosslinking ie PU1B with NCO/OH = 2.01, and the PU 1B-PAM IPNs are depicted in Fig 3.6. The behaviour of the materials is essentially that of viscoelastic nature, however an initial yield stress (σ_s) is observed which is attributed to enhanced entanglements on crosslinking. Yield stress is usually attributed to a possible drop in stress on appearance of a 'neck' owing to the breakdown of elements of supermolecular structure at sufficiently high stresses.The formation of a 'neck',usually corresponds to a transition in the horizontal part of a stress-strain diagram ,characteristic of a forced rubbery deformation (239). For the PU-PAM IPNs, the extended horizontal part of the curve which is obtained subsequent to 'necking' is not present. However the stress-strain curves for the PU1B-PAM IPNs,Fig. (3.6b-e), indicate increased yield stress and elongation compared to the homopolymer PU1B. This is indicative of more toughness

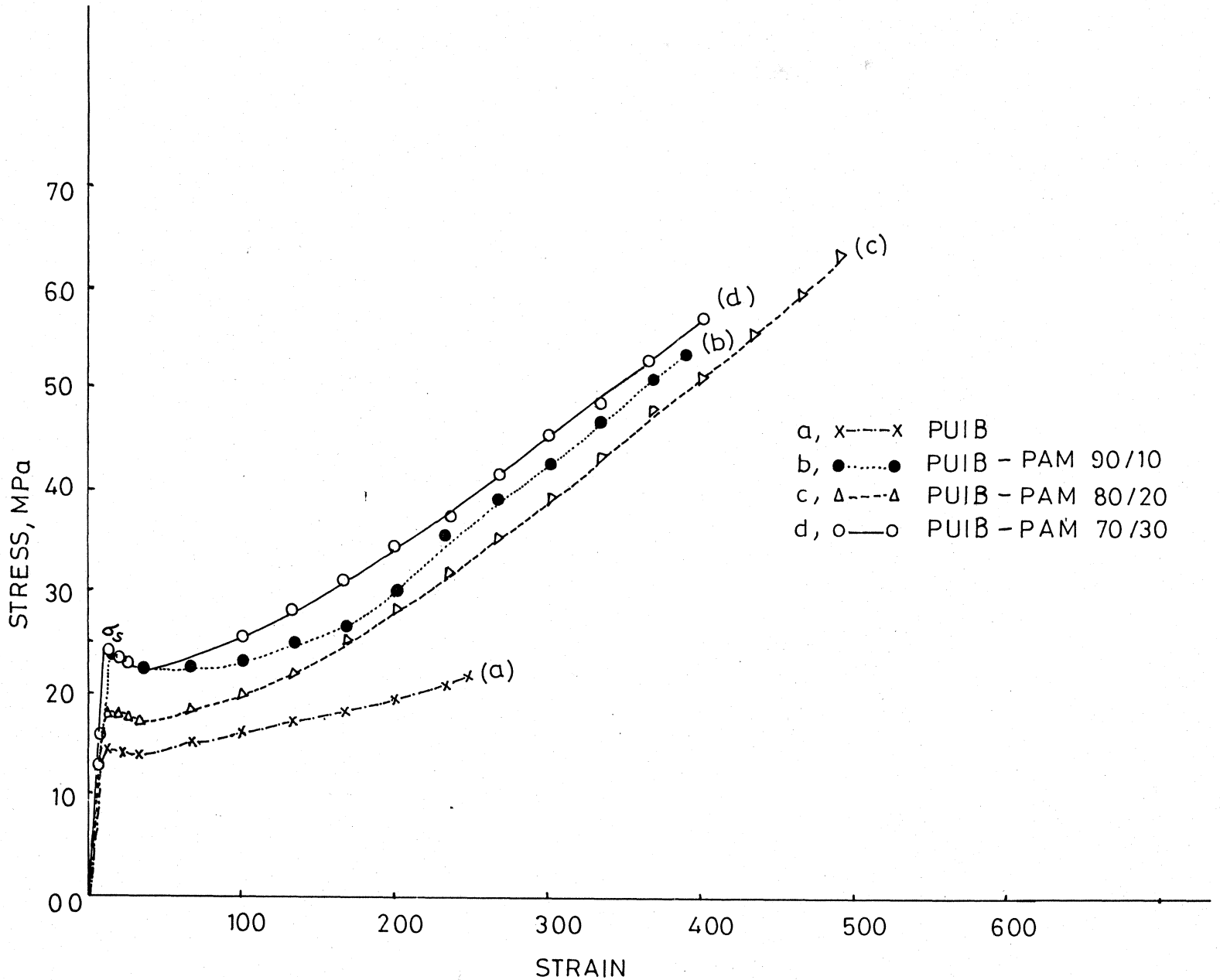


Fig.3.6. Stress VS Strain curves for TDI based polyurethane PUIB and PUIB PAM

for the IPNs which may be due to the enhanced entanglements on interpenetration. The higher isocyanate index of polyurethanes could therefore lead to better interpenetrated structures. The general mechanical behaviour observed both for the polyurethanes PU1A and PU2A and PU 3A (Table 3.VIII-3.X) and for their corresponding IPNs is that when the isocyanate index for the polyurethane is increased, the tensile stress increases, elongation decreases and modulus increases. The increase in tensile stress is not directly dependent on the decrease in elongation. Similar behaviour has been reported by Andrady et al (240,241) for polydimethylsiloxane networks. They attributed the increase of modulus and ultimate strength to the low incidence of dangling chain irregularities (241) and due to the non Gaussian effects arising from limited chain extensibility(240). As the PU-PAM IPNs have not been prepared by strictly controlling the incidence of dangling chains, the second reason of non-Gaussian effects from limited chain extensibility seen to be the more plausible one.

3.4.1.3. Effect of molecular weight of polyol on the mechanical behaviour of PU-PAM IPNs:

The molecular weight of the polyol PTMG is increased from 1010 in PU1A and PU1B series to 2000 in PU2A and PU2B series (Table 3.VIII and 3.IX).The mechanical behaviour dependence on molecular weight of the polyol is not the same for all compositions.Comparing the tensile stress,(Table 3.VIII and 3.IX),shows that at higher NCO/OH, the tensile stress decreases for both the

polyurethanes and IPNs on increasing the molecular weight of the polyol eg tensile stress of PU1B is 22.84 MPa which is decreased to 16.86 MPa in PU2B (except in the case of the PU 2B-PAM 70/30 IPN). The decrease of tensile stress is accompanied by a corresponding increase of elongation and a decrease of modulus. The increase of elongation can be attributed to an increase of soft segment (C-O-C) groups in a higher molecular weight polyether or a greater distance between two crosslinks. At lower NCO/OH ratio, the polyurethane follows the same trend. The tensile stress of PU1A is 14.12 MPa, which is decreased to 4.8 MPa for PU2A. However, the PU-PAM IPNs show an interesting behaviour. Comparing the values of tensile stress for the IPNs of PU2A series, (Table 3.IX) one can see that PU1A-PAM 90/10, PU1A-PAM 80/20, and PU1A-PAM 70/30 have less tensile stress and elongation than PU2A-PAM 90/10, PU2A-PAM 80/20 and PU2A - PAM 70/30 IPNs. A plausible reason for the enhanced tensile stress of PU2A could be the increased flexibility obtained by the more number of C-O-C groups in PU2A, to accomodate more polyacrylamide resulting in a larger domain size for the polyacrylamide network as reported by us(242) Touhsaent et al (39) have reported that unequal domain size in compatible IPNs gives rise to increased tensile stress, with the IPNs behaving like plastic reinforced rubber. In case of the PU2B series, where the polyol molecular weight is again 2000, the crosslinking is increased in comparison to PU2A. The flexibility of the soft segments of PU2B is therefore much decreased due to the enhanced interlocking of polyol segments, which in turn, could

restrict the formation of larger domain sizes for polyacrylamide. The more crosslinked PU2B-PAM IPNs may therefore be more phase mixed and have finer domain sizes. The realization of such a morphology decreases tensile stress than what would have been obtained if there were unequal domain sizes. The resultant effect is reflected as an increased tensile stress for PU1B-PAM series with polyol molecular weight of 1010 over that of the PU2B - PAM series.

TABLE 3.VIII

MECHANICAL PROPERTIES OF POLYURETHANE (TDI-PTMG1010-TMP)-PAM IPNS

Polymer	Ultimate Tensile stress, MPa	% Elongation at break	Modulus at 100% elongation MPa
NCO/OH = 1.09			
PU 1A	14.12	746	5.69
PU1A-PAM 90/10	16.67	715	3.73
PU1A-PAM80/20	18.73	700	2.75
PU1A-PAM 70/30	14.02	700	3.14
PU1A-PAM 50/50	25.69	581	7.35
NCO/OH = 2.01			
PU1B	22.84	217	18.82
PU1B-PAM 90/10	55.20	447	20.98
PU1B-PAM 80/20	56.37	415	19.60
PU1B-PAM 70/30	57.84	386	27.25

TABLE-3.IX

MECHANICAL PROPERTIES OF POLYURETHANE(TDI-PTMG2000-TMP)-PAM IPNS

Polymer	Ultimate Tensile stress,MPa	Percent elongation at break	Modulus at 100% elongation MPa
NCO/OH = 1.09			
PU2A	4.80	897	0.49
PU2A-PAM90/10	36.67	1318	3.04
PU2A-PAM80/20	35.20	1315	1.37
PU2A-PAM70/30	30.10	1299	3.04
PU2A-PAM50/50	6.06	1210	1.23
NCO/OH = 2.01			
PU2B	16.86	932	3.82
PU2B-PAM90/10	42.55	735	7.45
PU2B-PAM80/20	48.63	740	10.00
PU2B-PAM70/30	61.18	940	3.11
PU2B-PAM50/50	15.39	408	4.49

TABLE-3.X

MECHANICAL PROPERTIES OF POLYURETHANE(TDI-PPG2000-TMP)-PAM IPNS

Polymer	Ultimate Tensile stress,MPa	Percent elongation at break	Modulus at 100% elongation MPa
NCO/OH = 1.09			
PU3A	1.60	350	0.69
PU3A-PAM 90/10	4.49	1456	0.98
PU3A-PAM80/20	1.55	666	0.54
PU3A-PAM 70/30	0.97	333	0.70
PU3A-PAM50/50	4.25	899	0.81
NCO/OH = 1.68			
PU3C	4.80	580	3.43
PU3C-PAM90/10	8.17	790	3.04
PU3C-PAM80/20	2.41	190	2.45
PU3C-PAM70/30	3.14	170	3.73

3.4.1.4. Effect of the nature of the polyol on the mechanical properties of PU-PAM IPNs :

When polypropylene glycol (PPG) molecular weight 2000 was used as polyol, increased tensile stress and modulus are observed (Table 3.X), on increasing NCO/OH ratio. Elongation values are generally decreased. The values of tensile stress are not as

much as in the PTMG series (Table 3.VIII and 3.IX). The asymetric nature of PPG with bulky (-CH3) groups could be preventing the ordering of the macromolecules required to build the mechanical properties (242). In addition the bulky (-CH3) groups may be reducing the intercellular spaces and hindering efficient penetration of polyacrylamide networks. Consequently, the tensile stress values for PU3A-PAM IPNs are lesser than that for PU2A-PAM IPNs, even though the molecular weight of polyols and NCO/OH ratio are the same for both the series.

3.4.1.5. Effect of the nature of the isocyanate on the mechanical properties of PU-PAM IPNs:

In the (PTMG 1010-TDI-TMP) PU-PAM IPNs, NCO/OH was maintained at 1.09 and isocyanate was changed to MDI. As MDI is more symmetric than TDI, increased ordering of chains and increased tensile stress for the polyurethane can be expected. Crosslinking reactions during biuret formation can also be expected to be more efficient for MDI structure due to its more symmetric nature, which would also increase tensile stress and modulus. The tensile stress for the MDI based polyurethane PU4A and its IPNs (Table3.XI) is comparitively higher than that of TDI based polyurethane PU1A and its IPNs (Table 3.VIII). Increased crosslinking with polyurethane continuous phase in MDI based IPNs reduces the elongation in comparison to that of the TDI based PU1A and its IPNs. A reverse trend is observed with PAM becoming a co-continuous phase at PU4A-PAM 70/30 (Table 3.XI) in MDI based IPNs.

TABLE-3.XI

MECHANICAL PROPERTIES OF POLYURETHANE(MDI-PTMG1010-TMP)-PAM IPNS

Polymer	Tensile stress MPa	Percent elongation at break	Modulus at 100% elongation MPa
PU 4A	30.78	563	10.90
PU4A-PAM 90/10	37.94	539	10.39
PU4A-PAM80/20	37.55	513	11.18
PU4A-PAM70/30	57.35	704	12.65
PU4A-PAM50/50	49.12	758	11.70

TABLE 3.XII

MECHANICAL PROPERTIES OF VINYL POLYMERS

Polymer	Ultimate Tensile stress, MPa	Percent Elongation at break
2% crosslinked PAM	1.96	-
2% crosslinked PMMA	10.88	-
2% crosslinked PHEMA	23.73	-
2% crosslinked PVP	2.94	-

3.4.2. Effect of varying the second monomer in TDI based IPNs on the mechanical properties of IPNs:

The (PTMG 1010-TDI-TMP) PU of NCO/OH=1.09 ie. PU1A was selected for studying the effect of varying the second monomer in the IPN. The second polymer was changed from PAM to polymethyl-methacrylate,(PMMA),poly2-hydroxyethyl methacrylate,(PHEMA), and polyvinyl pyrrolidone,(PVP). The crosslinking of the two polymers were not varied mainly for two reasons. The first one, being that crosslinking of the second monomer has been reported to be not influencing the IPN formation(239) and secondly higher crosslinking ratios of the polyurethane, though they give rise to

more compatible IPN formation in the PU-PAM IPNs, are not desirable for biomedical applications, especially blood contacting and soft tissue applications owing to their high rigidity.

Table 3.VIII,3.XIII and Fig 3.7 depict the changes of the mechanical properties on varying the second monomer. PU-PMMA IPNs have higher tensile stress values than PU-PAM IPNs. PU-PAM and PU-PHEMA have almost similar tensile properties while PU-PVP IPNs have the least strength.The tensile stress of PU1A-PVP 90/10 IPN is even less than that of the homopolymer polyurethane PU1A. The lower tensile stress of PU1A-PVP 90/10 IPN compared to PU1A, could be attributed to the greater segmental mobility of the polyvinyl-pyrrolidone units. However, the percent elongation at break,(Table3.XIII), do not show the increased values normally associated with a rubbery structure. This may partly be due to the crosslinked nature of the IPNs. Another reason reported by us (243) could be that the bulky-CH3 groups of TDI and the cyclic units of PVP may be hindering the free alignment and ordering of polymer chains. In the PU-PMMA IPNs, an increase in elongation value is noted for the 90/10 IPN which may be attributed to a plasticizing effect of the acrylate component. The individual IPN series with PMMA,PHEMA, and PVP show maxima and minima in tensile stress similar to those found for the PU-PAM series. It is also observed that addition of 10 wt% of any vinyl monomer can itself produce IPNs with optimum mechanical properties.

TABLE-3.XIII

MECHANICAL PROPERTIES OF (TDI-PTMG1010-TMP)PU AND IPNS

NCO/OH = 1.09

Polymer	Ultimate Tensile stress, MPa	Percent elongation at break	Modulus at 100% elongation MPa
PU1A	14.12	746	5.69
PU-PMMA IPNs			
PU1A-PMMA90/10	35.78	1188	5.10
PU1A-PMMA80/20	17.16	784	2.45
PU1A-PMMA70/30	23.53	693	2.75
PU1A-PMMA50/50	38.14	866	4.90
PU-PHEMA IPNs			
PU1A-PHEMA90/10	22.94	691	6.18
PU1A-PHEMA80/20	15.29	660	5.88
PU1A-PHEMA70/30	18.24	613	6.76
PU1A-PHEMA50/50	17.84	583	8.53
PU-PVP IPNs			
PU1A-PVP 90/10	6.57	448	3.92
PU1A-PVP 80/20	10.69	551	4.51
PU1A-PVP 70/30	11.37	566	5.39.

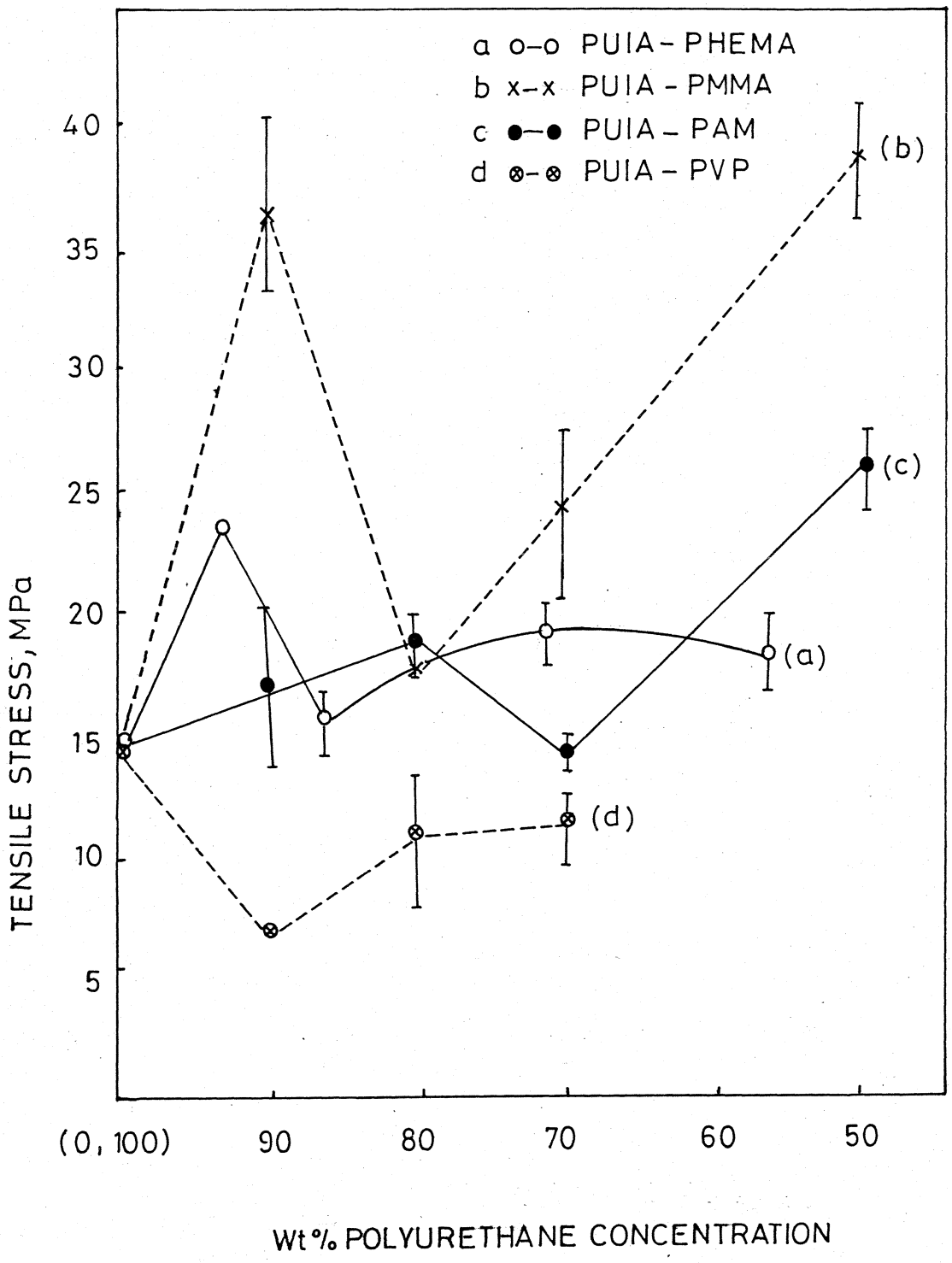


Fig. 3.7. Effect of second monomer on the tensile stress of TDI based polyurethane PUIA and IPNS.

3.4.3 Effect of changing the second monomer in the MDI based IPNs on the mechanical properties of the IPNs:

The second monomer was varied in the (MDI-PTMG 1010-TMP) polyurethane PU4A. The NCO/OH of the polyurethane was 1.09. Table 3.XI gives the tensile test results of the PU4A-PAM IPNs and Table 3.XIV comprises the results of the other PU4A based IPNs. Tables 3.XI,3.XIV and Fig 3.8, show that on increasing the second polymer content, the tensile stress of the IPN is increased over that of the polyurethane PU4A. While the elongation is decreased, not much change is observed in modulus values. Increases in elongation could be due to a plasticizing action of the second polymer. The increase of the tensile stress may be attributed to the enhanced interlocking of polymeric chains on IPN formation. Lipatova has reported (11) that the presence of heterogenous interfacial regions may contribute to the mechanical properties. The random increases of tensile stress could be due to such interfacial region contributions. An interesting increase of tensile stress is observed in the case of the PU4A-PVP IPNs, unlike the case of the TDI based PU1A-PVP IPN. The PVP homopolymer, has a very low tensile stress of 2.94 MPa Table 3.XII. Synergism of the tensile stress value on IPN formation for polyurethane PU4A and PVP could not be the sole reason for the increased tensile stress of PU4A-PVP IPN. A possible reason could be the formation of a lamellar type of structure composed of the cyclic units of PVP in one plane and the symmetric MDI units forming another plane. Such a structure could contribute to enhanced tensile

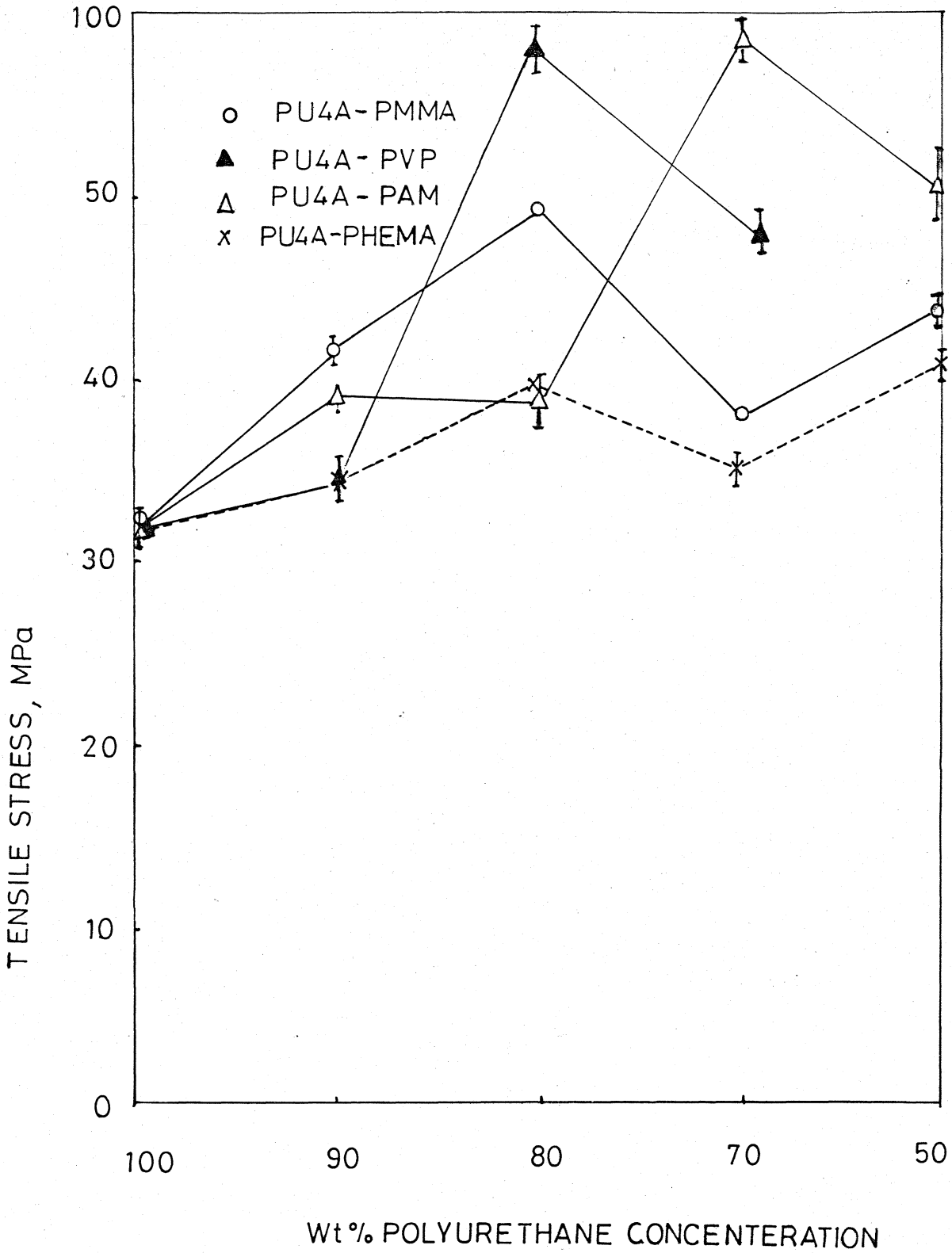


Fig.3·8· Effect of second monomer on tensile stress of MDI based polyurethane PU4A and IPNS.

stress and elongation. Fig 3.8 gives the comparative tensile stress values for the PU4A IPNs. A clear trend of the superior IPNs at all compositions similar to that in case of(Fig 3.7) for the TDI based IPNs cannot be observed. However, at the 90/10 composition it can be seen (Fig 3.8) that PU4A-PMMA90/10 has more tensile stress than PU4A-PAM 90/10 IPN which in turn is higher than that for PU4A-PHEMA and PU4A-PVP IPNs.On the whole, the values of tensile stress, and modulus for the MDI based polyurethane and IPNs are more than that for the TDI based system. However, the elongation values of the MDI PU and IPNs, except for PU4A-PVP IPNs,are lesser than that of the TDI IPNs, probably due to more efficient crosslinking in the MDI system.

In summary , the mechanical properties of polyurethane-polyacrylamide IPNs are seen to be influenced by parameters such as molecular weight and nature of polyols, crosslinking ratio of polyurethane, extent of acrylamide penetration, phase mixing, phase separation and interfacial region contributions. For the other IPNs, only one polyurethane and one crosslinking ratio was studied and a comparison of the TDI based and MDI based IPNs demonstrated the superior mechanical properties of MDI polyurethane and IPNs. Incorporation of 10 wt% of vinyl monomers itself can give IPNs of superior and consistent mechanical properties.Among the different 90/10 IPNs of both MDI and TDI system, the PU-PMMA 90/10 IPN emerged as the one with the best mechanical properties followed by PU-PAM and PU-PHEMA IPNs. The PU-PVP 90/10 IPNs had the least mechanical properties in both MDI

and TDI system. However in the MDI system, the tensile stress values for PU4A-PVP IPNs were more than that for the homopolymer PU4A and this have been attributed to the formation of a lamellar like structure for the PU4A-PVP IPNs.

TABLE-3.XIV

MECHANICAL PROPERTIES OF POLYURETHANE(MDI-PTMG1010-TMP) AND IPNS

Polymer	Ultimate Tensile stress, MPa	Percent elongation at break	Modulus at 100% elongation MPa
PU4A	30.78	563	10.90
PU-PMMA IPNS			
PU4A-PMMA 90/10	40.59	593	13.14
PU4A-PMMA 80/20	47.84	682	13.14
PU4A-PMMA 70/30	36.87	603	15.29
PU4A-PMMA 50/50	42.55	448	14.51
PU-PVP IPNS			
PU4A-PVP 90/10	33.33	686	11.67
PU4A-PVP 80/20	56.86	796	12.35
PU4A-PVP 70/30	46.86	633	12.65
PU-PHEMA IPNS			
PU4A-PHEMA 90/10	33.24	490	13.53
PU4A-PHEMA 80/20	38.73	565	15.69
PU4A-PHEMA 70/30	33.04	490	16.67
PU4A-PHEMA 50/50	39.22	450	12.75

3.5. Dynamic Mechanical Properties:

Dynamic mechanical properties like dynamic modulus, loss modulus or internal friction express the mechanical properties of materials as they are deformed under periodic forces. The dynamic modulus indicates the inherent stiffness of material under dynamic loading conditions. The mechanical damping or internal friction indicates the amount of energy dissipated as heat during the deformation of the material. The internal friction of the material is important as a property index and for environmental and industrial applications. These dynamic parameters have been used to determine the glass transition region, relaxation spectra, degree of crystallinity, molecular orientation, crosslinking, phase separation, structural or morphological changes resulting from processing and chemical composition of polymer blends, graft polymers and copolymers(244). The dynamic loss modulus, or internal friction, is sensitive to many kinds of molecular motion, transitions, relaxation processes, structural heterogenities, and the morphology of multiphase systems (crystalline polymers, polymer blends, and copolymers). Therefore, interpretations of the dynamic mechanical properties at the molecular level are of great scientific and practical importance in understanding the mechanical behaviour of polymers.

3.5.1. Theory of Dynamic mechanical analysis:

The stress applied to a viscoelastic body results in a linear or non linear dynamic response. The applied force and the

resulting deformation both vary sinusoidally with time;For linear viscoelastic behaviour, the strain alternates sinusoidally but it is out of phase with the stress. This phase lag results from the time necessary for molecular rearrangements and is associated with relaxation phenomena (245). The stress σ and strain ϵ can be expressed as follows (244):

$$\sigma = \sigma_o \sin (wt + \delta) \qquad \ldots\ldots 3.1$$

$$\epsilon = \epsilon_o \sin wt \qquad \ldots\ldots 3.2$$

where w is the angular frequency and δ is the phase angle. Then $\sigma = \sigma_o \sin wt \cos \delta + \sigma_o \cos wt \sin \delta$ 3.3

The stress can be considered to consist of two components, one in phase with the strain ($\sigma_o \cos \delta$) and the other 90 degree out of phase ($\sigma_o \sin \delta$). When these are divided by the strain, the modulus can be separated into an in-phase (real) and out of phase (imaginary) component.

$$\tan \delta = E'' / E' \qquad \ldots\ldots 3.4$$

The real part of the moduli E' is called the storage moduli and is related to the storage of energy as potential energy and its release in the periodic deformation. The imaginary part of the moduli E", is called the loss moduli and is associated with the dissipation of energy as heat when the materials are deformed. The loss tangent $\tan \delta$, called internal friction or damping, is the ratio of energy dissipated per cycle to the maximum potential energy stored during the cycle (244).

3.5.2. Primary and secondary transitions:

The dynamic mechanical properties of polymers are usually

studied over a wide temperature range (-150→300 Degree C). Typical dynamic mechanical properties as a function of temperature (244) plots, indicate that in the region where the dynamic modulus temperature curve has an inflection point, the internal friction (tan δ) curve goes through a maximum. This transition region is called the glass transition region where the dynamic modulus E' changes from approximately 1 GPa in the glassy state to about 1 MPa in the soft rubbery state.

In the transition region, the damping is high owing to the initiation of microbrownian motion in molecular chains. Microbrownian motion is concerned with the cooperative diffusional motion of main chain segments. This transition is so conspicuous that it is called the primary dispersion (α peak). This peak is usually associated with the glass transition temperature. The loss modulus E" goes through a peak at a slightly lower temperature than the internal friction E"/E'.

Other relaxation transitions can be found in a glassy state on the lower temperature side of the primary dispersion. These are called secondary dispersions and are usually designated β, γ etc. in order of decreasing temperature.

3.5.3. Loss factor behaviour of the TDI based IPNs:

The dependence of loss tangent on temperature for different IPN systems of 90/10 composition based on PU1A with TDI as curative is shown in Fig 3.9. In the case of polyurethane (PU1A), the loss factor exhibits a maximum at -22 degree C corresponding to glass transition. In the case of IPNs based on 90% PU1A the

location of this transition peak is shifted to higher temperatures indicating enhanced compatibility between the components of the IPNs.

Generally, if two polymers are incompatible, the loss factor of the blend exhibits maxima corresponding to the Tgs' of the components. If the two components are completely compatible, the blend shows a single transition peak at a temperature intermediate to the respective transition temperatures (246). In the case of IPNs also, Frisch et al (43) have reported a single transition that is intermediate in temperature to the Tgs' of the component networks for compatible IPNs. However, Klempner et al (19) also state that two inwardly shifted transitions are indicative of semicompatible IPNs. Lipatov et al (247) have reported a third transition as being a contribution of interfacial region.

Thus, Fig.3.9, indicates that there exists some amount of compatibility between the components of IPNs in PU1A. The magnitude of tan δ max and its temperature of occurence for the various IPNs are shown in Table 3.XV. The temperatures at which,Tg is obtained, do not strictly follow the random copolymer,or Fox equation (22). The shift in Tg of IPNs to higher temperatures than calculated Tg from equation could be due to increased hydrogen bonding in the IPN system. Such behaviour of departure of Tg has been reported (248) for weakly phase segregated urethanes.

The second polymer polymethyl methacrylate (PMMA) used in the TDI based IPNs is more hydrophobic than the polyurethane PU1A

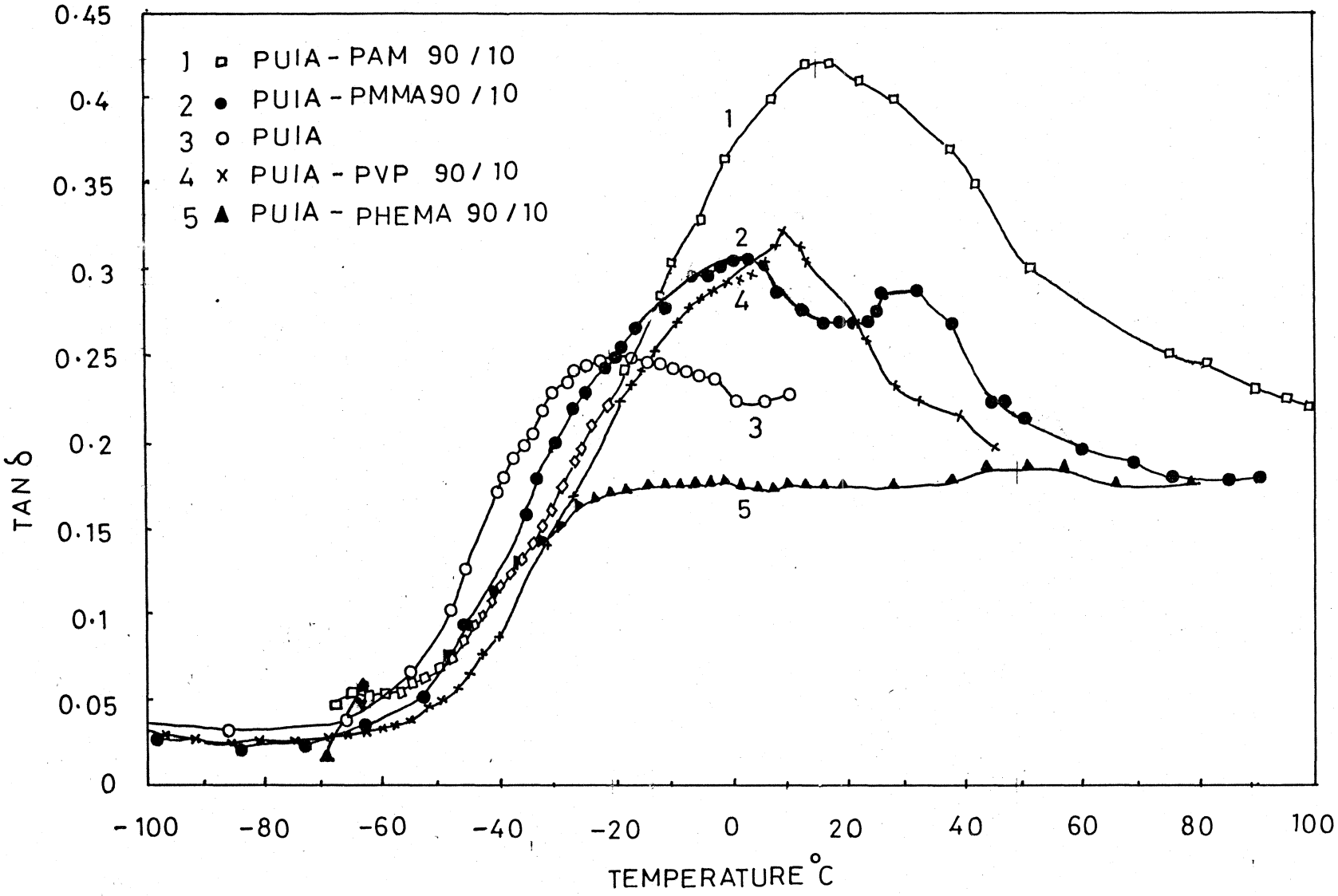


Fig 3.9 Tan δ vs temperature for TDI based PUIA and IPNS.

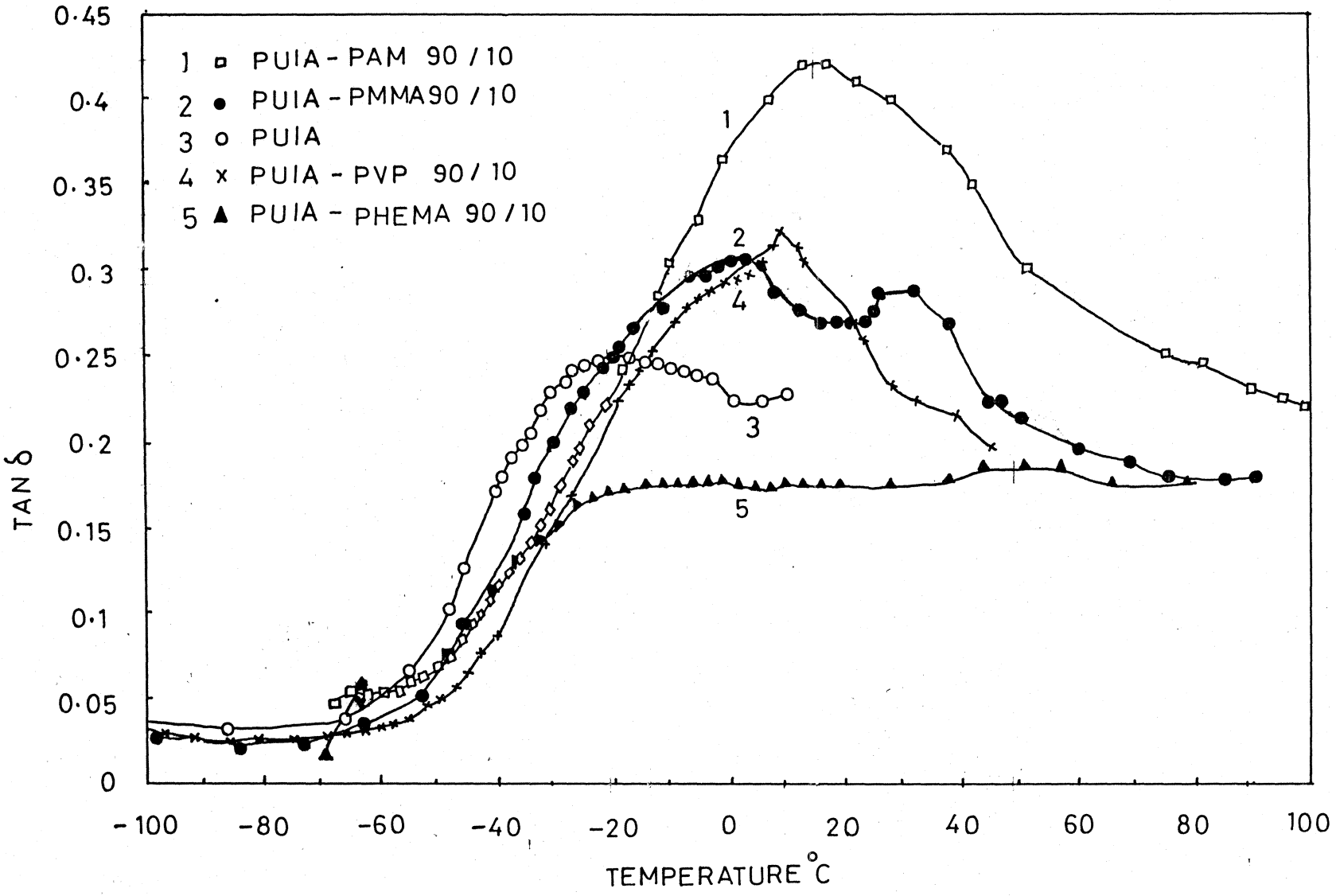


Fig 3.9 Tan δ vs temperature for TDI based PUIA and IPNS.

Polyacrylamide, (PAM), polyhydroxyethyl methacrylate (PHEMA), and polyvinyl pyrrolidone, (PVP) are more hydrophilic than PU1A.

The structure of PAM and PHEMA which have free -CONH2 group and -OH group and PVP with -OH and -C=O groups can contribute to hydrogen bonding which in turn could raise the temperature of Tg.

The 90/10 PU1A-PHEMA IPN system shows an unusually broad tan δ peak and is eminently suitable for damping applications.

The original interpretation of a single broad transition was that different regions of space had different compositions each yielding its own glass transition temperature (27). Sperling et al (22) report that if the minimum volume required for independent contributions to the relaxation spectrum is the same or smaller than that required to yield homogenous overall compositions, a broadened transition will result.

Alternately, Lipatov et al (247) have reasoned that a centrally located Tg, arises from extensive interfacial boundary material.

Akay et al (229) have concluded that a broad transition is in effect a compound transition generated by a spectrum of quasi crosslink densities which are a manifestation of the restriction imposed by rigid polymer content on the segmental mobility of the elastomer.

From Table 3.XV, it is observed that except for PU1A-PHEMA 90/10 IPN, all the other TDI based IPN systems exhibit higher tan δ_{max} values than PU1A. Many investigators (229) have however reported, that the tan δ max values will be reduced in case of

TABLE-3.XV

LOSS TANGENT PEAK PARAMETERS OF TDI BASED POLYURETHANE IPNS

Polymer	Tan δ Deg.C.	Tan δ max value
PU1A	-22	0.253
PU1A-PMA 90/10	12 (BROAD)	0.425
PU1A-PMMA 90/10	0,32 "	0.315, 0.294
PU1A-PVP 90/10	10 "	0.33
PU1A-PHEMA 90/10	(-14 TO 49)"	0.175

IPNs but Frisch (249) states that a departure of two phase medium behaviour can be expected for IPNs with a complex morphological situation in which the interpenetration results in a third phase or where no phase is properly dispersed in another. In such cases, the properties of the IPNs would not satisfy in good approximation, the predictions of mean field theories or strictly be bounded by properties of series and parallel combination of two network phases. The observed trend of increased values of tan δ max and other properties for certain IPNs may be therefore attributed to such complex behaviour. The tan δ max values of all IPNs are however lower than that of the acrylic polymers Table 3.XVI. As the formation of sequential IPNs is reported to result

in smaller domain sizes and more compatibility (22), an enhanced compatibility and smaller domain sizes can therefore, be expected for the PU1A-PHEMA 90/10 IPN which is of sequential type. This enhanced compatibility can contribute to the reduction of tan δ max of PU1A-PHEMA 90/10 when compared to PU1A.

TABLE-3.XVI

LOSS TANGENT PEAK PARAMETERS OF VINYL POLYMERS

Polymer	Tan δ Deg.C.	Tan δ max value
PHEMA	138	1.05
PVP	69	0.87
PAM	180	0.8
PMMA	150	0.4

3.5.4. Loss factor behaviour of PU1A-PMMA IPN systems:

The effect of composition on loss tangent of PU1A-PMMA IPNs is shown in Table 3.XVII and Fig 3.10. It is observed that tan δ max value due to to PU1A increases on incorporation of PMMA to form the IPN system. The transition is also shifted inwards. After 30% PMMA content there is an inversion in this value. Liptova (42) observed heterogenity even when 10 wt% of polyacrylate in a polyurethane-polyacrylate IPN and predicted phase inve-

rsion around 40% of the second network. The complex behaviour of IPNs discussed by Frisch (249) and the presence of interfacial material discussed by Lipatov (42) could be responsible for increasing the values of tan δ max over that of PU1A. The shoulders obtained at 32 degree C and 14 degree C for 90/10 and 50/50 PU1A-PMMA IPN support this assumption. The phase inversion at 70/30 PU1A-PMMA IPN could be responsible for the exceptional high value of tan δ max for this IPN.

TABLE-3.XVII

LOSS TANGENT PEAK PARAMETERS OF TDI BASED PU-PMMA IPNS

Polymer	Tan δ Deg.C.	Tan δ max value
PU1A	-22	0.253
PU1A-PMMA 90/10	0,32	0.315,0.294
PU1A-PMMA 70/30	7	0.49
PU1A-PMMA 50/50	4,14	0.351,0.37
PMMA	150	0.5

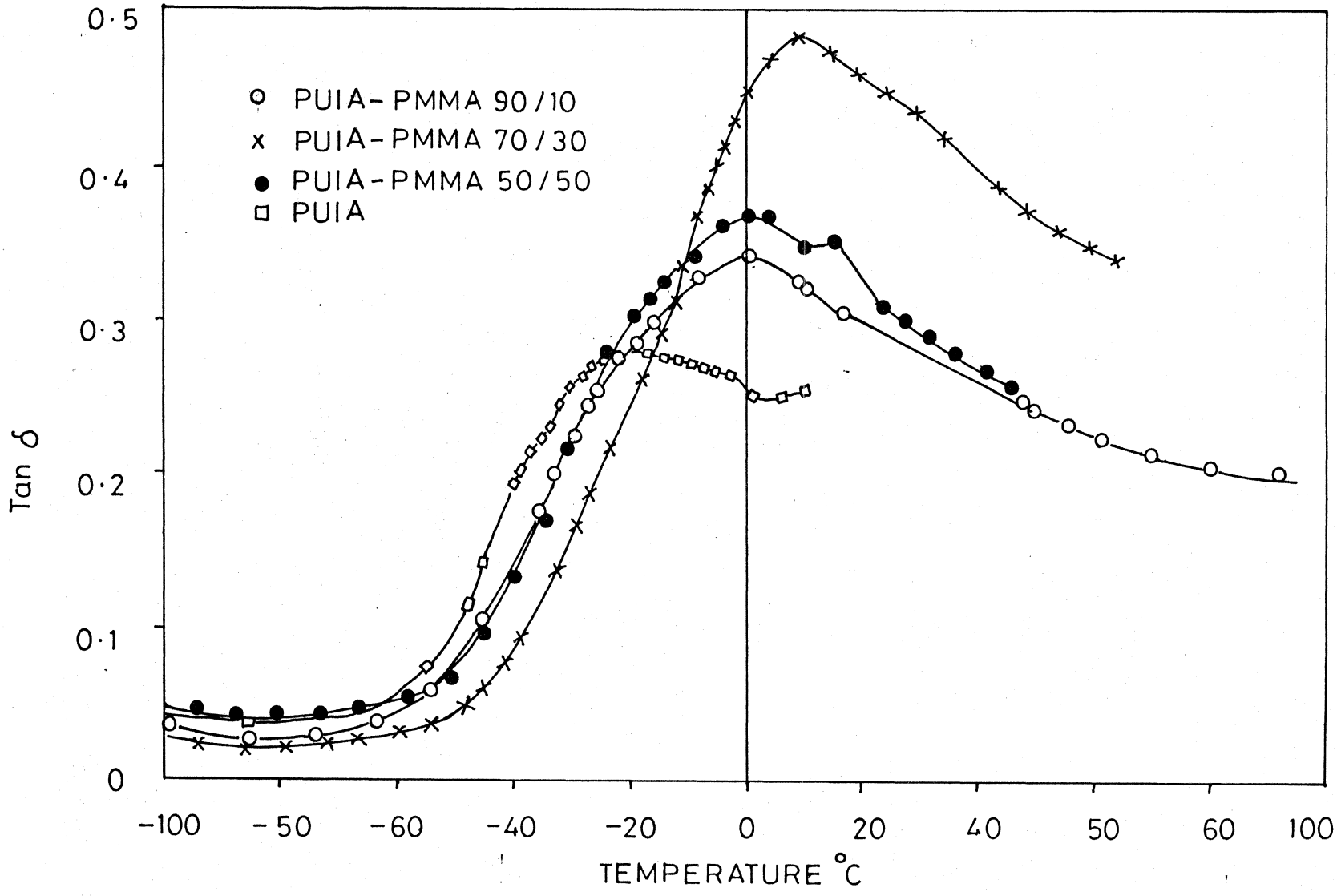


Fig. 3·10. Effect of composition on tan δ of PUIA-PMMA IPNS.

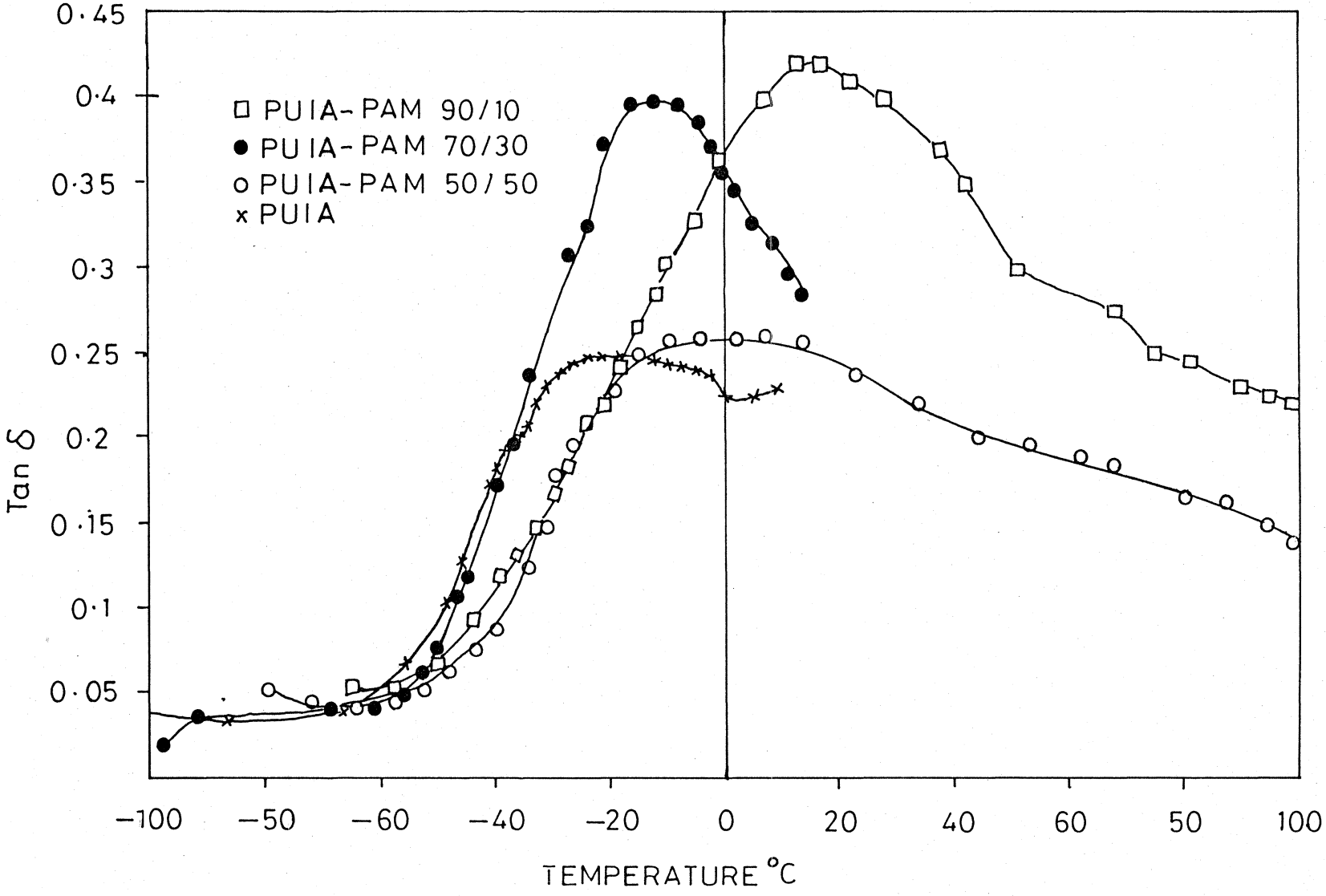
3.5.5. Loss factor behaviour of PU1A-PAM IPN system:

The effect of composition on the loss tangent of PU1A-PAM IPN is shown in Table 3.XVIII and Fig 3.11. A single broad tan δ peak is observed, which is shifted inwards. The value of tan δ max is less than that of PAM but increased in comparison to PU1A. However, phase inversion at 70/30 ratio is not observed as the tan δ max values are gradually decreasing.

TABLE-3.XVIII

LOSS TANGENT PEAK PARAMETERS OF TDI BASED PU-PAM IPNS

Polymer	Tan δ Deg.C.	Tan δ max value
PU1A	-22	0.253
PU1A-PAM 90/10	12	0.425
PU1A-PAM 70/30	-11	0.37
PU1A-PAM 50/50	-20 TO 20	0.25
PAM	180	0.8



Fig·3·11· Effect of composition on tan δ of PUIA-PAM IPNS.

3.5.6. Storage modulus behaviour of TDI based IPN systems:

The dynamic modulus-temperature plot for the 90/10 TDI based IPNs are depicted in Fig 3.12. The values of storage modulus, E', fall in the temperature range -70 degree C to -20 degree C, which is characteristic of the glass to rubber transition. The broad temperature range over which the dynamic storage modulus decreases is an indication of increased degree of intermixing as reported by Lee et al (250). The dynamic modulus values for the IPNs namely, PU1A-PMMA 90/10, PU1A-PHEMA 90/10 and PU1A-PAM 90/10 are higher than that for the pure polyurethane PU1A. The modulus value of PU1A-PMMA 90/10 IPN is the highest and that for PU1A-PVP IPN is the lowest. Synergism of modulus has been noted for compatible PPO-PS blends (251) and has been ascribed to an increase in packing density on blending. FIPNs of PPO-PS have also been reported (252)to exhibit an increased modulus which has been attributed to the amount of permanent chain entaglements between the two networks giving a resultant increase of packing density. In the present case, the increase of the dynamic storage modulus for PU1A-PMMA 90/10 IPN, PU1A-PAM 90/10 IPN and PU1A-PHEMA 90/10 IPN could be attributed to a similar enhancement of permanent chain entanglement or in other words increased intermixing of the two networks. PMMA with a solubility parameter of 9.3 $(cal/ml)^{1/2}$ is very close to a polyurethane solubility parameter of 10 $(cal/ml)^{1/2}$ (229) and hence, is expected to be more compatible and contribute to greater chain entaglement. The highest increase of the dynamic modulus for this

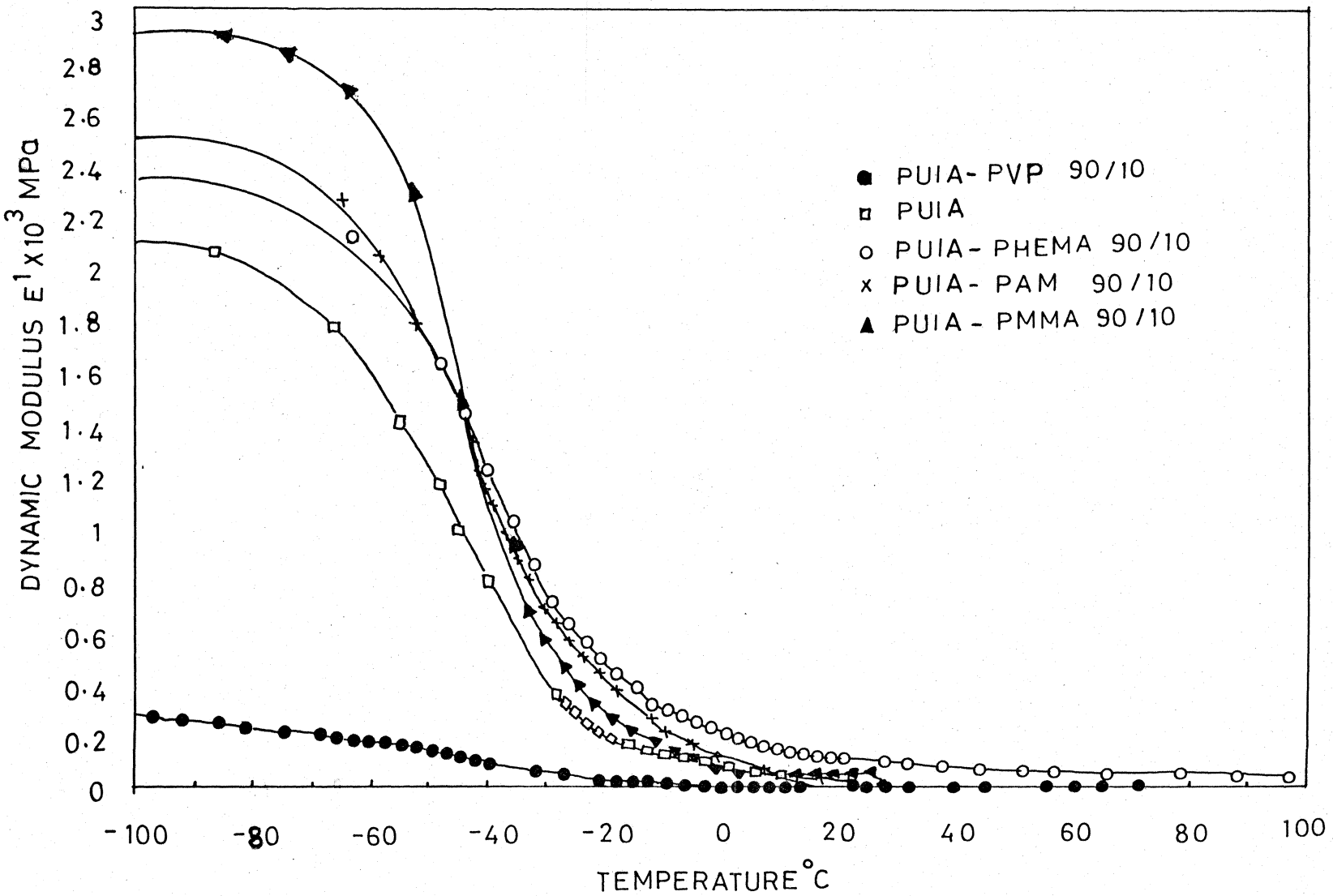


Fig. 3.12 Dynamic modulus - temperature plot of TDI based polyurethane

IPN substantiates the expected observation. PU1A-PVP 90/10 IPN with its highly amorphous and less phase mixed structure as discussed in section 3.4.5. could be expected to have a decreased intermixing in the IPN and hence the dynamic modulus for this IPN is decreased in magnitude. After the Tg region, the dynamic modulus values are nearly constant and equal to 10^6 Pa indicating the crosslinked nature of the IPNs. The effect of composition of the PU1A-PMMA IPNs and PU1A-PAM IPNs on the values of dynamic modulus are given in Table 3.XIX. Values of storage modulus for the IPNs are measured at the start of the transition (-100 degree C). It is observed that the modulus of the IPNs are higher than that of the homopolymer polyurethane PU1A. A phase inversion around 30 wt% of acrylic polymer is also seen evidenced by the drop of modulus for the 50/50 composition.

TABLE-3.XIX

EFFECT OF COMPOSITION OF TDI BASED IPNS ON THE STORAGE MODULUS

Polymer	Storage modulus MPa	Polymer	Storage modulus MPa
PU1A	2.1		
PU1A-PAM 90/10	2.5	PU1A-PMMA 90/10	2.9
PU1A-PAM 70/30	3.0	PU1A-PMMA 70/30	4.7
PU1A-PAM 50/50	2.3	PU1A-PMMA 50/50	3.2

3.5.7. Comparison of the MDI and TDI based systems:

The dependence of loss tangent on temperature for different IPN systems 90/10 composition based on PU4A with MDI as curative is shown in Fig 3.13 and Table 3.XX. In the case of PU4A the loss factor exhibits a maximum at -24 degree C corresponding to the glass transition. In the case of the IPNs based on 90% PU4A the transition is shifted to higher temperatures indicating the enhanced compatibility between the components of the IPNs. The higher glass tansition temperature for the TDI system has been attributed by Yu Yu Kercha et al (253) to a homogenization of the system. Tan δ max values for the PU4A based IPNs do not show appreciable changes which could be due to the formation of structure with less interfacial material.

TABLE-3.XX

LOSS TANGENT PEAK PARAMETERS OF MDI BASED IPNS

Polymer	Tan δ Deg.C.	Tan δ max value
PU4A	-24	0.24
PU4A-PAM 90/10	-15,15 (BROAD)	0.24
PU4A-PMMA 90/10	0 "	0.26
PU4A-PVP 90/10	-15,14 "	0.26,0.225
PU4A-PHEMA 90/10	-10,10 "	0.25,0.225

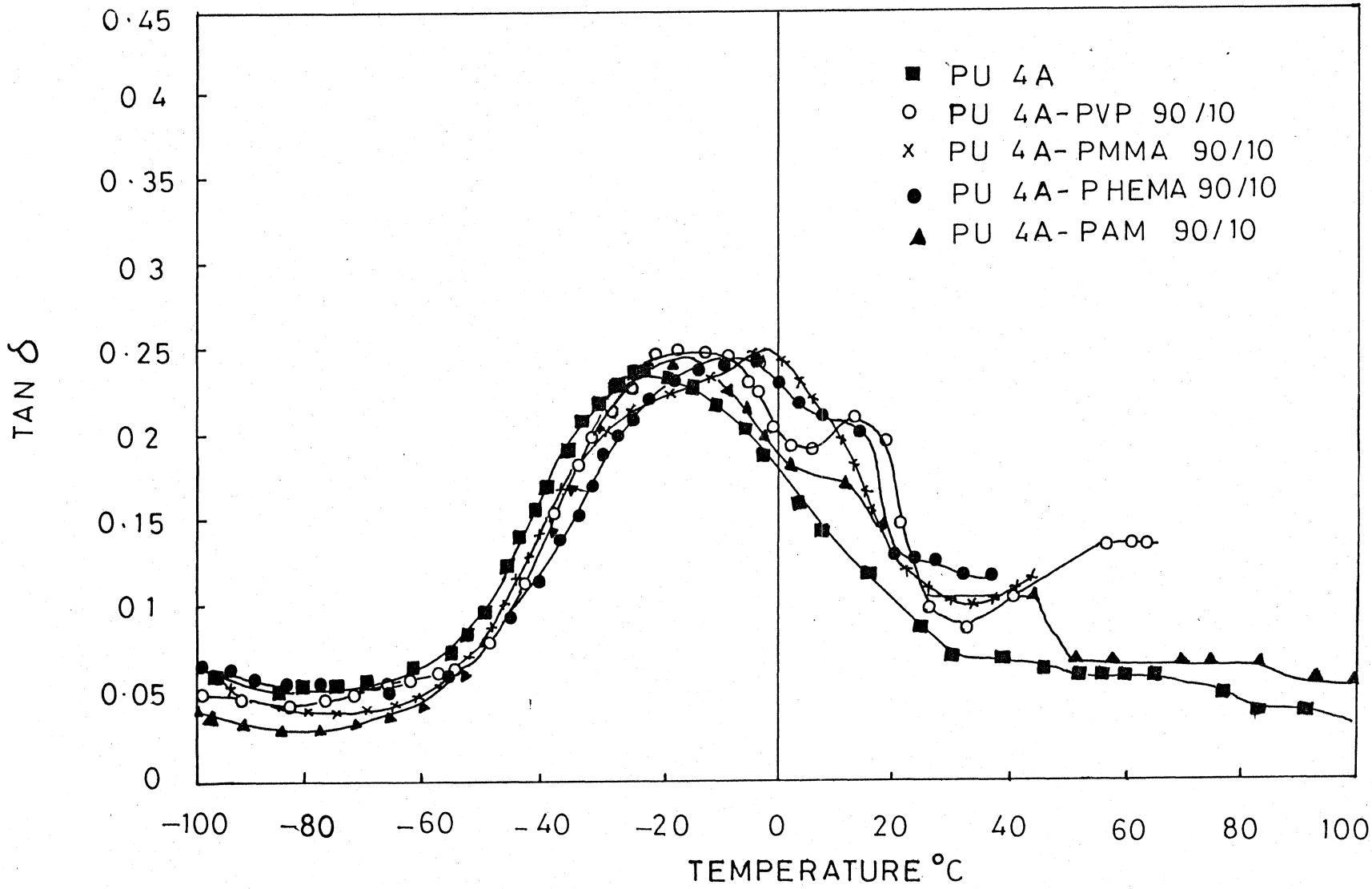


Fig. 3.12 Tan δ vs temperature for MDI based PU/4A and IPNS

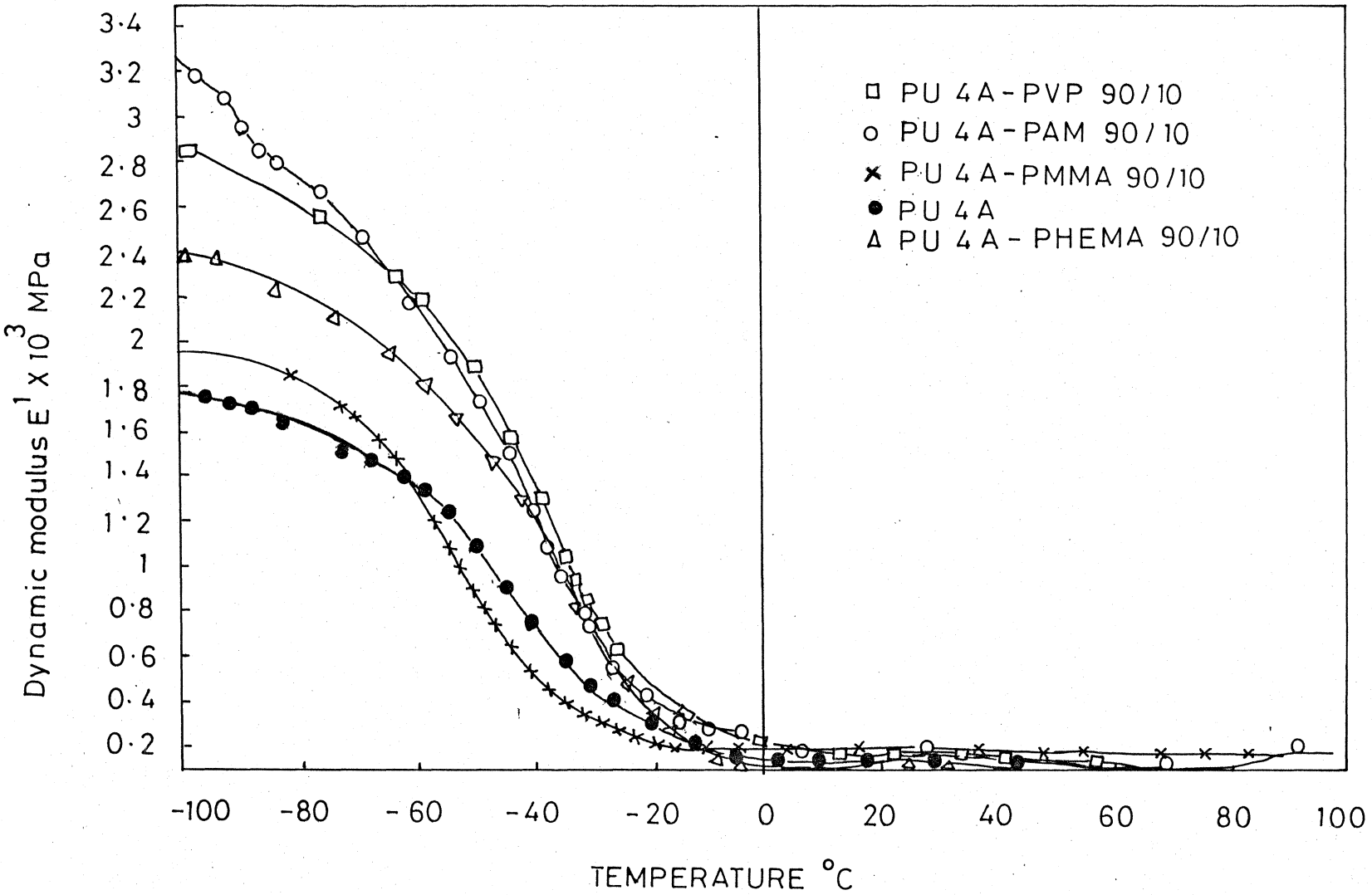


Fig. 3.14. Dynamic modulus temperature plot of MDI based polyurethane PU 4A and IPNS

The dynamic storage modulus-temperature plot for the MDI based IPN, Fig 3.14, indicate that the modulus values are similar to those obtained for TDI systemm. The E' for the PU4A based IPN systems falls from 10^8 - 10^9 Pa to 10^6 Pa. The E' values fall in a broad range of -80 degree C to 10 degree C. The broad region could be due to the greater interpenetration of MDI IPNs. Greater interpenetration of MDI based IPNs is also borne out by the fact that in all cases the dynamic modulus values before the transition are higher than that for pure polyurethane PU4A. Section 3.4.7 discusses probable reasons for a greater mixing of PU4a-PVP IPNs. This greater mixing could be contributing to an increase of packing density and subsequent increase of dynamic modulus for PU4A-PVP 90/10 IPN compared to PU4A unlike the case of PU1A series.

3.6 Thermal analysis:

3.6.1. Glass transition behaviour:

Polymers, undergo a phase change from glassy to rubbery state as the temperature is increased. Rubbery polymers become stiff and brittle below this glass transition temperature, Tg. Most polymer physical properties, such as brittleness, modulus and heat capacity, undergo a marked change at Tg.

On a molecular scale, the glass transition signals the beginning of large scale molecular motion. Below Tg, the molecules are confined to vibrate in a localized lattice, although there is no large scale molecular order. Many theories have been proposed to explain the glass transition phenomena. An excellent review is that of Shen and Eisenberg(254).

The glass transition appears to be a thermodynamic effect superimposed on a kinetic effect. Therefore, Tg is often referred to as a pseudo-second order phase transition since the glassy state is a quasi-equilibrium state. In the glassy state, the polymer molecules are stable in terms of short range molecular motion, whereas they are unstable with respect to long range motion.

The study of glass transitions is complementary to morphological studies, The Tgs' of IPN's can be studied in a variety of ways. The methods available to measure Tg may be conveniently divided into two groups: mechanical and nonmechanical. The most widely used nonmechanical method is differential scanning calorimetry, DSC. Many attempts (255-258) have been made to predict the Tg for compatible polymer blends. Most of these treatments have been empirical in nature. Frisch et al (19,43) have analysed the Tg behaviour, beginning from the random copolymer equation $Tg\ (av) = w_1 (Tg_1) + w_2 (Tg_2)$ where Tg_1 and Tg_2 represent the glass transition temperatures of polymer 1 and polymer 2, respectively. w_1 and w_2 are their weight fractions and Tg(av) is the predicted value of the glass transition temperature of the IPN. The equation finally derived by the Frisch et al.

$$\frac{-\theta}{1+\theta} = \frac{Tg - Tg\ (av)}{Tg\ (av)}$$

where θ is a measure of interpenetration of networks and according to Frisch et al (43) should have a value between 0 and 1 to

depict ideal interpenetration.

3.6.1.1. Glass transition behaviour of IPNs:

The glass transition temperature of the TDI based polyurethane, PU1A, vinyl polymers: polymethyl methacrylate, PMMA; poly 2-hydroxyethyl methacrylate, PHEMA; polyacrylamide, PAM; poly vinyl pyrrolidone, PVP; and IPNs of 90 wt.% PU1A composition were evaluated by DSC. The experimental and calculated values of Tg along with the θ values are given in Table 3.XXI. The values of θ lie between 0 and 1 indicating that the IPNs are well interpenetrated structures. The values of Tg from DSC do not exactly coincide with the value of Tg obtained from DMA measurements mainly due to the different nature of the measuring method. The values obtained from DMA are higher. Hourston et al(259) have also reported higher values of Tg obtained by DMA, especially when the measurements were carried out at 35 Hz, as in the present case.

The glass transition temperatures obtained by DSC, for the MDI based polyurethane PU4A and IPNs of 90 wt% composition of PU4a are given in Table 3.XXII. θ is again between 0 and 1 indicating the interpenetrated structure.

The 90/10 IPNs, of both the TDI based PU1A and MDI based PU4A, are therefore compatible IPNs.

TABLE-3.XXI

GLASS TRANSITION BEHAVIOUR OF TDI BASED IPNS

Polymer	Tg °K (expt.)	Tg(av)°K (calc.)	θ
PU1A	247	-	-
PU1A-PMMA 90/10	258	265.4	0.029
PU1A-PAM 90/10	261	266.1	0.019
PU1A-PHEMA 90/10	260	263.0	0.012
PU1A-PVP 90/10	253	256.5	0.014
PMMA	431	-	-
PAM	438	-	-
PHEMA	407	-	-
PVP	342	-	-

$$Tg(av) = w_1 Tg_1 + w_2 Tg_2$$

$$\frac{-\theta}{1+\theta} = \frac{Tg - Tg(av)}{Tg(av)}$$

TABLE-3.XXII

GLASS TRANSITION TEMPERATURES OF MDI BASED IPNS

Polymer	Tg °K (expt.)	Tg(av)°K (calc.)	θ
PU4A	253	-	-
PU4A-PMMA 90/10	268	270.8	0.010
PU4A-PAM 90/10	267	271.3	0.017
PU4A-PHEMA 90/10	264	268.4	0.016
PU4A-PVP 90/10	258	261.9	0.015

TABLE-3.XXIII

GLASS TRANSITION TEMPERATURES OF (TDI-PTMG1010)PU-PAM IPNS

Polymer	Tg °K (expt.)	Tg(av)°K (calc.)	θ
PU1A	247	-	-
PU1A-PAM 90/10	261	266.1	0.019
PU1A-PAM 80/20	251	285.2	0.135
PU1A-PAM 70/30	263	304.3	0.157
PAM	438	-	-

TABLE-3.XXIV

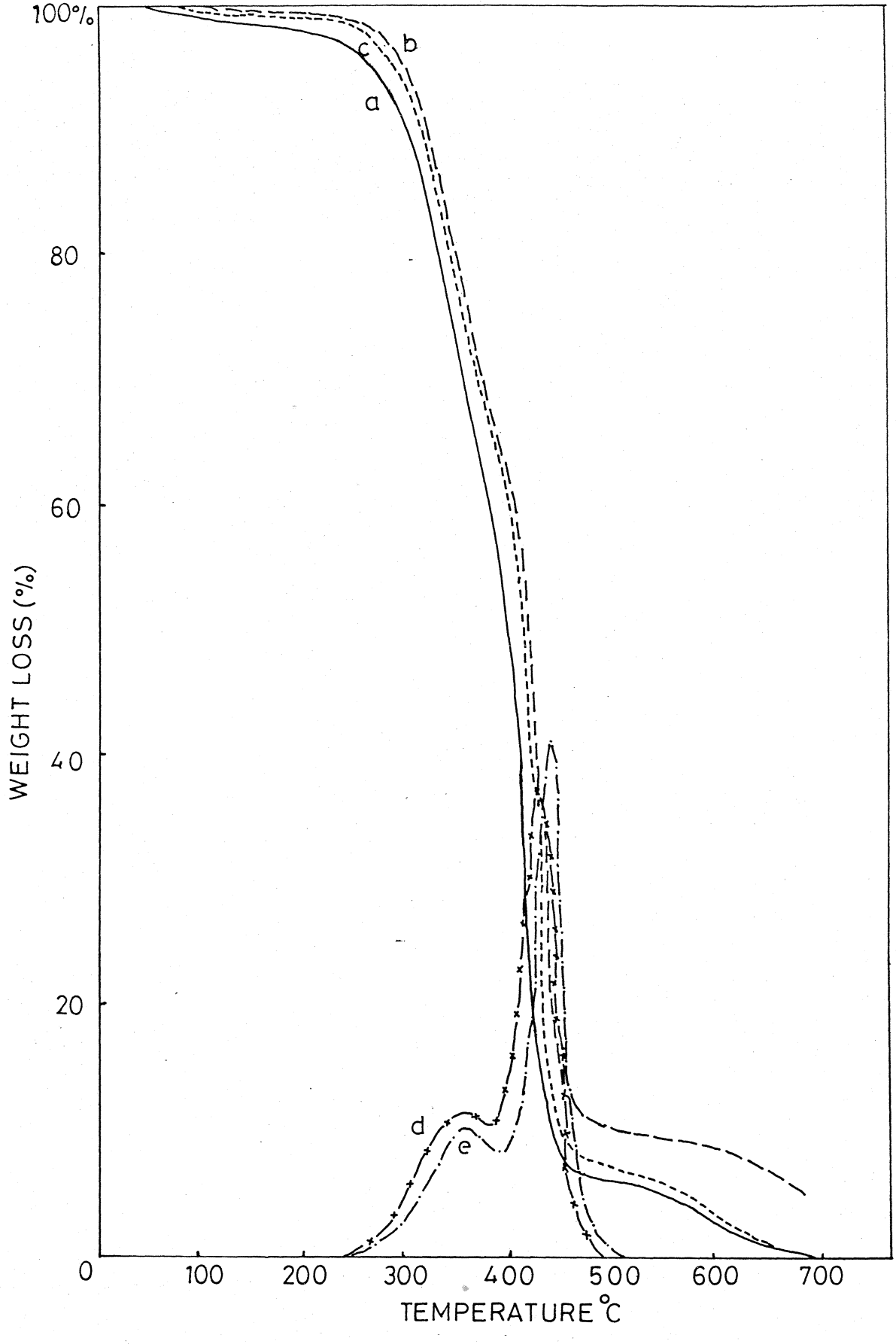
GLASS TRANSITION TEMPERATURES OF (TDI-PTMG2000)PU-PAM IPNS

Polymer	Tg °K (expt.)	Tg(av)°K (calc.)	θ
PU2A	188	-	-
PU2A-PAM 90/10	207	213	0.029
PU2A-PAM 80/20	193	238	0.233
PU2A-PAM 70/30	202	263	0.300

On increasing the concentration of the second monomer, the compatibility gradually decreases, as evidenced by the gradually increasing values of θ in PU-PAM IPNs. Representative examples of such increasing θ values are given in Table 3.XXIII and 3.XXIV. However, as the value of θ do not exceed 1, the present IPNs are not considered as phase separated.

3.6.2. Thermogravimetric analysis:

The technique of TGA involves change in weight of a material under examination as the temperature is increased at a predetermined and preferably at a linear rate. Applications of TGA to polymers include comparisons of relative thermal stability, the effect of additives on the thermal stability, study of degradation kinetics, oxidation stability etc.



Fig·3·15. Thermogravimetric analysis (TGA) curves of TDI based polyurethane and IPN
(a) PUIA, (b) PUIA–PAM 90/10 IPN
(c) PUIA–PAM 80/20 IPN, (d) DTG of PUIA

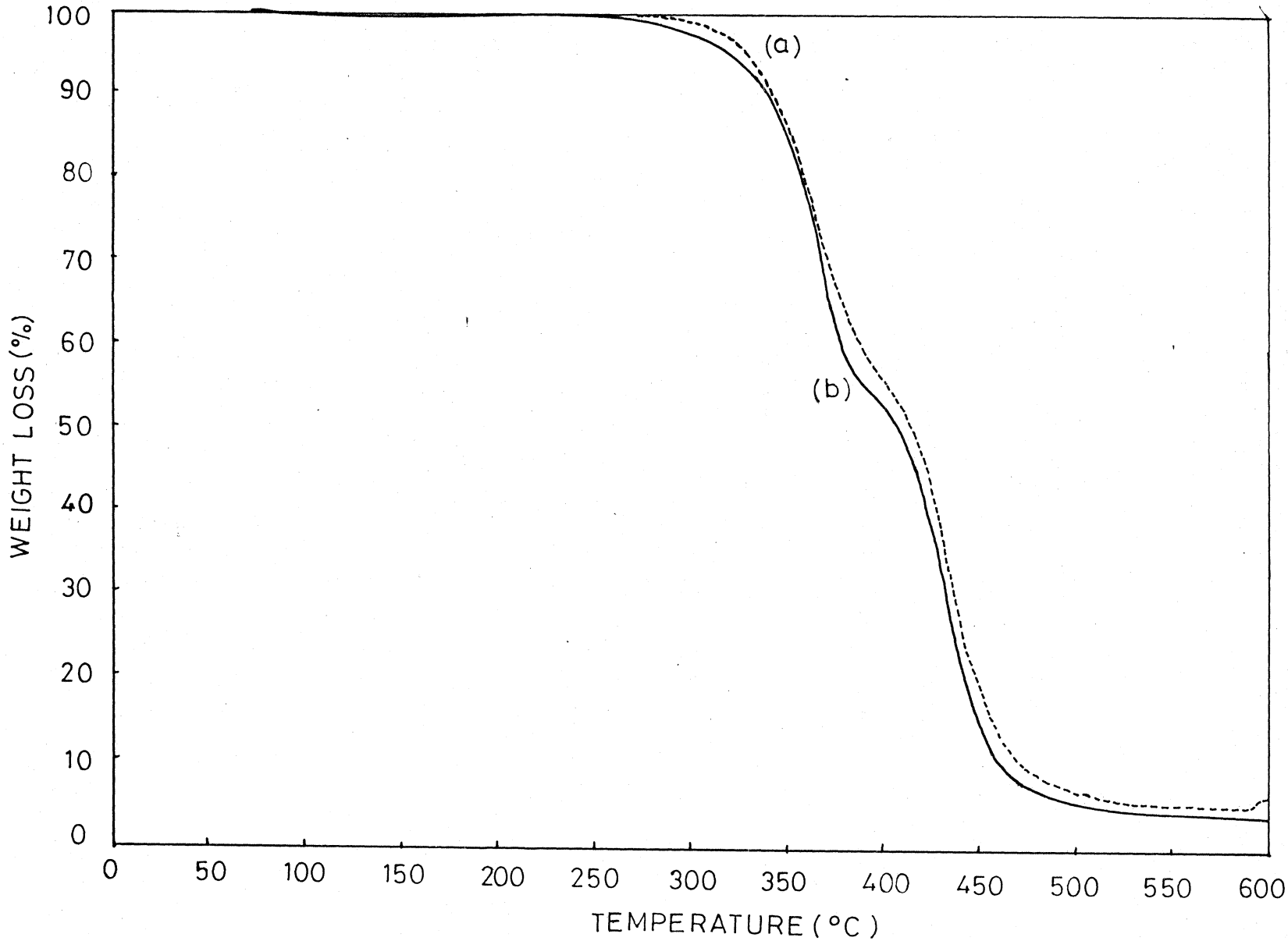


Fig . 3.16 . Thermogravimetric curve of MDI based polyurethane a = PU4A
b = PU4A-PAM 90/10 IPN

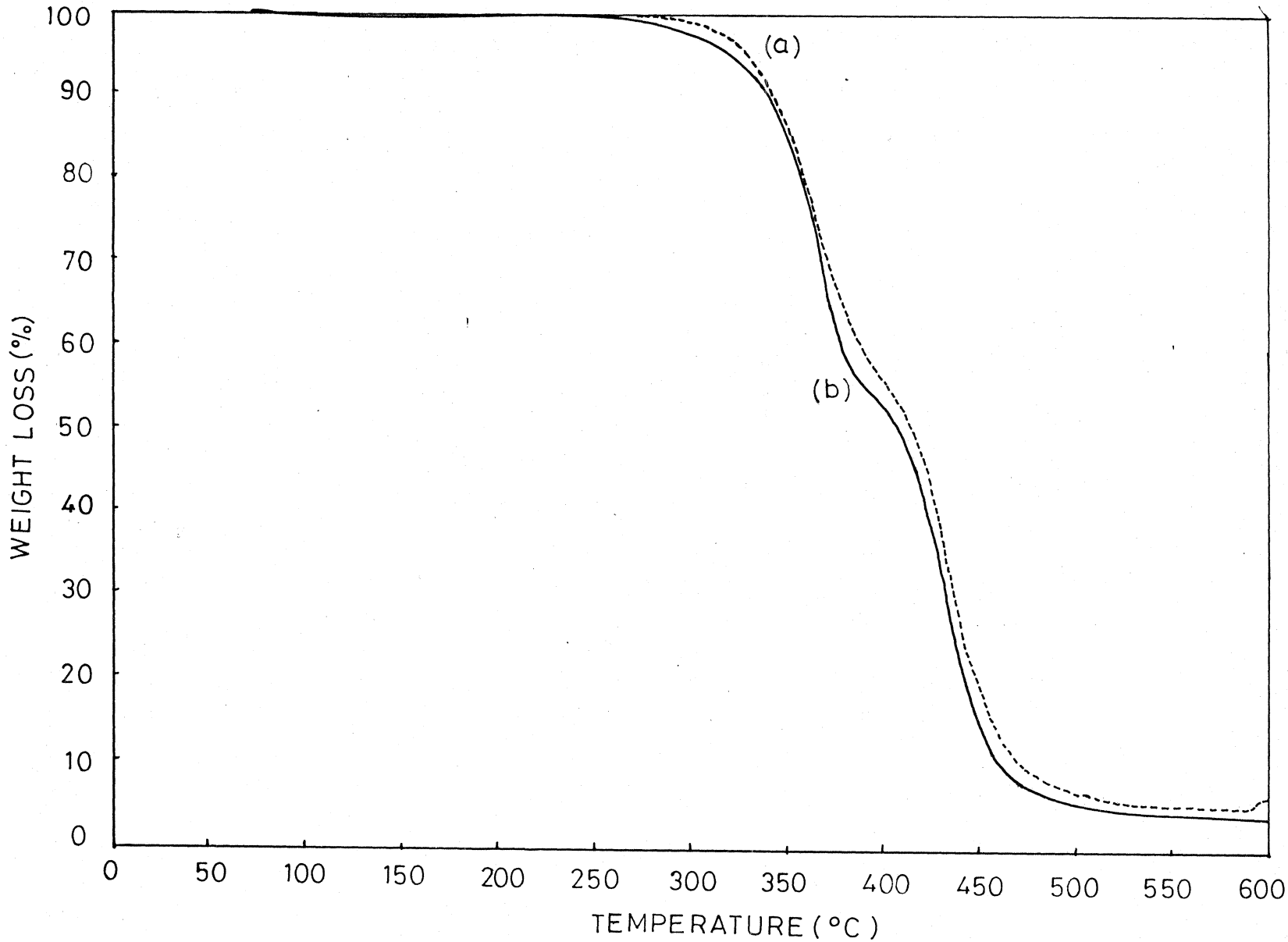


Fig . 3.16 . Thermogravimetric curve of MDI based polyurethane a = PU4A
b = PU4A-PAM 90/10 IPN

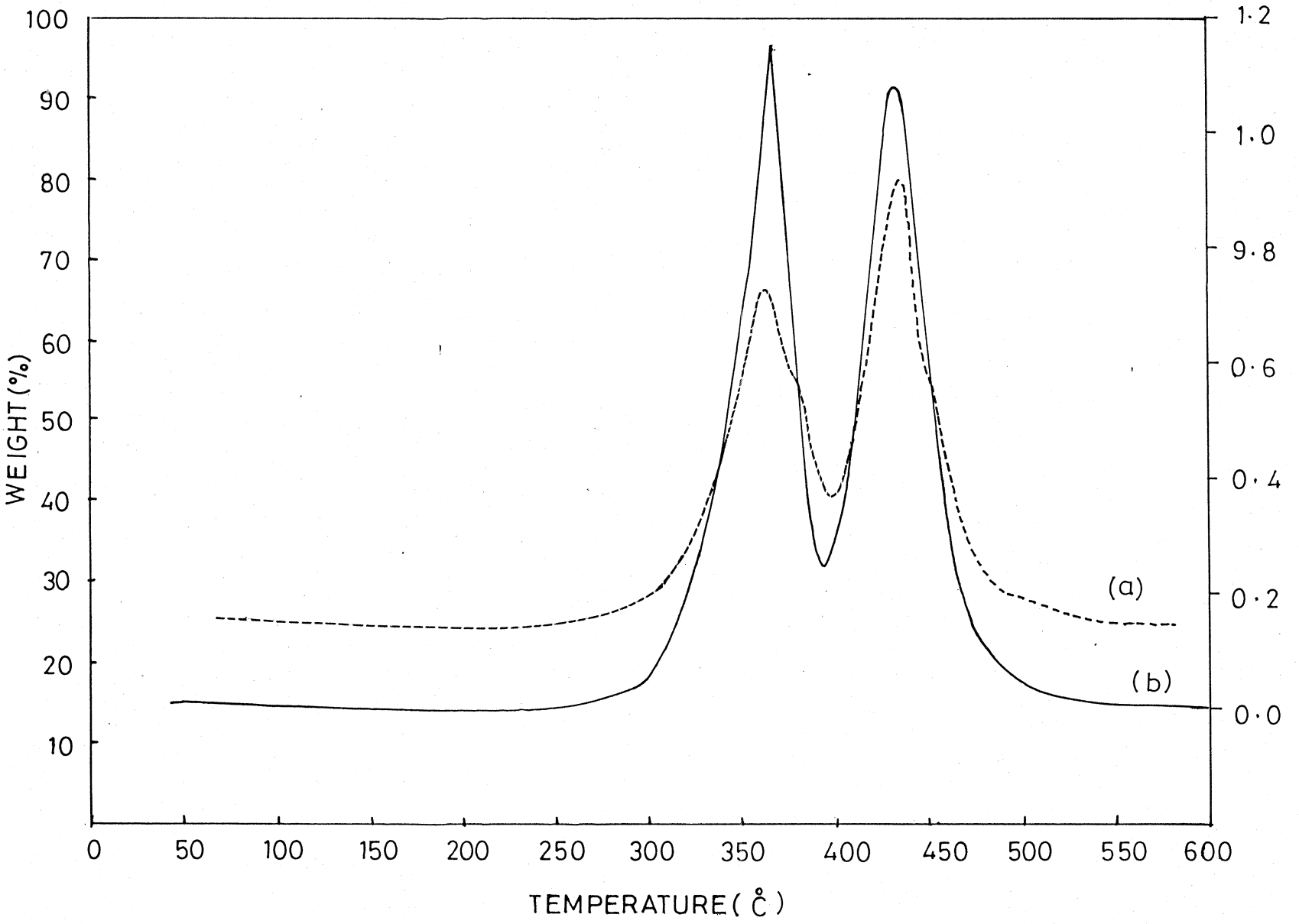


Fig 3.17 DTG trace of MDI based polyurethane and IPN
(a) PU4A (b) PU4A-PAM 90/10 IPN

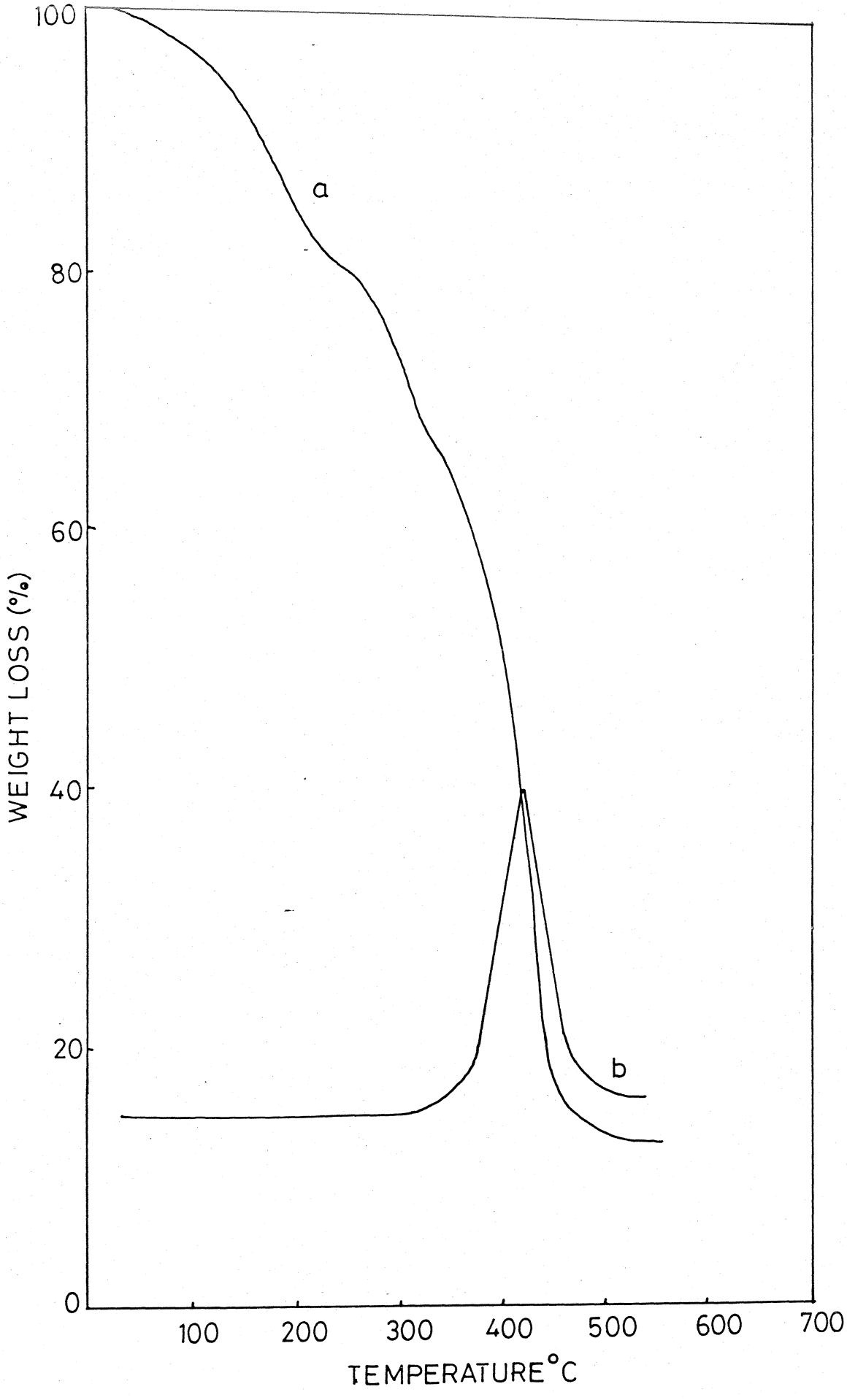


Fig 3.18 Thermogravimetric analysis curve of polyacrylamide (a) TGA (b) DTG

Thermogravimetric studies on the polyurethanes and IPNs of 90 wt% PU composition were carried out . Fig 3.15 shows a typical thermogram of the TDI based, PU1A and PU1A -PAM IPNs. The thermograms show two distinct stages of decomposition. The first stage of decomposition corresponds to the urethane bond breaking and occurs at 350 Deg.C (Fig 3.15a). Stage II is the polyol decomposition which occurs at 435 Deg C for the polyurethane while for the IPN (represented by PU1A-PAM 90/10) it is at 450 Deg C. Similar thermograms were obtained for the MDI based polyurethane PU4A and IPNs of PU4A . Fig. 3.16 is a representative TGA thermogram of PU4A and PU4A-PAM IPN. Fig.3.17 shows the DTG curves of PU4A and PU4A-PAM 90/10 IPN with the characteristic two step decomposition of the polyurethanes. The thermogram for the vinyl polymers is represented by the thermogram of polyacrylamide, Fig 3.18. Similar curves were obtained for the other vinyl polymers, PMMA, PHEMA, PVP. In all the cases of the vinyl polymers, a single stage decomposition is obtained which is indicative of main chain scissions of the polymer chain.

3.6.2.1. Thermal stability of IPNs:

A measure of thermal stability of polyurethanes and their IPNs can be ascertained from the temperature of 50% decomposition. The thermal decomposition temperatures are given in Table3.XXV. Decomposition temperatures for initial degradation, at 50% weight loss and the final decomposition of the TDI based PU and IPNs are indicated. Slight enhancement of thermal stability is observed for the IPNs over that of the polyurethane PU1A.

TABLE 3.XXV

THERMAL DECOMPOSITION TEMPERATURES OF TDI BASED IPNS

Polymer	Initial decomposition temp. Deg.C.	50 % Decomposition temp. Deg.C.	Final Decomposition temp. Deg.C.
PU1A	270	400	455
PU1A-PAM 90/10	285	420	470
PU1A-PMMA 90/10	265	410	460
PU1A-PVP 90/10	280	400	470
PU1A-PHEMA 90/10	280	415	485

The thermogravimetric curves are, however, clustered around a narrow region. The decomposition temperatures of the MDI based polyurethane, PU4A, and its IPNs are shown in Table 3.XXVI. In this case, however,no significant increase of thermal stability of IPNs over that of the polyurethane is observed. Table 3.XXVII, gives the thermal degradation temperatures of the vinyl polymers. Except in the case of PVP, the other three polymers, PMMA, PAM and PHEMA are less stable than their respective IPNs. The commonly observed clustering curves for the IPNs is however, evident. This behaviour of clustering of curves has also been observed by Kim et al (20) for PU/PMMA IPNs.

They have attributed this behaviour for similar thermal degradation behaviour of polyurethane and IPNs. Belyakov (260) has suggested a synergistic radical mechanism for the thermal degradation of PU/PMMA IPNs.This mechanism requires a close juxtaposition of the two polymers, which may be enhanced by IPN formation.

In the present case, clustering of the thermal degradation curves indicate the close juxtaposition of the polymers obtained during IPN formation.

TABLE-3.XXVI

THERMAL DECOMPOSITION TEMPERATURES OF MDI BASED IPNS

Polymer	Initial Decomposition temp. Deg.C.	50 % Decomposition temp. Deg.C.	Final Decomposition temp. Deg.C.
PU4A	335	410	475
PU4A-PAM 90/10	325	410	465
PU4A-PMMA 90/10	327	410	470
PU4A-PVP 90/10	340	410	490
PU4A-PHEMA 90/10	330	412	480

TABLE-3.XXVII

THERMAL DECOMPOSITION TEMPERATURES OF THE VINYL POLYMERS

Polymer	Initial Decomposition temp. Deg.C.	50 % Decomposition temp. Deg.C.	Final Decomposition temp. Deg.C.
PAM	150	400	475
PMMA	290	386	430
PVP	400	449	475
PHEMA	380	407	465

3.7. Surface study by contact angles:

A surface cannot simply be considered as an extension of the bulk material. The local chemistry, forces and bonding characteristics in the vicinity of the surface are generally considered different than those within the bulk. Furthermore, they are not invariant, and can change significantly depending on the nature and number of other phases the material surface has contacted.

The surface characteristics of biomaterials are believed to be more related to their blood-material interaction. A measure of surface free energy and/or surface wettability of solid materials is most readily and simply obtained by measuring the contact angle of a diagnostic liquid on the solid surface. This is an extremely sensitive technique for identifying changes in the surface composition (261). Though contact angle is usually measured in the advancing mode (262), for those polymers which have a significant degree of surface mobility and can readjust their surface region in response to their local environment, the contact angle measured in air or vapour is not generally satisfactory. More direct information related to polymer-water interfaces is obtained via the captive air or captive bubble technique (132).

3.7.1. Contact angles of PU-PAM IPNs:

The air-water contact angle and octane-water contact angles for a lightly crosslinked, NCO/OH = 1.09 and more crosslinked, NCO/OH = 2.01, PU-PAM IPNs are depicted with respect to composition of the IPNs in Fig 3.19. The air-water contact angle roughly decreases with increase in acrylamide cont-

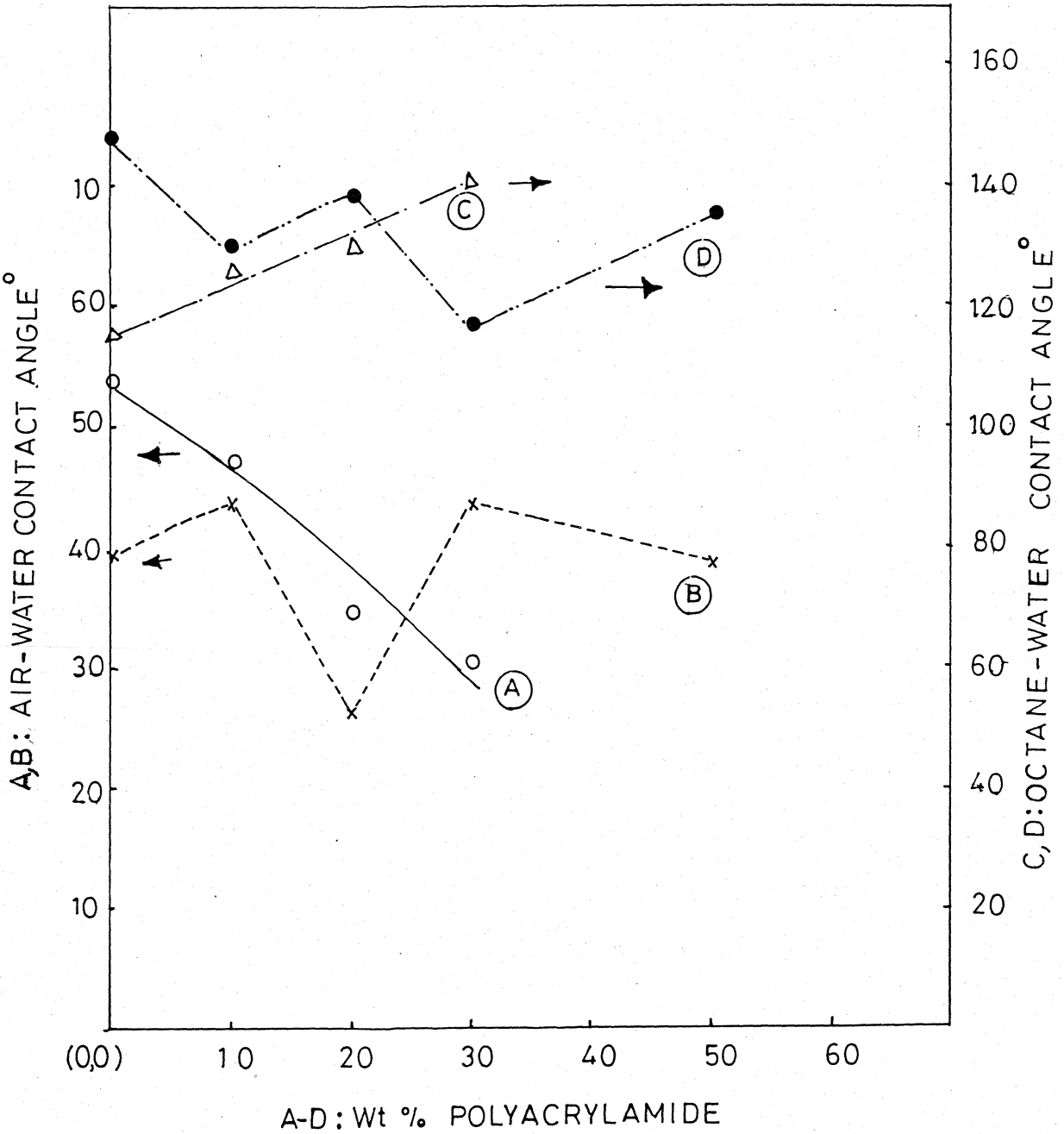


Fig. 3.19. Contact angles of (TDI-PTMG 1010) PU-PAM IPNS : A, C = PUIA-PAM IPN, NCO/OH = 1·09. B,D = PUIB-PAM IPN, NCO/OH = 2·01 .

ent while the octane-water contact angle increases in a NCO/OH = 1.09. PU-PAM IPN system (3.19 A,C). Such behaviour is indicative of the more hydrophilic surface of the PU-PAM IPN, on increasing acrylamide content. The IPNs of the more crosslinked network NCO/OH = 2.01 however, show random changes of the contact angle as seen in Fig 3.19 B and 3.19D. This may be due to the inability of the surface to orient itself when equilibrated with water in a more crosslinked system, Holly and Refojo (71) have suggested that a (PHEMA) surface is capable of changing its free energy through reorientation of the polymer side chains and chain segments depending on the nature of the adjacent phase. From the biomaterials point of view, the surface of the lower crosslinked IPNs NCO/OH = 1.09 is more suitable due to its capacity for orienting itself.

3.7.2. Contact angles of the TDI and MDI based IPNs:

The air-water contact angle and octane-water contact angle of the TDI based polyurethane PU1A and IPNs of 90 wt% PU1A are given in Table 3.XXVIII. As the decrease of air-water contact angle and increase of octane-water contact angle is taken as a measure of hydrophilicity(132), the PU1A-PMMA 90/10 IPN can be considered as relatively the most hydrophobic. The trend of decreasing hydrophilicity is given by PU1A-PVP 90/10 > PU1A-PHEMA 90/10 > PU1A-PAM 90/10 > PU1A > PU1A-PMMA 90/10. The surface hydrophilicity of IPNs is therefore influenced by even 10 wt% of the second polymer. From the values of air-water contact angle and octane-water contact angle and utilizing the several assumpt-

TABLE 3.XXVIII

CONTACT ANGLES & SURFACE PARAMETERS OF TDI BASED IPNS

POLYMER	θ_{air} °	θ_{octane} °	$(\gamma_{sv} - \gamma_{sw})$ dynes/cm	I_{sw} dynes/cm	γ_{sv}^{d} dynes/cm	γ_{sv}^{p} dynes/cm	γ_{sv} dynes/cm	γ_{sw} dynes/cm
PU1A	53.6	115.0	42.73	71.86	21.37	25.56	46.93	4.2
PU1A-PMMA 90/10	61.2	110.0	34.69	67.77	17.62	22.74	40.36	5.69
PU1A-PAM 90/10	43.7	130.3	52.06	83.16	19.45	34.24	53.69	1.63
PU1A-PHEMA 90/10	42.5	130.0	53.08	82.97	20.62	34.08	54.70	1.62
PU1A-PVP 90/10	40.0	135.0	55.16	86.20	19.50	36.79	56.29	1.14

ions (132) of surface energy and from the Young's equation (263) of $\gamma_{sv} - \gamma_{sl} = \gamma_{lv}\cos\theta$, one can calculate the interfacial free energy of the hydrated-gel-water (γ_{sw}), the interfacial free energy for hydrated-gel-water vapor (γ_{sv}). ($\gamma_{sv} - \gamma_{sw}$) is commonly called adhesion tension. Isw is the non dispersive polar interaction at the gel water interface. γ_{sv}^{d} and γ_{sv}^{p} are the dispersion and polar components to the surface free energy. The values of these parameters are given in Table 3.XXVIII. The minimum interfacial free energy hypothesis (264,70) of protein adsorption states that if the gel-water interface has a very low interfacial free energy, then protein adsorption should be very low and highly reversible. Though the hypothesis has been found to be more applicable to the fully hydrated hydrogel system, the IPNs in the present case also have the interfacial free energy γ_{sw} tending towards 0, especially in the more hydrophilic PU1A-PVP 90/10 IPN.

The air-water and octane-water contact angle of the MDI based PU4A and IPNs of 90 wt% composition PU4A are given in Table 3.XXIX. The same trend of decreasing hydrophilicity with change of second monomer to a more hydrophobic one is observed as in the case of the TDI IPNs and is as PU4A-PVP 90/10 > PU4A-PHEMA 90/10 >PU4A-PAM90/10 > PU4A > PU4A-PMMA 90/10. Comparatively the MDI based IPNs on the whole are more hydrophilic than the TDI based IPNs which may be due to the more hydrophilic nature of the MDI based polyurethane itself. The interfacial energy contributions of the MDI IPNs, except in the case of PU4A-PMMA90/10 IPN are all tending towards 0. The MDI based IPNs of the present study may

TABLE 3.XXIX

CONTACT ANGLES & SURFACE PARAMETERS OF MDI BASED IPNS

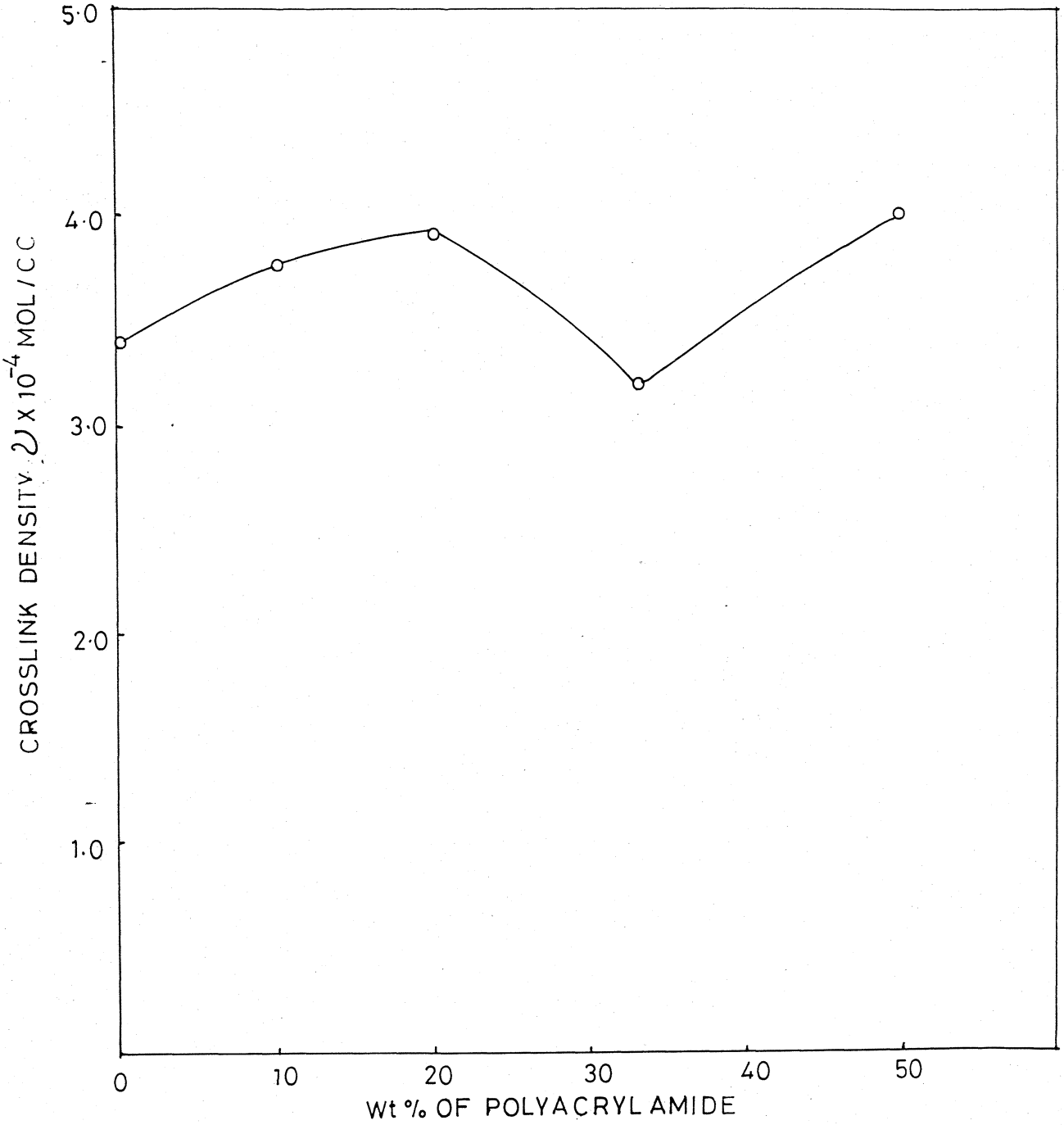
POLYMER	θ_{air} °	θ_{octane} °	$(\gamma_{sv} - \gamma_{sw})$ dynes/cm	I_{sw} dynes/cm	γ_{sv}^{d} dynes/cm	γ_{sv}^{p} dynes/cm	γ_{sv} dynes/cm	γ_{sw} dynes/cm
PU4A	40.3	136.0	54.91	86.81	18.71	37.31	56.01	1.10
PU4A-PMMA 90/10	51.0	120.0	45.31	75.75	20.09	28.41	48.5	3.19
PU4A-PAM 90/10	36.0	143.0	58.25	90.83	18.08	40.84	58.92	0.67
PU4A-PHEMA 90/10	39.0	140.0	55.95	89.18	17.48	39.37	56.86	0.91
PU4A-PVP 90/10	34.0	148.0	59.69	93.32	17.13	43.12	60.24	0.55

therefore be quite suitable for blood contacting applications based on the assumption of the minimal interfacial energy hypothesis.

3.8. Density and Crosslink density:

The crosslink densities of the TDI based polyurethane PU1A, and IPNs of PU1A are given in Table 3.XXX. The crosslink densities were calculated from the swelling values of the materials in toluene as discussed in Chapter II. The variation of crosslink density with the amount of polyacrylamide is shown in Fig.3.20. There exists a similarity between variation of crosslink density and tensile strength with the amount of plastic content as is evident from the comparison of Fig.3.20 with Fig 3.7, (Chapter 3). Although any conclusive and self standing implications on chain stretching effects arising due to interpenetration are not possible based on crosslink density data, the close similarity of the trend of variation of crosslink density with that of mechanical property is interesting. Incorporation of 10 wt% polyacrylamide increases the crosslink density of the IPN. At 30 wt% of polyacrylamide, the crosslink values decrease. This decrease could be attributed to the onset of the phase separation process. The data can be rationalised on the same grounds as for the anamolous mechanical property by suggesting uncoiling of chain segments and further stretching, resulting in increased free volume between the chains in juxtaposition.

This permits increased swelling and results in apparent decrease in crosslink densities. The average molecular weight, $\bar{M}c$,



Fig·3·20·Variation of crosslink density of PUIA-PAM IPN with the concenteration of PAM.

TABLE-3.XXX

DENSITY, CROSSLINK DENSITY AND AVERAGE MOLECULAR WEIGHT BETWEEN CROSSLINKS OF TDI BASED POLYURETHANE AND IPNS, NCO/OH = 1.09

Polymer	Density (eval.) g/cc	Crosslink density x 10-4 mol/cc	Average Molecular weight between crosslinks, $\overline{Mc}$
PU1A	0.833	3.39	2950
PU1A-PAM 90/10	0.915	3.75	2667
PU1A-PAM 80/20	0.918	3.88	2577
PU1A-PAM 70/30	0.914	3.17	3155
PU1A-PAM 50/50	0.917	4.00	2500
PU1A-PMMA 90/10	0.844	4.45	2247
PU1A-PMMA 80/20	0.836	4.10	2439
PU1A-PMMA 70/30	0.893	4.24	2358
PU1A-PMMA 50/50	0.885	4.52	2212
PU1A-PHEMA 90/10	0.925	4.00	2500
PU1A-PHEMA 80/20	0.865	3.75	2667
PU1A-PHEMA 70/30	0.918	3.81	2625
PU1A-PHEMA 50/50	0.923	3.74	2674
PU1A-PVP 90/10	0.940	3.23	3096
PU1A-PVP 80/20	0.925	3.42	2924
PU1A-PVP 70/30	0.917	3.35	2985

TABLE-3.XXXI

DENSITY, CROSSLINK DENSITY AND MOLECULAR WEIGHT BETWEEN CROSSLINKS OF MDI BASED POLYURETHANE AND IPNS, NCO/OH = 1.09

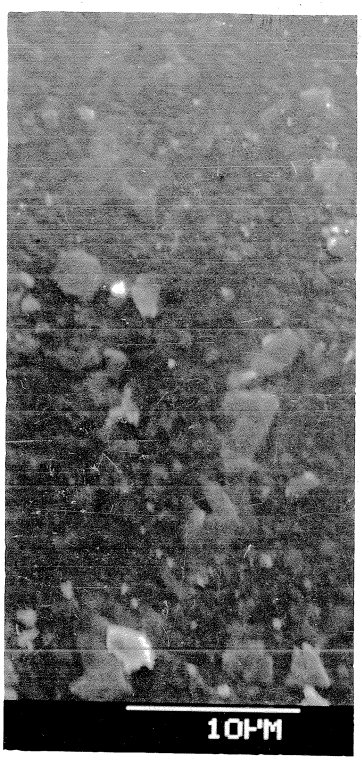
Polymer	Density (eval.) g/cc	Crosslink density x 10-4 mol/cc	Average Molecular weight between crosslinks, $\bar{M}c$
PU4A	1.014	4.83	2070
PU4A-PMMA 90/10	1.036	5.12	1953
PU4A-PMMA 80/20	1.130	5.30	1887
PU4A-PMMA 70/30	1.114	4.98	2008
PU4A-PMMA 50/50	1.126	5.06	1976
PU4A-PAM 90/10	1.018	5.00	2000
PU4A-PAM 80/20	1.027	4.96	2016
PU4A-PAM 70/30	1.033	5.36	1866
PU4A-PAM 50/50	1.058	5.32	1880
PU4A-PHEMA 90/10	1.026	4.86	2058
PU4A-PHEMA 80/20	1.063	4.97	2012
PU4A-PHEMA 70/30	1.087	4.88	2049
PU4A-PHEMA 50/50	1.116	4.98	2008
PU4A-PVP 90/10	1.035	4.85	2062
PU4A-PVP 80/20	1.068	5.54	1805
PU4A-PVP 70/30	1.109	5.32	1880

between crosslinks also (Table 3.XXX) showed the reverse trend. The density changes on IPN formation (Table3.XXX) however, do not show any substantial changes. Shibiyama et al (265) have also observed that density values would not change much during IPN formation.

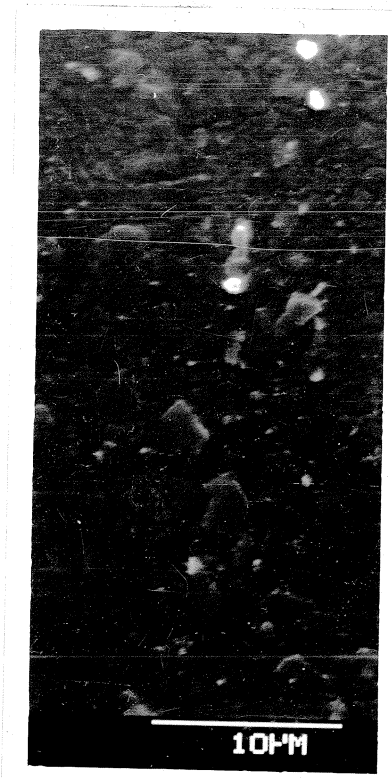
The density, crosslink density, and average molecular weight between crosslinks for MDI polyurethane and IPNs are given in Table 3.XXXI. The same trend of similarity of crosslink density and tensile stress data is observed as in the case of the TDI IPNs. The individual values of crosslink density of MDI IPNs are much higher than that of TDI IPNs. The average molecular weight between crosslinks obtained in case of MDI IPNs is lower than in case of TDI IPNs. This increased crosslinking of MDI IPNs could be contributing to the increased tensile stress obtained in case of the MDI polymers.

3.9. Morphology:

Morphology was studied by scanning electron microscopy. Fig.3.21A is the microphotograph of the TDI based polyurethane, PU1A. The microphotograph is essentially featureless, with no observable domain structure. Fig3.21B is the SEM of PU1A-PAM 90/10 IPN. The microphotograph of the IPN does not contain any distinguishable features that differentiate it from the basic SEM of PU1A. More compatibility of the two component polymers could be responsible for generating such a SEM. A similar morphology is obtained in the case of PU1A-PMMA 90/10 IPN (Fig.3.21C). The morphology of PU1A-PVP 90/10 IPN and PU1A-PHEMA 90/10 IPN as



A



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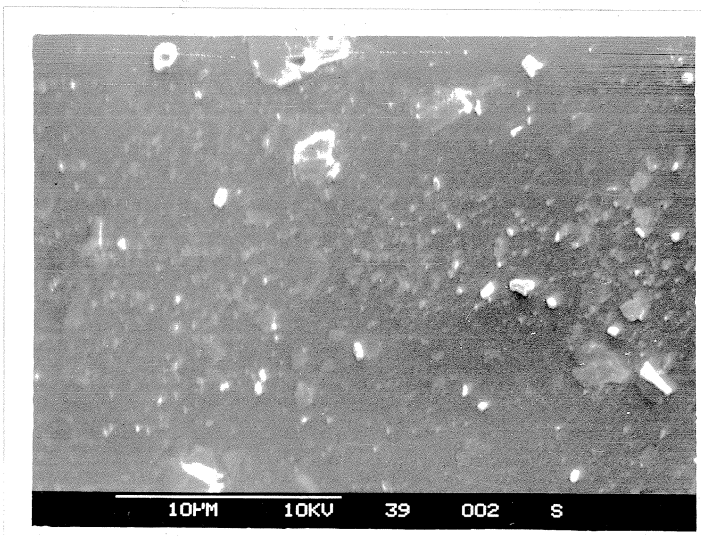

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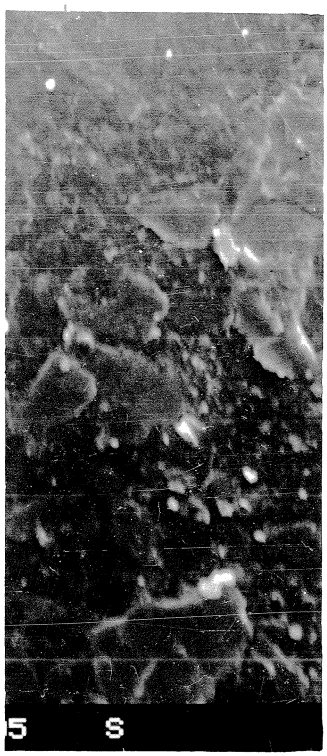

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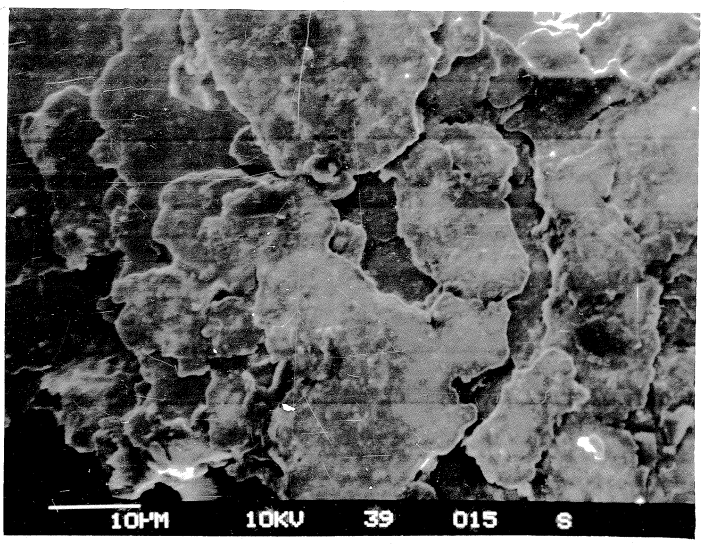
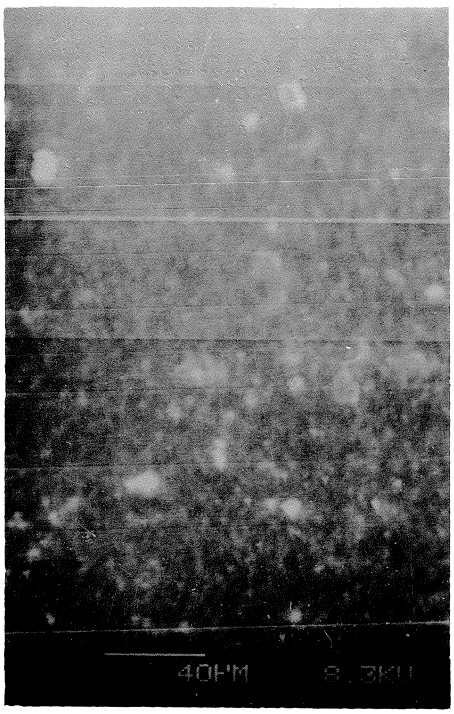
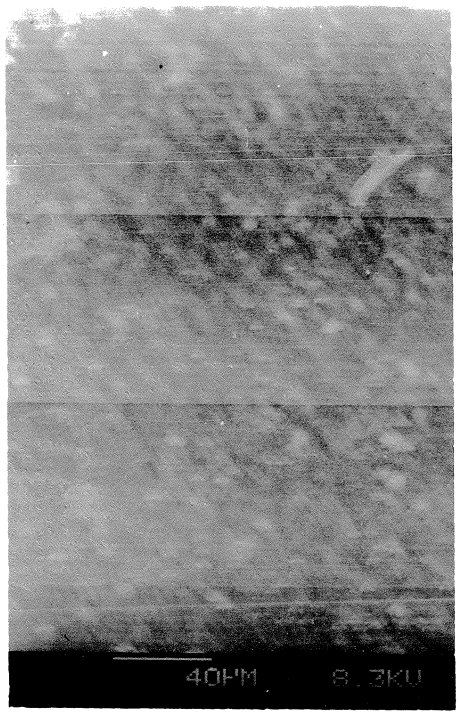


F

Fig. 3.21 : Scanning electron microphotographs of TDI based PU and IPNs. A-PU1A, B-PU1A-PAM 90/10, C-PU1A-PMMA 90/10, D-PU1A-PVP 90/10, E-PU1A-PHEMA 90/10, F-PU1A-PMMA 50/50 IPNs.



A



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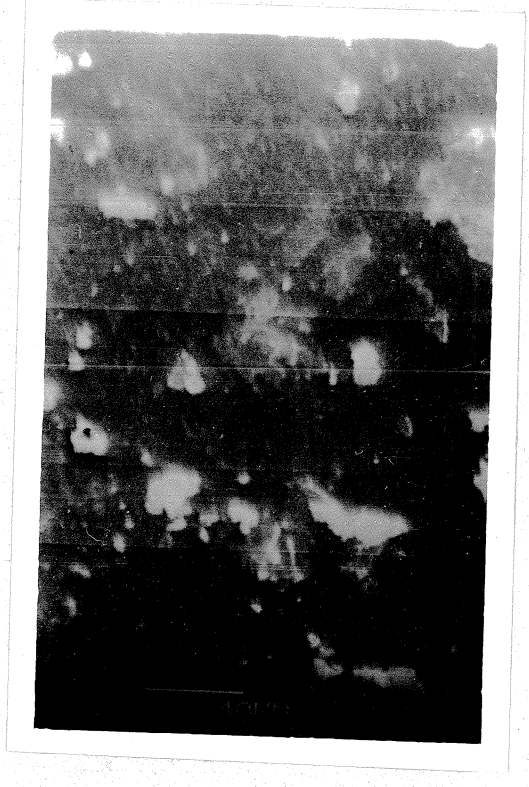
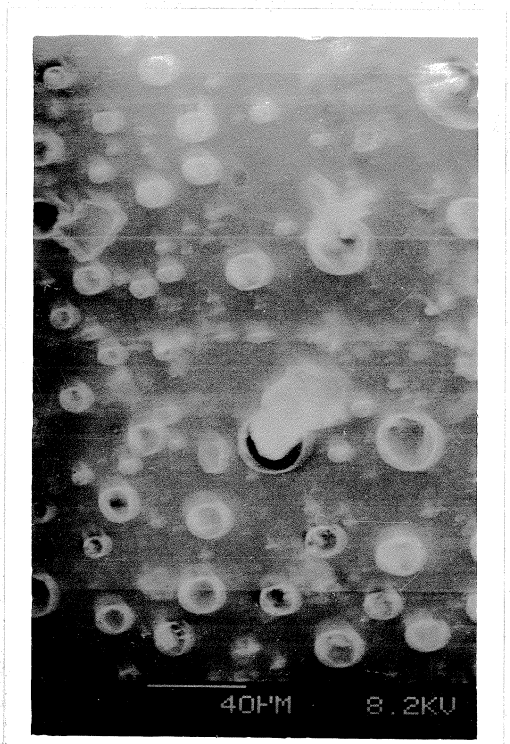


D

E

Fig. 3.22 : Scanning electron microphotographs of MDI based PU and IPNs. A-PU4A, B-PU4A-PMMA 90/10, C-PU4A-PAM 90/10, D-PU4A-PHEMA 90/10, E-PU4A-PVP 90/10 IPNs.

A



B

Fig. 3.23 : Scanning electron microphotographs of IPNs depicting phase separation. A-PU4A-PAM 50/50, PU4A-PMMA 50/50 IPNs.

depicted in the microphotographs (Fig.3.21D and 3.21E) reveal the semicompatible nature of these IPNs. Semicompatibility is evident from the different phases seen in the microphotograph. On increasing the second component (especially at equal ratios of 50/50), the SEM depicts more phase separation which is represented by the SEM of PU1A-PMMA 50/50 IPN (Fig.3.21F).

The SEM of the MDI polyurethane PU4A is depicted in Fig.3.22A. The SEM is again essentially featureless. Fig.3.22B is the SEM of the PU4A-PMMA90/10 IPN. The compatible nature of the PU4A-PMMA 90/10 IPN is clearly seen in the figure. Fig 3.22C and 3.22D are the SEM of PU4A-PAM 90/10 IPNand PU4A-PHEMA 90/10 IPN, respectively. Some differentiation of phases can be observed which are representative of less compatibility. However, as the DMA studies (Section 3.7) do not indicate phase separation, the PU4A-PAM 90/10 IPN and PU4A-PHEMA 90/10 IPN can be considered as semicompatible. Fig.3.22E is the SEM of the PU4A-PVP90/10 IPN which shows more phase separation than PU4A-PAM90/10 or PU4A-PHEMA 90/10 IPN. As the concentration of the second component polymer increases, the phase separation increases. Fig3.23A and Fig.3.23B are representative morphologies of the PU4A-PAM 50/50 IPN and PU4A-PMMA 50/50 IPN.

3.10. Radiation stability:

The TDI based polyurethane PU1A and IPNs of 90 wt% composition of PU1A were evaluated for their radiation stability upto a total dose of 2.5 Mrads. Table 3.XXXII gives the results of tensile stress and percent elongation at break after γ irradiation to

TABLE-3.XXXII

MECHANICAL PROPERTIES OF TDI BASED POLYURETHANES AND IPNS ON γ IRRADIATION, NCO/OH = 1.09.

Polymer	Original tensile stress, MPa	Final tensile stress, MPa	Original % elongation	Final % elongation
PU1A	14.12	13.56	746	726
PU1A-PAM 90/10	16.67	15.93	715	700
PU1A-PMMA 90/10	35.78	34.64	1188	1146
PU1A-PHEMA 90/10	22.94	21.79	691	656
PU1A-PVP 90/10	6.57	6.28	448	425

2.5 Mrads. The results indicate that the materials are all radiation stable and the changes observed in tensile stress or elongation are within the standard deviation of the results. Similar results (Table 3.XXXIII) are obtained on irradiating the MDI polyurethane PU4A and IPNs of 90 wt% composition of PU4A.

TABLE-3.XXXIII

MECHANICAL PROPERTIES OF MDI BASED POLYURETHANE AND IPNS ON γ IRRADIATION, NCO/OH = 1.09

Polymer	Original tensile stress, MPa	Final tensile stress, MPa	Original % elongation	Final % elongation
PU4A	30.78	28.56	563	534
PU4A-PAM 90/10	37.94	36.84	739	702
PU4A-PMMA 90/10	40.59	39.34	593	573
PU4A-PHEMA90/10	33.24	32.56	490	473
PU4A-PVP 90/10	33.33	31.66	686	656

3.11 Solid state ^{13}C Nuclear magnetic resonance (NMR) studies:

^{13}C solid state NMR studies of the polyurethanes and 80/20 weight fraction of polyurethane and vinyl polymers were carried out to study the structure and interactions if any.

3.11.1 ^{13}C NMR spectra of the homopolymers:

The ^{13}C NMR resonances of the TDI based polyurethane PU1A are given in Fig.3.24A. The peaks at 70.9 and 27.1 ppm are attributed to the $-CH_2-O$ and CH_2 carbons of polytetramethylene glycol (PTMG). The resonance at 17.5 ppm is due to the CH_3 carbon of the toluene diisocyanate (TDI). The peaks at 156.9, 136.5, 130.5, 121.2, and 114.9 are attributed to aromatic carbons of the biuret of TDI. The signals at 178.5, 174.5, and 163.9 ppm are due to the C=O carbons of the biuret of TDI-PTMG units.

The ^{13}C NMR signals of MDI based polyurethane PU4A are given in Fig. 3.24B. The peaks at 70.8 and 27.019 ppm are attributed to $-CH_2-O$ and CH_2 carbon atoms of the polyol units of (PTMG). The resonances at 40.012 is due to CH_2 carbons of MDI. Peaks at 95.182, 124.2, 130.3, 136.13, 154.99, are assigned to aromatic carbons of the biuret of MDI. The C=O carbons of the biuret of MDI-PTMG units show resonances at 176.7, 170.9 and 164.7 ppm.

Fig. 3.24C is the ^{13}C NMR spectrum of polyacrylamide (PAM). The peaks at 179.78 ppm is due to the C=O. The Cα and Cβ resonances are 41.577 and 36 ppm respectively.

The ^{13}C NMR of polymethylmethacrylate (PMMA) is shown in Fig. 3.24D. The resonances at 177.7 ppm is due to the C=O group. The OCH_3 group gives a signal at 51.994 ppm, while the Cα and Cβ

give the peaks at 44.919 and 51.994 ppm respectively. The peak at 16.551 ppm is assigned to CH_3.

Fig. 3.24E is the ^{13}C NMR of polyhydroxy ethylmethacrylate (PHEMA). The resonance corresponding to C=O is at 178.82 ppm. $-CH_2OH$ gives the peak at 67.234 ppm while $-OCH_2$ gives the peak at 60.033 ppm. The resonances at 45.126 and 55.034 ppm are assigned to C α and C β respectively. The signal at 16.313 ppm is attributed to the CH_3 group.

Fig. 3.24F is the ^{13}C NMR of polyvinyl pyrrolidone (PVP). The resonances at 176.844ppm is assigned to the C=O group. The C-N group at the C(5)carbon atom of PVP gives the signal at 63.452 ppm. Carbons at 4 and 3 position (Fig 3.24F) give the merged signal at 31.849 ppm. The carbon at 2 position gives the peak at 18.505 ppm, while the peak at 43.782 ppm is assigned to the carbon atom position 1.

3.11.2 ^{13}C NMR spectra of IPNs:

Typical ^{13}C NMR spectra of IPNs of TDI and MDI are depicted in Fig.3.24 G-J . Fig 3.24G is the spectra of a MDI based PU4A-PMMA 80/20 IPN. A weak signal at 53 ppm may be due to the carbon resonance of PMMA. Fig 3.24H is the ^{13}C NMR of the TDI based PU1A-PVP 80/20 IPN. Weak resonances at 42.42 and 50.44 ppm may be attributed to peaks coming from PVP. Also a shift in the carbonyl peak is observed. This may be due to the weak hydrogen bonding interaction of the polyvinyl pyrrolidone with the polyurethane in the IPN matrix. This was also reflected in the maxima and minima of tensile stress as discussed in section 3.4.

Fig. 3.24I is the ^{13}C NMR of MDI based PU4A-PHEMA 80/20 IPN. All the characteristic peaks corresponding to PHEMA at 66.92, 59.683, 54.36 and 44.66 ppm are observed.

Fig. 3.24J is the ^{13}C NMR spectrum of TDI based PU1A-PAM 80/20 IPN. The spectra is identical to that of polyurethane. The resonances of the CH_2 and CH carhon atoms of acrylamide are so weak that they are merged in the intense peaks of the aliphatic region of the polyurethane.

The NMR spectra therefore, indicate that interpenetration of the constituent polymers takes place on IPN formation. Grafting reactions of the polyurethanes and vinyl polymers may be ruled out. The NMR also indicate, that a small degree of interaction of the constituent networks takes place through hydrogen bonding in the polyurethane with the formation of the PU-PHEMA and PU-PVP IPNs.

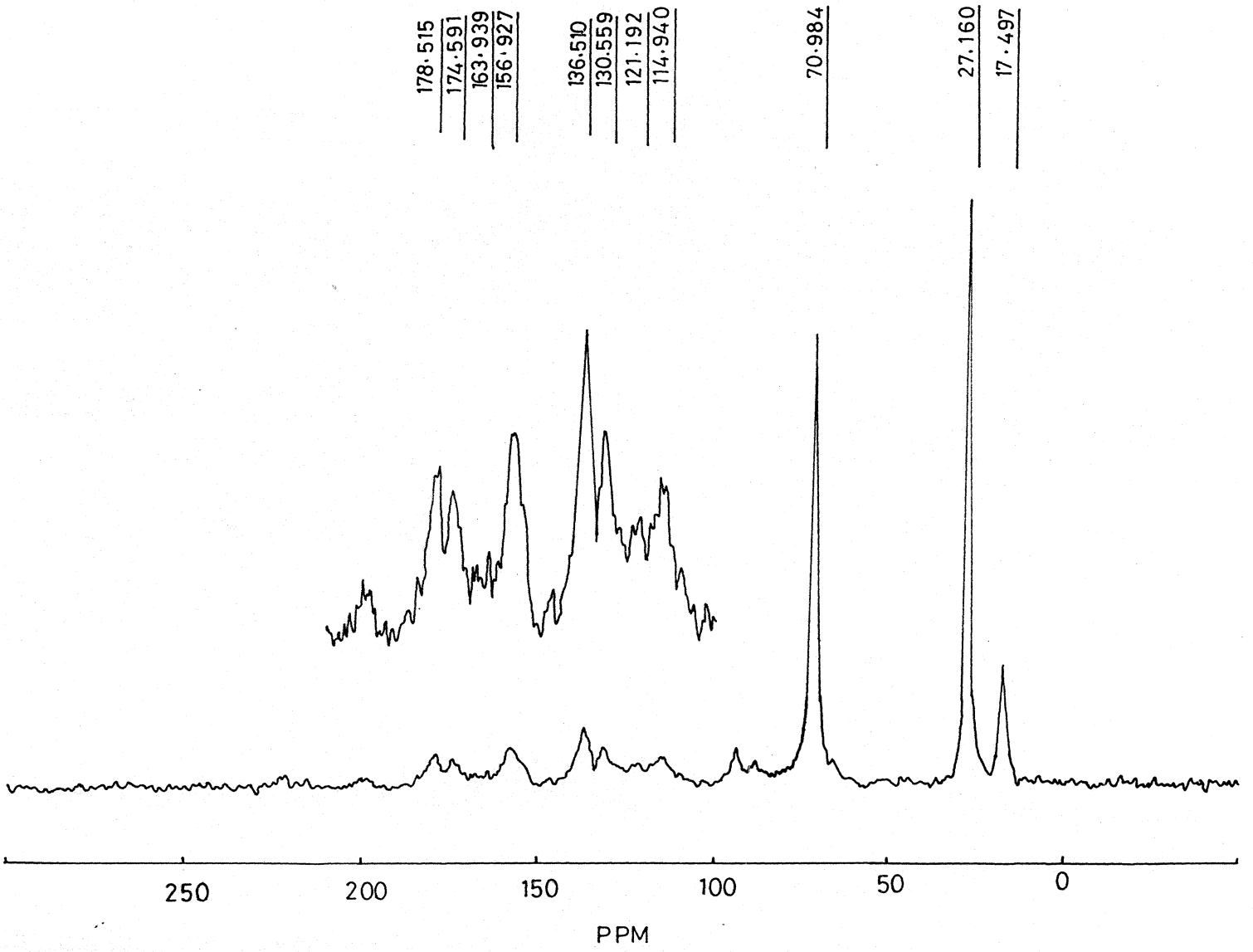


Fig.3.24A : ^{13}C NMR spectrum of TDI based polyurethane PUIA.

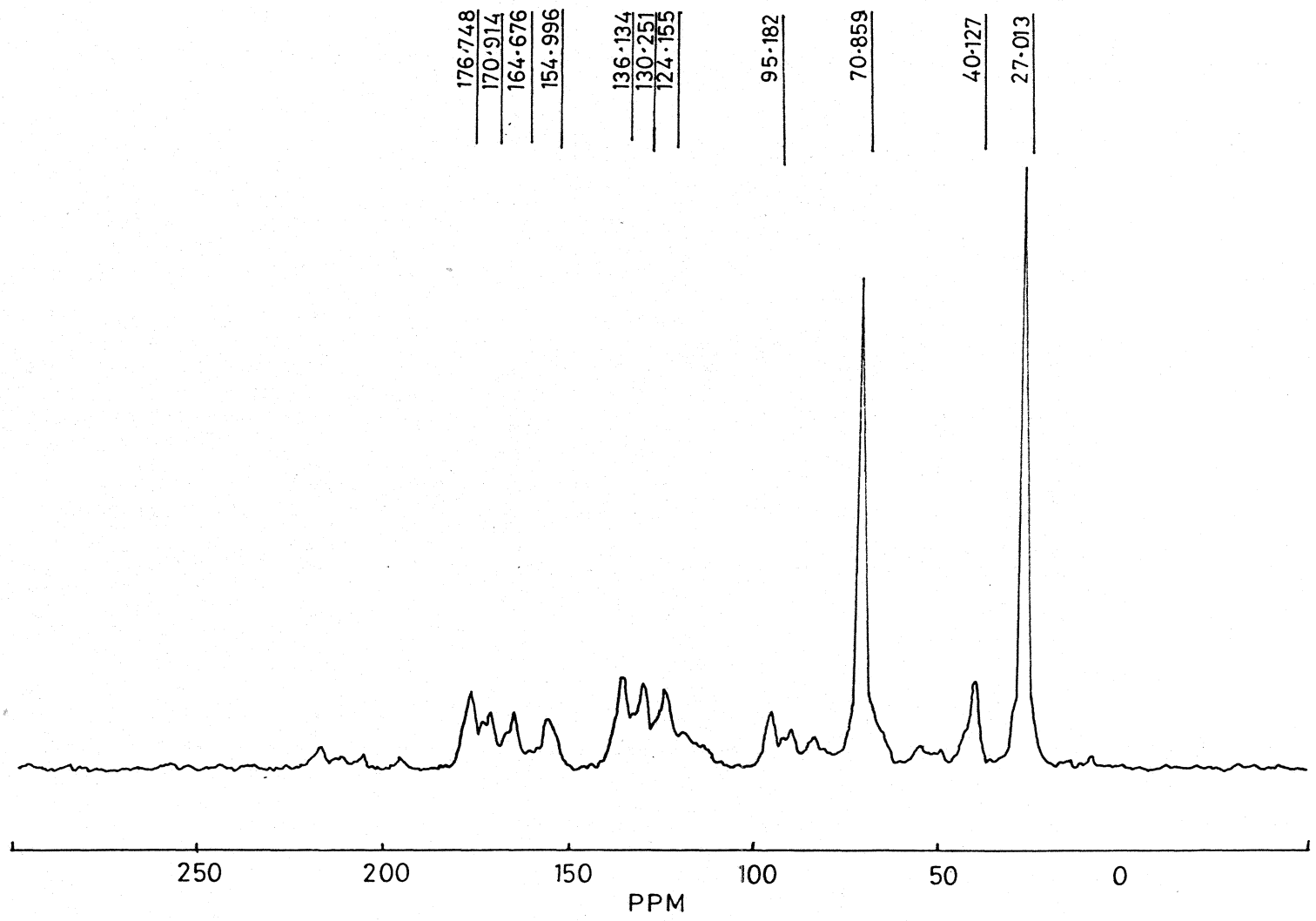


Fig-3.24B : ^{13}C NMR spectrum of MDI based polyurethane PU4A.

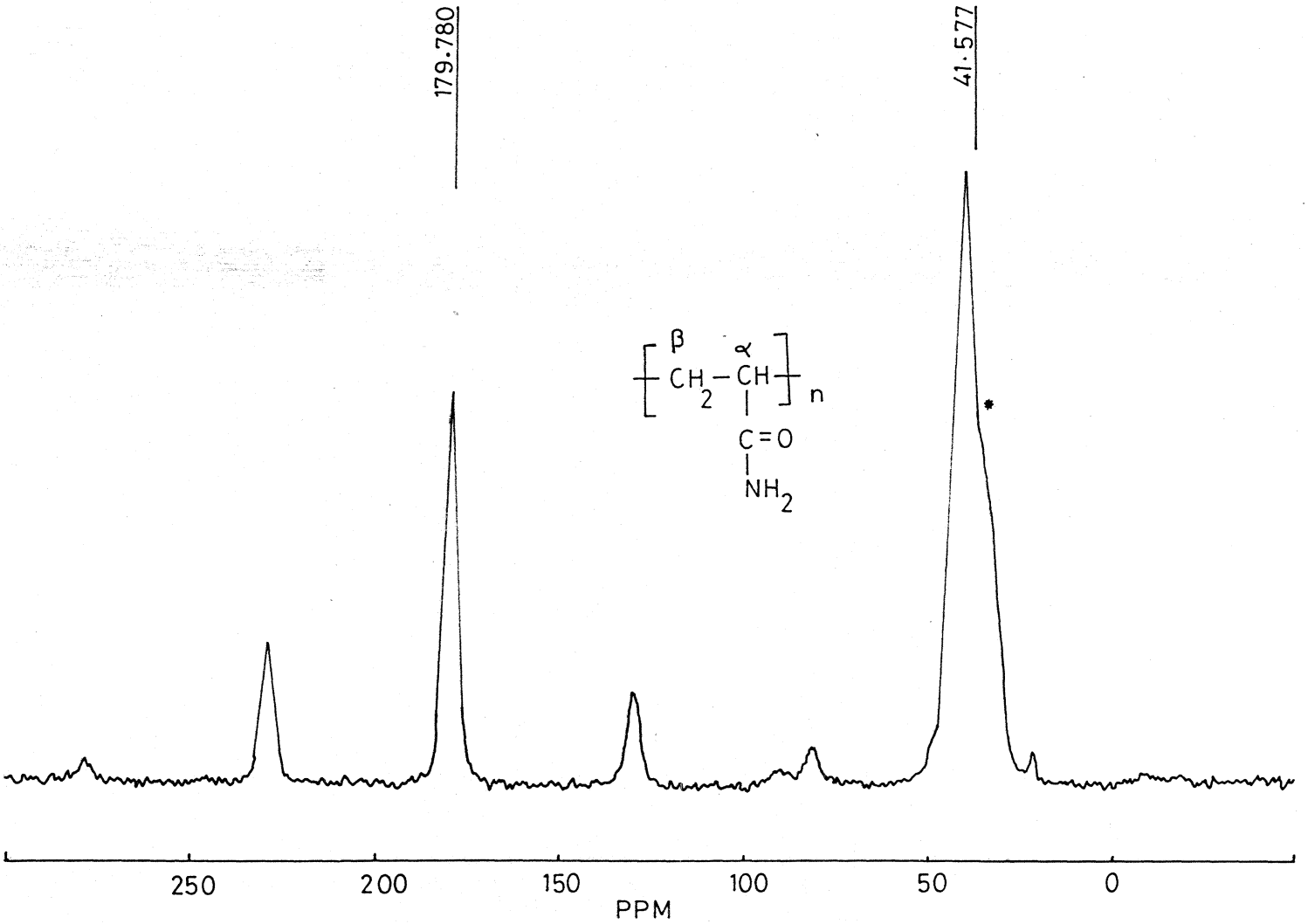


Fig.324C: ^{13}C NMR spectrum of polyacrylamide (PAM).

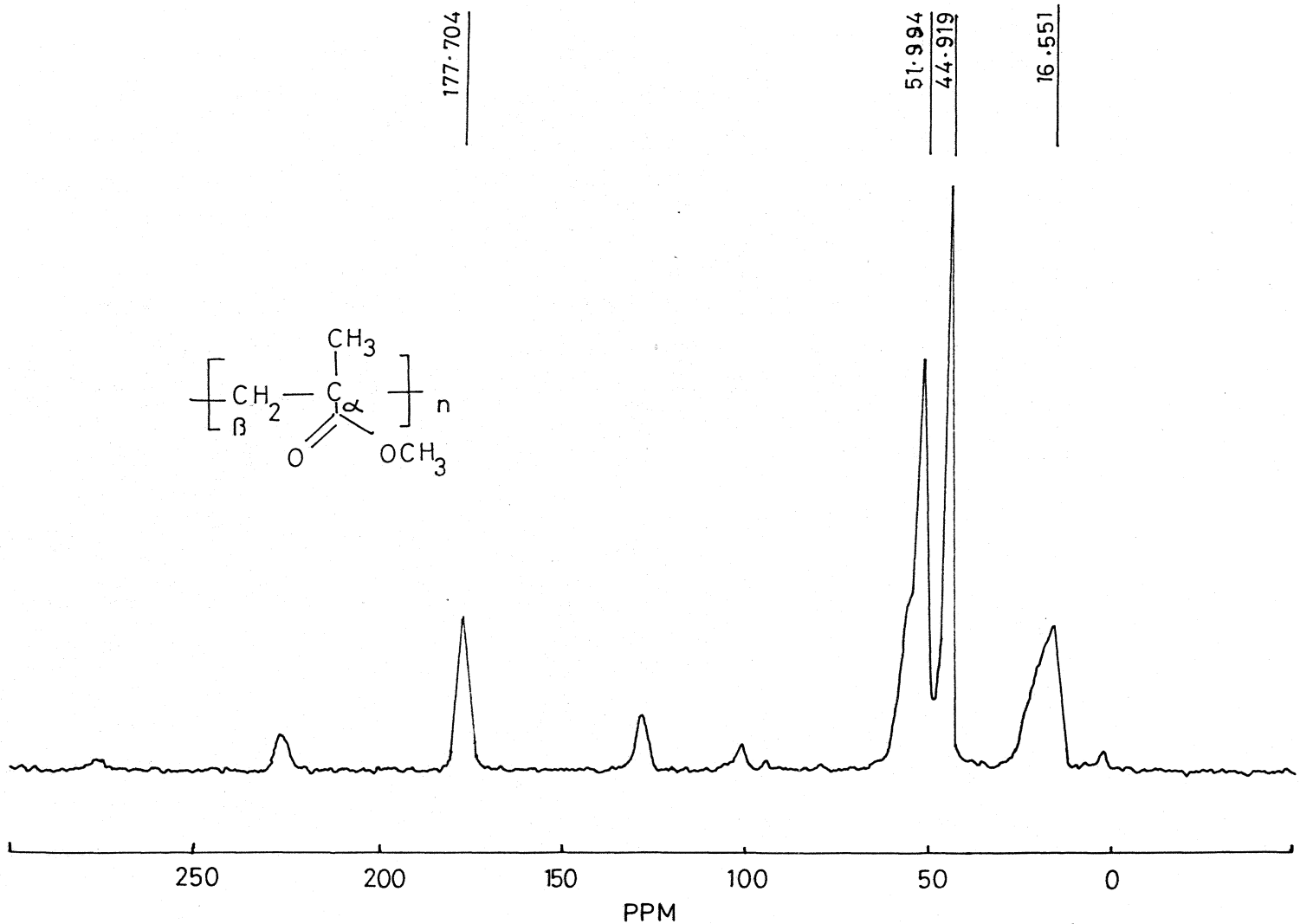


Fig:3.24 D : ^{13}C NMR spectrum of polymethyl methacrylate (PMMA).

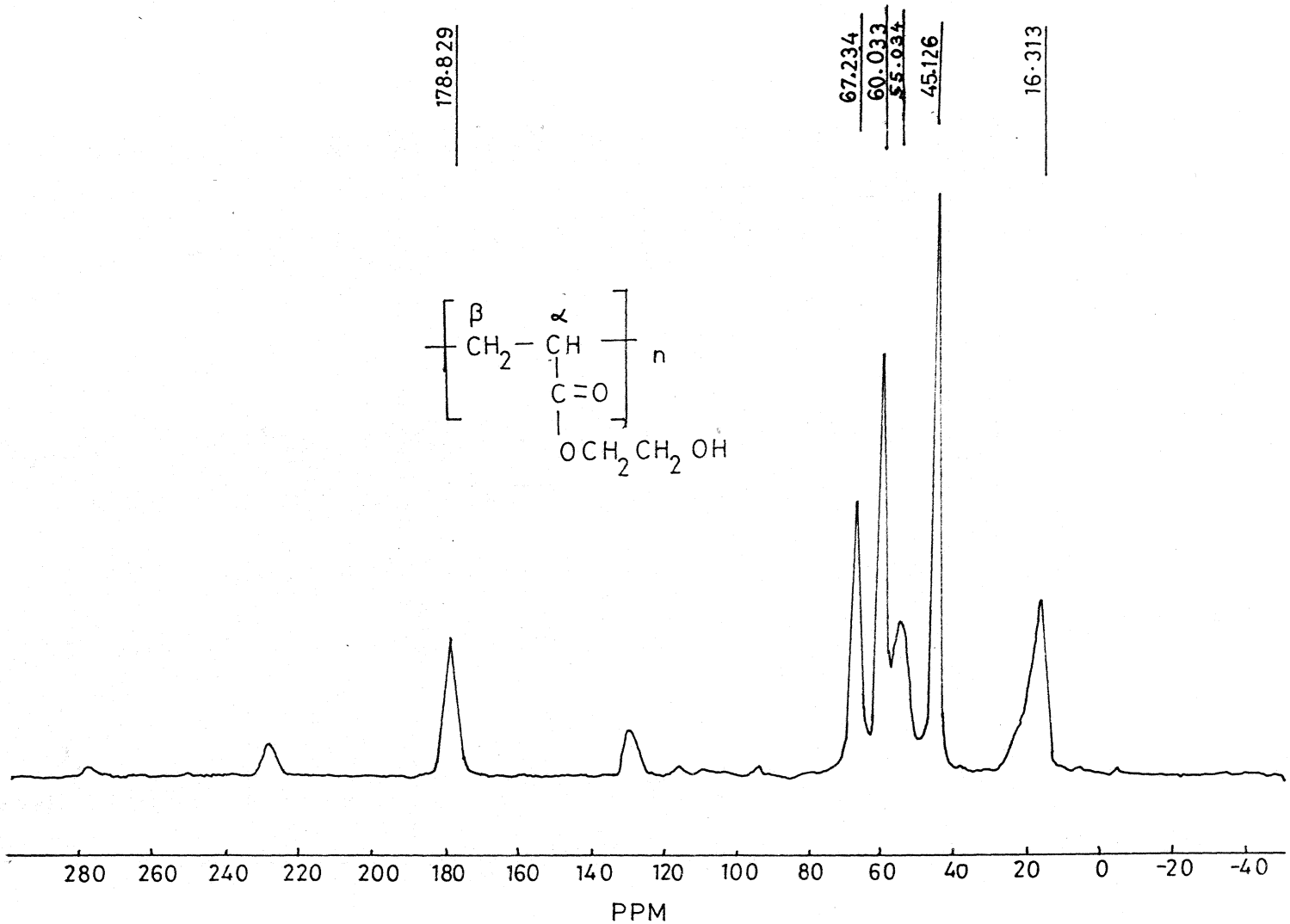


Fig.3.24E : ^{13}C NMR spectrum of polyhydroyethyl methacrylate (PHEMA).

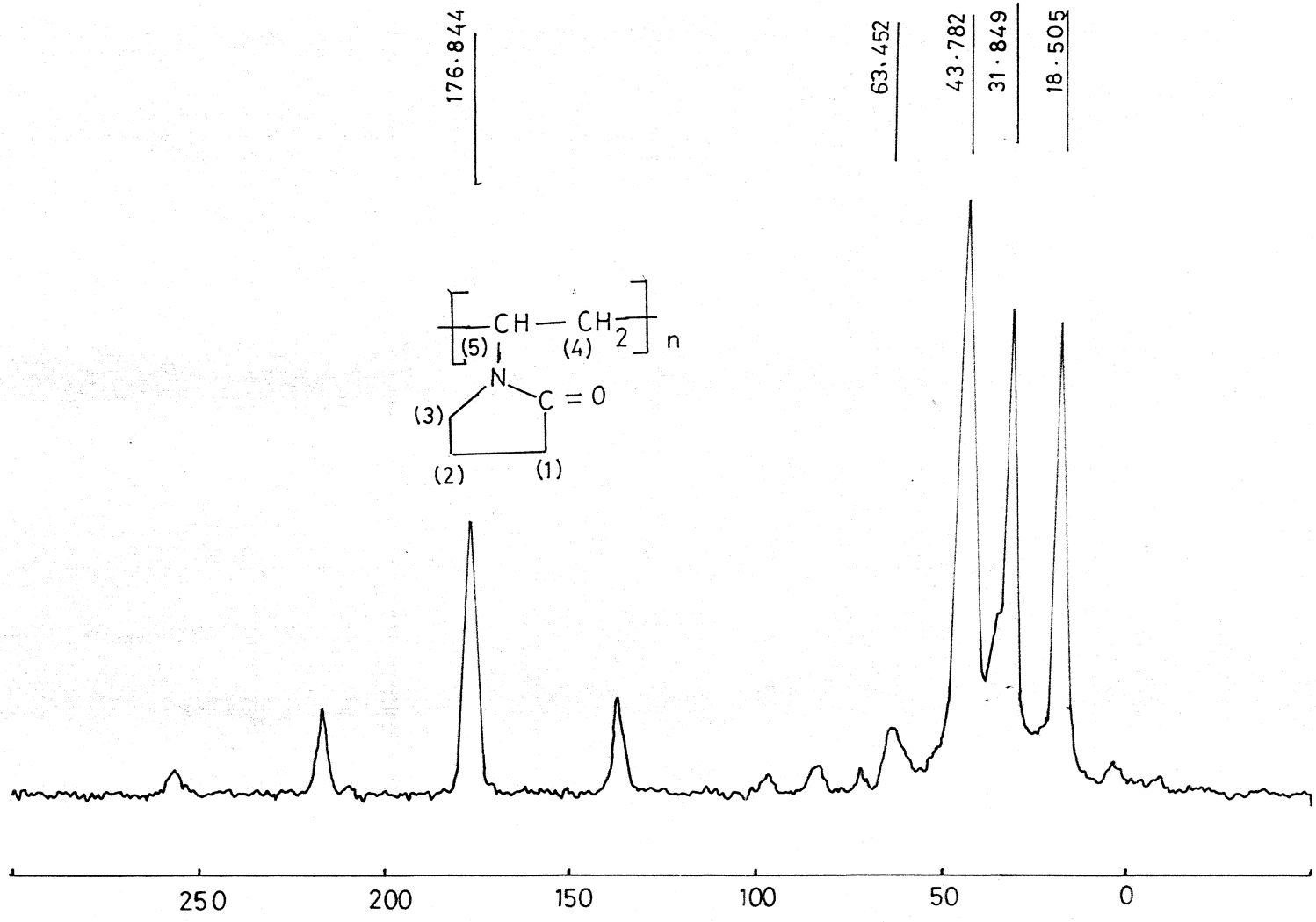


Fig. 3.24F : ^{13}C NMR spectrum of polyvinyl pyrrolidone (PVP)

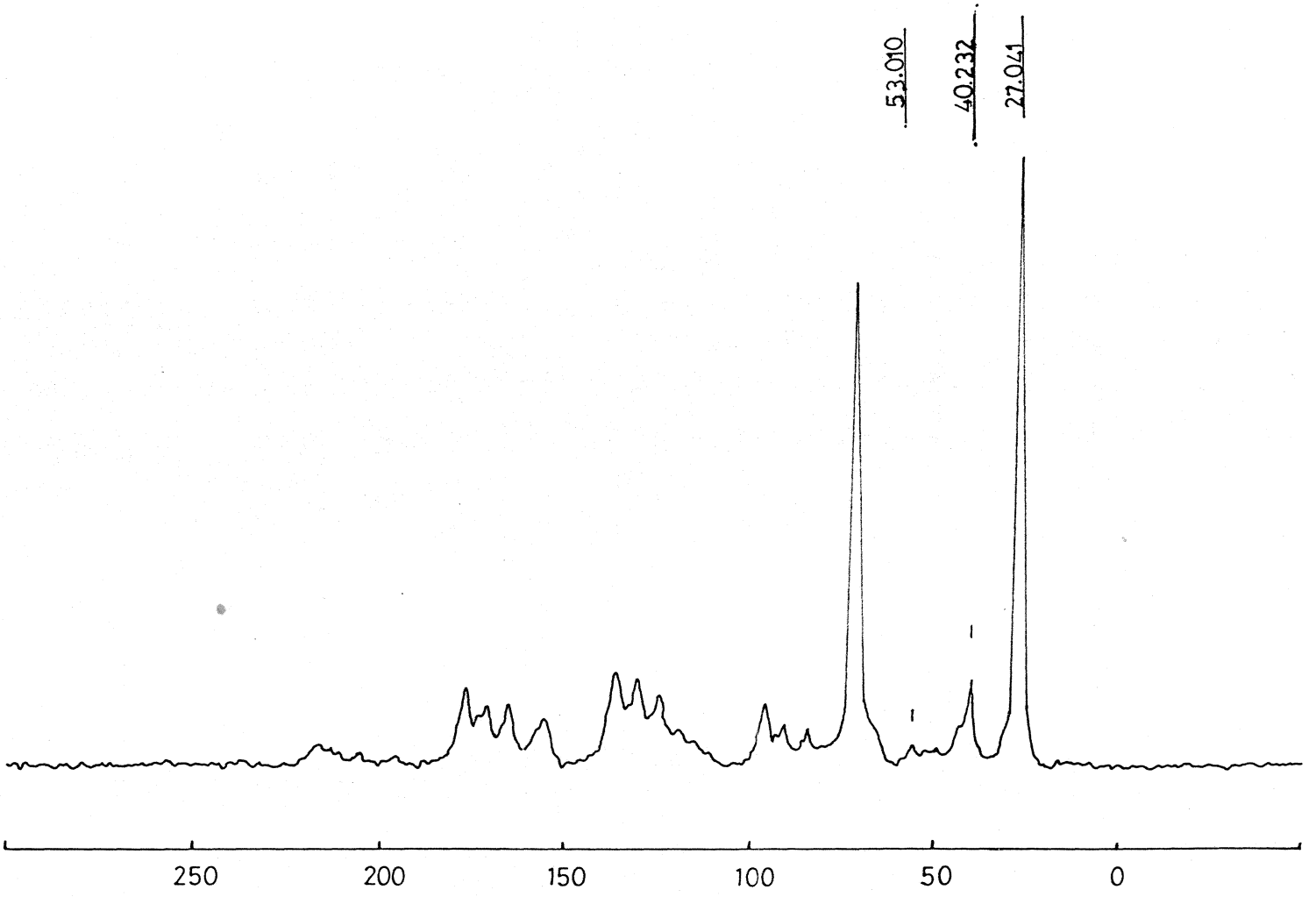


Fig3.24G : ^{13}C NMR spectrum of PU4A-PMMA 80/20 IPN.

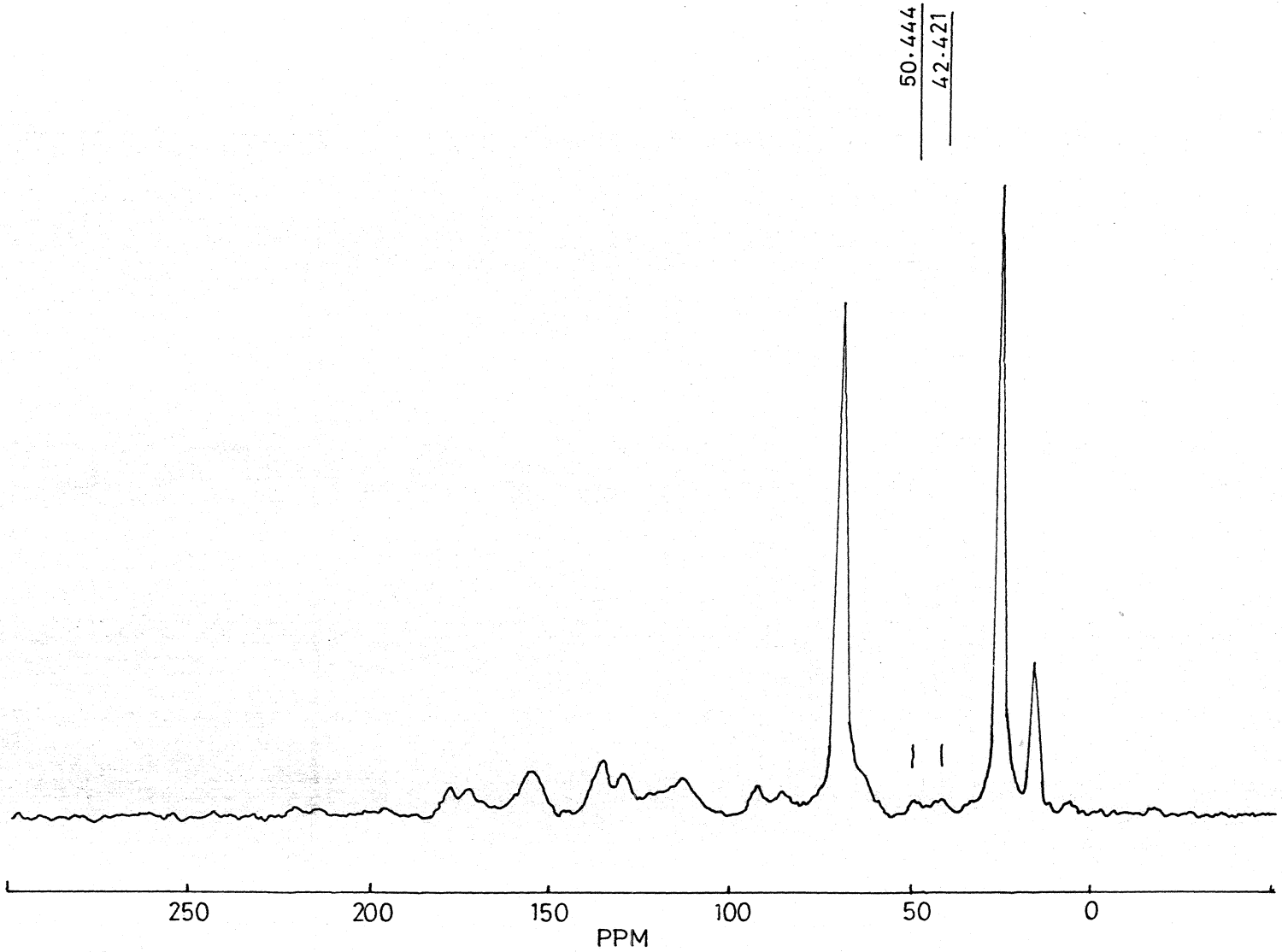


Fig.3.24H: ^{13}C NMR spectrum of PUIA-PVP 80/20 IPN.

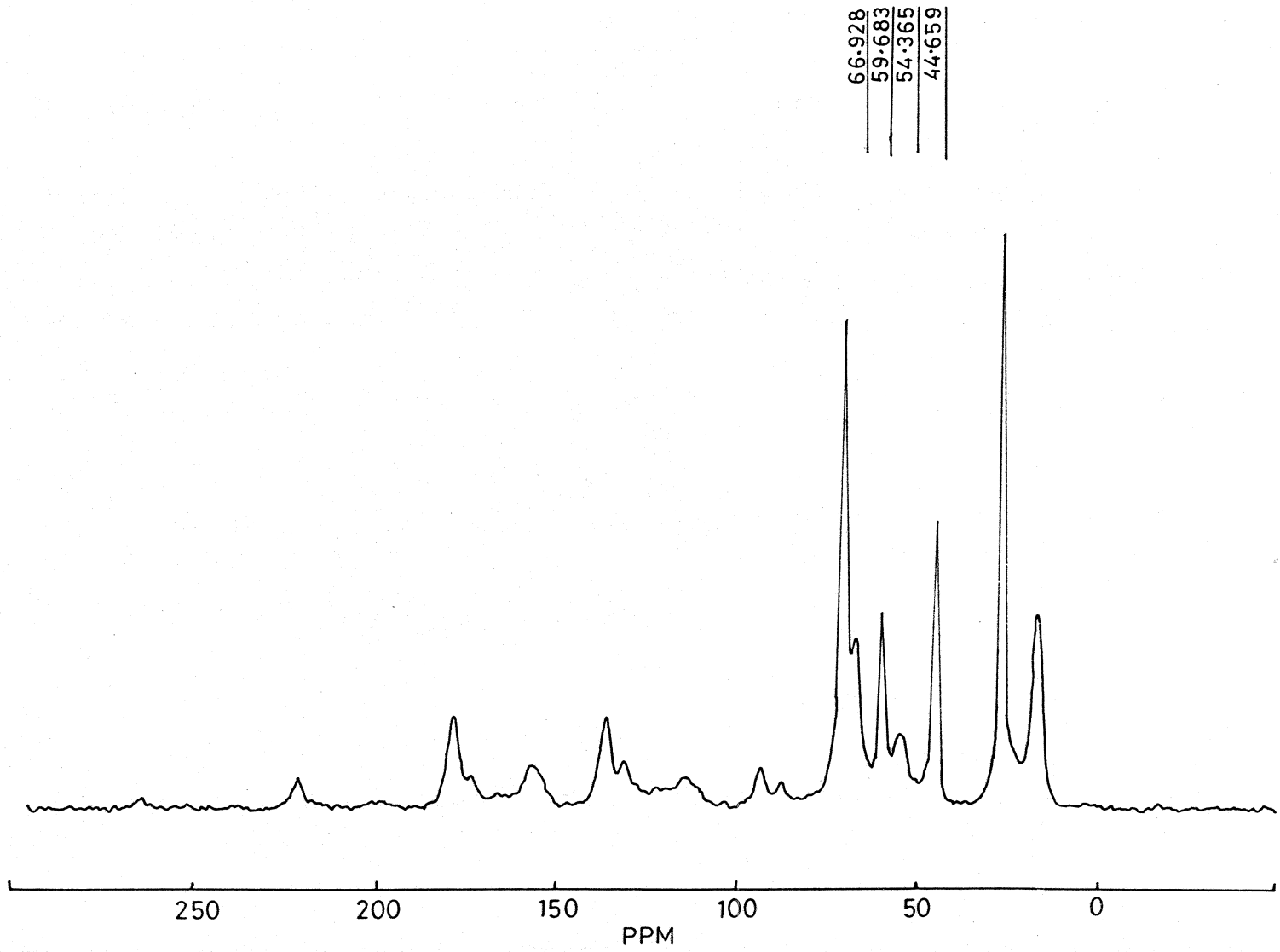


Fig 3.24I : ^{13}C NMR spectrum of PU4A-PHEMA 80/20 IPN.

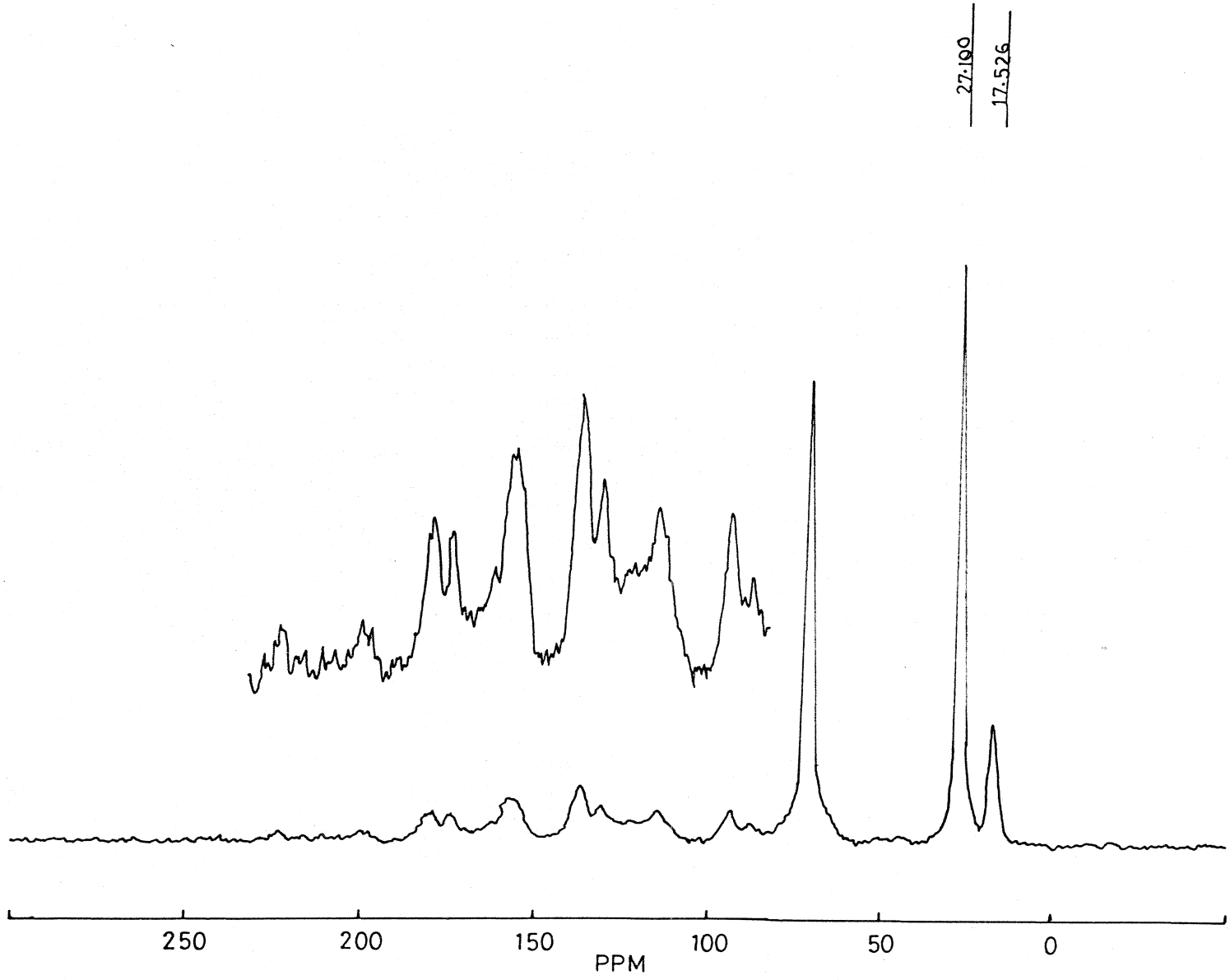


Fig.3.24J: ^{13}C NMR spectra of PUIA-PAM 80/20 IPN

INVITRO STUDIES

CHAPTER-IV

During recent years a large number of investigations have been undertaken to develop blood compatible biomaterials which offer a variety of applications in medicine, surgery and artificial organs. The physiology of the human body is such that it can recognise any foreign surface and promote clot formation on it. The question of how the interface triggers clot or thrombus formation is not completely understood. The suggested sequence of events (266) at the polymer interface leading to the formation of a thrombus is depicted in Fig.4.1.

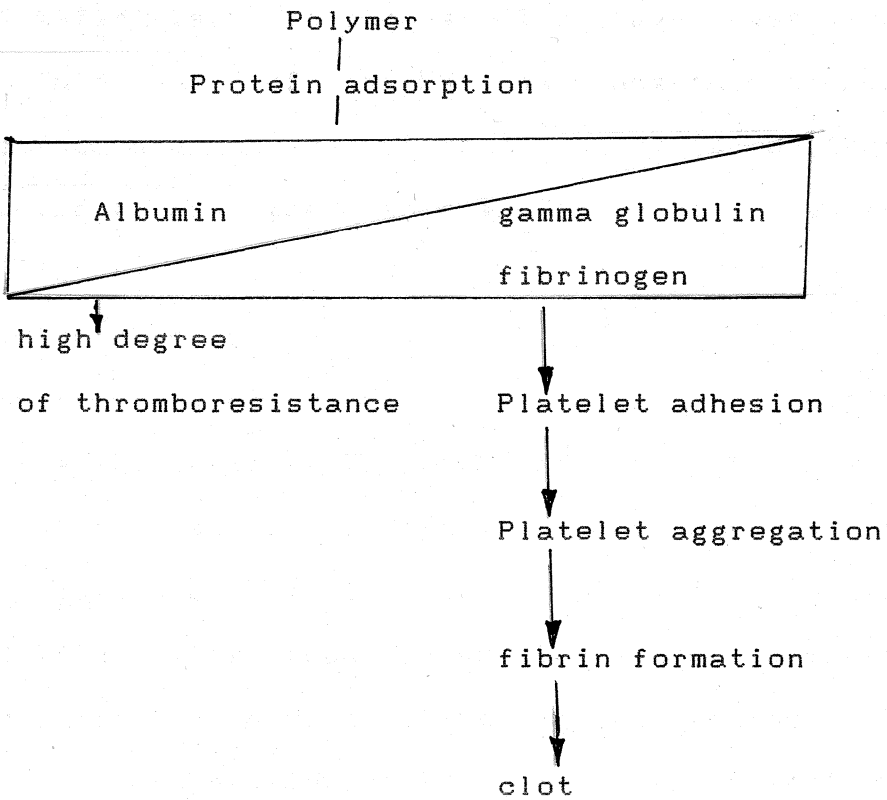


Fig.4.1-Sequence of events at the polymer interface

In addition,it is also reported that the decrease of intracellular cyclic AMP, the rapid adsorption and desorption of denatured thrombin, hemolysis of red cells, adhered white blood cells, surface activation of intrinsic coagulation factors and/or the release of adsorbed fatty acids may cause the formation of thrombus (95). A thrombus is then the end result of a complex interaction of various processes. Several investigations (95,267) have dealt in detail with the cascading series of pathways that lead to the final formation of fibrin threads.

The present work deals with the development of a biocompatible IPN material. The following sections deal with the invitro studies carried out to estimate the blood contacting potential of the IPN materials. Invitro studies have been recommended by the Guidelines of the National Institute of Health (268) mainly for the larger number of samples that can be tested, and are not expected to give the complete picture of events at the invivo situation.

4.1. Recalcification time test:

In this test citrated plasma is recalcified and clotting takes place via the intrinsic pathway, being initiated by the surface activity of the materials of the clotting tube.The recalcification time obtained for the control platelet rich plasma (calf blood) (PRP) in a glass tube coated with a blood compatible commercial polymer-Tecoflex 60D,the TDI based polyurethane PU1A and IPNs of 90 wt% composition of PU1A are given in Table 4.I. The normal range of recalcification time (RCT) reported for

TABLE-4.I

RECALCIFICATION TIME OF TDI BASED IPNS

Polymer	R.C.T. secs.	Polymer	R.C.T secs
Control PRP	75	PU1A-PMMA 90/10	80
Tecoflex 60D	78	PU1A-PAM 90/10	100
PU1A	78	PU1A-PHEMA 90/10	86
		PU1A-PVP 90/10	110

domestic animals is 65 to 100 secs (269). The RCT values obtained for the materials all fall in the normal range except for PU1A-PVP 90/10 for which a slightly prolonged time is obtained. A prolonging of recalcification time within limits is considered as an indication of increasing nonthrombogenicity. All the materials can therefore be considered as nonthrombogenic. The blood contacting behaviour is either similar or even slightly better in some cases than the biomedical grade polyurethane used in similar conditions. Recalcification time for the control PRP in glass tube, Tecoflex 60D, the MDI based polyurethane PU4A and IPNs of 90 wt% composition of PU4A are given in Table 4.II. The values are again observed to be within the normal limits of RCT of domestic animals. PU4A with RCT below even the control PRP value, is however, observed to be more thrombogenic than the other materials. The TDI based IPNs in general, are more non

TABLE-4.II

RECALCIFICATION TIME OF MDI BASED IPNS

Polymer	R.C.T. secs.	Polymer	R.C.T. secs.
Control PRP	75	PU4A-PMMA 90/10	78
Tecoflex 60 D	78	PU4A-PAM 90/10	87
PU4A	72	PU4A-PHEMA 90/10	80
		PU4A-PVP 90/10	89

thrombogenic than the MDI based IPNs due to the more prolonged RCT times obtained. eg PU1A-PAM 90/10 has a RCT of 100 secs while PU4A-PAM 90/10 has a RCT value of 87 secs. The increased thrombogenicity of MDI IPNs in comparison to TDI IPNs could be due to the original thrombogenic nature of the MDI polyurethane PU4A. IPN formation with hydrophilic and hydrophobic monomers seem to have synergistically increased the nonthrombogenic character of the MDI polyurethane. It is also observed in Table 4.I and 4.II that incorporation of more hydrophilic monomer (Section 3.7) results in an increasing nonthrombogenic character for the IPNs. The PU-PHEMA IPNs are however, an exception and PU1A-PHEMA 90/10 though more hydrophilic than PU1A-PAM 90/10 is also more thrombogenic than PU1A-PAM 90/10. Other factors for eg. the heterogenous structure of this IPN (section 3.5) may contribute towards such behaviour.

4.2. Haemolysis :

This test was conducted mainly to see the effect of the materials on the red blood cells. Damage to red cells as a result of exposure to foreign surfaces and rheological stresses have been reported (270). Indeglia et al also report that the canine erythrocytes release several lipids from the cell membrane when a flowing suspension of cells is exposed to a foreign surface. The position of red cells in thrombosis is rather unclear. However, they can adhere to a surface and if haemolysis (or breaking up the red cells with the release of haemoglobulin) occurs, erythrocyte ghosts are formed. Red cells also contain both clot promoting factor (erythrocytin) and platelet aggregating substance (ADP) which become available by haemolysis (267). Attempted phagocytosis of the ghost by the platelet triggers platelet release reaction (271) leading onto platelet adhesion and aggregation. The complex mechanisms of the red cell interaction with surfaces is poorly understood. However, Autian et al (272) report upto 5% haemolysis is permissible for a biomaterial. The Table 4.III gives the % haemolysis values of plasma exposed to the TDI and MDI polyurethanes and IPNs. The values are either less than or near about 2% making the IPNs suitable candidate materials for further studies.

TABLE-4.III

PERCENT HAEMOLYSIS OF PLASMA IN CONTACT WITH THE IPNS

Sample	% Haemolysis	Sample	% Haemolysis
PU1A	2.0	PU4A	2.3
PU1A-PMMA 90/10	1.8	PU4A-PMMA 90/10	2.0
PU1A-PAM 90/10	1.7	PU4A-PAM 90/10	1.8
PU1A-PHEMA 90/10	1.5	PU4A-PHEMA 90/10	1.9
PU1A-PVP 90/10	1.0	PU4A-PVP 90/10	1.5

4.3 Platelet Aggregation:

The adhesion of platelets to each other is called platelet aggregation. When blood contacts an artificial surface, the immediate effect is protein adsorption, which is followed by platelet adhesion and platelet aggregation. The initial adhesion process cannot be validly initiated outside the living vessel as the mechanism is difficult to investigate experimentally.The process of aggregation on the other hand, can be observed in vitro by various methods in which it appears to operate much as in vivo (273). In vitro, human platelets are caused to aggregate by adenosine5'-diphosphate (ADP), adrenaline, 5-hydroxytryptamine thrombin, collagen, vasopressin, arachidonic acid and its metabolites, and platelet activating factor (PAF) as well as by several other agents less immediately relevant to haemostasis. Platelets of other mammalian species are also aggregated by some of these

agents but not all of them are active in all species (274). The mechanisms of the platelet activation, aggregation have been reviewed(275,276). Usually the effects of added ADP on platelets causing aggregation is studied with reference to differences with other agents. A spectrophotometic method (221) is adopted for the study of platelet aggregation. The platelet suspension is first exposed to the foreign surface or IPN materials. The foreign surface could induce changes in the aggregatory properties of platelets. The treated platelet suspension is then induced for aggregation with added ADP. The aggregation potential of the treated platelet suspension is measured with reference to the original untreated platelet suspension. The rate of aggregation is measured as the slope of the change in optical density trace obtained on adding ADP as in the inset of Fig. 4.2. Fig 4.2 is a representative reciprocal plot of the rate of aggregation for platelet suspension in contact with different material versus concentration of added ADP. The reciprocal of the intercept on the (X) axis gives half maximal saturation concentration (HMSC) of the agonist ADP. In other words, it is the concentration of agonist required for getting half the maximum aggregation. The reciprocal of the (Y) axis intercept gives the R max or the rate of maximum aggregation. Table 4.IV gives the half maximal saturation concentration values (HMSC) of the TDI based and MDI based IPNs. A Tecoflex 60D material was used as a control material. The values of the HMSC for the samples are comparable with the values obtained for Tecoflex 60D. The aggregatory poten-

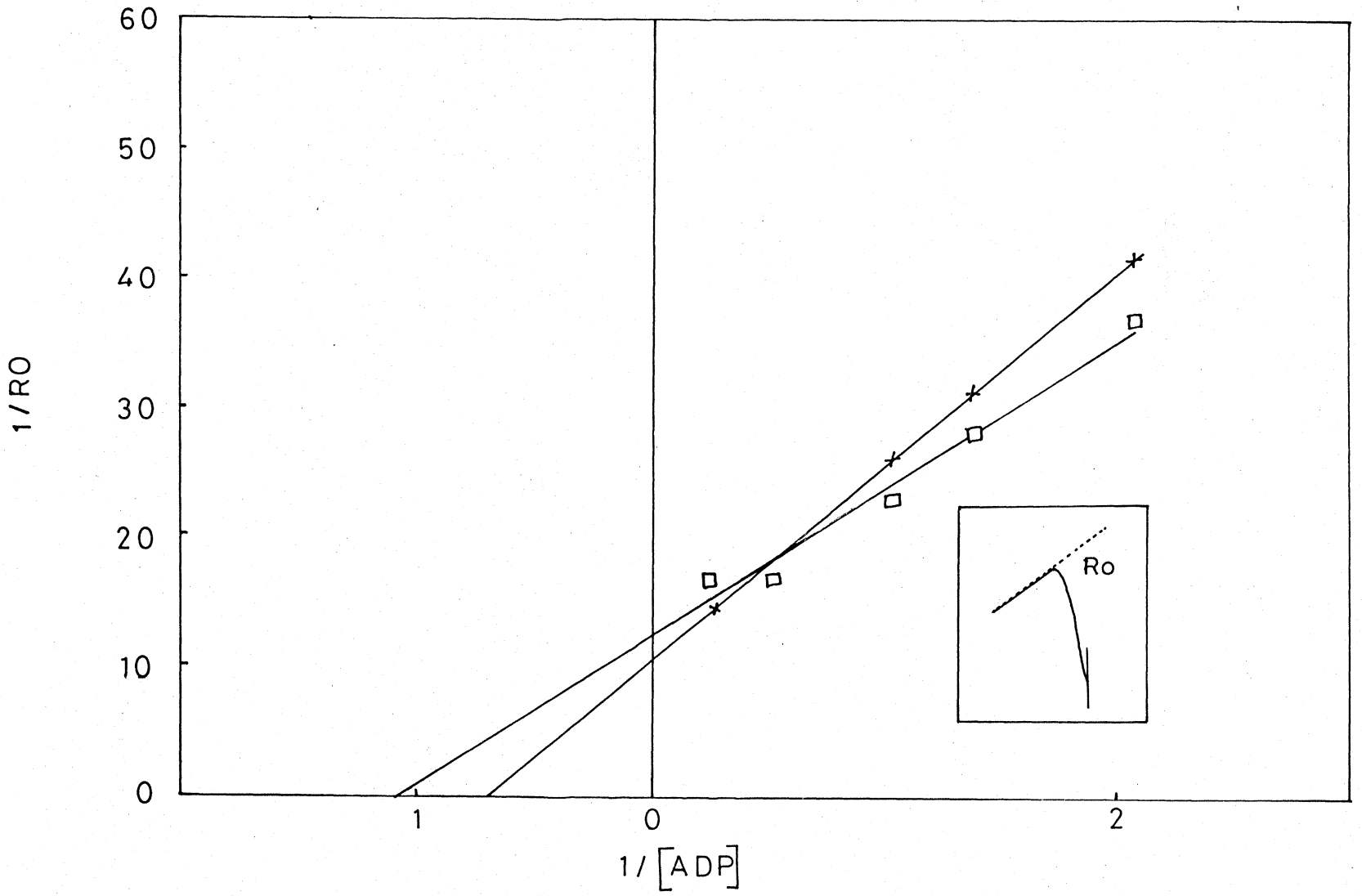


Fig. 4.2 Representative platelet aggregation curve □-Tecoflex 60D X-PUIA-PMMA 90/10 IPN Inset shows representative spectrophotometric trace whose slope is Ro.

TABLE-4.1V

ADP INDUCED PLATELET AGGREGATION OF PLASMA EXPOSED TO PU-IPNS

Polymer	HMSC ADP μM	Polymer	HMSC ADP μM
TECOFLEX 60D	0.95		
PU1A	0.90	PU4A	0.80
PU1A-PAM 90/10	0.99	PU4A-PMMA 90/10	0.85
PU1A-PVP 90/10	1.08	PU4A-PAM 90/10	0.96
PU1A-PHEMA 90/10	1.15	PU4A-PHEMA 90/10	0.98
PU1A-PMMA 90/10	1.43	PU4A-PVP 90/10	1.12

tial of the IPN materials can therefore be termed as equivalent or even slightly less than the Tecoflex material. The platelet aggregatory properties of the MDI based polyurethane PU4A and an IPN, PU4A-PMMA 90/10 and TDI based polyurethane, PU1A are observed to be more than that of Tecoflex 60D. due to the lower value of HMSC obtained for these two materials. A lower value of HMSC indicates less amount of ADP is needed for aggregation of platelets. This could be a consequence of the material interaction with the platelets leading to the early release of ADP , and hence, less amount of added ADP is required for subsequent aggregation in comparision to the reference untreated platelet suspension. Higher amount of HMSC within limits can mean that the material has better platelet contacting properties. The materials

with the exception of PU4A and PU4A-PMMA90/10 can therefore be considered as candidates for potential blood contacting application.

A point to be noted in the context of invitro studies is that the tests cannot accurately predict that a surface will turn out to be bland and unreactive in vivo in long term use. The use of invitro static and dynamic tests for assessment of blood material interactions is controversial (268). However, there is general agreement that invitro tests are most useful in detection of artificial surfaces that are highly reactive with various blood components and produce rapid activation of the blood coagulation sequences or other blood cells markedly.

4.4. Stability in phosphate buffered saline:

Fig.4.3 shows the tensile stress changes of the TDI based polyurethane PU1A and IPNs of 90 wt% composition of PU1A.The tensile stress is only nominally decreased. Fig.4.4 shows the corresponding changes in percent elongation at break for the same materials. Slight increases of elongation are observed in some IPNs The changes in both the tensile stress and % elongation at break fall within the standard deviation limits, so it can be concluded that practically no change takes place on exposing the TDI based IPNs to an aqueous environment.Fig.4.5 and Fig 4.6 are the change n tensile stress and per cent elongation at break for the MDI based polyurethane, PU4A and the IPNs of 90 wt% composition of PU4A respectively. Again no substantial changes occur suggesting that both MDI and TDI IPNs are quite stable in an aqueous environment.

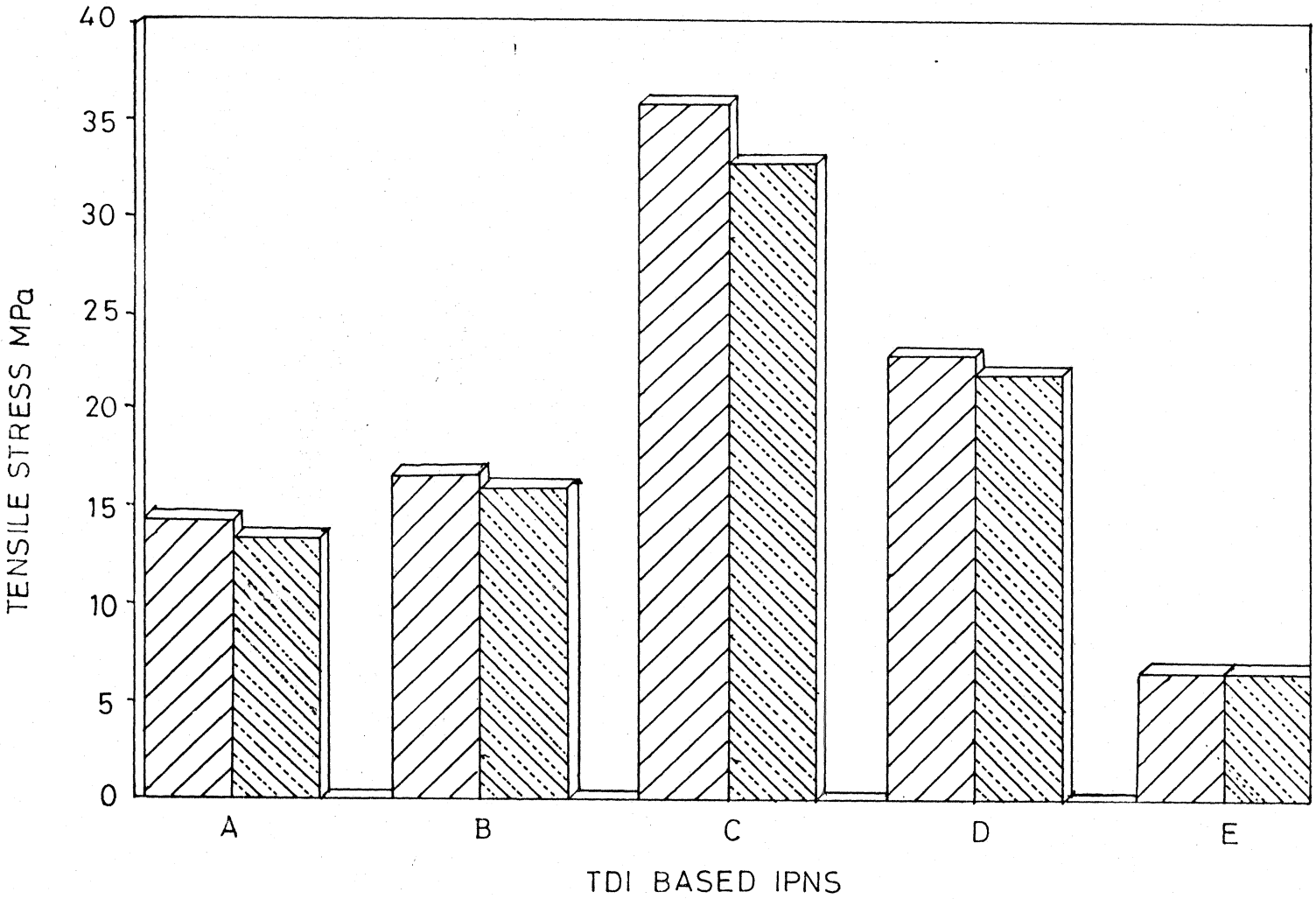


Fig . 4.3. Changes of tensile stress of TDI based IPNS on storing in phosphate bufferred saline ▨ initial tensile stress ▨ final tensile stress A = PUIA, B = PUIA-PAM 90/10 IPN, C = PUIA-PMMA 90/10 IPN, D = PUIA-PHEMA 90/10 IPN, E = PUIA-PVP 90/10 IPN.

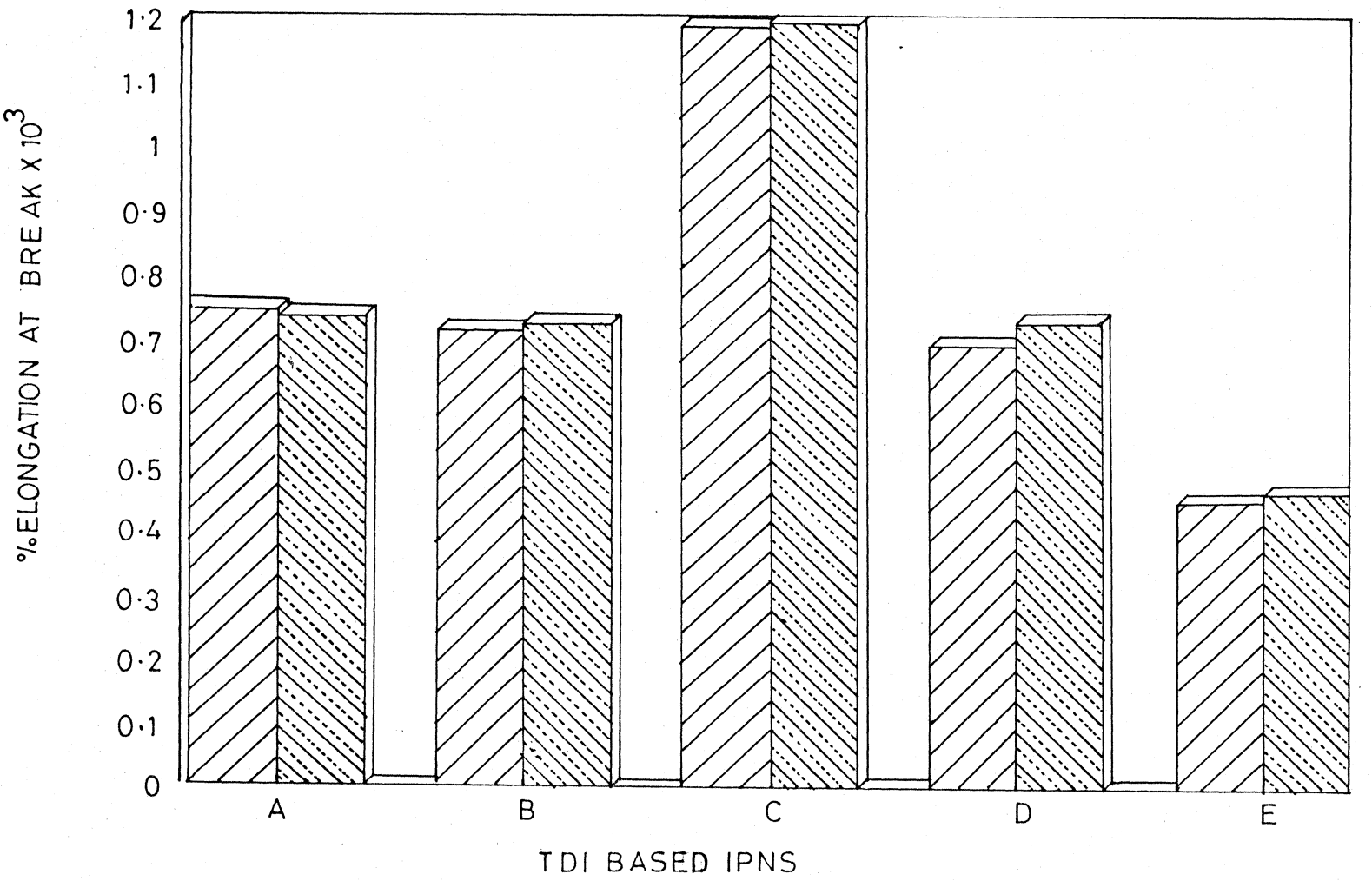


Fig .4.4. Changes of % elongation at break of TDI based IPNS on storing in phosphate bufferred saline ▨ initial elongation ▨ final elongation A=PUIA, B = PUIA-PMMA 90/10 IPN, D - PUIA PHEMA 90/10 IPN E PUIA PVP 90/10 IPN

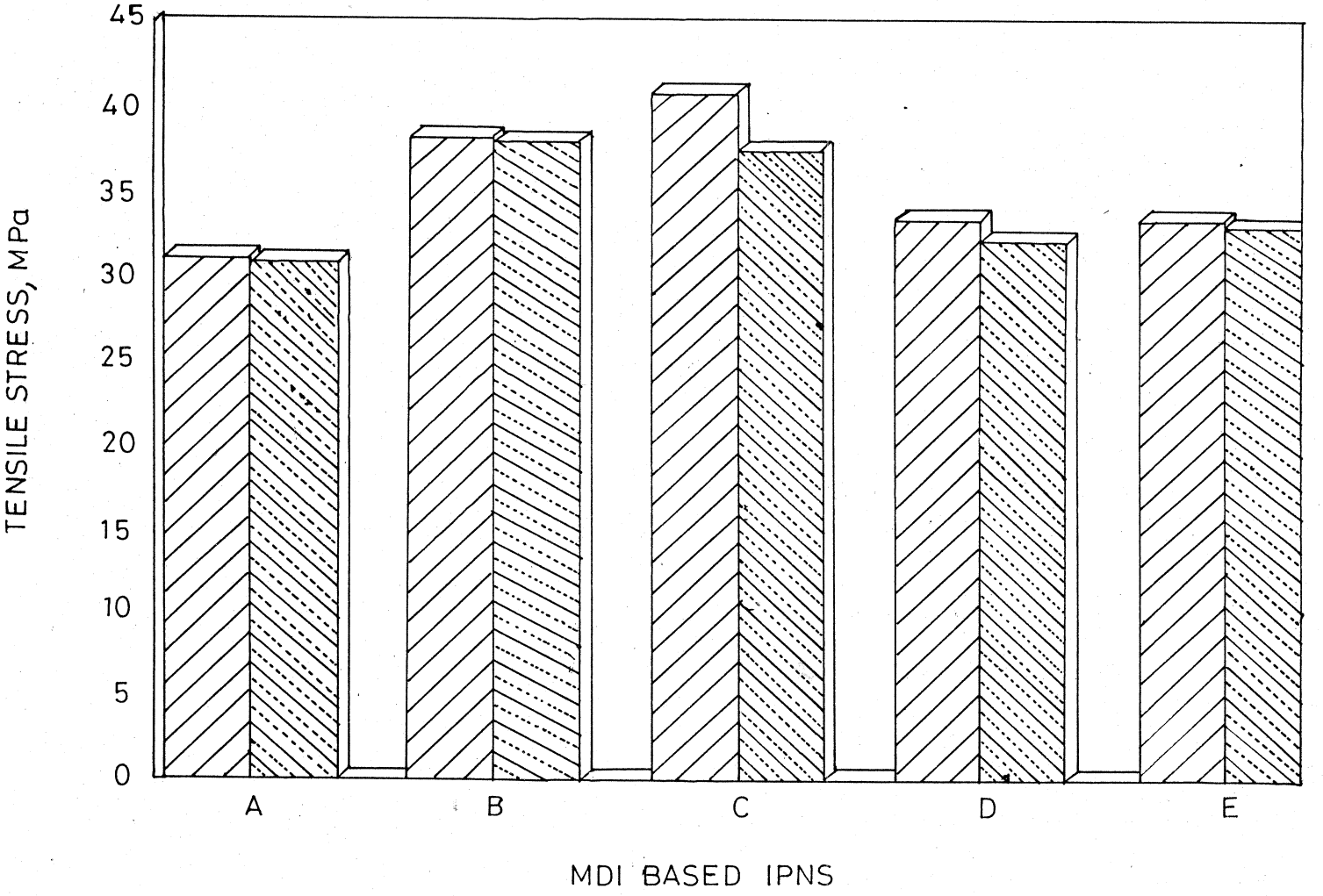


Fig . 4.5. Changes of the tensile stress of MDI based IPNS on storing in phosphate bufferred saline ▨ Initial tensile stress ▨ final tensile stress A = PU4A , B= PU4A-PAM 90/10 IPN, C = PU4A-PMMA 90/10 IPN, D= PU4A-PHEMA 90/10 IPN, E = PU4A PVP 90/10 IPN.

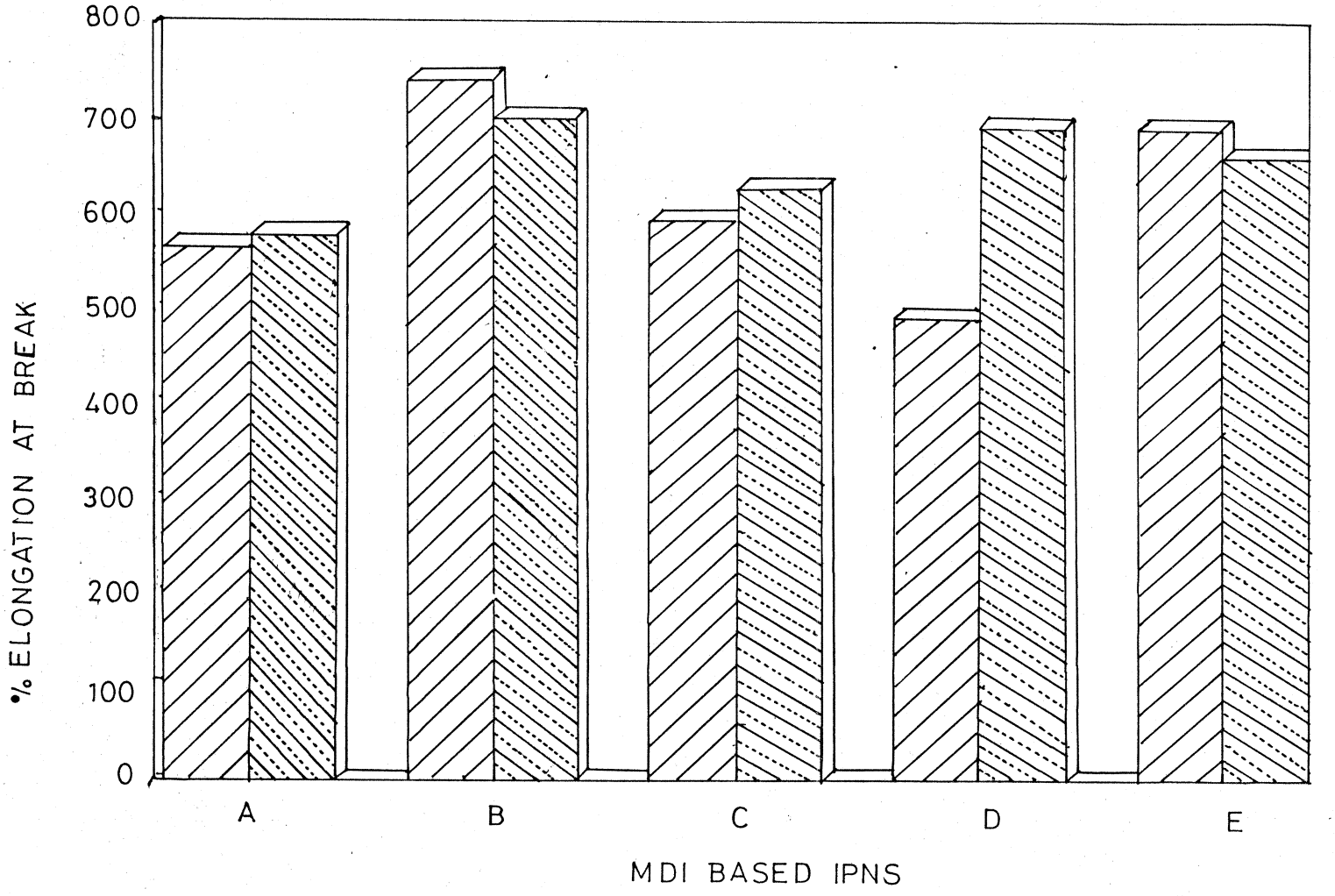


Fig. 4.6. Changes in % elongation at break of MDI based IPNS on storing in phosphate bufferred saline ▨ intial elongation ▨ final elongation. A = PU4A , B = PU4A-PAM 90/10 IPN, C = PU4A-PMMA 90/10 IPN, D = PU4A-PHEMA 90/10 IPN, E = PU4A-PVP 90/10 IPN.

IN VIVO STUDIES

Chapter V

5.1 Toxicological Analysis of Materials:

5.1.1. Acute systemic injection test:

This test is an acute toxicological test useful to detect the presence of injurious leachable substances in a material. Mice subjected to the systemic injection test with the extracts of the test materials,(as reported in Chapter II), showed no signs or symptoms suggestive of systemic toxicity upto 7 days. They were alert, active and normal in their habits and feeding. There was no change in the behaviour or loss of body weight of these animals from those of the control group which received either, sodium chloride injection IP or refined cotton seed oil, the media of extraction.

5.1.2. Intracutaneous irritation test:

The intracutaneous test carried out in rabbits with the extracts of sodium chloride injection IP and refined cotton seed oil did not elicit significant erythema, oedema or necrosis suggestive of cutaneous irritation. The scores obtained for the test samples were well comparable to those of control.

The results of the two tests detailed above indicate that the candidate materials are devoid of gross toxicity and show promise for further consideration as biomaterials.

5.2. Biostability:

Prolonged contact of a biomaterial with biological systems often results in alterations of the chemical and physical properties of the biomaterial. There are few biomedical applications such as absorbable sutures or some controlled drug release systems, in which biodegradation of the material is a desirable characteristic, but it is undesirable for most applications.

Biodegradation and/or biotransformation may take the form of biological molecules attaching to, or penetrating into, the polymer or of biological reactions altering the polymeric structure of the material. The result may be an increase or decrease in crosslinking, degradation, or fragmentation of polymer chains with a concomitent change in physical, mechanical and biocompatibility characteristics. These degradation products,when they are not assimilated, may initiate or participate in local or systemic toxic reactions, hypersensitivity reactions or other adverse effects.

In general, invitro tests are of little value, in accurately estimating, the performance of materials in the complex biological environment. In the present study, the IPNs were implanted for a post implantation period of three months in subcutaneous pouches of wistar rats. The mechanical properties of the materials before and after implantation were evaluated to estimate the changes in properties of the material on implantation. The changes in mechanical properties are a reflection of the changes in the micromorphology of the materials.

5.2.1. Changes in the mechanical properties of TDI based IPNs:

In general, the tensile stress of the TDI based polyurethane PU1A, and the IPNs of 90 wt% composition of PU1A is observed to be decreased on implantation for a period of 3 months. Fig 5.1 represents the decrease of tensile stress and Fig.5.2 represents the corresponding changes in the elongation of the PU1A and its IPNs. The tensile stress decrease is accompanied by an increase in the elongation for the IPNs but the polyurethane shows no changes in elongation. Table 5.I gives the values of percent decrease of tensile stress and the percent increase of elongation at break. It can be clearly seen that the percent decrease of tensile stress for PU1A-PMMA 90/10 IPN and PU1A-PVP 90/10 IPN is the least. The decrease of tensile stress is also accompanied by a relatively increased elongation. This is suggestive of a plasticizing action of water and other biological molecules which may be absorbed by the material in the invivo environment. As the percent decrease of tensile stress for the PU1A-PAM 90/10 IPN and PU1A-PHEMA 90/10 IPN is relatively more, plasticizing action of absorbed molecules may not be solely responsible for the decrease of tensile stress for these latter mentioned IPNs. The decrease of tensile stress could be due to chain scissions of the molecules in these cases. The PU1A-PAM 90/10 IPN which contains free -CONH2 groups is also prone to enzymatic attack. This sort of degradation has been reported for nylon polymers also containing -CONH2 groups (277). Though the PU1A-PHEMA 90/10 IPN does not contain -CONH2 groups, the morphol-

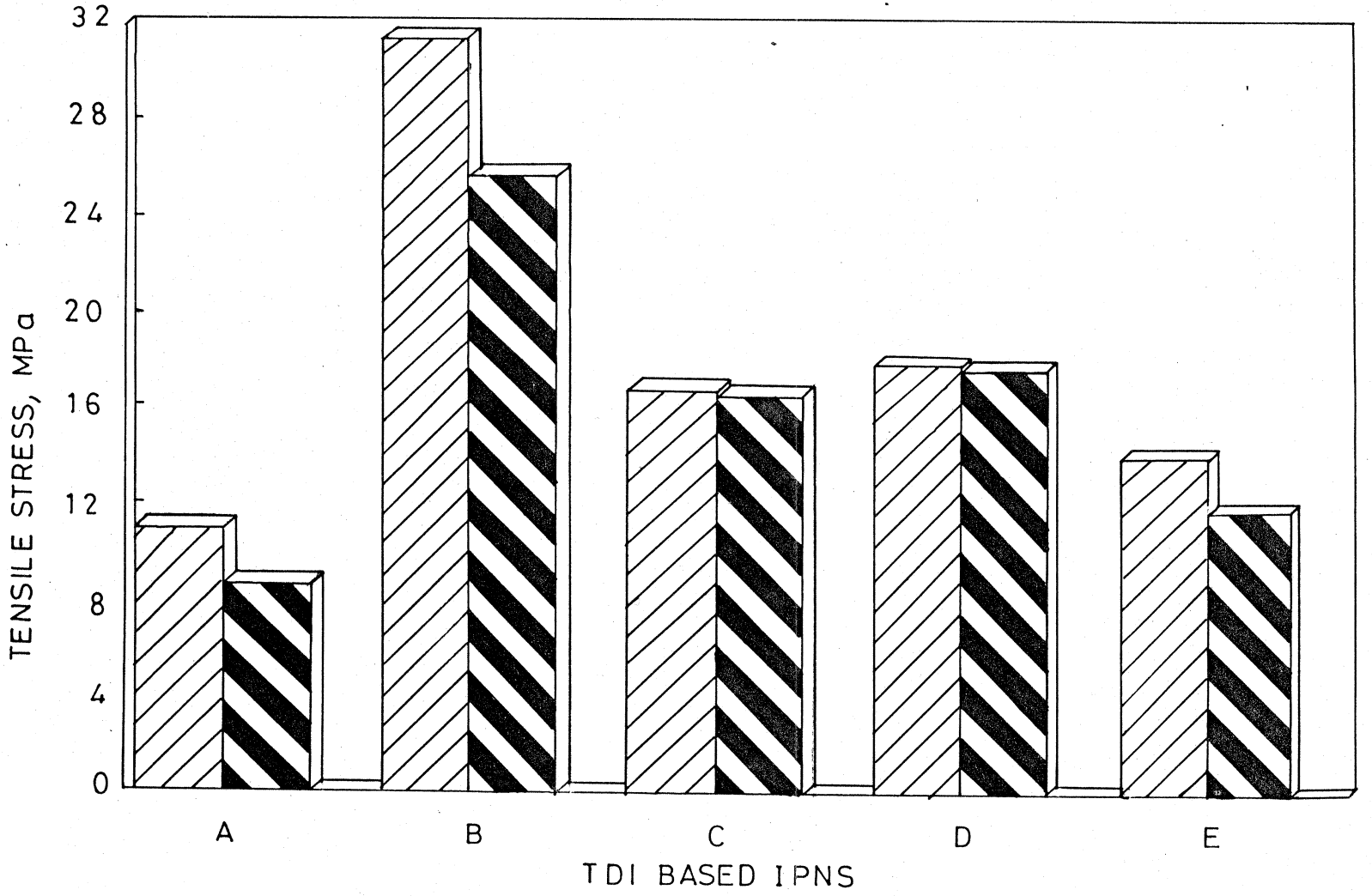


Fig. 5.1. Changes of tensile stress on implantation for 3 months, ▨ - initial tensile stress ▩ - final tensile stress; A = PUIA, B = PUIA - PAM 90/10, C = PUIA - PMMA 90/10, D = PUIA - PVP 90/10, E = PUIA - PHEMA 90/10. IPNS

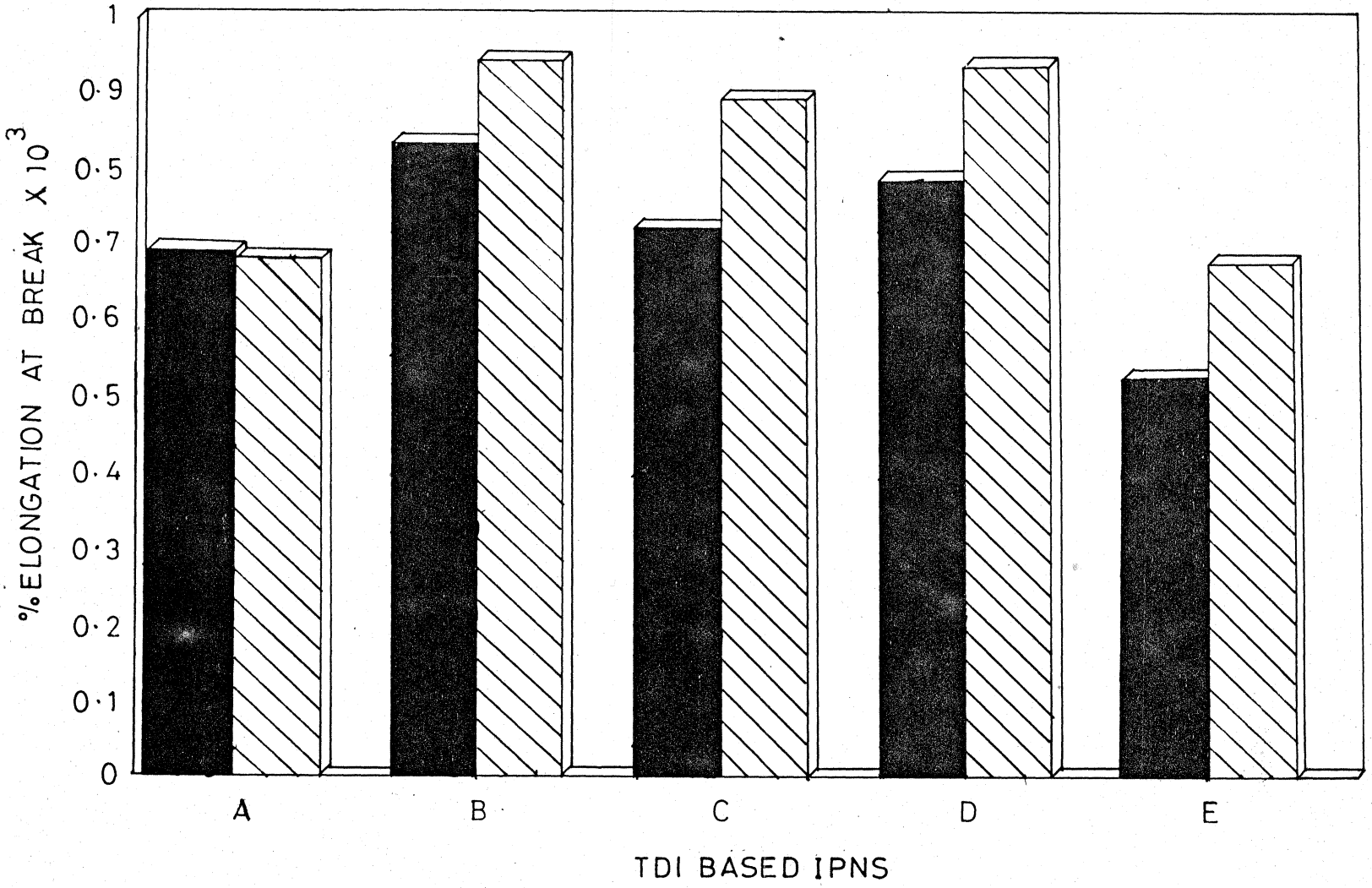


Fig. 5.2 Changes of % elongation on implantation for 3 months ■ initial elongation ▨ final elongation A = PUIA, B = PUIA-PAM 90/10, C = PUIA-PMMA 90/10 IPNS D = PUIA-PVP 90/10, E = PUIA-PHEMA 90/10 IPN

TABLE-5.I

PERCENTAGE CHANGES OF MECHANICAL PROPRETIES ON IMPLANTATION

Polymer	% Decrease of Tensile stress	% Increase of Elongation
TECOFLEX 60D	35	20
PU1A	20	0
PU1A-PAM 90/10	18	13
PU1A-PMMA 90/10	1	22
PU1A-PVP 90/10	1	19
PU1A-PHEMA 90/10	15	27
PU4A	10	17
PU4A-PAM 90/10	12	27
PU4A-PMMA 90/10	23	78
PU4A-PVP 90/10	28	30
PU4A-PHEMA 90/10	14	21

ogy of the PU1A-PHEMA 90/10 IPN as realised by DMA studies (section 3.5) is a heterogenous one. The heterogenous structure could account for the degradation of this IPN.

The homopolymer, polyurethane PU1A has the maximum per cent decrease of tensile stress with practically no change in elongation. The polyurethane may therefore be undergoing considerable chain scission reactions in the hostile physiological environment

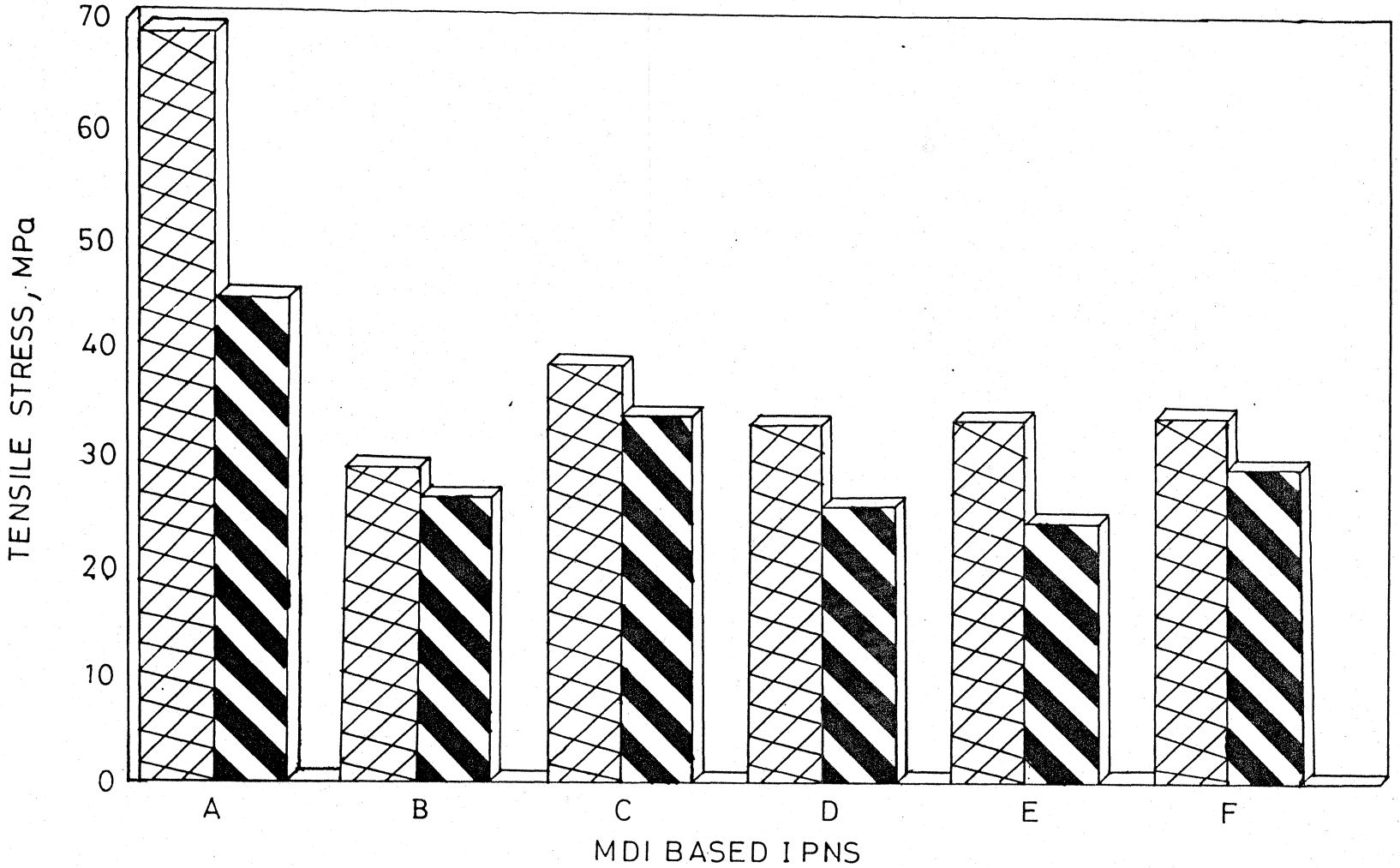


Fig. 5.3. Changes of tensile stress on implantation for 3 months ▨-initial tensile stress ▨ final tensile stress; A=TECOFLEX, B=PU4A, C=PU4A-PAM 90/10, D=PU4A-PMMA 90/10, E=PU4A-PVP 90/10, F-PU4A-PHEMA 90/10. IPNS

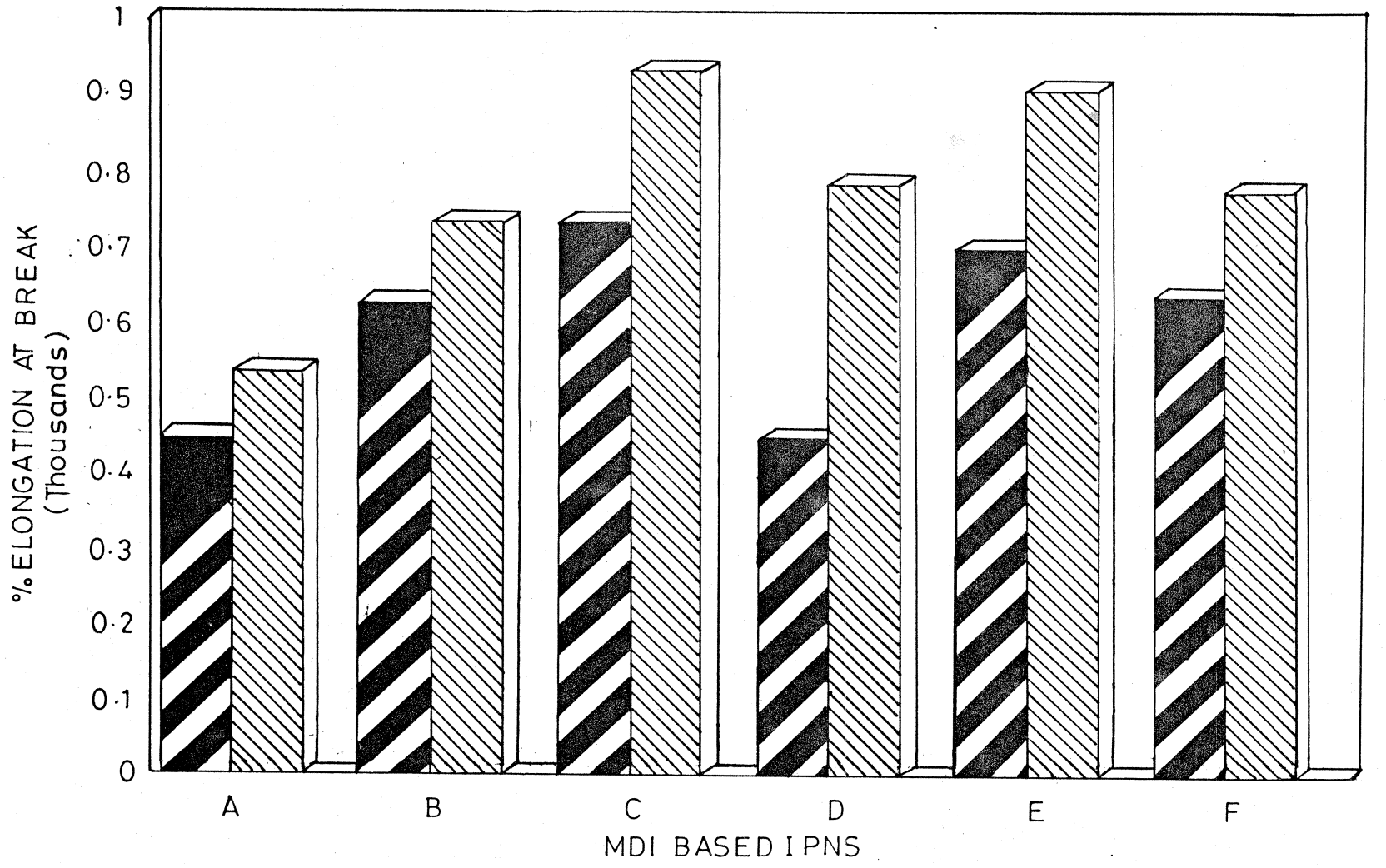


Fig . 5·4 · Changes of % elongation on implanation for 3 months ▨-intial elongation ▨ - final elongation; A=TECOFLEX , B=PU4A, C=PU4A-PAM 90/10, D=PU4A-PMMA 90/10, E=PU4A-PVP 90/10, F-PU4A-PHEMA 90/10· IPNS. .

ment. A linear biomedical grade polyurethane Tecoflex 60D also showed (Fig.5.3 and5.4) a substantial decrease of tensile stress and increase of elongation. Modification of polyurethane homopolymer to IPN structures may therefore serve to reduce the extent of invivo degradation.

5.2.2. Changes in the mechanical properties of MDI based IPNs:

Fig.5.3 and Fig.5.4 represent the change in tensile stress and change in elongation on implanting the MDI based polyurethane PU4A and the IPNs of 90 wt % composition of PU4A. The changes of the biomedical grade polyurethane Tecoflex 60D is also included in the figures for comparision. In comparis on to the TDI polyurethane, the MDI polyurethane seems to possess better stability as the percent decrease of tensile stress is less for the PU4A. It is also accompanied by relatively increased elongation. However, the MDI based IPNs have relatively decreased tensile stress in comparison to the TDI based IPNs especially in case of the PU4A-PVP 90/10 IPN and PU4A-PMMA 90/10 IPN. The PU4A -PMMA 90/10 IPN shows a substantial increase of elongation (Table 5.I) which could be due to the plasticizing action of biological molecules. This plasticizing action could contribute to the decrease of tensile stress. The fact that increase of elongation of the PU4A-PVP 90/10 IPN is comparable to that obtained for other IPNs, indicates that plasticization alone could not be responsible for the decreased tensile stress. The structure of the PU4A-PVP 90/10 IPN is considered as a lamellar one (section 3.4). PVP being a hydrophilic polymer could selectively absorb

water leading to structural reorganisation of the lamellar structuare. The structural reorganisation could result in phase separation and decrease of tensile stress. So plasticization and phase separation could together contribute to the decrease in tensile stress for PU4A-PVP IPN and there may not be much degradation. In general, all the TDI and MDI based IPNs, are quite stable in the biological environment. The degradations observed in certain IPNs, as discussed above,are minor. The changes of tensile stress can be mainly attributed to plasticizing action of water and biological molecules.

5.3. Histopathological studies:

Implantation techniques primarily are used for safety (or biocompatibility) assessment of materials or devices that will be in contact with subdermal and soft parenteral tissues. The testing of a new biomaterial in man, regardless of its proposed specialized use, usually follows the gross and microscopic examination of the response to the material implanted in test animals. The extent and duration of the acute and chronic inflammatory response evoked by subcutaneous or intramuscular implants anticipates the response to them in parenchymal organs or other specialized sites (278). Furthermore, the extent and duration of the inflammatory response are more or less similar in rodent, dog rabbit or in primates, allowing inferences to be obtained for the anticipated responses in man (279).

5.3.1. Histopathological evaluation of TDI based IPNs:

The tissue responses to the TDI based IPNs are scored as

per the method of Turner et al (225), for their histological criteria (Table 5.II-5.IV). Other parameters evaluated were calcification, necrosis and haemorhage. The thickness of the fibrous capsule was also noted. The necrosis varied from mild to moderate while there was neither haemorhage nor calcification in any of the samples. The mean fibrous capsule thickness was 20 μm for all the samples. The responses were further classified into either inflammatory or connective tissue responses. A predominance of neutrophils in the inflammatory reaction is termed as an acute inflammatory response designated (A). A response with macrophages, lymphocytes and plasma cells is termed as a chronic inflammatory response (B), which may be without giant cells or with giant cells (C). Presence of a response with eosinophil (D) would indicate hypersensitivity. Connective tissue responses are the combination of a cellular response consisting of a predominance of fibroblasts and fibrocytes (E) or a collagenous response which consists of mainly collagen fibres with sparse fibrocytes (F). The total reaction is summed up based on the relative increase of A,B,C,D,E or F. The summing up of the response is also carried out following a numerical rating system (Table 5.V) where $\pm$ = 5, + =10, 2+ = 20, 3+ = 30 etc. The numerical scoring system is advantageous to distinguish the tissue response to different materials.

The results of 7 day post implantation study of the TDI based IPNs of 90 wt % PU1A,polyurethane PU1A and a control biomedical grade polyurethane Tecoflex 60D, are summarised in Table 5.II.

TABLE-5.II

7 DAYS POST IMPLANTATION OF TDI BASED IPNS,

HISTOPATHOLOGICAL EVALUATION OF ADJACENT MUSCLE.

Histopathology	Control	PU1A	PU1A-PMMA 90/10	PU1A-PAM 90/10	PU1A-PHEMA 90/10	PU1A-PVP 90/10
Neutrophils-A	±	+	+	±	+	±
Macrophages	2+	3+	4+	3+	3+	3+
Lymphocytes B	±	±	+	±	+	0
Plasmacells	0	±	+	+	0	±
Giant cells C	2+	±	3+	+	±	3+
Eosinophils D	+	2+	+	3+	3+	2+
Fibroblasts E	3+	4+	4+	3+	4+	4+
Fibrocytes F	±	±	±	±	0	+
Fatty infiltrate	0	+	0	0	0	0

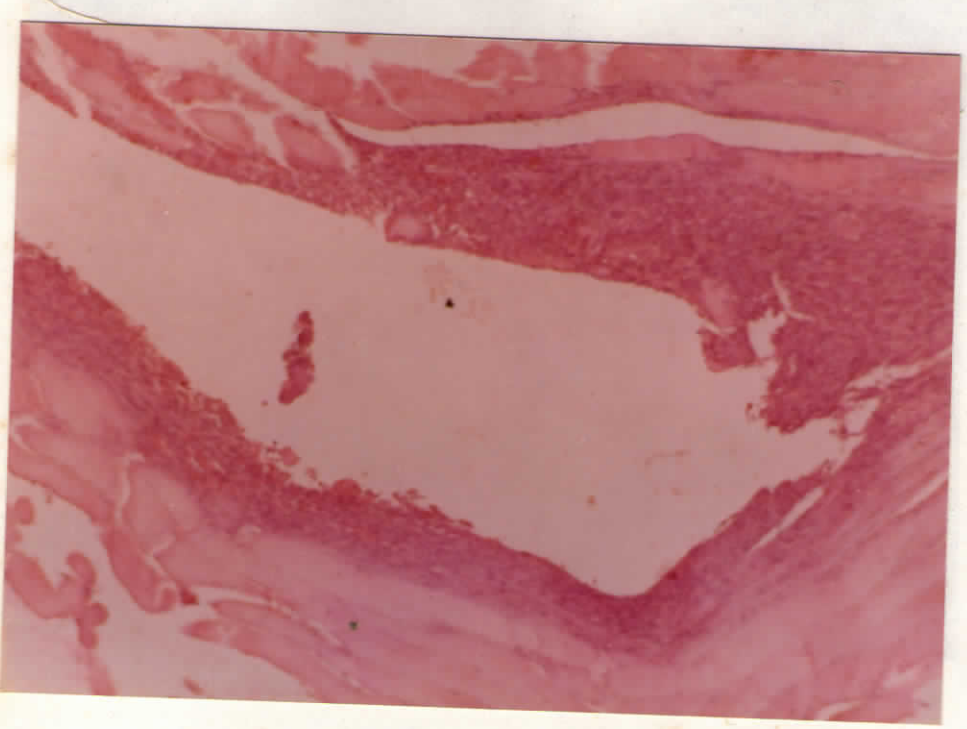
Scoring based on a 0 to 4+ scale, 0 = item not present.
± = item occasionally present. + = item present to a mild degree. 2+ = item present to a moderate degree. 3+ item present to a marked degree. 4+ = high degree.

A - acute inflammatory response, B - chronic inflammatory response C - chronic inflammatory response with giant cells, D-hypersensitivity, E - connective collagenous tissue response. F - connective cellular tissue response.

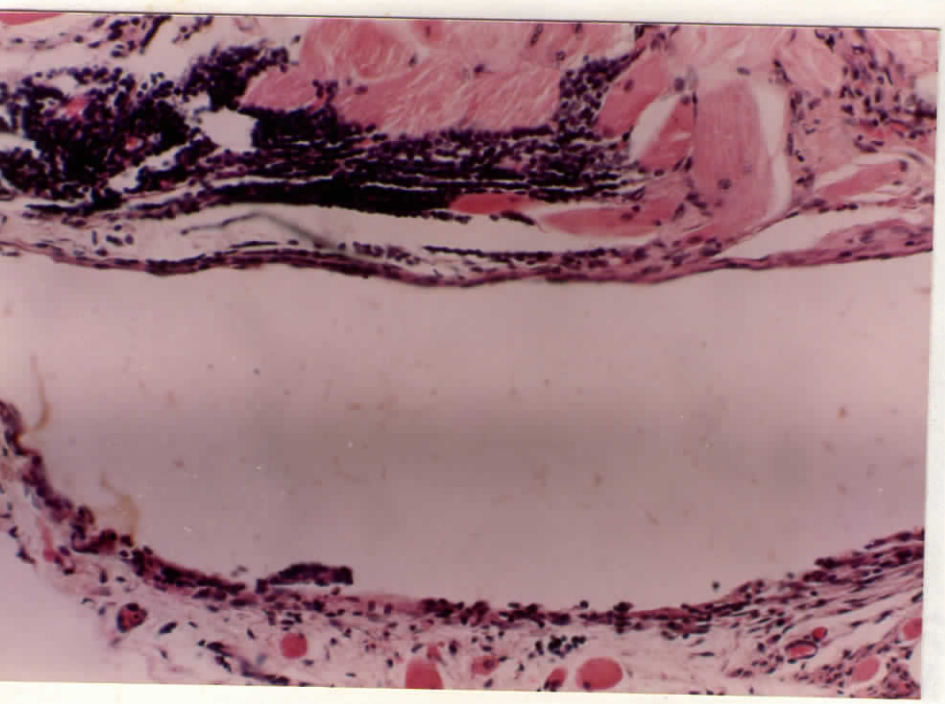
The tissue responses for all the samples as well as the control can be seen to be a mixture of inflammatory and connective tissue type. Various studies (280) of tissue response to implanted materials have indicated neutrophil migration into the wound site following implantation. Anderson (280) has stated that the preferential migration of neutrophils mediated through a chemotactic stimulus is a well known characteristic of the acute inflammatory response. However, monocytes and lymphocytes also migrate into the wound site during the seven day period after implantation and macrophages are also reported (280) to be present at their highest concentration during the same period.

Hence the classification of the inflammatory reaction as acute or chronic is erroneous at this period. The photomicrographs (Fig.5.5 and 5.6) of the tissue responses around the control and a respresentative test material PU1A-PAM 90/10 indicate that the responses are similar. Similar responses as observed for the materials of this study have also been reported for other biocompatible materials (281).

Histopathological findings of tissue site around implants for a post implantation period of one month are given in Table 5.III. Neutrophils are absent indicating the end of the acute inflammatory phase. Inflammation is still evident in the form of lymphocytes and macrophages as well as few giant cells around samples, PU1A and PU1A-PAM 90/10. However, fibrocytes along with collagen tending to form a capsule around implant is also seen [Fig 5.7(A-C)].

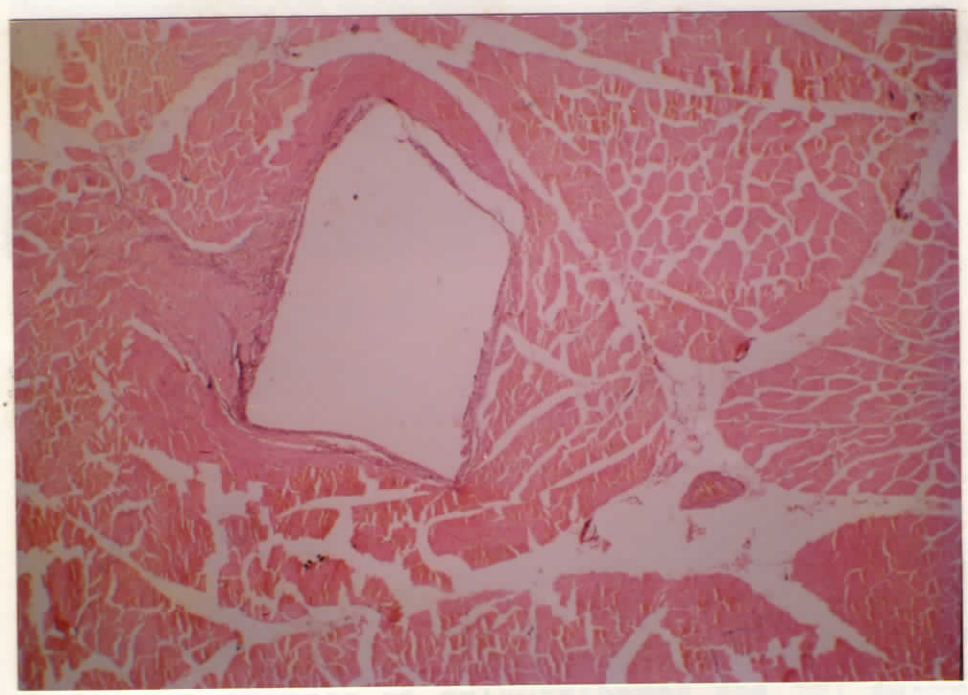


5.5 : Tissue response of control polyurethane at 7 days

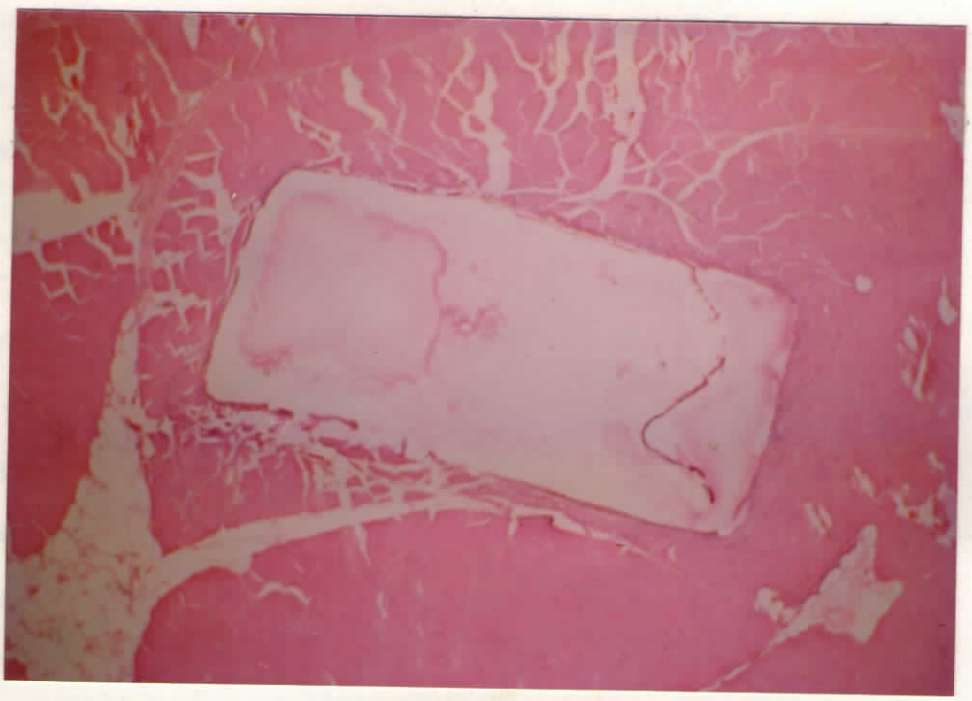


5.6 : Tissue response of PU1A-PAM 90/10 IPN at 7 days.

A



B



C

5.7:Tissue response of polyurethanes and TDI based IPN at one month. A-Control polyurethane,B-Polyurethane,PU1A, C-PU1A-PAM 90/10 IPN.

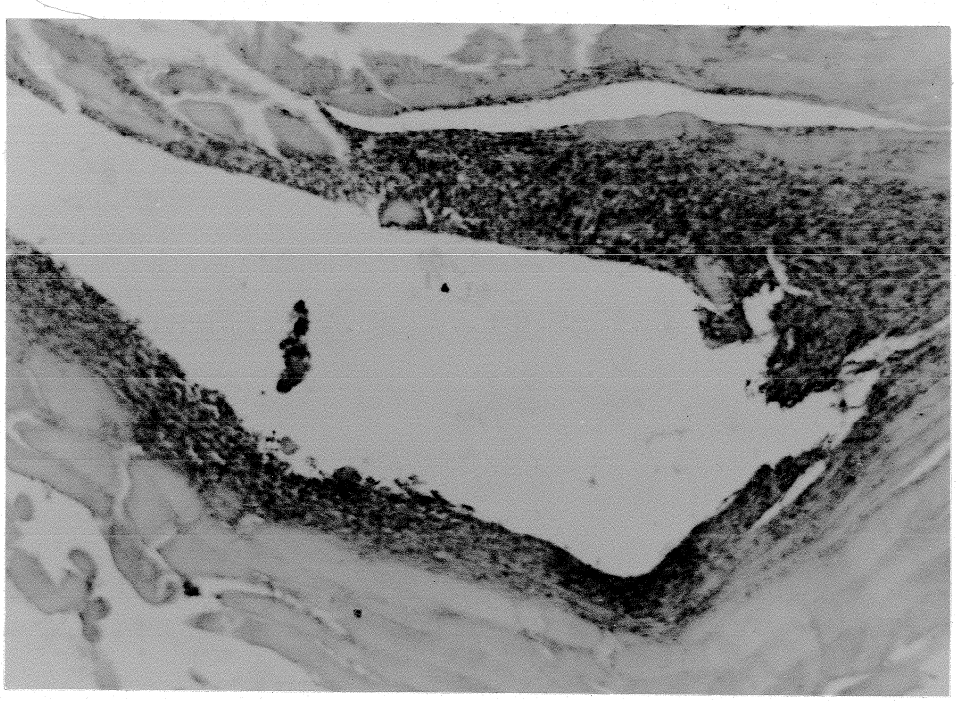


Fig. 5.5 : Tissue response of control polyurethane at 7 days

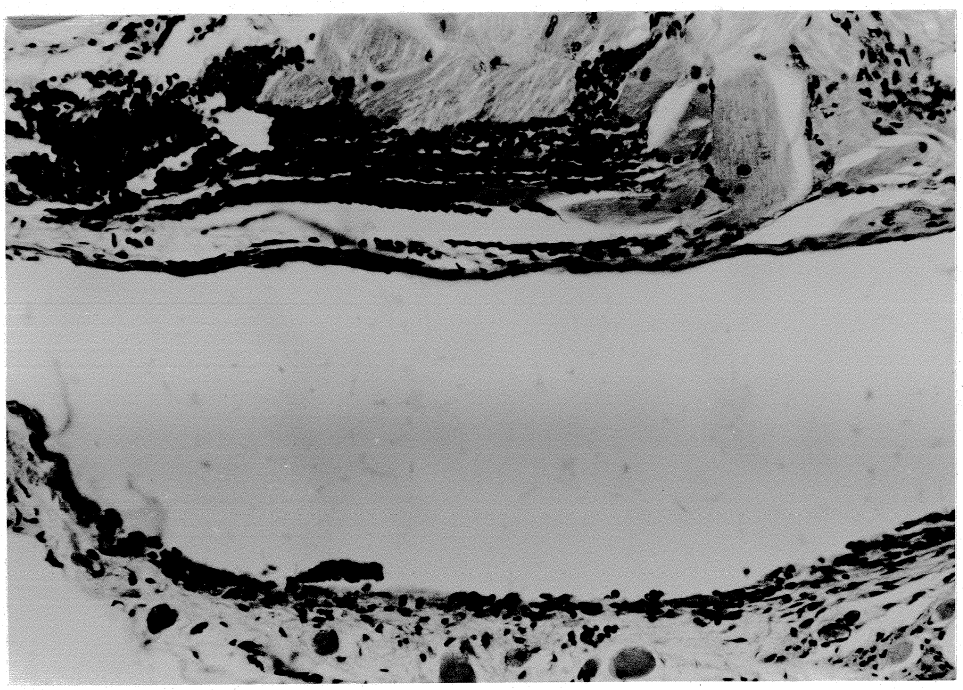
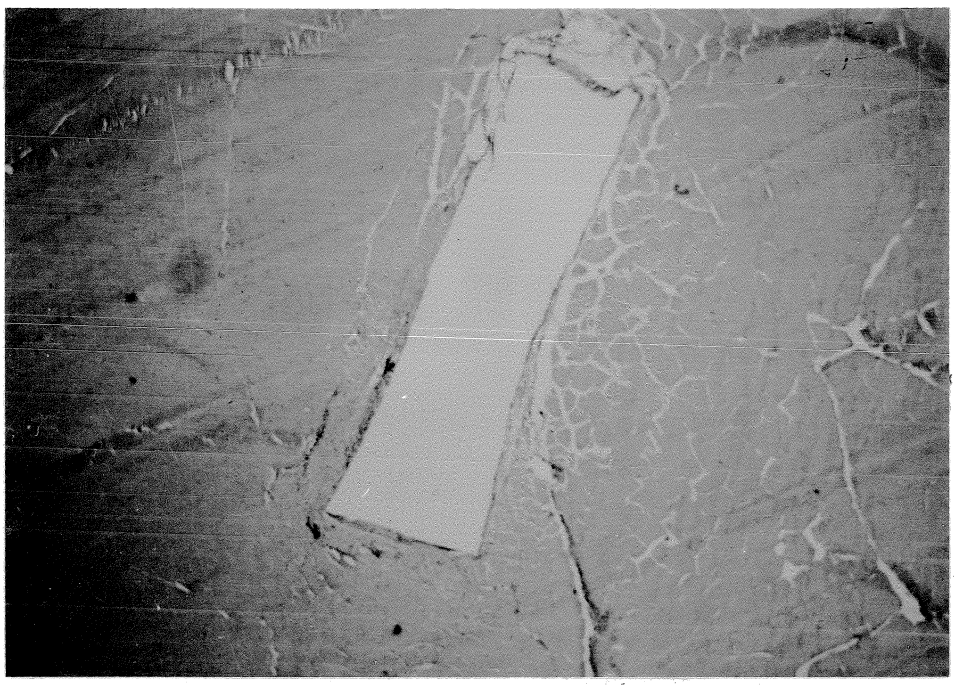
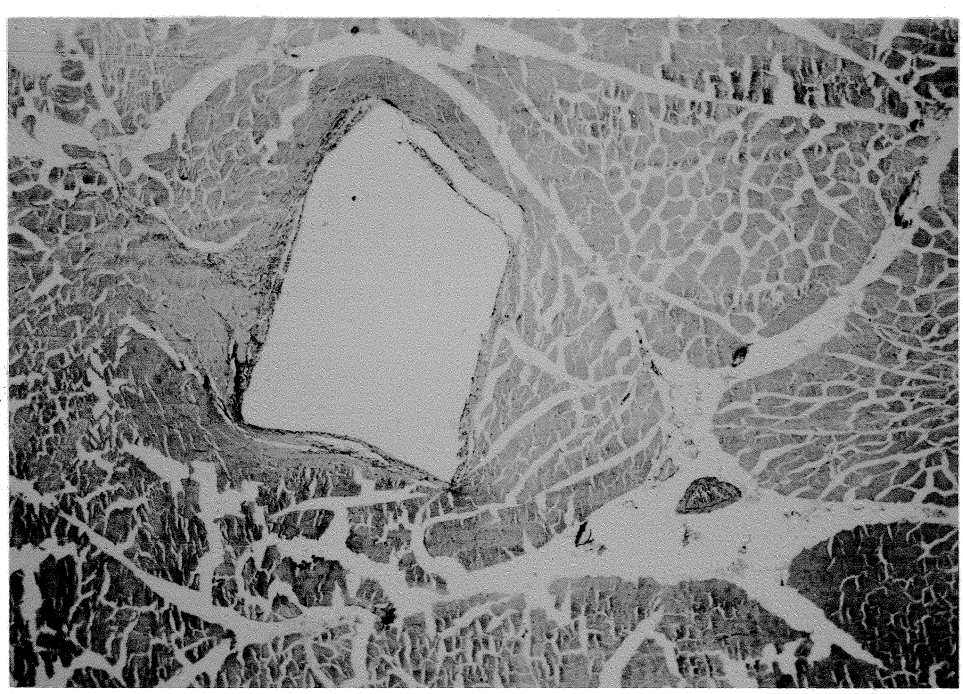


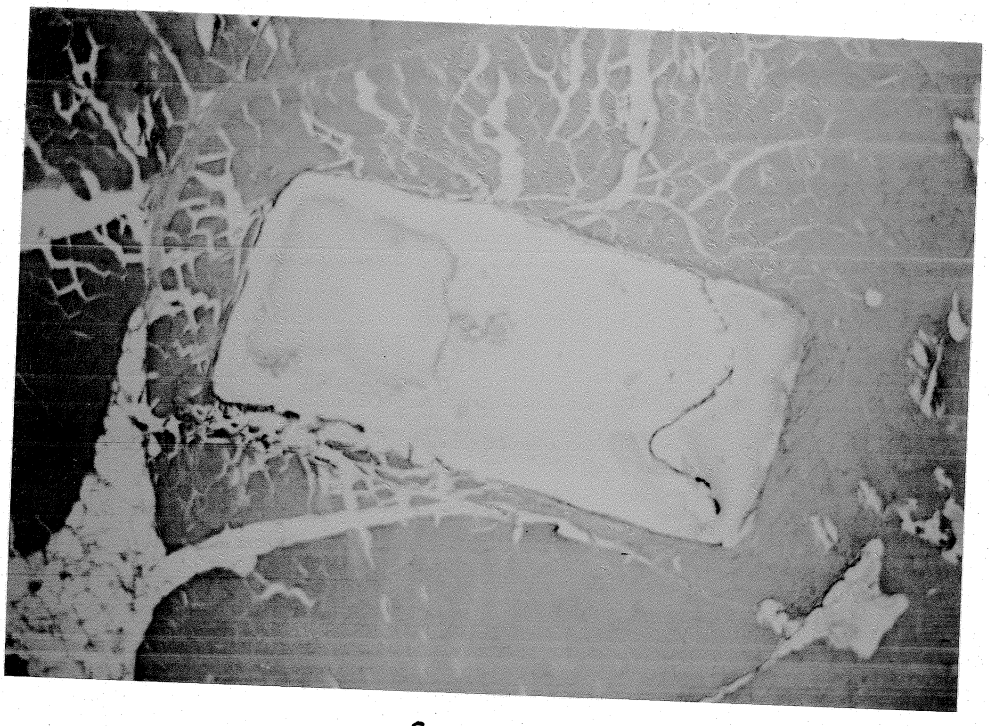
Fig. 5.6 : Tissue response of PU1A-PAM 90/10 IPN at 7 days.



A



B



C

Fig. 5.7:Tissue response of polyurethanes and TDI based IPN at one month. A-Control polyurethane,B-Polyurethane,PU1A, C-PU1A-PAM 90/10 IPN.

TABLE 5.III

ONE MONTH POST IMPLANTATION OF TDI BASED IPNS, HISTOPATHOLOGICAL EVALUATION OF ADJACENT MUSCLE.

Histopathology	Control	PU1A	PU1A-PMMA 90/10	PU1A-PAM 90/10	PU1A-PHEMA 90/10	PU1A-PVP 90/10
Neutrophils-A	0	0	0	0	0	0
Macrophages	2+	2+	3+	3+	2+	3+
Lymphocytes-B	2+	±	±	+	+	+
Plasma cells	0	0	0	±	0	0
Giant cells-C	0	±	0	±	0	0
Easinophils-D	0	0	0	0	0	0
Fibroblasts-E	2+	+	4+	3+	+	3+
Fibrocytes-F	+	+	2+	2+	3+	+
Fattyinfiltration.	±	0	+	+	0	+

Anderson (280) has speculated that foreign body giant cell formation is a function of polymer chain mobility at the surface which facilitates the motility of macrophages and their subsequent fusion to form foreign body giant cells. The low glass transition temperatures of the TDI based polyurethane and IPNs as discussed in section 3.6 could be an indication of the greater segmental mobility of the IPNs. This factor could be contributing to the presence of giant cells as speculated by Anderson (280). Table 5.V gives the numerical rating for characterising the tissue response. The connective tissue response rating which is indicative of the repair process is either equal to or more than the inflammatory response rating in case of the IPNs. The connective tissue responses are however, slightly lower than the inflammatory responses for the control polyurethane and the synthesised polyurethane. Hence, at the end of one month the responses of the IPNs indicate them to be more biocompatible than the polyurethanes studied.

The post implantation studies (Table 5.IV) of the TDI based IPNs at the end of the 3 months period showed that the inflammatory responses had subsided. However, some neutrophils are noted for the polyurethane PU1A. The PU1A-PAM 90/10 IPN and PU1A-PHEMA 90/10 IPN also show some lymphocytes which are normally associated with an immune response (123).

TABLE-5.IV

3 MONTH POST IMPLANTATION OF TDI BASED IPNS, HISTOPATHOLOGICAL EVALUATION OF ADJACENT MUSCLE

Histopathology	Control	PU1A	PU1A-PMMA 90/10	PU1A-PAM 90/10	PU1A-PHEMA 90/10	PU1A-PVP 90/10
Neutrophils-A	0	+	0	0	0	0
Macrophages	±	±	0	±	+	0
Lymphocytes-B	0	0	0	±	2+	0
Plasma cells	0	0	0	0	0	0
Giant cells-C	0	0	0	0	0	0
Eosinophils-D	0	0	0	0	0	0
Fibroblasts-E	±	2+	±	+	2+	0
Fibrocytes-F	+	2+	±	+	2+	±
Fatty-infiltration.	±	0	0	2+	±	±

TABLE-5.V

NUMERICAL RATING FOR TDI BASED IPNS

Samples	1 month implantation		3 month implantation	
	Inflammatory response	Connective tissue response	Inflamatory response	Connective tissue response
Control	40	30	5	15
PU1A	30	20	15	40
PU1A-PMMA 90/10	35	60	0	10
PU1A-PAM 90/10	50	50	10	20
PU1A-PHEMA 90/10	30	40	30	40
PU1A-PVP 90/10	40	40	0	5

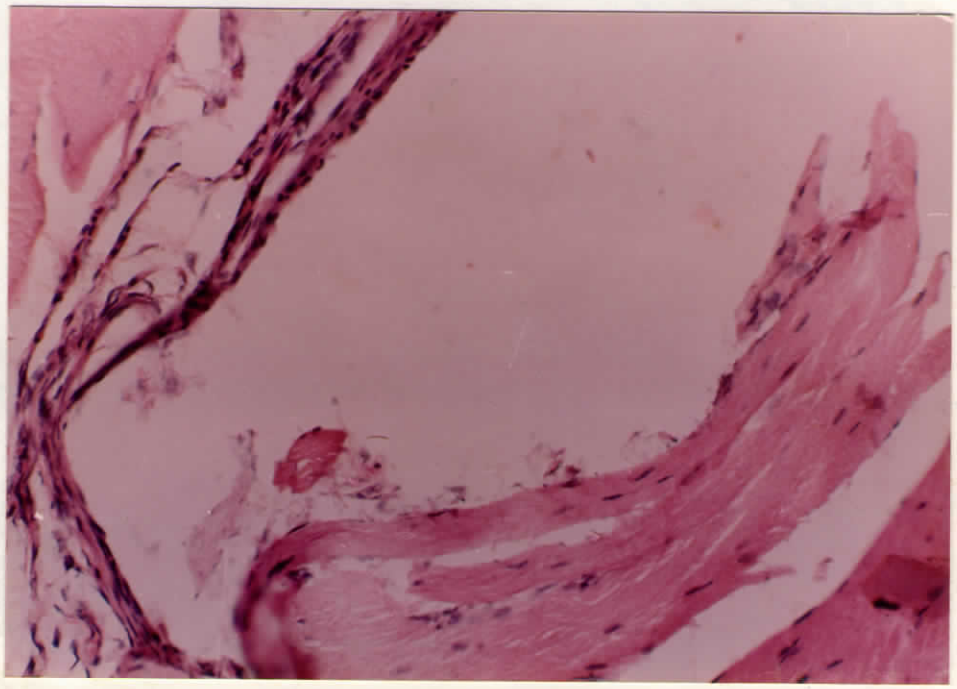
Scoring $\pm$ = 5, + = 10, 2+ =20, 3+ = 30, 4+ = 40

Inflammatory response = A+ B + C

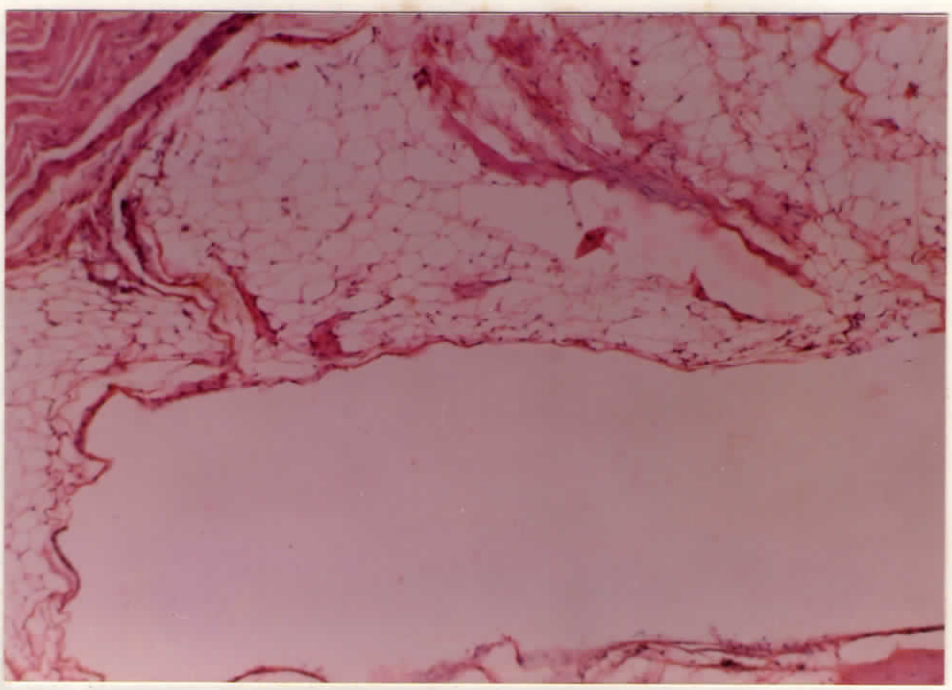
Connective tissue response = E + F

The numerical rating in Table 5.V indicates that in all cases the repair reaction is more than the inflammatory response for all samples. PU1A-PMMA 90/10 IPN and PU1A-PVP 90/10 IPN show a complete absence of inflammatory response and also have a minimum connective tissue response. Connective tissue responses though favourable for encapsulating a material and rendering it more inert, should not indefinitely increase so as to form a very thick capsule. The minimum connective tissue response at 3 month period for the PU1A-PMMA 90/10 IPN and PU1A-PVP 90/10 IPN can therefore be considered as the reactions of more biocompatible and inert materials.

A comparison of the numerical rating of responses at 1 month and 3 months (Table 5.V) indicate that the inflammatory response rating of one month is reduced for all the samples except PU1A-PHEMA 90/10 at the end of 3 months. The connective tissue response rating of all the samples, except PU1A and PU1A-PHEMA 90/10 IPN, is also reduced by 3 months. Hence the PU1A and PU1A-PHEMA 90/10 can be termed as more reactive to the tissue when compared to PU1A-PVP 90/10 or PU1A-PMMA 90/10IPN or the control polyurethane. The sample PU1A-PAM 90/10 IPN shows more reactivity to tissue than PU1A-PMMA 90/10 or PU1A -PVP 90/10 on account of the presence of some inflammatory response. However, the PU1A-PAM 90/10 is less reactive in comparison to the PU1A or PU1A-PHEMA 90/10 IPN. Among the PU1A and PU1A-PHEMA 90/10, though the response rating of PU1A is better than that of PU1A-PHEMA 90/10 on account of a lower rating of inflammatory response, the



A



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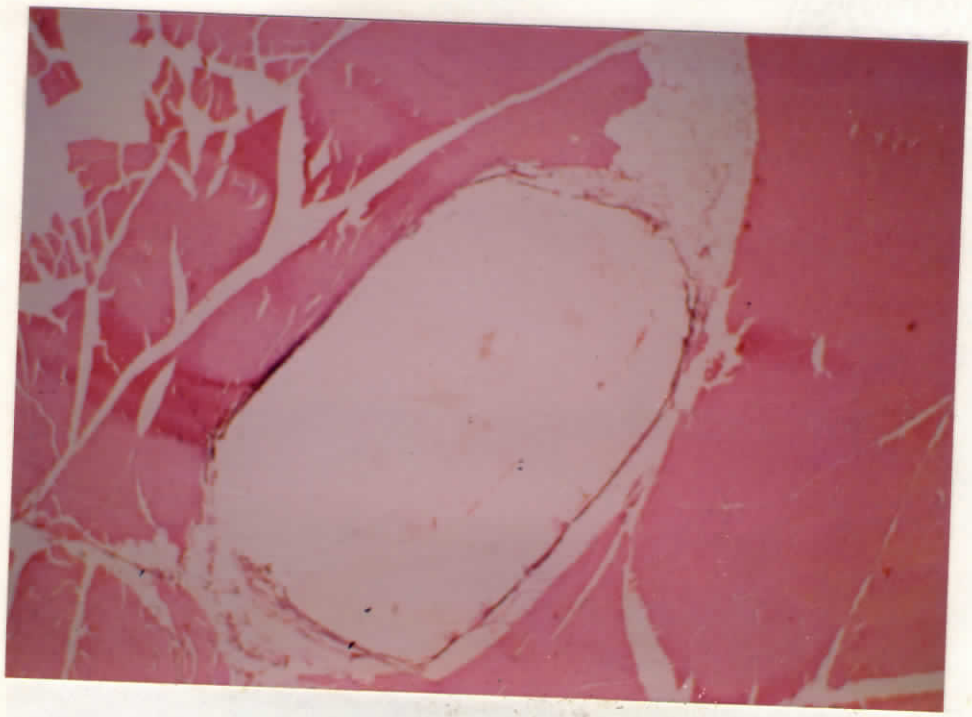
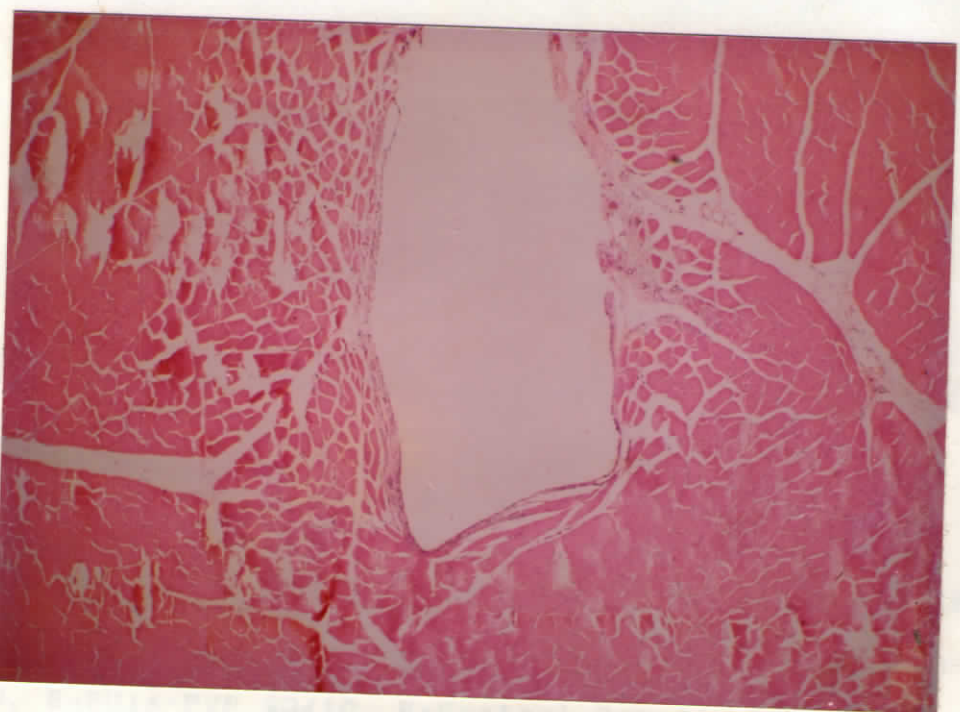


C



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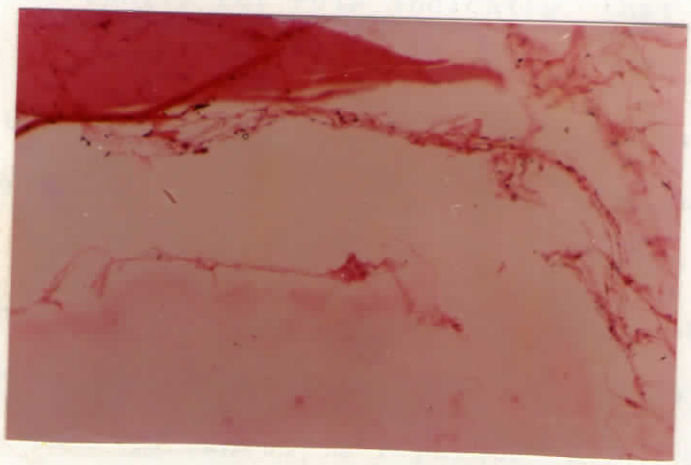
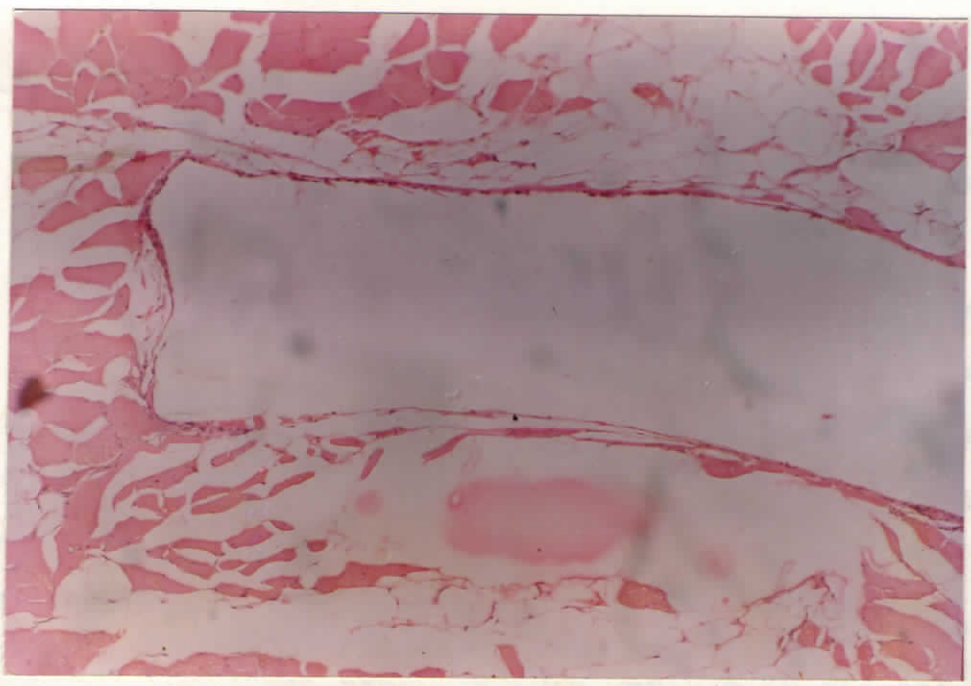


E



F

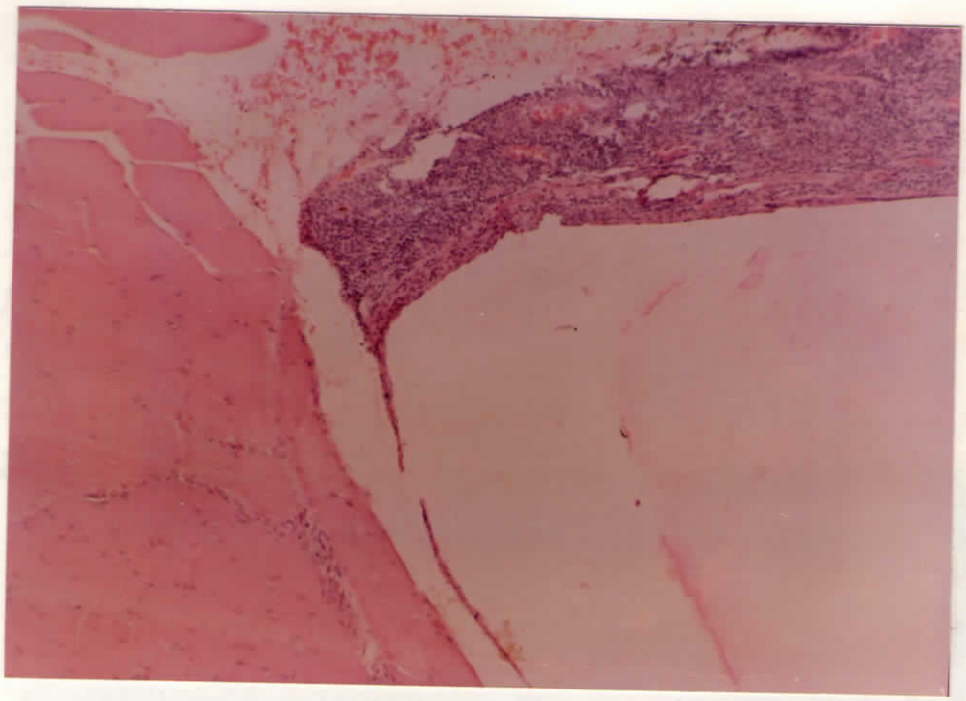
Tissue responses of polyurethanes and TDI based IPNs at
A-PU1A, B-PU1A-PMMA 90/10, C-PU1A-PAM 90/10, D-PU1A-
10, E-PU1A-PVP 90/10, F-Control Tecoflex 60D.

presence of neutrophils for PU1A indicates that PU1A could be more reactive than PU1A-PHEMA 90/10.

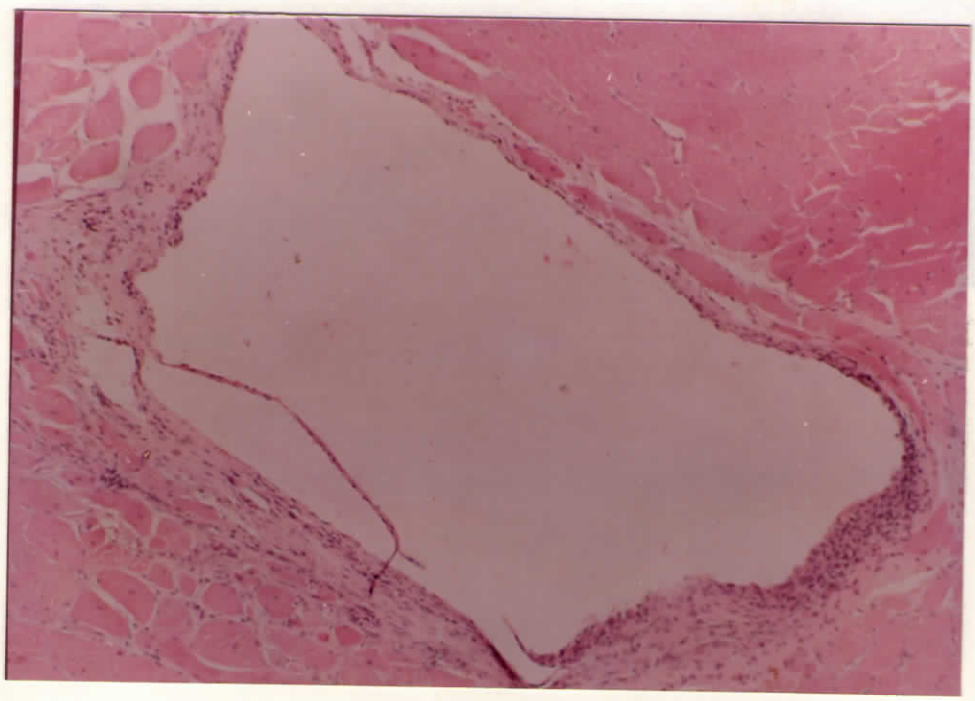
In all the cases, a thin capsule consisting of mature collagen with few fibrocytes is seen surrounding the implant. Fig.5.8(A-F) are the photomicrographs of the samples for the three month post implantation period, showing the capsule formation. The thickness of the capsule was found to vary between 20 um to 30 um. This thickness is reported (282) to be of ideal grading for biocompatibility.

5.3.2. Histopathological evaluation of MDI based IPNs:

The 7 day implantation characterising the acute inflammatory phase is more or less similar for all polymers and is detailed in section 5.3.1. 1 month post implantation study (Table 5.VI) indicate that neutrophils are absent except for a few in case of PU4A-PMMA 90/10 IPN. Macrophages and lymphocytes are observed around all the samples indicating that inflammation is still present. The rating for the inflammatory response of the MDI polymers at 1 month given in Table 5.VII indicates that the inflammatory response is more than the connective tissue response for all the IPNs except PU4A-PMMA 90/10. Though the connective tissue response with tendency to form capsule is present, the inflammatory reactions are more predominant. Fig 5.9 (A-C) depict the chronic inflammation around the MDI implants at one month.



A



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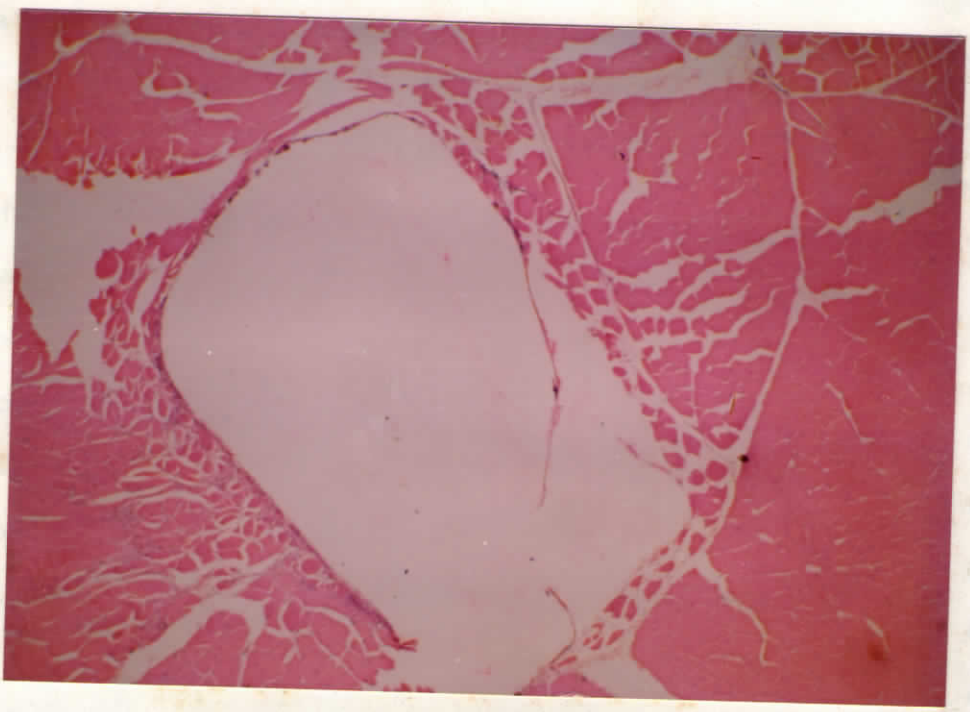


C

Tissue responses of MDI based IPNs at 1 month. A-PU4A,
90/10, C-PU4A-PHEMA 90/10.

TABLE-5.VI

ONE MONTH POST IMPLANTATION OF MDI BASED IPNS, HISTOPATHOLOGICAL EVALUATION OF ADJACENT MUSCLE

Histopatho-logy	Control	PU4A	PU4A-PMMA 90/10	PU4A-PAM 90/10	PU4A-PHEMA 90/10	PU4A-PVP 90/10
Neutrophils-A	0	0	±	0	0	0
Macrophages	2+	+	+	2+	±	0
Lymphocytes-B	+	+	+	+	2+	3+
Plasma cells	0	0	0	±	0	0
Giant Cells-C	±	0	0	0	+	0
Eosinophils-D	0	0	0	0	+	0
Fibroblasts-E	+	+	+	2+	+	+
Fibrocytes-F	2+	+	2+	+	+	+
Fatty-infiltration	0	0	0	0	0	0

TABLE-5.VII

3 MONTH POST IMPLANTATION OF MDI BASED IPNS, HISTOPATHOLOGICAL EVALUATION OF ADJACENT MUSCLE.

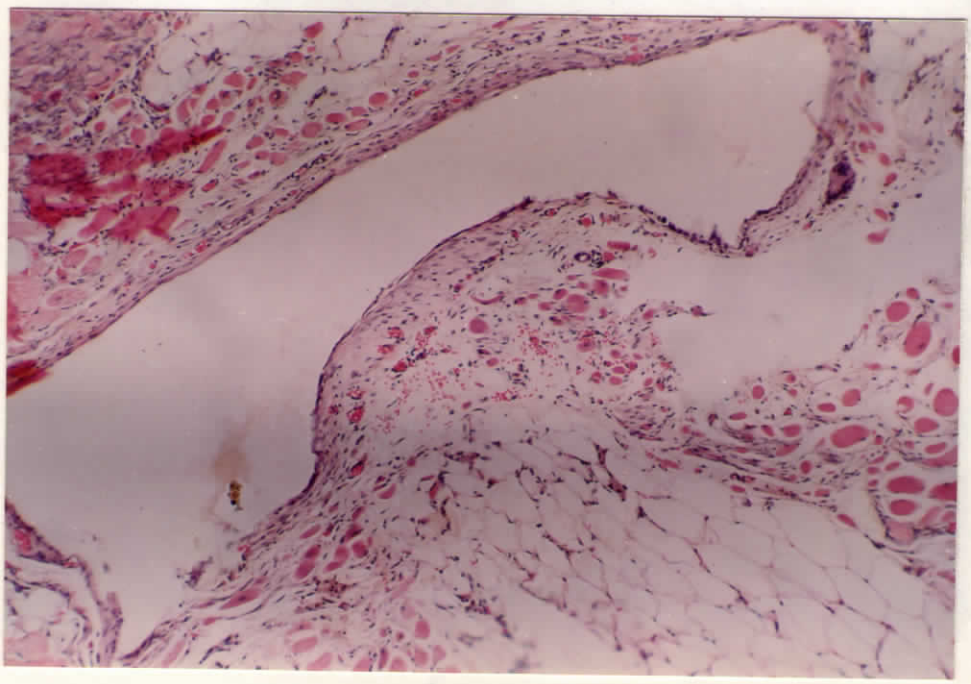
Histopathology	Control	PU4A	PU4A-PMMA 90/10	PU4A-PAM 90/10	PU4A-PHEMA 90/10	PU4A-PVP 90/10
Neutrophils-A	0	0	0	0	0	0
Macrophages	0	2+	0	0	0	0
Lymphocytes-B	+	2+	0	+	+	+
Plasma cells	0	0	0	0	0	0
Giant cells-C	0	0	0	0	0	0
Eosinophils-D	0	0	0	0	0	0
Fibroblasts-E	+	+	+	+	+	+
Fibrocytes -F	+	+	+	+	+	+
Fatty-Infiltration	+	±	0	0	+	0

TABLE-5.VIII

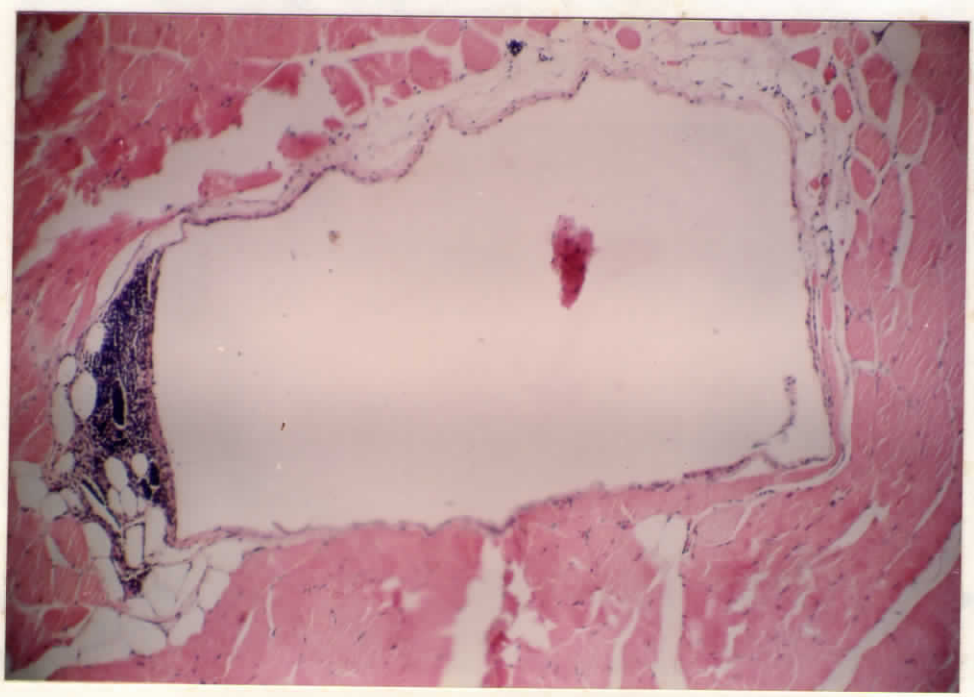
NUMERICAL RATING FOR MDI BASED IPNS

Samples	1 month implantation		3 month implantation	
	Inflammmatory response	Connec-tissue response	Inflammatory response	Connec-tissue response
Control	35	30	10	20
PU4A	20	20	40	20
PU4A-PMMA 90/10	25	30	0	20
PU4A-PAM 90/10	35	30	10	20
PU4A-PHEMA 90/10	35	20	10	20
PU4A-PVP 90/10	30	20	10	20

At the end of the 3 month period, the inflammatory responses for all the materials except the homopolymer PU4A have subsided and a thin capsule is laid down Fig.5.10(A-D). Mean thickness of capsule is around 30 um so the materials can be termed to be biocompatible as in case of TDI based IPNs. The responses given in Table 5.VII indicate that some lymphocytes remain in case of all samples except PU4A-PMMA 90/10 IPN even after 3 months. Lymphocytes are round 5-10 um cells derived both from the bone marrow and from lymph nodes.They are characteristically present at



A



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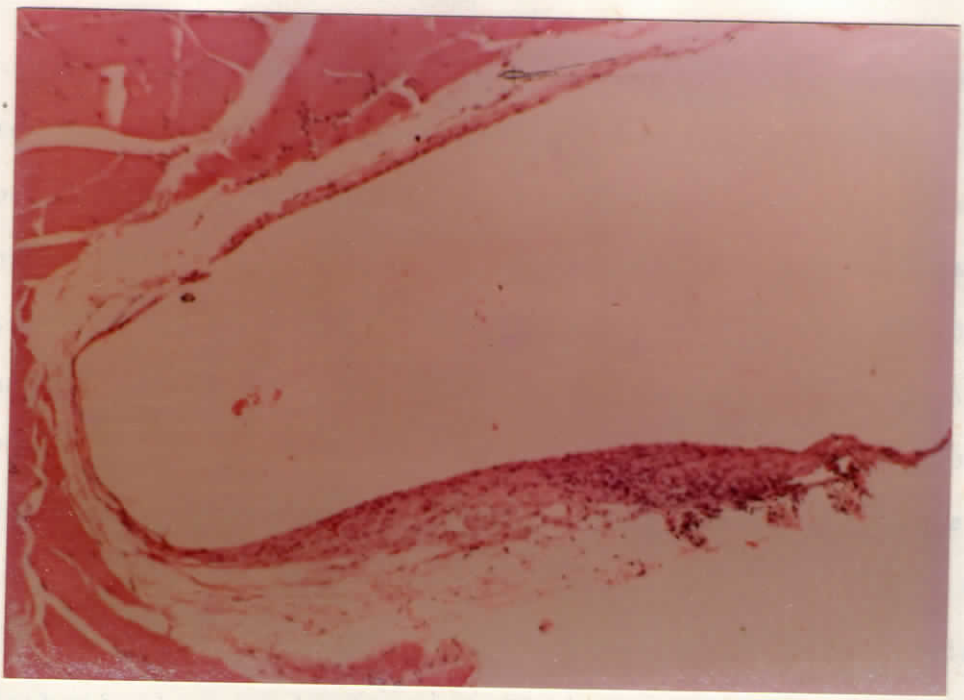

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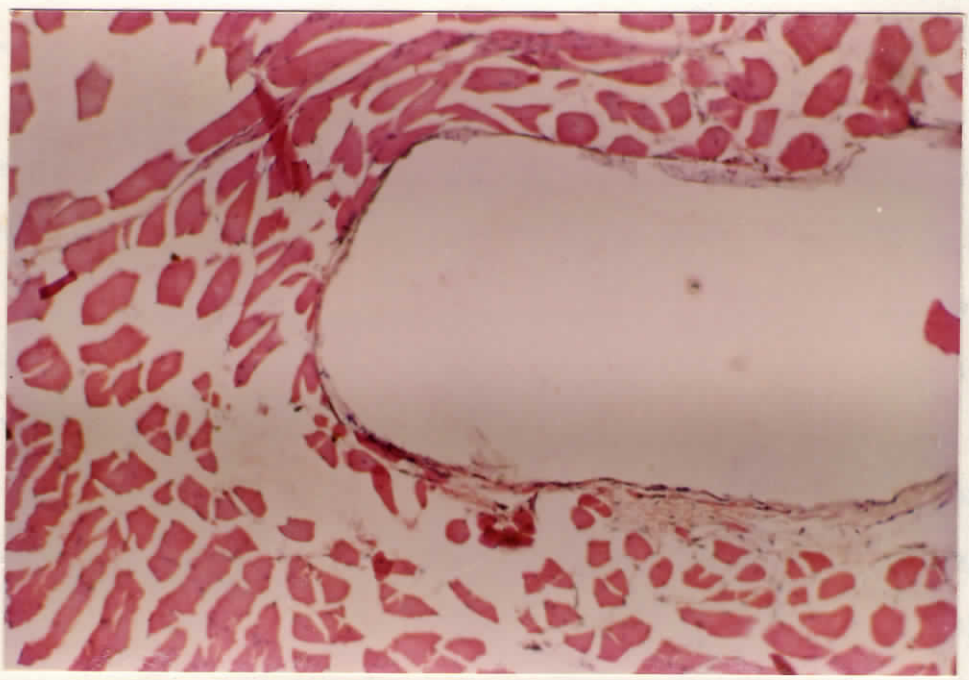

D

Fig. 5.10: Tissue responses of MDI based IPNs at 3 months.
A-PU4A, B-PU4A-PMMA 90/10, C-PU4A-PHEMA 90/10, D-PU4A-PVP
90/10.

sites of chronic inflammation (282) with small numbers of lymphocytes being present at sites of resolving injury. Large collections of lymphocytes are usually characteristic of immunological injury . Implants having antigenic properties eg amino acids are also known to elicit the presence of lymphocytes(282). The presence of lymphocytes at the MDI polyurethane PU4A and IPNs PU4A-PHEMA 90/10 and PU4A-PVP 90/10 could be due to some minor degradative product. The increased stiffness of the MDI IPNs could also facilitate the lymphocyte migration at the edges of the implant site as is observed in the present case,Fig.5.10(A-D). As both the control and MDI polymers could show minor degradations,(section 5.2), the lymphocytes are seen in both cases. The MDI are therefore not as biocompatible as the TDI IPNs. However, their biocompatibility is comparable with that of a control biomedical grade polyurethane. The response ratings at the end of 3 months (Table 5.VIII) show that except for PU4A-PMMA 90/10 IPN all the MDI IPNs are similar in their responses.

5.3.3. Influence of material properties on the histological response:

The role of material properties in the determination of histological response is rather unclear, though some reports exist (67, 119) on the role of surface topography or shape of implant.

Of the various theories (65-70) proposed for blood compatibility evaluations, the minimal interfacial energy hypothesis (70) seems to have gained widespread acceptance going by the number of

materials prepared utilizing this concept. According to this concept, the interfacial free energy of the material surface should be 0. This concept has however, not been correlated to invivo tissue responses. The 3 month post implantation histological responses of the TDI based IPNs indicate that PU1A-PVP 90/10 and PU1A-PMMA 90/10 IPNs are most inert and PU1A-PAM 90/10, PU1A-PHEMA 90/10, PU1A are slightly bioreactive. The surface properties of the TDI IPNs as discussed in section 3.7 indicate that PU1A-PMMA 90/10 IPN is the most hydrophobic and PU1A-PVP90/10 IPN is the most hydrophilic while PU1A-PAM 90/10 IPN, PU1A-PHEMA 90/10 IPN and PU1A are having intermediate hydrophobicity or hydrophilicity. The interfacial energy of the PU1A-PMMA 90/10 IPN (section 3.7) is 5.674 dyn/cm. Hence the requirement for blood compatibility that interfacial free energy (γ_{sw}) should be 0 may not have much significance for the correlation of tissue responses. Moreover, PU1A-PAM 90/10 and PU1A-PHEMA 90/10 with rsw of 1.619 dyn/cm and 1.633 dyn/cm respectively are relatively more reactive than PU1A-PMMA 90/10. It could therefore be speculated that the relative hydrophobicity or hydrophilicity of the surface may be a more important factor determining the tissue response. In the case of intermediate hydrophobicity or hydrophilicity, other factors may also come into play in determining the tissue response. Some neutrophil is observed (Table5.IV) with PU1A during 3 months, Woodward et al (283) also have observed neutrophil infiltration for weeks after subcutaneous deposition of methyl 2 cyanoacrylate. The presence of

the neutrophils have been attributed (282)to be from a variety of circumstance eg. infection, degradation of biomaterials or extensive necrosis of tissue due to other causes. The PU1A undergoes some degradation as discussed in section 5.2.1. The emergence of the neutrophils for PU1A could therefore be due to this degradation. The increased connective tissue response rating of 40 observed for PU1A at 3 months (Table 5.V) could be aimed at encapsulating the material more efficiently. PU1A-PHEMA 90/10 also shows minor degradation and has a total inflammatory response rating of 30 at 3 months (Table 5.V) is PU1A-PHEMA 90/10. PU1A-PHEMA 90/10 is the sequential IPN which is synthesised by swelling the polyurethane with HEMA monomer as discussed in Chapter II. The swelling process increases the volume fraction of the material due to the dimensional changes involved. Though subsequent polymerisation, curing and extraction methods result in shrinkage, the resultant pore size of the PU1A-PHEMA 90/10 materials would be different from that of the other materials. Pure polyHEMA material though very biocompatible (284) has also been known to elicit tumorogenesis and calcification (285) when used in porous form.The increased inflammatory response for PU1A-PHEMA 90/10 IPN could thus be a result of the altered porosity and the minor degradation.

The order of inertness for the TDI based IPN materials taking into account all the above mentioned factors could therefore be PU1A-PMMA 90/10 = PU1A PVP 90/10 > PU1A-PAM 90/10 > PU1A -PHEMA 90/10 > PU1A.

In case of the MDI based polymers as discussed in section 5.3.2., lymphocytes are observed at the 3 month period. which is attributed to the slight degradation of the PU4A and its IPNs (section 5.2.2) The rating response is similar for all the MDI IPNs (Table 5.VIII) probably due to the influence of this degradation. Moreover, the connective tissue response rating is not increased for more encapsulation. No attempt has therefore been made to predict the trend of inertness for these IPNs. However, owing to the presence of these lymphocytes in general, the MDI polymers can be termed less compatible than the TDI polymers.

SUMMARY AND CONCLUSIONS

CHAPTER-VI

6.1. Summary and Conclusion:

The thesis comprises the author's efforts to synthesise and evaluate polyurethane based interpenetrating polymer networks for biomedical applications. Interpenetrating polymer networks (IPNs) of polyurethane and vinyl polymers having varying relative hydrophobicity and hydrophilicity have been synthesised. The IPNs synthesised are polyurethane-polymethylmethacrylate,(PU-PMMA polyurethane-acrylamide (PU-PAM), polyurethane polyvinylpyrrolidone (PU-PVP) and polyurethane-poly 2-hydroxy ethylmethacrylate (PU-PHEMA). Different polyurethanes were prepared by varying the polyols, isocyanates and the NCO content. Varying combinations of weight of polyurethane and vinyl polymers were used to prepare the different IPNs. The chapter II comprises the details of the synthetic procedures and the experimental details of the characterisation. The procedures used to study the invitro blood compatibility and stability and in vivo biocompatibility and biostability are also discussed.

Chapter III summarises the results and discussion of the characterisation of the synthesised IPNs. The IPNs were found to be quite stable in a wide range of solvents.The infra red spectra and NMR spectra demonstrated that there was no chemical interaction between constituent networks.The mechanical properties of the IPNs were seen to be influenced by extent of crosslinking of

polymer 1, molecular weight and nature of polyols, type of isocyanate and composition of polymer 2. Phase mixing, phase separations and interfacial region contributions could influence the mechanical properties. The MDI based IPNs had superior mechanical properties in comparison to the TDI based IPNs. Incorporation of 10 wt % of vinyl monomers itself can give IPNs of superior and consistent mechanical properties. Among the different 90/10 IPN of both MDI and TDI system, the PU-PMMA 90/10 IPN emerged as the one with the best mechanical properties followed by PU-PAM and PU-PHEMA IPNs. The PU-PVP 90/10 IPN had the least mechanical properties in both MDI and TDI system. However, in the MDI system, the tensile stress values for PU4A-PVP IPN were more than that for the homopolymer PU4A and this has been attributed to the formation of a lamellar like structure for the PU4A-PVP IPN. Synergism of ultimate tensile stress of the constituent polymer networks was observed for almost all IPNs.

The results of the dynamic mechanical analysis of the 90/10 IPNs are dealt with in section 3.5. The loss tangent obtained for the both TDI and MDI based IPNs was a single broad peak which was obtained at a temperature intermediate to the glass transition temperatures of individual homopolymers. The loss tangent shifted when the composition of the IPNs were varied. A phase inversion was observed at 70 wt% of polyurethane in PU-PMMA IPNs. The storage modulus values for all IPNs except the TDI based PU1A-PVP 90/10 IPN showed an increase over the storage modulus value of the respective polyurethane. This was attributed to the

increase of packing density obtained on IPN formation. The dynamic mechanical analysis studies therefore served to indicate the IPN formation. The glass transition behaviour was also studied by DSC and results summarised in section 3.6. The 90/10 IPNs of TDI based PU1A and MDI based PU4A were determined to be compatible IPNs. On increasing the concentration of the second monomer, the compatibility was observed to decrease without extensive phase separation. The thermogravimetric analyses showed a clustering of curves for the IPNs. No significant increase of thermal stability was observed, but the clustering of the curves indicated the close juxtaposition of the two networks usually obtained on IPN formation.

The air-water and octane-water contact angle of the 90/10 IPNs were estimated to obtain relative hydrophobicity or hydrophilicity. The MDI based IPNs were relatively more hydrophilic than the TDI based IPNs. The PU-PMMA IPNs were found to be relatively most hydrophobic followed by PU-PAM IPN, PU-PHEMA and PU-PVP IPN. The surface energy parameters were evaluated for the IPNs. It was observed that except in case of PU-PMMA IPN, the interfacial free energy of all the IPNs tended towards 0. The crosslink density of IPNs showed an increase on IPN formation in most of the cases. The morphology determined by SEM showed phase mixing in case of the PU-PMMA IPNs of TDI and MDI indicating enhanced compatibility of the polyurethane and PMMA networks. Other IPNs showed varying degrees of compatibility. It was also observed that an increase of the second

component led to more phase separation. The 90/10 IPNs were found to be radiation resistant on sterilization with γ rays.

Chapter 4 comprises the results of the invitro studies which were carried out to estimate the blood contacting potential of the 90/10 IPNs. The results of the recalcification time test indicated a prolonged recalcification time for almost all IPNs indicating the nonthrombogenic behaviour. The nonthrombogenicity was comparable and in some cases even better than a control biomedical grade polyurethane. Haemolysis studies indicated the non haemolytic nature of the IPN materials. Platelet aggregation of plasma exposed to the IPN materials was estimated. With the exception of the MDI polyurethane PU4A and PU4A-PMMA 90/10 IPN, all the other IPNs could be considered as candidates for potential blood contacting applications on the basis of invitro tests. In vivo tests in blood contacting sets would be required to estimate the actual blood contacting potential. Chapter IV also deals with stability of the materials on storing in a simulated physiological fluid of phosphate buffered saline for one month. The materials were found to be unaffected by the aqueous environment.

In Chapter V, the results of the toxicological studies and the invivo implantation procedures are discussed. The acute systemic injection test in mice showed no signs or symptoms suggestive of systemic toxicity upto 7 days. Intracutaneous irritation test carried out in rabbits did not elicit significant erythema, oedema or necrosis suggestive of cutaneous irritation. The two

tests therefore served to indicate the nontoxic nature of the IPN materials.

Biostability of the IPN materials were assessed by implanting strips of the 90/10 IPNs in subcutaneous pouches of wistar rats and evaluating the changes of mechanical properties. The mechanical property changes were mostly due to plasticization by water and biological molecules. However some minor degradation was observed in case of the TDI based polyurethane as well as the PU-PAM and PU-PHEMA IPNs. The rest of the IPNs were quite stable in biological environment. The biostability of TDI based IPNs were also seen to be superior to the MDI based IPNs.

Histopathological studies of the tissues in which the IPN materials were implanted for a period of 3 months, were carried out. Necrosis of tissues is evident at 7 days in common with most other biomedical polymers. However, by the end of 3 months, reactions of inflammation had subsided and a repair process which begun by about 1 month completed. The materials were thus all encapsulated by a thin capsule which could indicate the biocompatible nature of the IPNs. Differences in the individual tissue reactions were rated using a numerical system. The TDI IPNs in general were more inert than the MDI IPNs. Among the TDI IPNs, the PU-PVP 90/10 IPN, which was relatively the most hydrophilic, and PU-PMMA 90/10 IPN which was relatively the most hydrophobic emerged as the most inert materials. Other TDI IPNs had intermediate tissue responses. The differences in the tissue reaction were attributed to a simultaneous interplay of the relative

hydrophobicity and hydrophilicity and any accompanying degradative process.

In conclusion, several IPNs have been synthesised and assessed for their physicochemical characteristics and biocompatibility aspects. These could be utilized for use as biomaterials according to the appropriate response required. For requirements of more inertness, the TDI based PU1A-PVP 90/10 IPN and PU1A-PMMA 90/10 IPN are suggested, with PU1A-PMMA 90/10 IPN as a more tough material and PU1A-PVP 90/10 IPN as a soft material.

6.2 Scope and Future work :

The study indicates that IPNs can be tailor made with specific properties for specific biocompatibility requirements. The future work on these IPNs is mainly concerned with the applications to which they would be utilized. Permeability characteristics of the IPNs are to be carried out before they could be used in extracorporeal devices. Other parameters to be standardized are the processing parameters. Further, though the blood contacting characteristics are favourable, for use as vascular grafts, more experiments of invivo blood contacting applications are to be carried out. This is mainly to assess the blood contacting potential under flowing conditions and in a complex biological environment. However, the IPNs could be used as such for soft tissue contacting applications.

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APPENDIX

APPENDIX-A

A.1 ACD :

Trisodium citrate = 2.2 g

Citric acid = 0.8 g

Dextrose = 2.5 g

Dissolved in 100ml of distilled water, ph = 5 to 5.1

A.2 Tris buffer. HCl :

Dextrose = 1.000 g

Magnesium chloride = 0.199 g

Potasssium chloride = 0.402 g

Sodium chloride = 8.120 g

Trizma base = 1.756 g

Calcium chloride = 5.5 mg

Dissolved in 900 ml distilled water, ph adjusted to 7.4 by dil.HCl, made upto 1 litre.

A.3 Phosphate buffered saline (0.15M) :

Disodium hydrogen phosphate.$2H_2O$ = 21.42 g

Sodium dihydrogen phosphate.$2H_2O$ = 4.689 g

Sodium chloride = 8.599 g

Total volume made up to 1 litre by dissolving in distilled water, ph = 7.4.

APPENDIX-B

PUBLICATIONS FROM THIS THESIS :

1. Mechanical Properties of polyurethane-polyacrylamide IPNs
   Acta Polymerica in press.

2. Polyurethane-Polyacrylamide IPNs 1. Synthesis and characterisation.
   J. Polym. Sci. Polym. Chem. ed. 1990, 28(13), 3775.

3. Studies on the histocompatibility of interpenetrating polymer networks.
   Accepted in Biointeractions'90, 21-23rd Aug. 1990, Oxford,U.K.

4. Hydrophobic-hydrophilic IPNs for biomedical applications
   Proceedings of Polymer'91 conference, India, Tata-McGraw Hill, 1991, Vol 2, 1003.

APPENDIX-C

LIST OF ABBREVIATIONS :

PU - Polyurethane

PTMG - Polytetramethylene glycol

PPG - Polypropylene glycol

TDI - Toluene diisocyanate

MDI - Diphenyl methane diisocyanate

TMP - Tri methylolpropane

PU1A - Polyurethane of PTMG(molecular weight=1010),TDI,TMP
NCO/OH = 1.09

PU1B - Polyurethane of PTMG(molecular weight=1010),TDI,TMP
NCO/OH = 2.01

PU2A - Polyurethane of PTMG(molecular weight=2000),TDI,TMP
NCO/OH = 1.09

PU2B - Polyurethane of PTMG(molecular weight=2000),TDI,TMP
NCO/OH = 2.01

PU3A - Polyurethane of PPG(molecular weight=2000),TDI,TMP
NCO/OH = 1.09

PU3B - Polyurethane of PPG(molecular weight=2000),TDI,TMP
NCO/OH = 1.68

PU4A - Polyurethane of PTMG(molecular weight=1010),MDI,TMP
NCO/OH = 1.09

PAM - Polyacrylamide

PMMA - Polymethylmethacrylate

PHEMA- Poly 2-hydroxyethyl methacrylate

PVP - Polyvinylpyrrolidone

BOP - Benzoyl peroxide

AIBN - Azobisisobutyronitrile

DBTL - Dibutyl tin dilaurate

EGDMA- Ethylene glycol dimethacrylate

IR - Infrared spectroscopy

DMA - Dynamic mechanical analysis

DSC - Differential scanning calorimetry

TGA - Thermogravimetric analysis

DTG - Differential thermogravimetry

SEM - Scanning electron microscopy

ADP - Adenosine di phosphate

ACD - Acid citrate dextrose

μM - Micromoles