STUDIES ON THE RADIATION GRAFTING OF HYDROPHILIC MONOMERS ONTO PLASTICIZED POLY (VINYL CHLORIDE) TO PREVENT PLASTICIZER MIGRATION

A thesis presented

by

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CERTIFICATE

I, Kalliyana Krishnan V, hereby certify that I had personally carried out the work depicted in the thesis entitled "STUDIES ON THE RADIATION GRAFTING OF HYDROPHILIC MONOMERS ONTO PLASTICIZED POLY (VINYL CHLORIDE) TO PREVENT PLASTICIZER MIGRATION" except where external help sought are acknowleged.

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Date: 07-11-1990

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DECLARATION

This is to certify that Sri. Kalliyana Krishnan, V. in he Division of Polymer Technology of the Sree Chitra Tirunal nstitute for Medical Sciences and Technology, has fulfilled the equirements of regulations relating to the nature and prescribed eriod of research for the Ph.D degree of that Institute. The ork relating to his thesis entitled "STUDIES ON THE RADIATION RAFTING OF HYDROPHILIC MONOMERS ONTO PLASTICIZED POLY(VINYL LORIDE) TO PREVENT PLASTICIZER MIGRATION" was carried out under ur joint supervision.

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entitled

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KALLIYANA KRISHNAN V.

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SYNOPSIS

The phenomena of plasticizer migration from flexible poly(vinyl chloride)(PVC) based devices used in medical applications has been the subject of numerous investigations (50, 52, 81). The safety of using low molecular weight organic plasticizers such as di(2-ethylhexyl) phthalate (DEHP) to impart flexibility and better low temperature properties to PVC used in medical applications has been questioned (86, 123). DEHP has been reported to cause adverse effects in the pitutary gland and in the liver (71, 125). It has also been reported to be a potential carcinogen (68, 44). Different attempts have been made by earlier workers either to prevent or to retard the plasticizer migration from flexible PVC. This includes glow discharge treatment of PVC and the use of alternate plasticizers (3, 18). This thesis deals with the studies on the effect of grafting hydrophilic monomers using radiation from a Co^{60} source onto medical grade PVC sheetings to prevent or retard plasticizer migration. The suitability of such modified migration resistant PVC in medical applications has been investigated.

The introductory chapter reviews the various aspects of plasticizer migration from PVC based medical devices and the toxicological problems associated with the migration of DEHP. It critically reviews the various techniques used for graft

modification of polymers with particular emphasis on PVC as the trunk polymer. The rationale of using gamma radiation grafting of hydrophilic monomers onto flexible PVC to prevent or retard the migration of low molecular weight plasticizers such as DEHP is also outlined in this chapter.

Chapter II describes the various experimental methods and materials employed during the course of this investigation. This includes purification of the monomers, the grafting procedure, characterization of the graft polymer using gravimetric, spectrophotometric, electron microscopic and contact angle methods, methods employed for quantifying the migration of the plasticizer DEHP into organic solvents as well as physiological media such as plasma, and the mechanical, optical and medico-biological properties of the migration resistant PVC sheetings.

Chapter III deals with the results obtained on the grafting of hydrophilic monomers such as 2-hydroxyethyl methacrylate [HEMA], N-(vinyl pyrrolidone)[NVP] and methacrylic acid [MAA] in different combinations and proportions onto flexible PVC using gamma radiation of various doses. The effect of monomer concentration and the radiation dose on the graft yield are discussed. Results obtained by using different monomer combinations in various proportions are also discussed. The advantages of carrying out the grafting reaction in the presence of small concentrations of Cu^{2+} in the grafting medium to prevent

the homopolymerization of monomer combinations such as HEMA and NVP are described. Atomic absorption estimation of residual Cu^{2+} was carried out to demonstrate that the metal ion in the graft polymer is within safety limits. Results on the characterization of the graft polymer using ATR-IR spectroscopy and scanning and optical photomicroscopy are also included in this chapter.

Evaluation of the surface energy parameters and estimation of the mechanical, optical and water absorption characteristics of the graft polymer in comparison with control ungrafted PVC are dealt with in Chapter IV. The polar and dispersion components ($\gamma_{s,v}^{p}$) and ($\gamma_{s,v}^{d}$) of the surface free energy ($\gamma_{s,v}$) have been evaluated using air-in-water and octane-in-water contact angle techniques. The drastic increase in the polar component and the corresponding decrease in the dispersion component values of the surface free energy of the graft modified PVC indicated the highly hydrophilic nature of the modified polymer. The mechanical properties estimated include tensile strength, elongation and hardness of the grafted sheets in the dry and the hydrated states again in comparison with unmodified control sheets. The results with sheets grafted on both sides as well as on one side are compared. The values obtained demonstrated that graft modification does not affect the mechanical properties in a significant manner. Water of hydration in the in graft polymer was estimated in order to assess the water absorptivity of the

grafted PVC. The percentage transmission of light in the 700-350nm region of the graft modified PVC sheetings has been found to be comparable with unmodified control sheets.

Chapter V deals with the thoroughly investigated migration studies of the plasticizer DEHP from the graft modified PVC sheets into potential extractant media. The media selected include organic extractants such as n-hexane, n-heptane and n-octane and biological extractants such as Cotton seed oil and Polyethylene glycol-400. Migration experiments were carried out using bags specially fabricated for this purpose. Such bags were filled with the monomer solutions and irradiated to the requisite doses to effect grafting only on the inner surface. PVC graft modified using a 5 vol% of NVP/HEMA showed the maximum reduction in the migration of DEHP into all organic extractants. The migration into n-hexane, a potential organic extracant was found to be less than 4% of the migration from unmodified control bags over a period of 5 h at 30°C. Most significantly, no plasticizer migrated into a USP recommended simulated biological extractant such as cotton seed oil over a period of 96 h at 70°C from the graft modified PVC bags. However, in polar media such as methanol and PEG 400, the reduction in migration was not as pronounced as observed in the case of hydrocarbon solvents or cotton seed oil. Attempts have been made to explain these observations based on the results. The effect of sterilization of the graft modified

PVC bags using gamma radiation as well as steam on the migration of plasticizer has also been investigated. The results demonstated that the above sterilization methods could be successfully adopted for the graft modified migration resistant bags.

Chapter VI contains the results of the platelet aggregation studies and migration work done using bovine and human plasma. The platelet aggregation induced by ADP in plasma stored in control and grafted bags was monitored by a spectrophotometric technique. The nature of platelet aggregation in bovine plasma stored in control and grafted sheets activated by agonists such as ADP were different and the grafted sheets tended to show better blood compatible properties compared to control. The migration of plasticizer into plasma stored in grafted bags also was found to decrease several folds compared to plasma stored in ungrafted bags.

In Chapter VII the conclusions derived from this investigation are listed and discussed. Considerable amount of work has been reported in the literature on the graft modification of PVC resin inorder to change the physical and mechanical properties of the polymer. However, no attempt seems to have been made by previous workers to graft hydrophilic monomers onto PVC in an effort to prevent or retard the migration of the low molecualr weight plasticizer such as DEHP from

flexible PVC used in medical applications. Use of high molecular weight plasticizers and glow discharge surface modification of PVC have been suggested in the literature to tackle the problem of plasticizer migration in PVC used in medical applications. Nevertheless, while the use of high molecular weight plasticizers is not a cost effective proposition, methods such as glow discharge treatment of the finished product is not a commercially feasible alternative on a large scale. Furthermore the physical and mechanical properties of PVC are drastically affected by such procedures. The grafting of hydrophilic monomers onto PVC using gamma radiation investigated and reported in this thesis provides a simple, reliable and reproducible technique to prevent or retard the migration of toxic plasticizers such as DEHP from PVC based medical devices. The work reported in this thesis is expected to offer a potential solution to the problem of plasticizer migration and its associated toxicologial implications in PVC based medical devices.

INTRODUCTION

CHAPTER I

INTRODUCTION

I.1. Role of Polymers in Medicine:

Polymers find a large number of applications in medicine (7, 8, 134). They are used in various forms such as films or sheets, moulded or extruded articles, foams and even fibres and woven structures. Poly(vinyl chloride), polyethylene, and polypropylene films are used in blood storage applications. They are also used for a wide variety of tubings and mouldings such as syringes, forceps, seals and connectors along with other polymers such as polycarbonates, polystyrene and nylons. Polyurethane and polyethylene foams are used for surgical dressings and supports. In addition, many prosthetic devices are made from polymers such as polyesters, polyacetals, polyurethanes, silicones, poly(methyl methacrylate) and poly(tetrafluoro ethylene).

The major use of polymers in hospital supplies is in the area of pre-sterilized disposable products. Disposables are desirable because they reduce the danger of transmitting infection from one patient to another. In 1985, approximately $4.4 billion was spent for medical disposable products in the United States alone (38). The plastics industry has estimated that disposables account for 80% of the medical market for

plastics. Great progress has also been made in developing biocompatible polymers ie., polymers that can co-exist with living tissue or with blood without causing thrombosis or without generating a reaction. The total world market for polymeric implants and artificial organs has been estimated to be 3 to 4 billion dollars (20).

I.1.1. Types of Medical Devices:

The various medical devices available in the market can be divided into different categories (24) depending on their mode of application. These include:

(a) Products included for long term implantations within the body tissues (e.g. artery grafts, hip prostheses)

(b) Products for long term contact with mucosal surfaces or conjunctiva (e.g. dentures, contact lenses)

(c) Products meant for short term use within the body or in contact with mucosal surfaces (e.g. endotracheal tubes, urological catheters)

(d) Products intended to be in long term contact with the skin (e.g. prosthetic legs)

(e) Products used to contain or administer substances, including blood and blood products to be introduced parenterally into the body, but not themselves making contact with the recepient's body tissues (e.g. hemodialysis unit, blood bags).

I.1.2. Criteria for Polymers to be used in Medical Applications:

Materials for biomedical applications differ from those used in other applications. In biomedical applications, one should consider not only the requisite mechanical and physical properties but also their influence on biological environment. Conversly, the influence of the biological environment on the materials themselves must be considered. The basic specifications for biomedical materials (122) can be summarized as follows:

(1) Intrinsic properties of materials:

(a) functional performance (e.g. permeability)

(b) structural performance (e.g. mechanical properties)

(c) adaptability of shape

(d) durability

(e) suitability for sterilization

(2) Influences of the biological environment:

(a) Resistance to biodegradation, especially by enzymatic hydrolysis.

(b) Resistance to chemical degradation, especially by water, salts, oxidants etc.

(c) Resistance to physical degradation as a result of stresses.

(3) Effect on the biological environment:

(a) Should not contain leachable toxic substances.

(b) Not cause allergic reactions or inflammation.

(c) Should be non-carcinogenic

(d) Should be non-thrombogenic.

(e) Should not cause denaturation of body proteins or interfere with normal cell structure.

(f) Should not produce degradation products

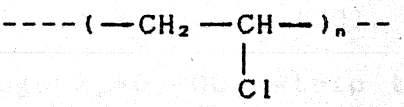
A major advantage that plastics materials have been able to provide to the medical profession is that it has become possible to use containers and other devices which are unbreakable, flexible and sterile all at the same time. Another major innovation, is the provision of 'one trip' or disposable devices which greatly reduce the risk of infection as well as abolishing the need for the time and labour spent in cleaning and sterilizing re-usable devices.

I.2. Role of Poly(vinyl chloride)(PVC) in the Biomedical Field:

I.2.1. Advantages of PVC:

Flexible PVC has assumed a leading position among plastics materials used for one trip medical products because of its economic and design advantages. It is a material of choice due to lower cost, greater availability or improved performance. It is a versatile polymer used in flexible, semi-rigid or rigid form. PVC resin is so amenable to widespread property modification that it accounts for the number one position in overall product volume and number of applications. PVC is produced by the polymerization

of vinyl chloride and has the structure:



Structure of Poly(vinyl chloride)/(PVC)

I.2.2. Applications of PVC in Medicine:

PVC is used for a variety of medical applications. It was first used in the United Kingdom for tubings in blood administration sets as long ago as 1958 (6). In this initial application, PVC tubing replaced glass and rubber. Because it was transparent, it could be seen to be clean and the flow of the liquid could be observed. The administration sets could be supplied as presterilized disposable packs, and from this a reduction was noted in the incidence of thrombophlebitis arising during blood administration (6). As a result, flexible PVC mouldings and extrusions became readily acceptable for a whole range of applications including heart-lung machines, hemodialysis apparatus, blood transfusion sets, catheters, endotracheal tubes, suction and drainage tubing and enema packs. Calendered PVC sheet is fabricated into bags used for storage of a variety of liquids including blood and intravenous solutions. On the whole, many of the life support systems in our hospitals are dependent upon the ready availability of flexible vinyls. Without flexible vinyls, many of these devices will not exist. Data indicate that about

87,000 metric tonnes of PVC polymer was used in medical applications in US in 1976 out of a total consumption of 4,82,000 metric tonnes of all polymers (79). Its use is expected to increase to a huge 2,40,000 metric tonnes by 1990.

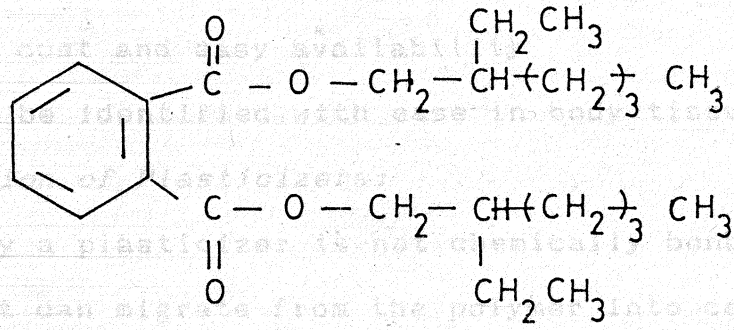
I.2.3. Role of Additives in PVC Compounding:

Plastics, apart from high polymers also contain oligomers, monomers and particularly additives. Formulation of any PVC compound requires incorporation of several additives to the basic PVC resin in order to enable it to be processed satisfactorily into a finished product of desired properties(80). These additives include plasticizer, stabilizer and lubricant. The plasticizers are mainly added to the resin to induce flexibility. Stablizers are added for inducing thermal stability and lubricants for easy processability. All these ingredients have to satisfy the requirements of medical device regulating agencies (For eg. the Food and Drug Administration [FDA] in the U.S.A.) regarding their suitability with respect to toxicological and other appropriate properties. As a result, the formulation of all flexible PVC in use today for medical applications is based on a very restricted range of additives as opposed to PVC used in general purpose applications.

I.2.3.1. Role of Plasticizers:

Of all the additives required in a flexible PVC compound, the plasticizer is the one which is present in the greatest

concentration ranging from 15% to 50%. Phthalates, citrates, phosphates, sebacates etc. are some of the common plasticizers used in the PVC industry (111). However, monomeric phthalate esters are commonly used in medical applications due to various reasons (6). The range of suitable phthalates has greatly been reduced over a period of years due to doubts about their toxicity. The octyl phthalates are preferred more in medical PVC plastics. Of these, di-(2-ethylhexyl) phthalate [DEHP] is the one which is commonly used (130). It has an outstanding record of over 40 years of service in some of these critical applications. It has the structure:



(DEHP)

1.2.3.2. Market for Plasticizers:

It is estimated that the annual production of phthalate esters in the U.S. alone is about 2,000,000 tons and that of DEHP is about half of this amount (92). It is also reported that 60 million pounds of phthalates are used in FDA regulated applications alone. These applications include food wraps, medical devices etc (88).

I.2.3.3. Advantages of DEHP:

DEHP is considered to be synonymous with bis(2-ethylhexyl) phthalate and has also been referred to as dioctyl phthalate (10, 123). It has a molecular weight of 391, a factor that is of some importance in so far as its toxicity is concerned. It has a low vapour pressure and has a boiling point of 387°C. The advantages of using this phthalate plasticizer (6, 123) in PVC medical applications are listed below:

(a) Most inert plasticizer currently available

(b) Provides optimum properties to PVC

(c) Available in highly pure form commercially.

(d) Low cost and easy availability

(e) Can be identified with ease in body tissues.

I.2.4. Migration of Plasticizers:

Generally a plasticizer is not chemically bonded to the polymer and it can migrate from the polymer into certain materials in contact with it. This is especially true for plasticizers that are incorporated in PVC, the loss of which makes the resin inflexible. Effectively, plasticizers behave as low volatile solvents for the resin. The 'permanence' of a plasticizer is determined (25) by a) its solvent properties vis-a-vis the resin and b) loss due to volatalization, extraction and by other means. This is physically manifested by movement of the plasticizer from the bulk of the resin to its surface and the

loss from the surface into the surrounding medium. In the field of medical applications, oily substances, such as the contents of the digestive system and blood or plasma are capable of extracting monomeric plasticizers from PVC tubings or collection sets (86). These plasticizers have also been reported to be readily soluble in lipid materials (81). The subsequent consequences are:

i) Changes in properties of the PVC due to loss of plasticizer.

ii) Possible toxic and biological effects arising from the transfer of plasticizer to a patient.

I.2.4.1. Background Work on Migration Studies:

Leachability of plasticizer from PVC containers and its subsequent presence in intravenous fluids, blood and blood products has been extensively documented (1, 22, 43, 50-52, 58, 115). Exposure of patients to significant quantities of phthalic acid ester plasticizers through contact with medical PVC plastic products is also well known (53, 76, 129). DEHP, the most commonly used phthalate plasticizer has been detected in the blood and tissues of patients receiving blood transfusions or undergoing hemodialysis treatments (96). Patients undergoing maintenance hemodialysis therapy would seem particularly at risk of potential toxicity from DEHP, due to regular exposure to the plasticizer over prolonged periods of time. Therefore, the subject has become extremely important in food packaging and

medical applications (91).

I.2.4.1.a. Migration into Blood Storage Systems:

It has been established for some years that blood or blood fractions can extract materials from plastic containers or tubing. Extensive studies have been carried out on the distribution of phthalate plasticizers after transfusion of blood stored in PVC packs (93, 107, 109). Valeri et al (128) found that whole blood took up plasticizer to a significant extent and the material was found almost entirely in the plasma confirming earlier results from Marcel and Noel (82) and Jaeger and Rubin (52). It has been reported that blood stored at 4°C took up 0.25mg/100ml/day and that platelets were particularly avid in this respect (54). Thus a 70 Kg patient receiving 5 bags of blood which had been stored for 4 weeks would receive 175 mg of DEHP, a dosage of 2.5mg/kg. The uptake of the plasticizer by plasma from transfusion bags was investigated by Vessman and Rietz (131) who studied extensively the analytical problems involved. Typically they report 10mg/100ml as the concentration of DEHP in plasma stored at 4°C for 5 weeks. It has also been estimated that DEHP leaches at a rate of 100 µg/ml/day into platelet concentrate supernatant stored in PVC containers (70). It has also been found that the uptake of plasma was significantly correlated with the concentration of triglycerides but not related with the amount of cholesterol present (82).

I.2.4.1.b. Migration from Hemodialysis:

In the hemodialysis of patients with kidney failure there is again exposure of blood to PVC and this aspect was investigated by Easterling, Johnson and Napier (26). Easterling et al measured concentrations of DEHP in plasma circulated through plastic tubes connected to dialysis equipment. They have estimated that about 10 mg of DEHP would enter a patient in typical dialysis ie., about 0.14 mg/kg for a 70 kg subject. Ono et al(89) measured the free phthalic acid and DEHP present in whole blood working both with patients under dialysis and with an artificial model. In 3h circulation in the model, 1 litre of blood was found to dissolve 0.5mg DEHP. The uptake of plasticizer by their patients is difficult to interpret since metabolic elimination occurs but the authors stress that in 100-150 treatments in a year, a patient can receive significant quantitites of the ester. More recently it has been estimated by Gibson et al(33) that as much as 150 mg of DEHP could be transferred to a patient undergoing dialysis for 5 h. This is greater than the upper limit (15 mg) inferred from the results of Fayz et al (27) who tested 3 types of tubing plasticized with DEHP in a model system they devised as an improvement on those referred to above. They also found that the adipate ester in other types of tubing was transferred more extensively than the phthalate. Based on the best available estimates of DEHP delivery during hemodialysis, patients may

receive 20g or more of DEHP during the course of a year (33).

I.2.4.1.c. Migration from Food Packaging Material:

Phthalic acid esters used as plasticizers in food packaging materials have been known to migrate into food material stored in them and their toxic effects have been studied (114). The Food Additives Amendment to the Federal Food, Drug and Cosmetic Act in 1958 in the U.S. has restricted the use of phthalates in food packaging material. The restriction has not been applied to DEHP and diisooctyl phthalate because the available toxicological data would not support unlimited migration into fatty foods.

I.2.4.2. Toxic Effects due to Migration of Plasticizer:

Plasticizer migration from PVC into various media has attracted the interest of numerous investigators due to the high consumption figures of this polymer used in the plasticized form (14, 26-28, 34, 45, 66, 74, 81, 83, 94, 104, 105, 118, 119, 133, 136, 137) . The toxic aspects of the migrated plasticizers have also been extensively studied (4, 11, 37, 124). Although a low order of toxicity is associated with acute and sub-chronic administration of DEHP or its de-esterified metabolites in experimental animals(125), long term feeding studies suggest adverse effects on major organ systems. The LD_{50} values for DEHP has been summarized by Thomas et al (125) as follows:

Rat/oral	:	26g/kg
Guinea pig/dermal	:	10g/kg
Rabbit/oral	:	34g/kg
Rabbit/dermal	:	20 g/kg
Mouse/i.p	:	14.2g/kg
Rat/i.p/LD_{10}	:	0.3g/kg
Human/TD_{10}	:	0.143g/kg

I.2.4.2.a. Toxic Effects in New Born Children:

Residual DEHP has been shown to be present in postmortem heart and gastrointestinal tissue from critically ill infants who had umbilical catheters in place and who had received varying amounts of blood products(42). Newborn infants who receive exchange transfusions will be exposed to considerable quantities of DEHP and since the immature liver of these infants have lower metabolizing capacity than adults, they may easily be susceptible to possible harmful effects of this plasticizer (117).

I.2.4.2.b. Hepatic Toxicity of DEHP:

The phthalate ester plasticizer DEHP has been shown to produce liver enlargement and hepatic peroxisome proliferation in rats (71, 85, 112) and in mice (103) and to increase the incidence of liver tumors in these two species (68). DEHP has also been found to induce cytosolic epoxide hydratase and glutathione S-transferase activity in rodent liver (40).

I.2.4.2.c. Toxic Effects on Reproductive Systems:

The most notable effects of DEHP toxicity involve the reproductive organs (95). Most of the attention with regard to DEHP induced changes in the reproductive system has been focused upon its effects upon the fetus. Early studies by Shaffer et al. employing a 90 day feeding period and using a diet containing varying amounts of DEHP revealed tubular atrophy and degeneration in the rat testes (110). Very recent studies by Garvin et al. suggest that high doses of DEHP seem to cause changes in the reproductive system of experimental animals (32). They have also evaluated the teratogenic potential of plasma soluble extracts of PVC in rats. Seth et al examined the effect of DEHP on rat gonads and has reported that the activities of succinic dehydrogenase and adenosine triphosphate were significantly reduced (113). Furthermore, long term dietary intake of DEHP and its hydrolysis product MEHP has been reported to cause testicular atrophy in male rats (29).

I.2.4.2.d. Carcinogenic Effects of DEHP:

The public preoccupation in DEHP was triggered by the publication of the US National Cancer Institute study in early 1980's (88) where DEHP was implicated as a possible carcinogen in addition to causing changes in pitutary gland tissue and testicular atrophy. In a two generation study, Carpenter et al. reported no adverse effect (12). However, a recent 2-year feeding

study conducted by the National Toxicology Programme showed an increased incidence of hepatocellular carcinoma in F-344 rats and B6C3F1 mice (68). IARC classifies DEHP as carcinogenic in animals (44).

I.2.4.2.e. Other Toxic Effects:

There have been reports of cellular toxicity of DEHP in tissue culture(35, 36, 49, 59). Using blood cells, several studies have dealt with the effects of DEHP on blood stored in plastic bags in regard to hemolysis (108), post transfusion survival of erythrocytes (121, 132), platelet function (53, 67, 90), and mitosis of lymphocytes (127). In addition, embryotoxic and teratogenic effects have been demonstrated in rodent studies with DEHP (116, 126).

Aside from these well defined organ toxicities, diverse metabolic effects have been noted following treatment with phthalate esters in various animal species. Changes in lipid metabolism (5) and hepatic microsomal drug-metabolizing enzyme activities have been reported with DEHP pretreatment(71, 97, 120) Similar effects on microsomal drug metabolizing enzymes were observed in rats following direct treatment with monoester metabolites of DEHP (30).

I.2.4.3. Difficulties in DEHP Analysis:

Attempts to predict the toxicologic consequences of long term exposure to DEHP in humans are hampered by the lack of

information concerning both the degree of exposure to and the metabolism of the plasticizer in man. Patients exposed to plasticizers through PVC medical devices comprise one of the most extensively studied populations. Several investigators have reported serum concentrations of DEHP in dialysis and surgical patients in μg/ml range (21, 23, 75). DEHP has also been identified in various tissues obtained from dialyzed renal failure patients (97).

A number of studies have been performed to show the toxic effects of the plasticizers in blood bags. The basic problem encountered when studying DEHP migration into blood stored or transfused has been its poor solubility in these media and hence it was very difficult to prepare a standard concentration. One must rather depend on the material leaching from the blood bag into the blood products. The levels achieved in the blood not only varied with the blood product used for testing but also with the amount of storage time and the bag composition. Many of the toxicity studies have therefore been performed using the time honoured method of feeding huge doses of the material to experimental animal. Human studies are complicated by the finding that about 70 percent of all humans transfused die within six months of having received the blood or blood products (60).

I.2.5. Search for an Alternative to DEHP:

The National Toxicology Conference on Phthalates (88)

discussed the safety element of use of phthalates in medical PVC devices and various results were presented. With a disturbing number of studies showing that there might be some effect of DEHP on the patient, the PVC manufacturers began to search for a better plastic that used no or a non-leachable plasticizer. The major studies have involved non-PVC plastics such as polyolefin (69) or a PVC plastic with non or poorly leachable plasticizer The plasticizer used, tri-(2-ethylhexyl) trimellitate (TOTM) was found to leach in smaller amounts from the plastic into the stored blood compared to DEHP (3). This compound is composed of a phthalate ring triply substituted at the 1,2 and 4 positions with ethylhexyl groups. However, this plasticizer is a high molecular weight compound compared to DEHP and economically not viable for use in PVC industry. It has also been reported that though storage time of platelets could be increased (15), red cells could not be stored in TOTM plasticized bags for longer than 21 days (87). Also, the production of DEHP is in millions of tons all around the world that the PVC industry is not just ready to switch over to a new plasticizer.

I.2.6. Modification of PVC Trunk Polymer:

Since attempts to change the plasticizer overnight may face considerable problems, attempts to modify the basic PVC material in order to prevent or reduce the migration to a negligible extent have been carried out by various groups. Of this,

modification by glow discharge technique seems to have had a certain amount of success (16, 46, 47, 135). However, this method has several limitations. Firstly, the technique cannot be employed for modifying large surface area of samples such as blood storage bags which are intended for a single use. Secondly, the plasma technique is often difficult to be reproduced. Thirdly, the cost factor involved makes it an unfavourable economic proposition for disposable devices. Glow discharge treatment increases surface wettability, but enhances the adhesion of platelets to the surface and causes morphological changes to them. Most of the platelets adhered to glow discharge treated PVC were spread with radiating pseudopods and lactate dehydrogenase was released from the plasma membrane of damaged platelets which was highly detrimental (48).

I.3. Purpose of this Study:

The purpose of this study involves:

1. To study the migration aspects of the plasticizer DEHP from different PVC sheetings used in medical devices.

2. To graft plasticized PVC sheets using hydrophilic monomers such as 2-(hydroxyethyl methacrylate)[HEMA], N-(vinyl pyrrolidone)[NVP] and methacrylic acid (MAA) using gamma radiation from a Co^{60} source in an effort to prevent or retard plasticizer migration from such modified sheets.

3. To characterize the physical, mechanical and surface properties of the grafted material and compare them with control samples.

4. To examine the migration behaviour of the plasticizer DEHP from the graft modified surfaces into various extraction media such as saturated hydrocarbons, cotton seed oil, poly ethylene glycol and plasma.

5. To assess the suitability of the graft modified PVC for migration resistant applications with emphasis on medical applications.

I.4. Use of Gamma Radiation for Grafting onto PVC:

Use of high energy irradiation has been a popular synthetic approach to produce graft copolymers of PVC, especially due to the labile nature of the chlorine atoms in the polymer. Three techniques have been mainly employed (13).

i) To irradiate the polymer alone at low temperatures in the absence of oxygen which is further reacted with a monomer to induce grafting.

ii) To irradiate the polymer in presence of air or oxygen to produce peroxy or hydroperoxy groups on the polymer matrix which is further used in thermal or redox initiations for grafting and

iii) Direct irradiation of the polymer in presence of monomer(s) to effect grafting. Charlesby and Pinner have reported

that (19) direct irradiation in presence of monomers resulted in improved properties for the polymer.

I.4.1. Surface Grafting of Polymers:

Surface grafting of various polymers with hydrophilic monomers such as HEMA, NVP, acrylamide(AA) etc. has been reported to enhance the blood compatibility and antithrombogenicity of many polymers used for blood contact applications (77, 99, 100). Since hydrogels are polymers which can retain a large quantity of water (>20%) within their structure, they can provide low interfacial free energy on contact with blood. The hydrophilic surfaces will help form a passivating layer. Hydrogels have been investigated in a variety of biomaterial applications. HEMA has been grafted onto polyurethanes and silicones and studies on the platelet adhesion to these surfaces have been made(56). Hoffman has studied the properties of hydrogel grafted silastic(102). In all these cases lower platelet adhesion and high hydrophilicity of surfaces with low interfacial tension was recorded which favoured blood compatibility.

I.4.2. Proposed Modification of PVC:

Though considerable amount of work has been carried out on the grafting of a variety of hydrophobic monomers onto PVC by different groups (17, 18, 41, 57, 72, 73, 78), very little is reported on grafting of hydrophilic monomers onto the polymer (9, 31). Furthermore, most of the grafting work reported so far

has been on virgin PVC granules and not on the finished product. Most importantly, no attempt has so far been made to examine the migration behaviour of the plasticizer from graft modified PVC surfaces. Surface modification by grafting of hydrophilc monomers onto PVC is expected to alter the migration behaviour of DEHP, in addition to improving the blood compatibility of the polymer. Hence this study is undertaken to examine the effect of grafting of hydrophilic monomers such as HEMA, NVP and MAA (either singly or in combination) onto DEHP plasticized PVC sheets using gamma radiation from a Co^{60} source. The graft modified material is characterized for its physical, mechanical and surface properties. The migration behaviour of the plasticizer DEHP from graft modified PVC surfaces into various hydrocarbon solvents such as n-hexane, n-heptane and n-octane and simulated physiological media such as cotton seed oil and polyethylene glycol-400 is examined. Finally, migration of DEHP from graft modified PVC into a biological medium such as bovine plasma is studied and platelet aggregation studies are also carried out to examine the blood compatibility of the grafted polymer.

MATERIALS & METHODS

CHAPTER II

MATERIALS AND METHODS

II.1. Materials:

II.1.1. Poly(vinyl chloride)(PVC) Sheets:

Calendered PVC sheets of medical grade having a thickness of 0.4 mm, received as a gift from Technoport Co, Japan and Terumo Corporation, Belgium were used in all the experiments.

II.1.1.1. Characterization of the Plasticizer in PVC:

The identity of the plasticizer present in the PVC sheeting used in the experiments was determined by extraction and characterization using spectroscopic and chromatographic methods. Extraction of the plasticizer using methanol and carbon tetrachloride (1:2 by volume) for 16 h in a Soxhlet apparatus from PVC sheets yielded nearly 15% of the total weight of the sheeting as plasticizer. The procedure followed was as per ASTM D-3421-75. Infra red spectrum of the extracted plasticizer (neat) recorded using a Perkin Elmer Model 597 instrument is shown in Figure 2.1. It was found to correspond with the standard spectrum of DEHP (Figure 2.2) exhibiting all its characteristic peaks. UV spectrum of the plasticizer recorded using a double beam Shimadzu UV-VIS 240 spectrophotometer in methanol showed absorption maximum at 274 nm having an extinction coefficient of

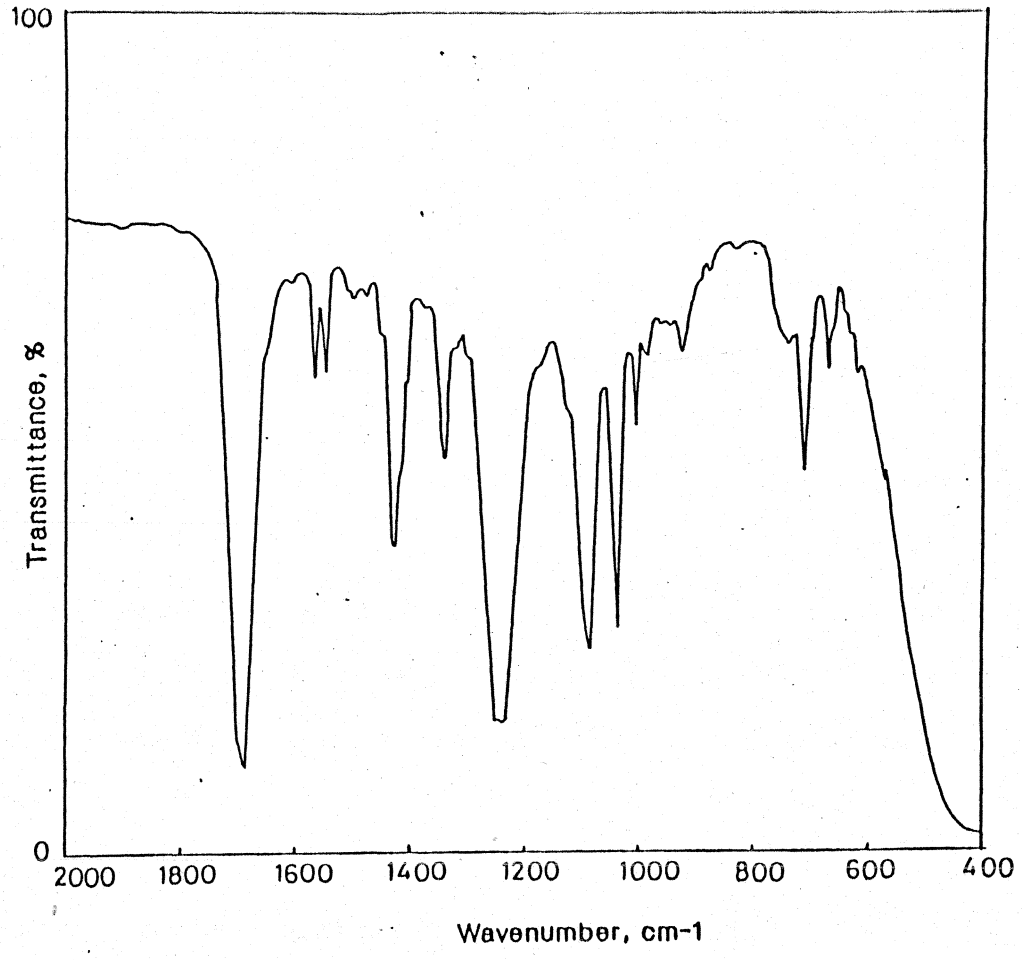


Figure 2.1. Infra Red spectrum of extracted plasticizer from PVC sheets used in the experiments.

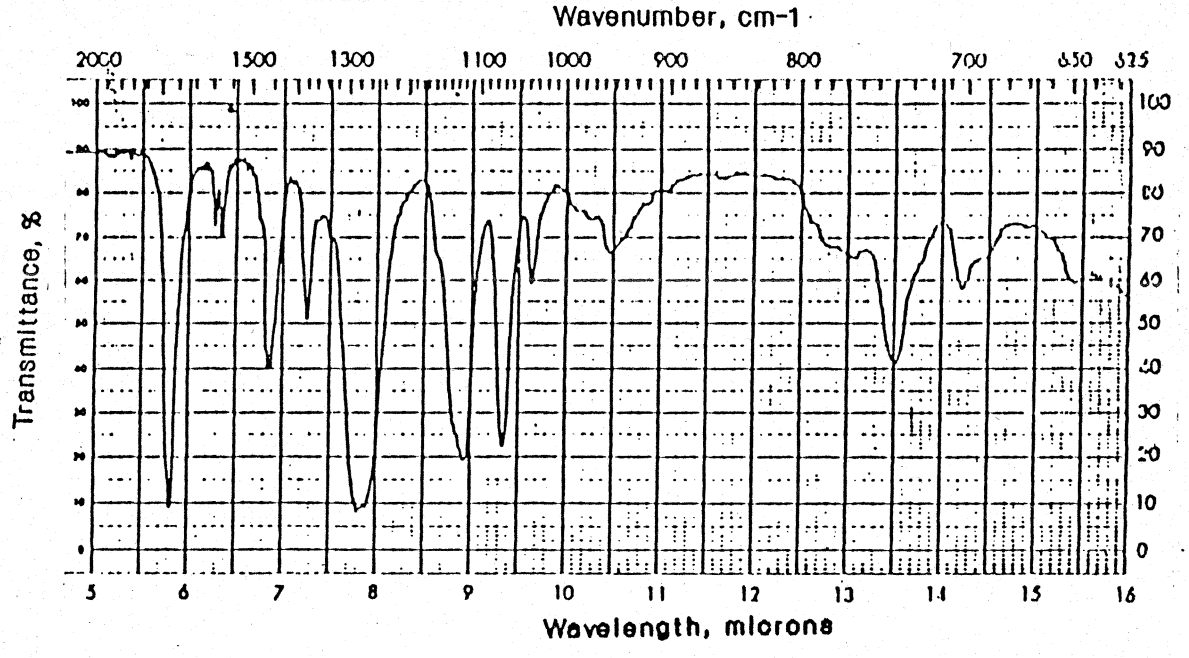


Figure 2.2. Standard infra red spectrum of di(2-ethylhexyl) phthalate [DEHP].

1512.6 cm^2/mole characteristic of DEHP (Figure 2.3). High Performance Liquid Chromatography (Water Associates, USA, 6000A solvent detection pump, U6K Injector and Model 440 UV absorbance detector, μ-porasil column, Mobile phase: CH_2Cl_2) analysis of the plasticizer showed a single prominent peak having strong absorption at 254 nm and elution time (nearly 4 min) similar to that of control DEHP (Figure 2.4). The refractive index of the plasticizer extracted was measured using a Model 3T ABBE refractometer (Atago, Japan). The refractive index value was found to be 1.4828 which corresponded to the reference value of DEHP confirming the identity of the plasticizer.

II.1.2. Chemicals:

Monomers 2-(hydroxyethyl methacrylate)(HEMA), N-(vinyl pyrrolidone)(NVP), ethylene glycol dimethacrylate (EDMA) and methacrylic acid(MAA) were from BDH, England. Spectroscopic grade methanol and AnalaR grade methanol (Glaxo and E. Merck, India) were used for spectroscopic, leaching and cleaning purposes respectively. Distilled n-hexane and n-heptane (E. Merck, India) and n-octane (BDH, England) were used for migration studies. Soap solution used for cleaning of PVC sheets was from Laxbro, India. All other reagents were of AnalaR or equivalent grade.

II.1.3. Blood Source:

Blood samples used for platelet aggregation and migration studies were taken from healthy calf by juglar venic puncture.

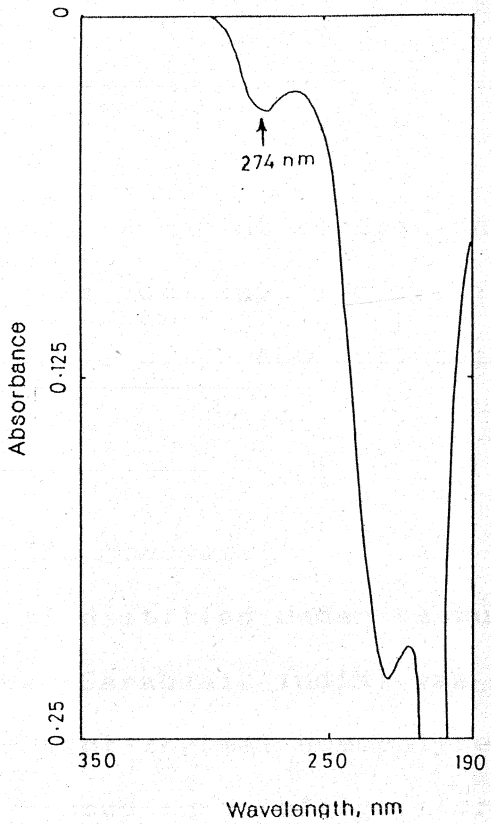


Figure 2.3. Ultra Violet spectrum of extracted DEHP.

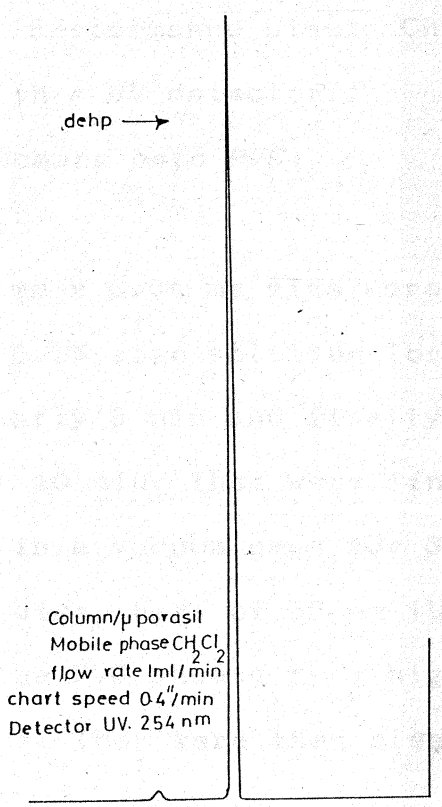


Figure 2.4. High Performance Liquid Chromatogram of DEHP

The animals were maintained in cement floored sheds, and fed chiefly on fodder and cattle feed supplied by Hindustan lever (Lipton), Bangalore, India. 1 ml of ACD anticoagulant was used for every 9 ml of blood.

II.2. Methods:

II.2.1. Purification of the Monomers:

The monomers were all distilled under vacuum before use. A pinch of cuprous chloride (Sarabhai, India) was added to the distilling monomer to prevent thermal homopolymerization. The distilled monomers were stored in a refrigerator at 4°C. Purity of the monomers was checked using IR spectroscopy (Model 597, Perkin-Elmer, USA) and High Performance Liquid Chromatography (Waters Associates, USA) with a UV detector.

II.2.2. Grafting of the Monomers onto PVC:

II.2.2.1. Cleaning of PVC :

Strips of 100 mm x 10 mm x 0.04 mm size were cleaned thoroughly by rinsing with 0.5% soap solution for 3 min, washed in running tap water for nearly 5 min and finally in double distilled water for further 10 min. They were finally rinsed with methanol for 15s and dried in a vacuum oven for 30 min at 50-55° C. For migration studies, bags of 56 mm (L) x 50 mm (W) size were fabricated from the PVC sheets by a high frequency welding machine (Figure 2.5). They were then cleaned in a similar fashion.

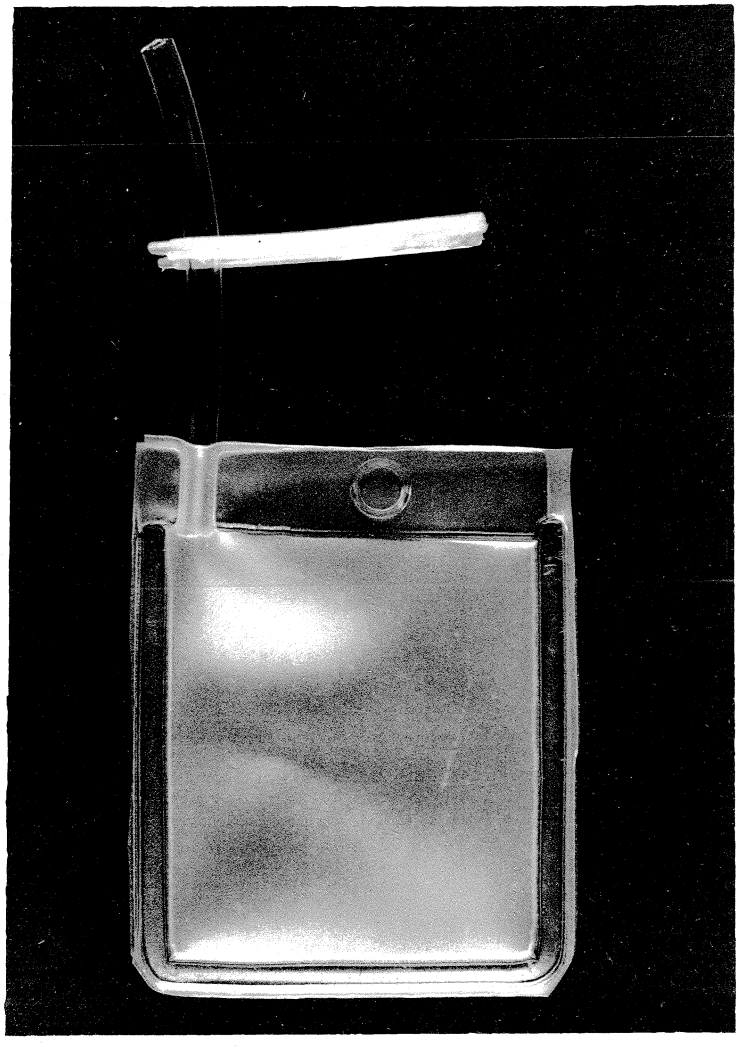


Figure 2.5. Photograph of the PVC bag specially fabricated for migration experiments into organic solvents and biological media.

II.2.2.2. Grafting Procedure:

Pre-weighed PVC strips (100 x 10 x 0.4 mm) were immersed in 20 ml monomer solutions of different concentrations containing various amounts of copper sulphate taken in screw-capped test tubes and degassed with nitrogen for nearly 3 min. The tubes were then stoppered and the samples were irradiated using a Co^{60} source (Panoramic Batch Irradiator) for various doses. After irradiation, the samples were washed for 24 h with frequent changes of the deionized water, rinsed in methanol for 15 s and dried in a vacuum oven at 50°C and weighed again. At least 3 samples were used in each experiment. For migration studies, bags fabricated as described in Section II.2.2.1. were employed. The inner surface of the bag was grafted by filling the bag with the monomer solution containing various concentrations of Cu^{2+} and irradiated to a dose of 0.5 Mrads. The bags were then washed free of the monomer, homopolymer etc. as described before.

II.2.3. Characterization of the Graft Polymer:

II.2.3.1. Gravimetric Estimation of the Graft Content:

The percentage graft yield was calculated using the following expression(98):

$$\frac{\text{(Wt. of grafted polymer) - (Wt. of ungrafted polymer)}}{\text{(Wt. of grafted polymer)}} \times 100$$

II.2.3.2. Spectrophotometric Characterization of the Graft:

A Perkin Elmer Infra Red Spectrophotometer (Model 597) with ATR accessory was used to record the spectra of the grafted surfaces. The samples were placed on a KRS-5 crystal and the spectra were recorded with the incidence angle of the IR beam at 45° for all samples.

II.2.3.3. Electron Microscopic Characterization of the Graft Surface:

The morphology of the grafted and the ungrafted surfaces was examined using Scanning Electron Microscopy. Samples were mounted on aluminium stubs using double sided tape, coated with gold or silver and examined in the microscope (Jeol JSM 35C, Japan or Cambridge Instruments, UK) (61, 62).

II.2.3.4. Optical Microscopic Characterization of the Graft Surface:

An optical microscope (Nikon Model XF 21, Japan) with phase contrast accessory was also employed to study the surface morphology of the control and modified surfaces of all samples.

II.2.3.5. Contact Angle Studies:

Captive air-in-water and octane-in-water techniques were used to measure the contact angles to determine the polar and dispersion components of surface energy of the ungrafted and grafted surfaces (39). A Contact Angle Goniometer (Rame'Hart, USA) was used for all contact angle measurements. All samples

were equilibrated overnight in distilled water before they were subjected to measurements. Surface energy parameters were calculated using the method of Andrade et al(2).

The grafted polymer samples were kept on microscopic slides and fastened on both ends using rubber bands. The slide was immersed in a Perspex tank containing double distilled water as shown in Figure 2.6. The sample was allowed to equilibrate for a few minutes again. The goniometer was aligned and focused on the polymer-water interface. Using a microsyringe with a bent needle, a tiny drop of octane or a tiny bubble of air was released onto the polymer surface. The apparent octane/water or air/water contact angle was then measured. Angles on both sides of the bubble were measured and averaged. A minimum of 6 values were taken on each surface. The measurements were then averaged and the mean and standard deviation calculated.

II.2.4. Migration Studies of Plasticizer:

II.2.4.1. Migration into Organic solvents:

Migration studies of DEHP into hydrocarbon solvents such as n-hexane, n-heptane and n-octane and other organic solvents were carried out at 30°C using specially fabricated bags. The bag was filled with 20 ml of the migration medium, their inlets and outlets were clamped using pinch clips and aliquotes of 100 µl were withdrawn at intervals of 1,2,3,4 and 5 h using a syringe having a 43 SWG gauge needle. An ungrafted bag filled with the

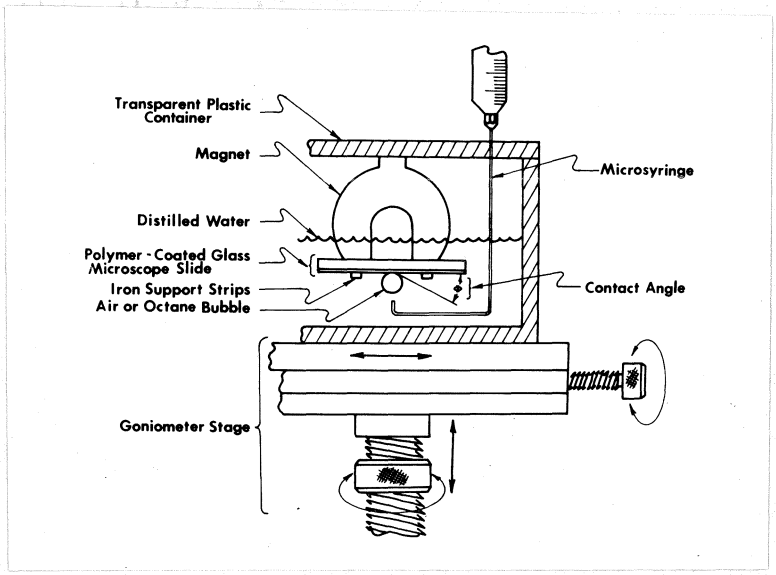


Figure 2.6. Contact angle experimental set up for determining air-in-water and octane-in-water contact angles.

same medium served as the control. A minimum of three bags were used in each experiment. The solvent was evaporated completly and the residue was dissolved in 3 ml of spectroscopic grade methanol and the absorbance was measured at 274 nm in the UV-VIS spectrophotometer where the plasticizer has a characteristic absorbance maximum (84). The amount of DEHP leached out into the medium at specific intervals was then calculated from a calibration curve for DEHP in methanol (Figure 2.7).

II.2.4.2. Migration into Cotton Seed Oil and Polyethylene Glycol:

The amount of plasticizer migrated into Cotton Seed Oil and polyethylene glycol-400 was determined by calculating the percentage loss of weight after specific intervals of time. Strips of control (ungrafted) and grafted material were immersed in 20 ml of the medium at 70° C and the pre-weighed samples were taken out at intervals of 24, 48, 72 and 96 h, washed with 0.5% soap solution for 5 min, rinsed with methanol and diethyl ether for 15 s each to remove the surface adhering oil, dried in a vacuum oven at 60° C for 60 min and weighed. Washing and drying were repeated till constant weight was achieved. The percentage loss of weight of plasticizer was then calculated.

II.2.4.3. Migration into Platelet Rich Plasma(PRP):

Migration experiments into PRP were carried out using freshly collected calf platelet rich plasma in pre-fabricated bags of 50 mm(L) x 56 mm(W) size (65). PRP was obtained by

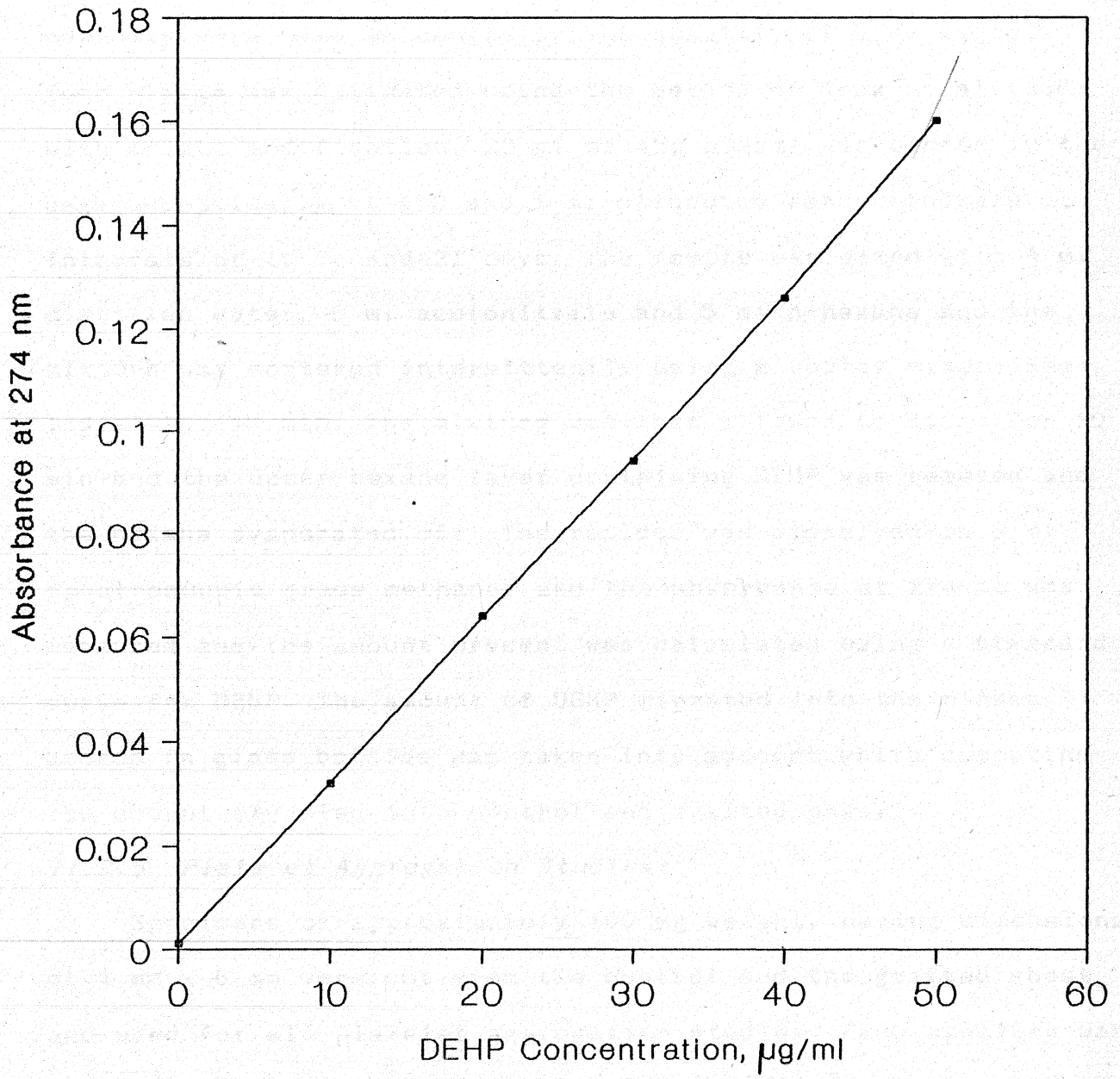


Figure 2.7. Calibration curve drawn using known concentrations for DEHP/Methanol system.

centrifuging citrated bovine blood in the standard fashion. Ungrafted bags of the same dimensions and glass bottles of 60 ml capacity were used as controls. The quantity of DEHP migrated into plasma was estimated using the method of Rock et al.(106) with slight modification. 20 ml of the plasma was stored in the bags asceptically at 4°C and 1 ml aliqoutes were withdrawn at intervals of 1, 7, and 21 days. The sample was mixed with 4 ml distilled water, 5 ml acetonitrile and 5 ml n-hexane and the mixture was vortexed intermittently using a vortex mixer (Remi, India) for 45 min. The mixture was then allowed to stand for 10 min and the upper hexane layer containing DEHP was removed and the hexane evaporated off. The residue was dissolved in 3 ml spectroscopic grade methanol and the absorbance at 274 nm was measured and the amount present was calculated using a standard curve for DEHP. The amount of DEHP migrated into the plasma stored in glass bottles was taken into account while computing the amount migrated into control and grafted bags.

II.2.5. Platelet Aggregation Studies:

Specimens of approximately 100 mg weight, having dimensions of 4 mm x 6 mm were cut from the control and the grafted sheet and used for all platelet aggregation studies. Each specimen was kept in 5 ml PRP at 31° C for 90 min. 1 ml of the plasma was then diluted to achieve the absorbance unit of nearly 0.8 at 540 nm (Approx. 8.0 x 10^4 platelets per µl suspension). The diluted

plasma was taken in a pair of siliconized glass cuvettes (pathlength 10 mm) and placed in the sample and reference positions of a UV-VIS spectrophotometer equipped with the thermostatted cuevette holders maintained at constant temperature (31±1° C). The instrument was set to read zero at 540 nm. After temperature equlibration, 10 µl agonist (ADP) was added to the sample cuvette and mixed using a glass stirrer. The ensuing changes in absorbance (turbidity) were recorded as a function of time and the initial rate of aggregation r_o was determined according to the method of Jamaluddin and Lissy (55).

II.2.6. Evaluation of Mechanical Properties:

The tensile strength and elongation of the test samples were measured using an Instron Model 1193 Universal Testing machine according to the ASTM Standard D882. Grafted strips of 100 mm(L) x 10mm(W) were used for all the measurements maintaining a gauge length of 60 mm. A cross-head speed of 500 mm/min and a chart speed of 500 mm/min were used (magnification ratio = 1). The strips were hydrated before the measurements by equilibrating them in distilled water for more than 48 h (63).

II.2.7. Hardness Measurements:

Shore A hardness values were estimated for all the grafted samples and the control using a hardness tester as per ASTM D-676-69T procedure. A minimum of 6 estimations were carried out for each sample.

II.2.8. Optical Transparency:

The optical transparency of the grafted and control specimens was checked by measuring the percentage transmission of light in the 700-350 nm region using a UV-VIS spectrophotometer.

II.2.9. Percentage Water of Hydration:

The percentage water of hydration present in the total polymer as well as in the graft was determined using gravimetric methods after equilibrating the grafted polymer in distilled water for a minimum of 48 h. The following relations were employed:

$$\text{Percentage Water}_{total} = \frac{\text{(Wt. of hydrated graft polymer)} - \text{(Wt. of dry graft polymer)}}{\text{(Wt. of hydrated graft polymer)}} \times 100$$

$$\text{Percentage Water}_{graft} = \frac{\text{(Wt. of hydrated graft polymer)} - \text{(Wt. of dry graft polymer)}}{\text{(Wt. of hydrated graft polymer)} - \text{(Wt. of ungrafted polymer)}} \times 100$$

The weighings were done using a high precision analytical balance (Ohaus, USA) having a sensitivity of 0.1 mg. The hydrated samples were pressed in between two #1 Whatman filter papers applying very little pressure before weighing so as to remove the adherent water.

II.2.10. Estimation of Residual Copper:

Since grafting medium contained Cu^{2+} in the concentration of 0.0025 to 0.01M, which was incorporated to prevent homopolymerization of the monomer, the residual copper content in the grafted polymer was determined in order to assess whether it was below toxic levels. This was carried out as per the recommended procedure of Department of Health and Social Security (DHSS), UK. Grafted sheets having 1250 cm^2 area were autoclaved in double distilled water at 120-123° C at 15 psi pressure ($1.03 \times 10^5 N/m^2$) for 20 min and the resultant extract was analysed for copper ions using an atomic absorption spectrophotometer (Instrumentation Labs, USA, Model 551). The amount of copper ions estimated in parts per million (ppm) was compared with acceptable limit values reported.

II.2.11. Sterilization:

II.2.11.1. Gamma Irradiaton:

All gamma sterilization work was carried out using a Panoramic Batch Irradiator (PANBIT), using a Co^{60} source for 2.5 Mrads at a dose rate of 0.40-0.49 Mrads/hour.

II.2.11.2. Autoclaving:

Autoclaving was carried out in a stainless steel autoclave at 121-123° C at 15 psi (1.03×10^5 N/m2) pressure for 10 min. The bags were filled with 5 ml of deionized water before autoclaving.

II.2.11.3. Ethylene Oxide Sterilization:

The samples were kept in an ETO chamber (Pest Control Co, Bombay, India; Freostar 2'x 2' x 4'), evacuated to 0.01 torr, purged with sterilization gas (88% Freon and 12% ETO) built up the pressure to 10 psi (0.69×10^5 N/m^2) at 50°C for 90 min, evacuated the gas and purged with air. The process was repeated three times.

RESULTS & DISCUSSION

CHAPTER III

RESULTS AND DISCUSSSION

III.1. Characterization of the Graft Polymer:

III.1.1. NVP:HEMA system:

III.1.1.1. Grafting of NVP/HEMA onto PVC:

III.1.1.1.a. Effect of Monomer Concentration on Graft Yield:

NVP and HEMA monomers were used in various proportions in the grafting experiments (61). Concentrations of 1 to 7 vol% were used for grafting. The percentage graft yield value is found to increase proportionately with monomer concentration in all the three different sub-systems studied (NVP:HEMA = 25:75; NVP:HEMA = 50:50; NVP:HEMA = 75:25) (all vol%). The amount of graft polymer on the surface was found to vary from nearly 0.16 mg/cm^2 at 1 vol% to 3.09 mg/cm^2 at 7 vol% monomer concentration for all the three systems. However, in certain instances, the radiation graft is likely to penetrate into the substrate polymer. Therefore, describing the degree of graft as graft/initial surface area may not be a completely meaningful expression of the extent of grafting. So the degree of graft has been expressed as the percent of graft in the final material. The results are plotted in Figure 3.1. Increase in concentration of NVP in the monomer mixture, however, did not result in any significant change in the

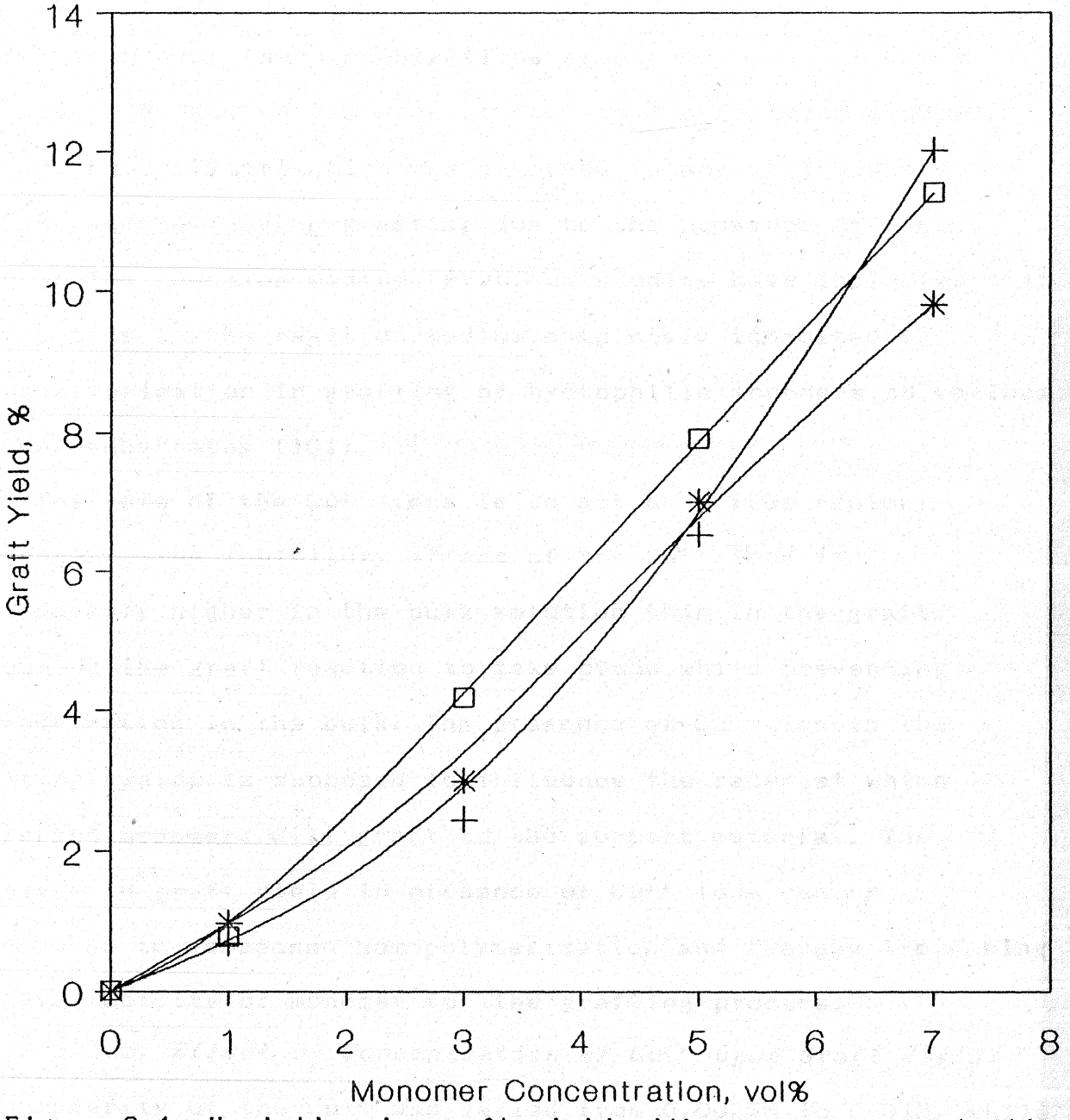


Figure 3.1. Variation in graft yield with monomer concentration for NVP:HEMA systems: Figure shows proportionate increase in graft yield with monomer concentration for NVP25:HEMA75 (+), NVP50:HEMA50 (*) and NVP75:HEMA25 (□) systems radiation grafted to PVC [0.005 M Cu^{2+}, 0.25 Mrads]. Standard Deviations (S.D.) are within $\pm$ 5% and not shown due to overlapping. A minimum of 5 samples was used for each system in all grafting experiments.

graft yield over the concentrations examined.

3.1.1.1.b. Effect of Presence of Cu^{2+} in the Grafting Medium:

No homopolymerization was observed in any of the above systems studied during grafting due to the presence of cupric ions in the reaction medium. Previous studies have indicated that cupric ions in the reaction medium completely inhibited homopolymerization in grafting of hydrophilic monomers to various polymer substrates (101).

The role of the Cu^{2+} ions is to act as a free radical scavenger. The inhibitory effect of the Cu^{2+} ions is considerably higher in the bulk solution than in the graft, favouring the graft reaction to take place while preventing polymerization in the bulk. The presence of Cu^{2+} ion in the grafting system is supposed to influence the rates at which different monomers will graft to the support material. The increase in graft yield in presence of Cu^{2+} ions can be attributed to decreased homopolymerization and thereby increasing the availability of monomer for the grafting process.

III.1.1.1.c. Effect of Concentration of Cu^{2+} upon Graft Yield:

Molarity of the Cu^{2+} was varied from 0.0025M to 0.01M, while monomer concentrations of 1, 3, 5 and 7 vol% were employed for grafting. The percentage graft yield was found to increase with increase in monomer concentrations in all the media studied (Figure 3.2). The degree of grafting for different monomer

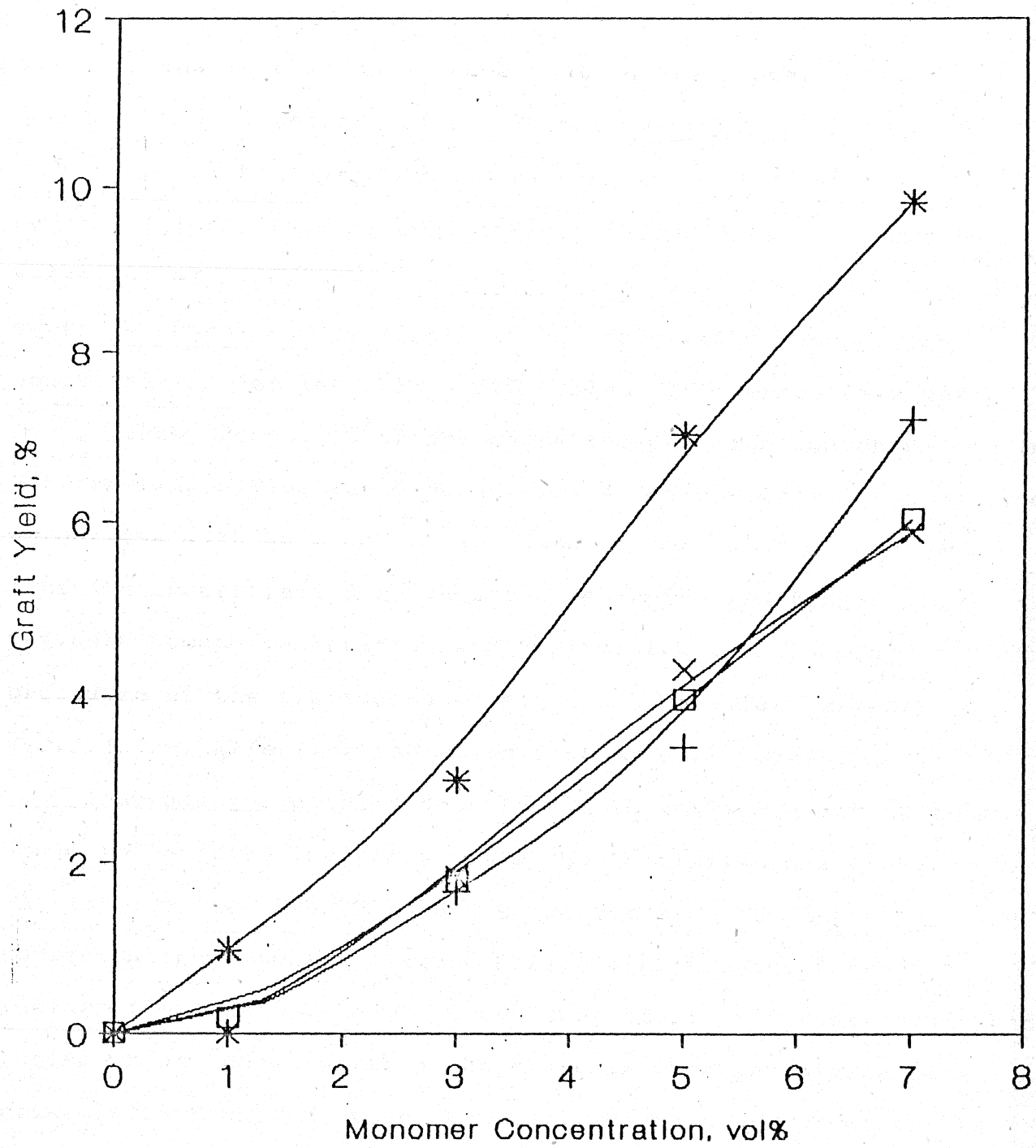


Figure 3.2. Effect of Cu^{2+} ion concentration on graft yield for NVP50:HEMA50 system: Figure shows variation in graft yield with monomer concentration for NVP50:HEMA50 system when grafted in aqueous media containing 0.0025M (+), 0.005M (*), 0.0075M (□) and 0.01M (x) Cu^{2+} ions [0.25 Mrads]. S.D. was within ± 5%.

compositions is seen to be dependent on the copper ion concentration. Samples grafted in the presence of 0.005M $Cu2^{+}$ showed the highest graft yield values compared to other concentrations. This is analogous to the observations made by Ratner et al. (101) for the grafting of hydrophilic monomers onto silicone rubber and is likely to be the critical copper ion concentration for (NVP/HEMA)-PVC system. The homopolymer was found to be present in traces where the Cu^{2+} ion concentration in the grafting medium was 0.0025M. The solutions were all clear and colourless with no trace of any homopolymer in other systems. Thus the incorporation of cupric ions in the grafting system prevents homopolymerization and facilitates the cleaning procedure of the grafted material to a significant extent.

III.1.1.1.d. Effect of Radiation Dose on Graft Yield:

Increasing radiation dose from 0.25 to 0.75 Mrads is also found to increase the graft yield substantially in a linear fashion for the NVP50:HEMA50 system for all the four concentrations studied (Figure 3.3). With increasing graft yields, the sheets tend to become more stiff in the dry state and curled up at concentrations above 5 vol% when irradiated to a dose of 0.5 Mrads or above. However, in the hydrated state the sheets became flexible and slippery in nature.

III.1.1.2. Effect of NVP Content on Optical Transparency:

An interesting observation during grafting was that optical

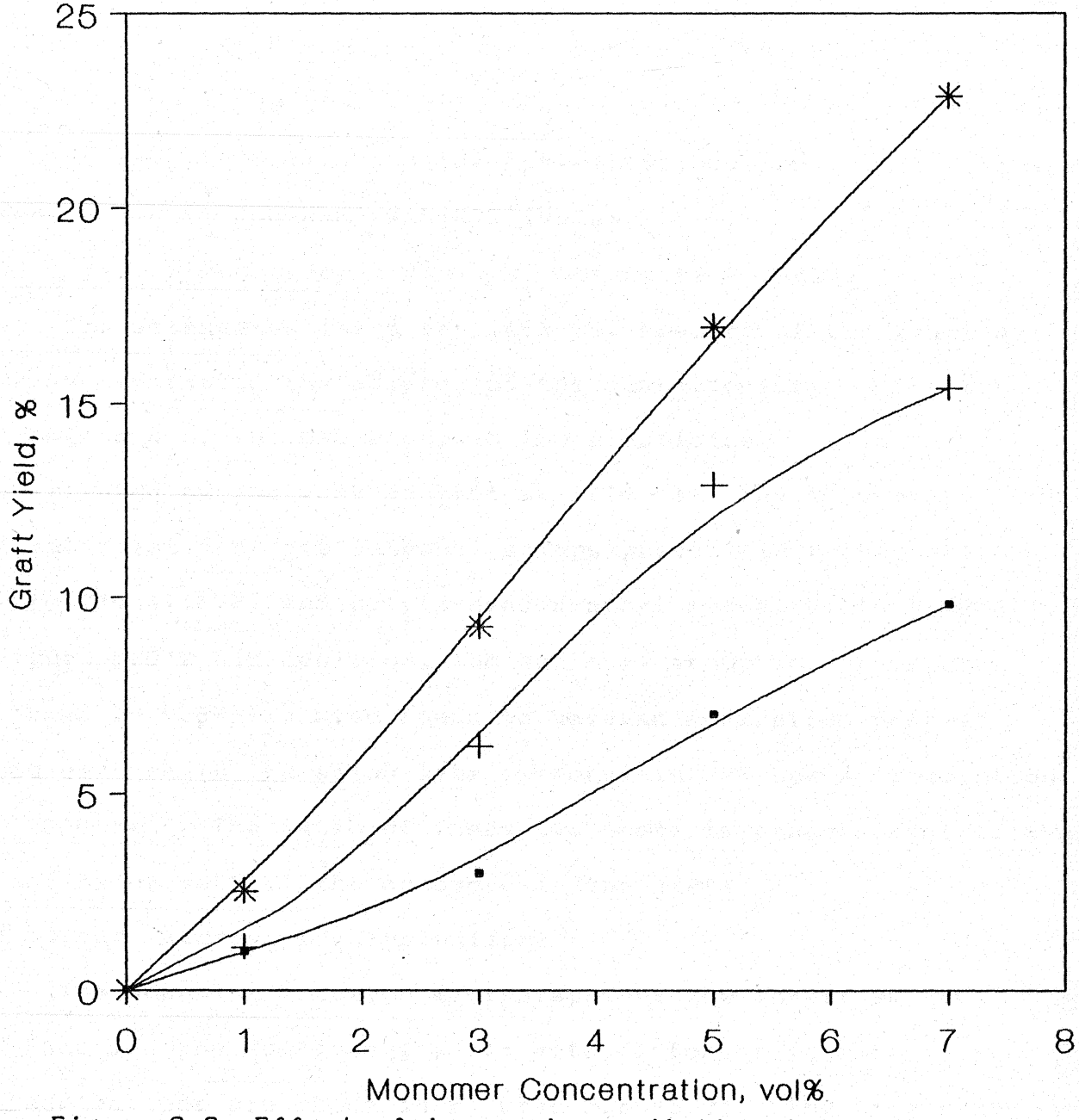


Figure 3.3. Effect of increasing radiation dose on graft yield for NVP50:HEMA50 system: Plot shows increase in graft yield with monomer concentration for NVP50:HEMA50 system grafted to PVC at 0.25 (.), 0.5 (+) and 0.75 (*) Mrads [0.005M Cu^{2+}]. S.D. was within $\pm$ 5%.

clarity (transparency) increased for 100% NVP content in the grafting medium whereas higher HEMA content in the system tended to make the sheets more opaque in all the concentrations studied (Figure 3.4). Thus the optical transparency varied in the order N75:H25 < N50:H50 < N25:H75 system.

III.1.1.3. Spectroscopic Analaysis of Graft Polymer:

The attenuated infra red (ATR-IR) spectra of the grafted surface indicated the absence of the characteristic 1725 cm^{-1} strong band of the C=O group in the plasticizer. It is substituted by the weak doublet at 1710 cm^{-1} and 1730 cm^{-1} characteristic of the carbonyl groups present in poly(vinyl pyrrolidone)(PVP) and poly(2-hydroxyethyl methacrylate)(PHEMA) (Figure 3.5). In addition, the carbonyl group in the ester linkage in PHEMA is also found to have an absorption peak at 1030 cm^{-1} while the amide type carbonyl in PVP has an absorption at 1008 cm^{-1}. The ratio of these two peaks is proportional to the fraction of each of the monomers in the graft.

III.1.1.4. Microscopic Evaluation:

The scanning electron micrographs of the ungrafted PVC surface and the surfaces grafted with different monomer concentrations are shown in Figures 3.6a-3.6j. The virgin PVC sheeting appears to a have a rough, irregular, non-uniform surface structure as seen in the photomicrograph (Figure 3.6a). It can be seen that the fine layer of graft at the surface alters

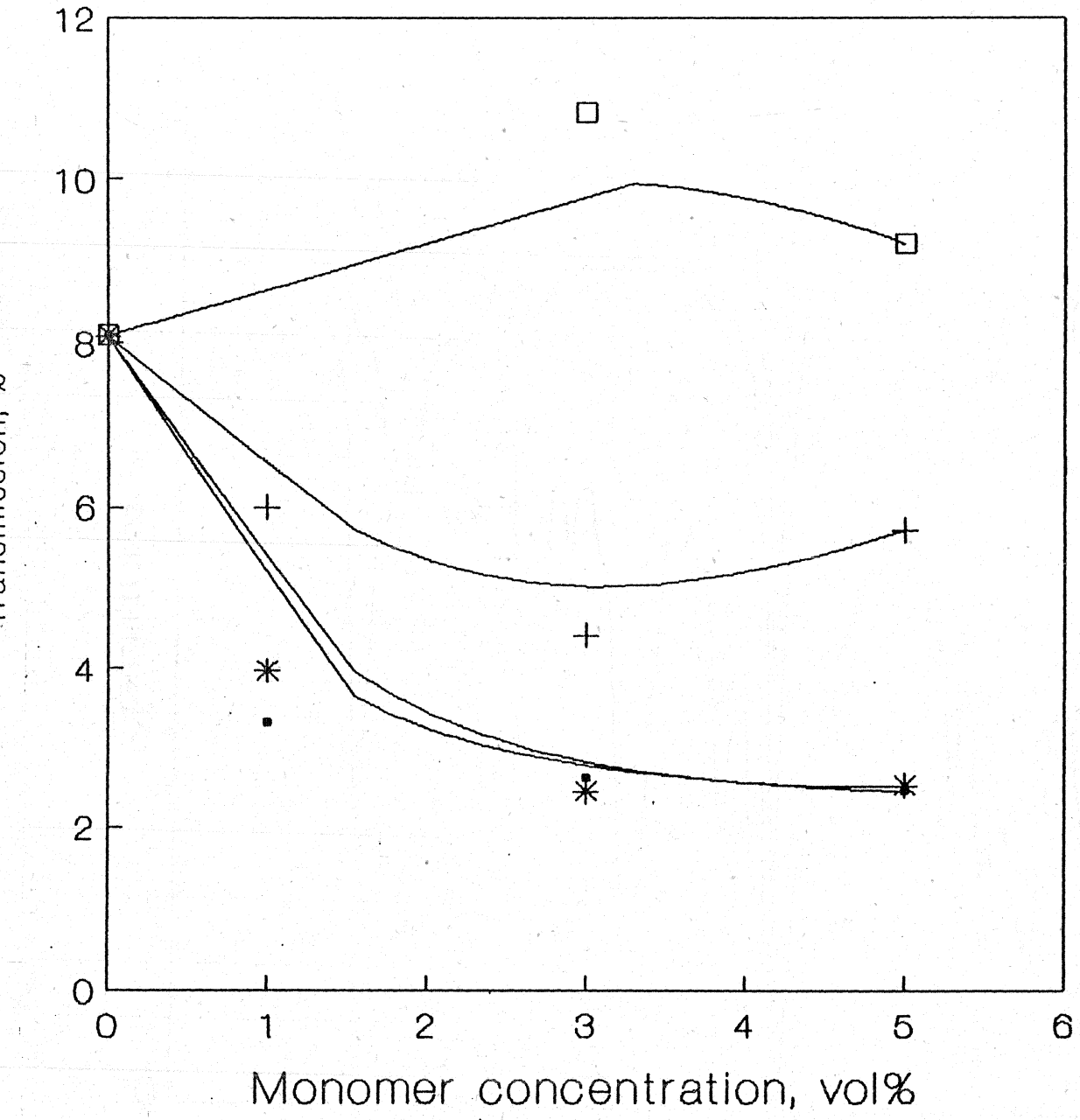


Figure 3.4. Variation in percentage transmission values with increasing monomer concentration for NVP:HEMA and NVP grafted PVC systems: The transmission values were determined at 700 nm using a double beam UV-VIS spectrophotometer. Figure shows values obtained for NVP25:HEMA75 (.), NVP50:HEMA50 (+), NVP75:HEMA25 (*) and NVP100 (□) systems radiation grafted to PVC [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 10%. A minimum of 4 samples was used for each system in all optical experiments.

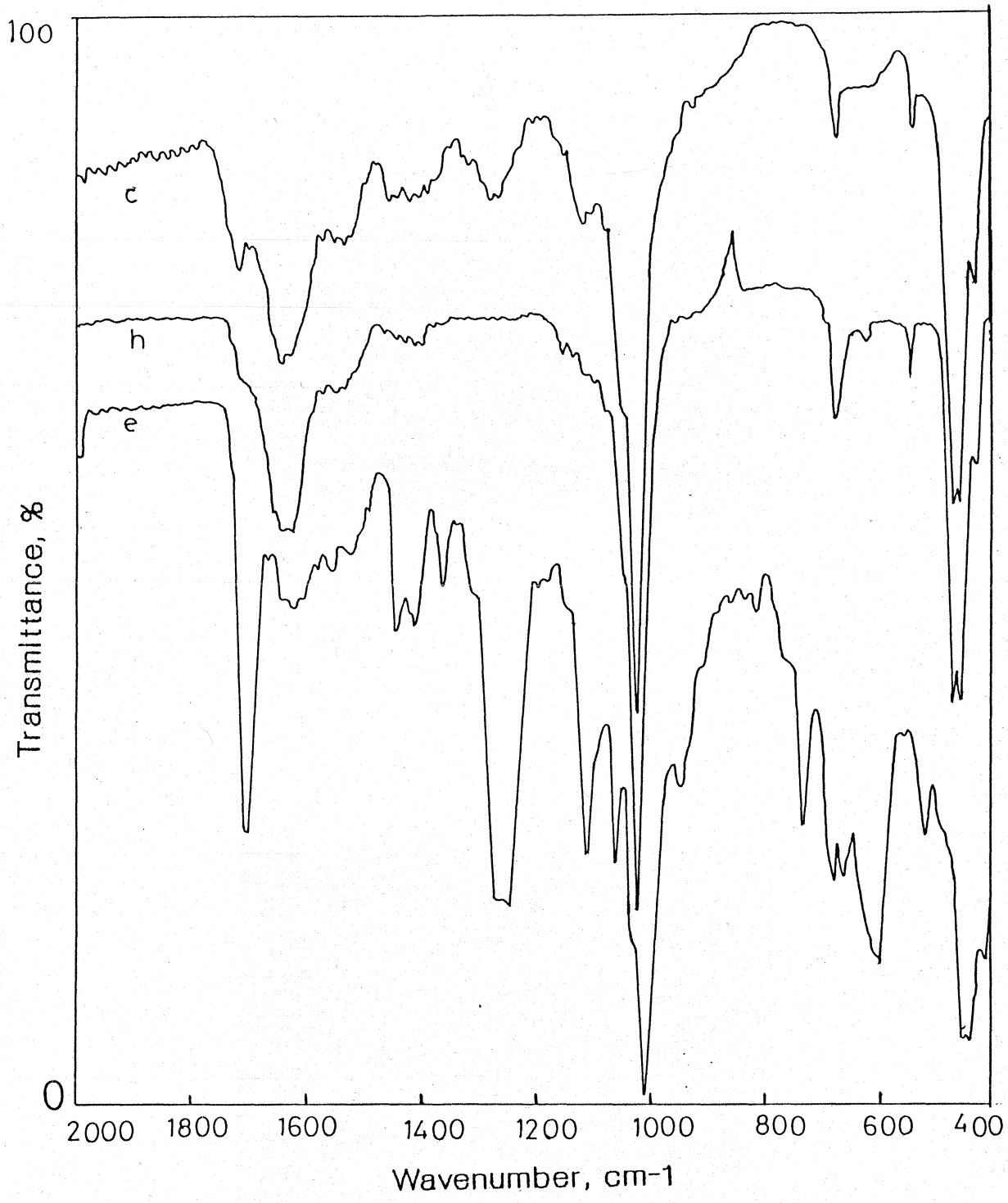


Figure 3.5. ATR-IR spectra of PVC surfaces grafted with NVP:HEMA monomer combinations: ATR-IR spectra of radiation grafted PVC with NVP25:HEMA75 (c), NVP50:HEMA50 (h) and NVP75:HEMA25 (e) monomer combinations and recorded at an incidence angle of 45° [all 5 vol%, 0.005M Cu^{2+}, 0.25 Mrads]

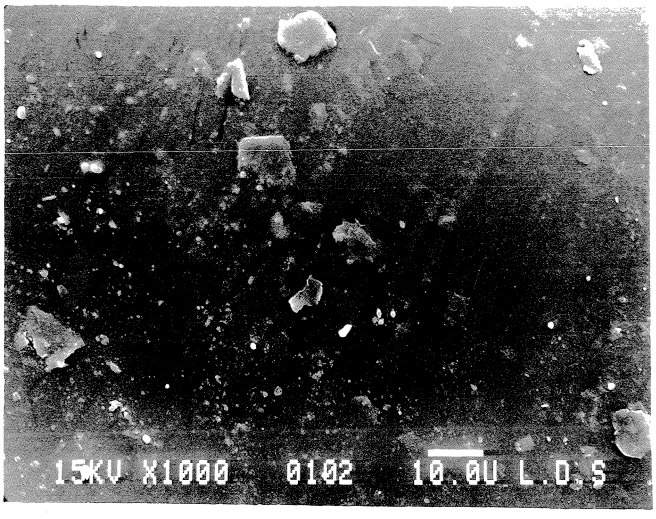


Figure 3.6a. Scanning Electron Micrograph of ungrafted PVC surface.

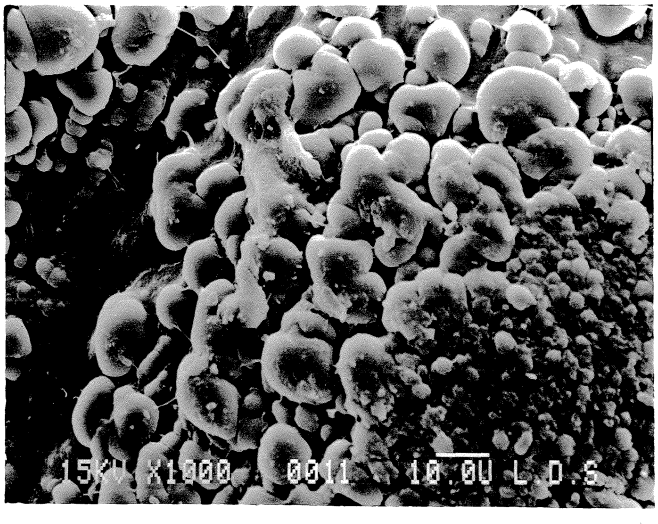


Figure 3.6b. Scanning Electron Micrograph of PVC surface grafted with 3% NVP25:HEMA75 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

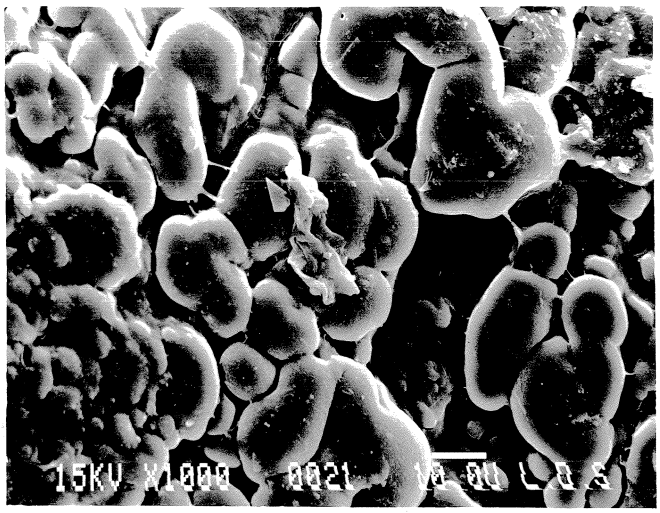


Figure 3.6c. Scanning Electron Micrograph of PVC surface grafted with 3% NVP50:HEMA50 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

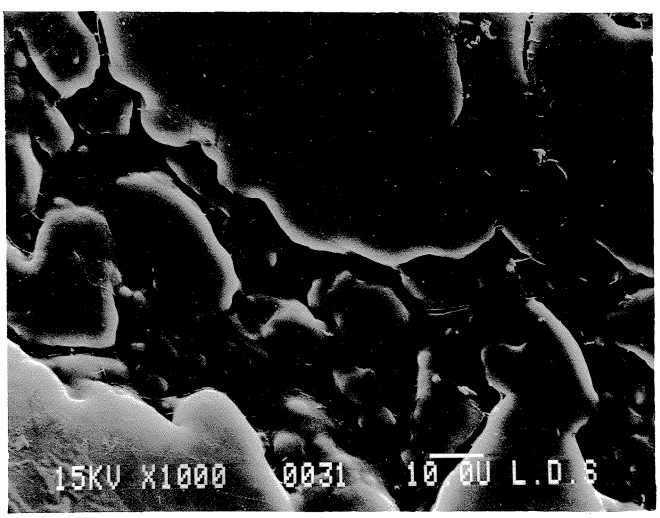


Figure 3.6d. Scanning Electron Micrograph of PVC surface grafted with 3% NVP75:HEMA25 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

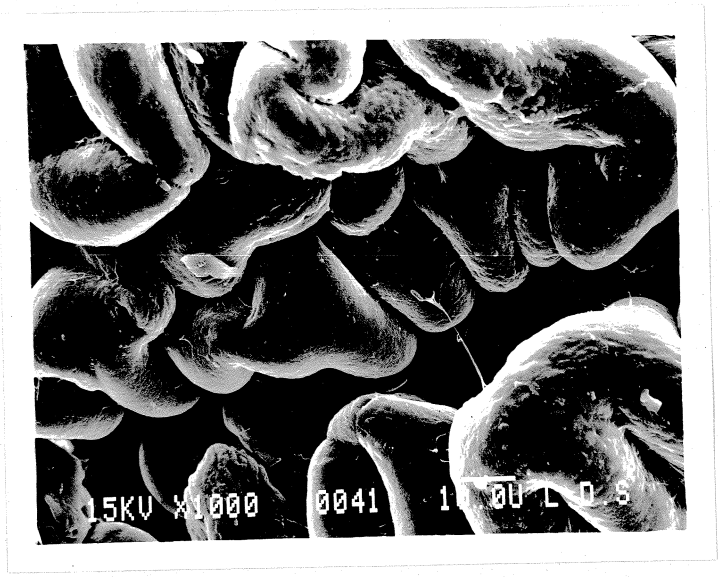


Figure 3.6e. Scanning Electron Micrograph of PVC surface grafted with 5% NVP25:HEMA75 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

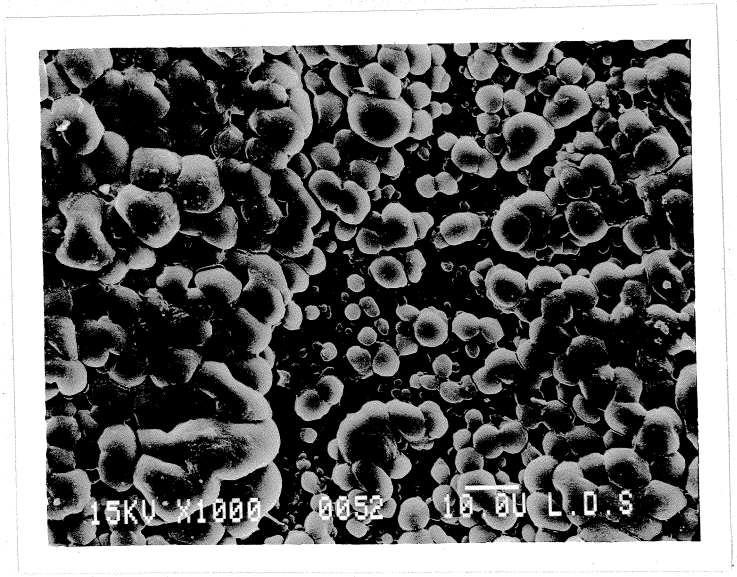


Figure 3.6f. Scanning Electron Micrograph of PVC surface grafted with 5% NVP50:HEMA50 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

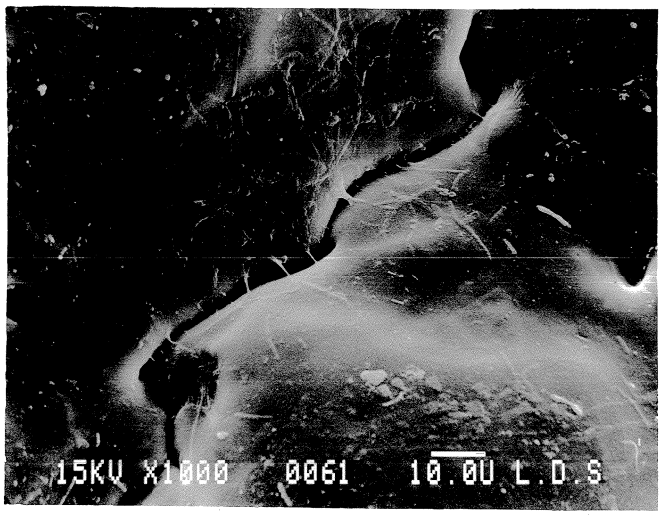


Figure 3.6g. Scanning Electron Micrograph of PVC surface grafted with 5% NVP75:HEMA25 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

Figure 3.6h. Scanning Electron Micrograph of PVC surface grafted with 7% NVP25:HEMA75 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

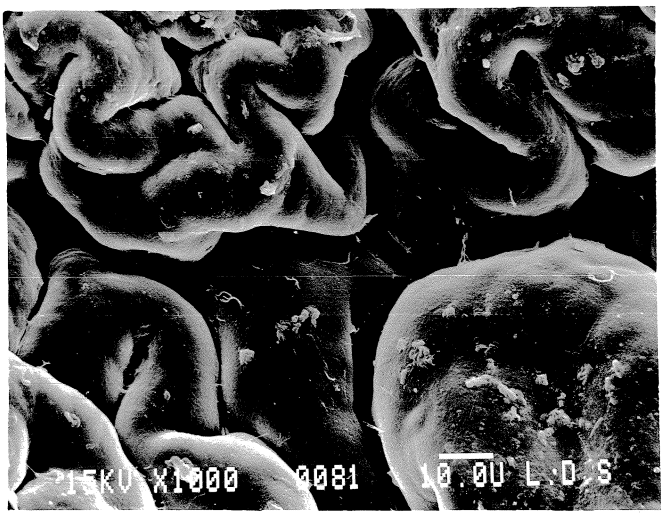


Figure 3.6i. Scanning Electron Micrograph of PVC surface grafted with 7% NVP50:HEMA50 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

Figure 3.6j. Scanning Electron Micrograph of PVC surface grafted with 7% NVP75:HEMA25 monomer combination[0.005M Cu^{2+}, 0.25 Mrads]

the surface morphology completely. It is observed that when the NVP content goes up, the coiled graft layers (due to PHEMA) becomes more discoid in shape due to the dominance of PVP in the graft layers. Samples grafted with NVP75:HEMA25 combination are totally discoid on the surface compared to the dominant coiled polymer structure due to PHEMA as in NVP25:HEMA75 system. Comparison of the optical photomicrographs of the control (Figure 3.7a) and grafted surfaces show the presence of the graft polymer on the grafted PVC surface (Figures 3.7b - 3.7d) with clear distinction on the the dominance of either PHEMA or PVP on the surface.

III.1.2. NVP System:

III.1.2.1.Grafting of NVP onto PVC:

III.1.2.1.a. Effect of Monomer Concentration on Graft Yield:

Concentrations of NVP in the range of 1 to 7 vol% were used in the experiments (62). The percentage graft yield was found to increase linearly with NVP concentration as in the previous system (Figure 3.8). A surface grafting of nearly 1.09 mg/cm^2 was obtained when 5 vol% NVP was used for grafting.

III.1.2.1.b. Effect of Presence of Cu^{2+} in the Grafting Medium:

No homopolymerization was observed while grafting NVP onto PVC due to the presence of cupric ions in the reaction medium as in the case of NVP/HEMA system. Figure 3.9 shows the extent to

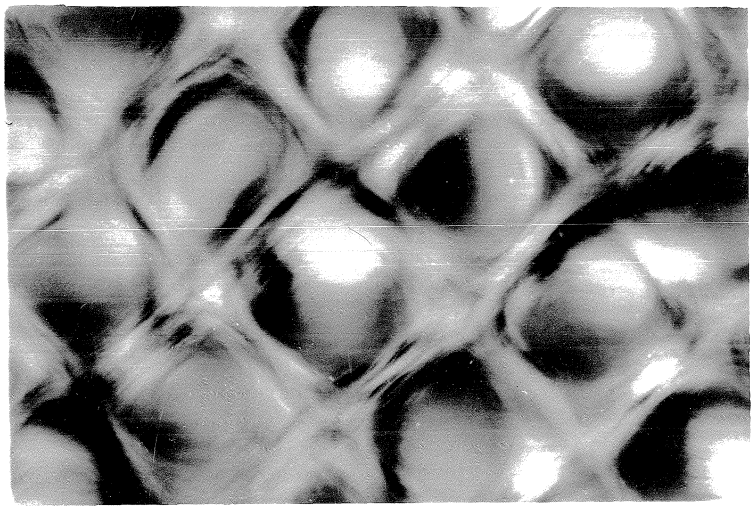


Figure 3.7a. Optical photomicrograph of ungrafted PVC surface (50x) photographed using a phase contrast Nikon microscope.

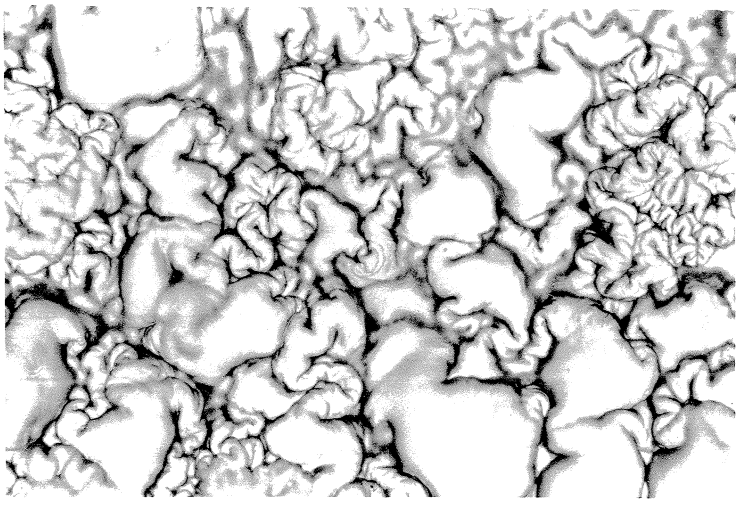


Figure 3.7b. Optical photomicrograph of PVC surface grafted with 5% NVP25:HEMA75 monomer combination[50x, 0.005M Cu^{2+}, 0.25 Mrads]

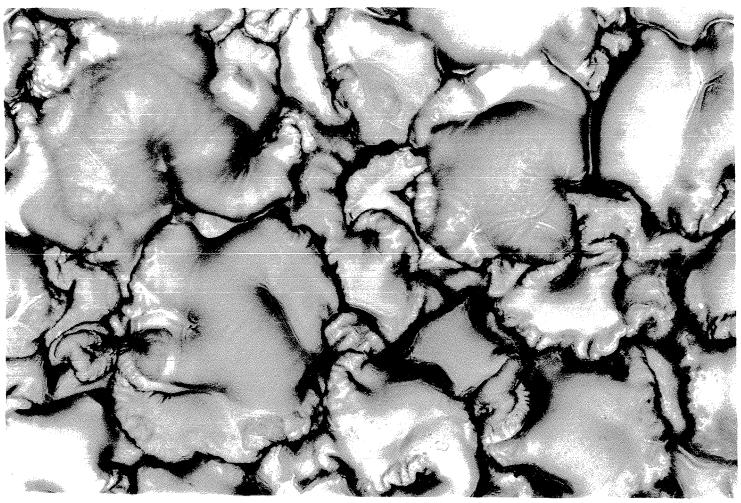


Figure 3.7c. Optical photomicrograph of PVC surface grafted with 5% NVP50:HEMA50 monomer combination[50x, 0.005M Cu^{2+}, 0.25 Mrads]

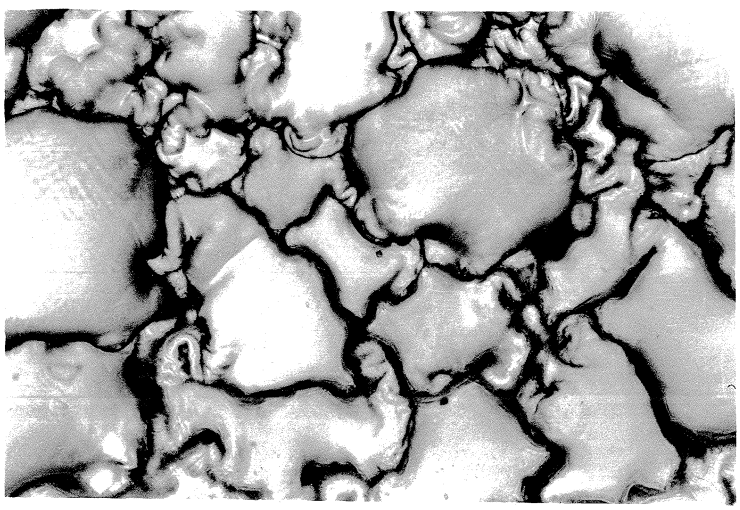


Figure 3.7d. Optical photomicrograph of PVC surface grafted with 5% NVP75:HEMA25 monomer combination[50x, 0.005M Cu^{2+}, 0.25 Mrads]

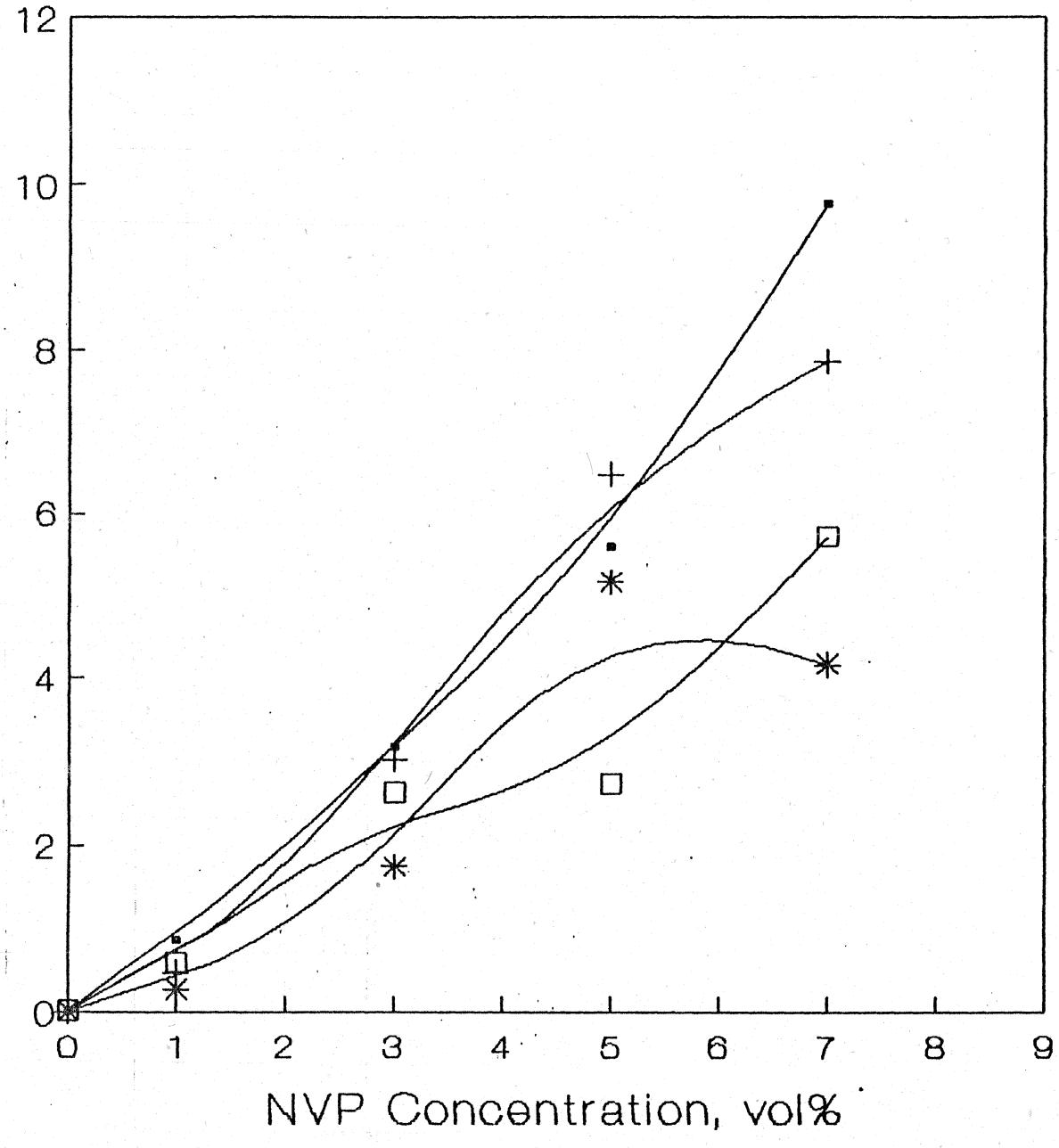


Figure 3.8. Effect of Cu^{2+} ion concentration on graft yield for NVP system: Figure shows increase in graft yield with NVP concentration for PVC sheets grafted with NVP in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions [0.25 Mrads]. S.D. was within ± 5%.

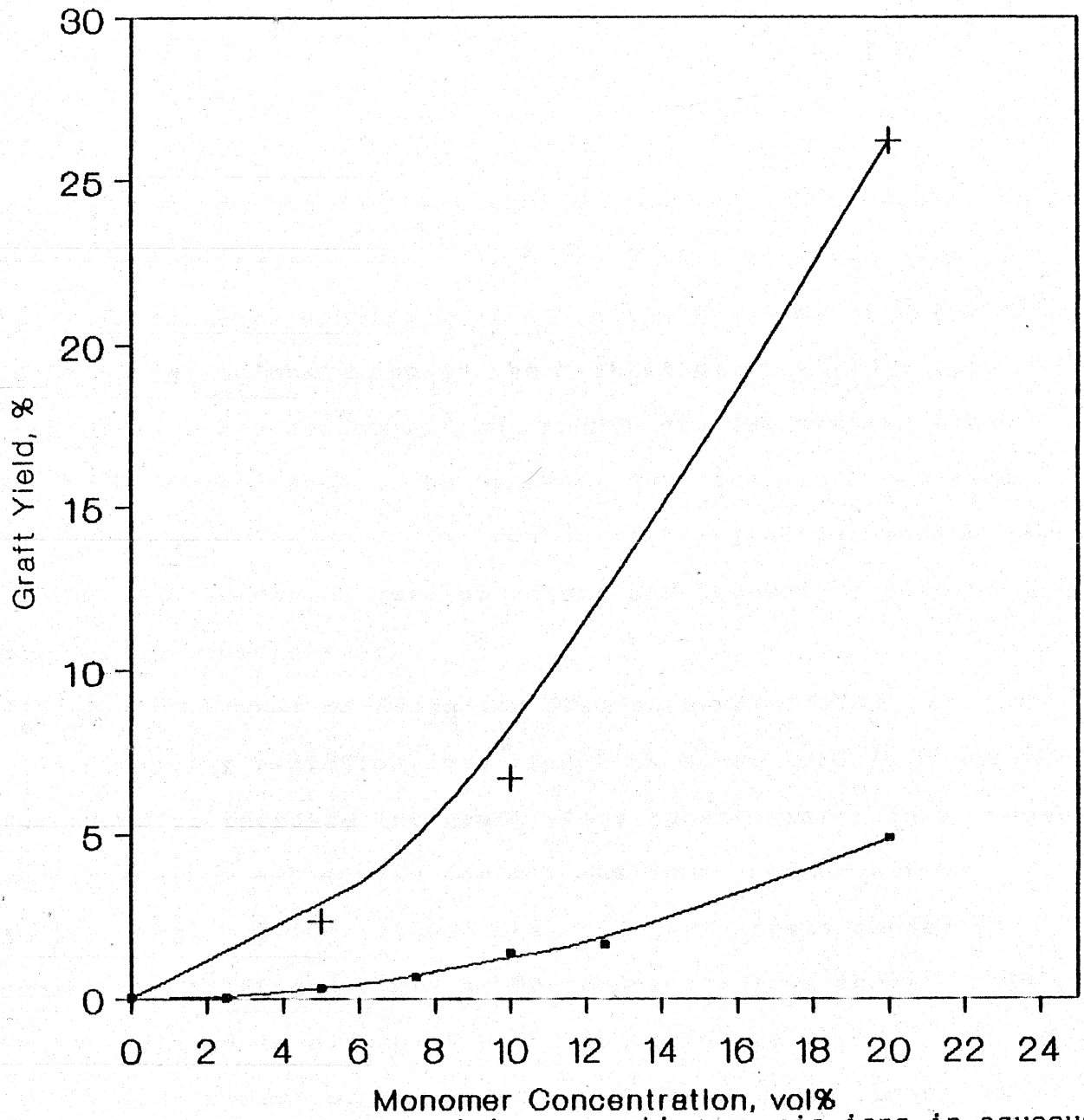


Figure 3.9. Advantage of incorporating cupric ions in aqueous grafting medium for improving graft yield: Figure shows drastic improvement in graft yield with NVP concentration for PVC sheets grafted with the monomer when 0.005M Cu^{2+} ions incorporated into distilled water (+) was used as the grafting medium compared to aqueous medium without metal ions (.) [0.25 Mrads]. No gel formation was observed in the former system. S.D. was within $\pm$ 5%

which the graft yield is enhanced when the aqueous grafting medium contained 0.005M of Cu^{2+} ions.

III.1.2.1.c. Effect of Concentration of Cu^{2+} upon Graft Yield:

Molarity of the Cu^{2+} was varied from 0.0025M to 0.01M, while monomer concentrations of 1, 3, 5 and 7 vol% were employed for grafting. However, samples grafted in the presence of 0.0025M to 0.005M copper sulphate showed the highest graft yield values compared to other concentrations in NVP grafted systems also (Figure 3.8). No trace of homopolymer was found to be present even when the Cu^{2+} ion concentration in the grafting medium was 0.0025M. The solutions were all clear and colourless with no trace of any homopolymer.

III.1.2.1.d. Effect of Radiation Dose on Graft Yield:

Increasing radiation dose from 0.25 Mrads to 0.75 Mrads is also found to increase the graft yield substantially in a linear fashion for the NVP system for all the four concentrations studied (Figure 3.10). It was observed that sheets tended to become more stiff and rigid at NVP concentrations above 5 vol% when irradiated to a dose of 0.5 Mrads or above.

III.1.2.1.e. Effect of the Presence of Cross-linker on Graft Yield:

The effects of small quantities of the cross-linker, ethylene dimethacrylate (EDMA) in the monomer is of interest as it is used to prepare crosslinked hydrogels for biomedical

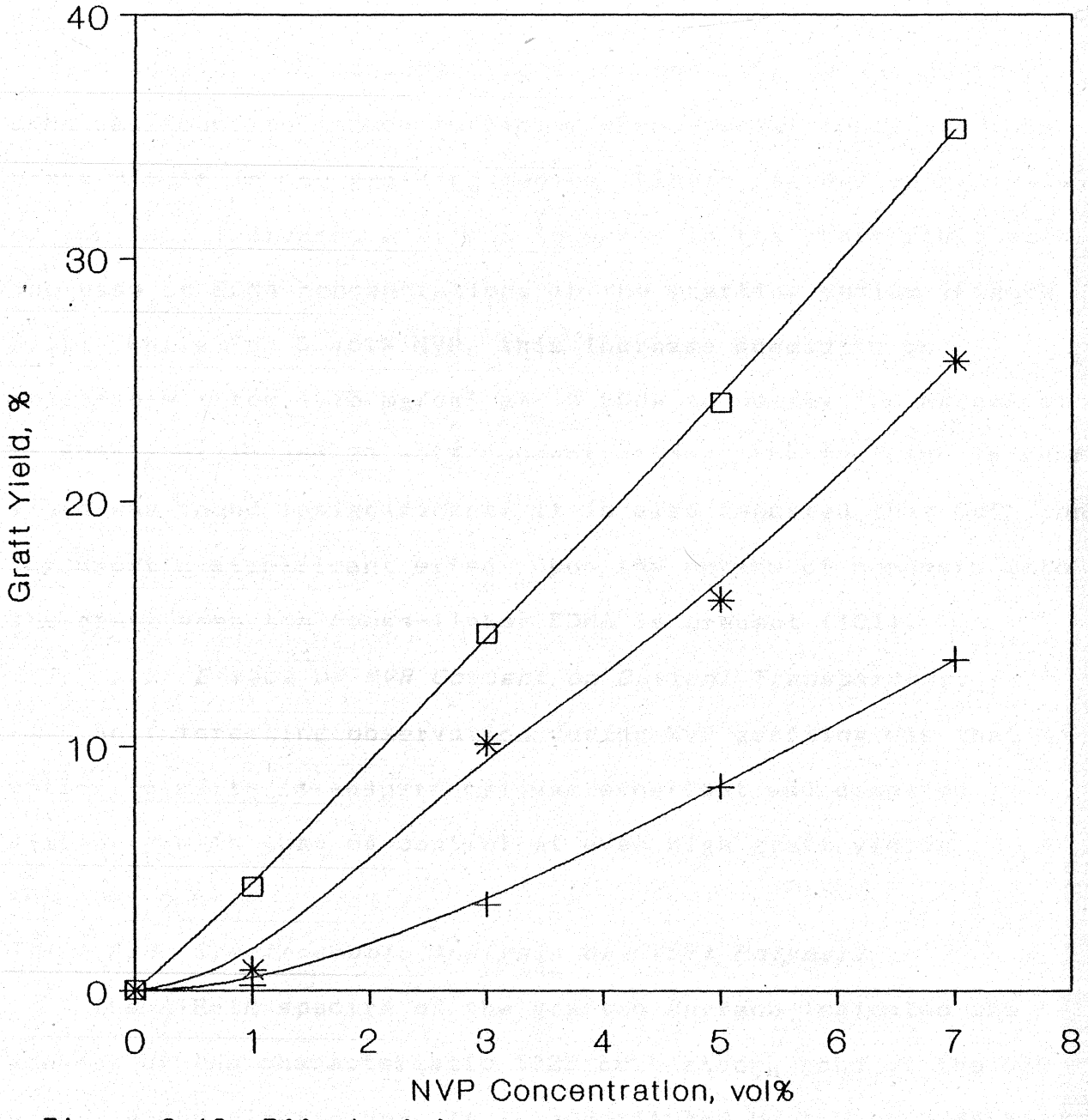


Figure 3.10. Effect of increasing radiation dose on graft yield for NVP system: Increase in graft yield is observed at higher radiation doses for different concentrations of NVP grafted to PVC at 0.25 (+), 0.5 (*) and 0.75 (□) Mrads [0.005M Cu^{2+}]. S.D. was within ± 5%.

applications. The effect of the presence of cross-linker on the graft yield was studied by varying EDMA concentrations from 1 to 5 vol% keeping NVP concentrations constant (5, 10 and 20 vol%). EDMA was found to induce turbidity when used at concentrations above 3 vol% in the grafting medium. Linear regression analysis of the data indicated a slight increase in the graft yield with increase in EDMA concentrations in the grafting medium (Figure 3.11). While for 5 vol% NVP, this increase seemed to be noticeable (from 1.13 mg/cm^2 at 1% EDMA to nearly 1.8 mg/cm^2 at 5% EDMA), at 10 and 20 vol% concentrations, the increase in graft yield was found insignificant. It is also reported that Cu^{2+} ion may exert a significant effect upon the uptake of monomers into the graft when the cross-linker EDMA is present (101).

III.1.2.2. Effect of NVP Content on Optical Transparency:

An interesting observation during NVP grafting was that optical clarity (transparency) was excellent and compared similarly with that of control at even high graft yields (Figure. 3.4).

III.1.2.3. Spectroscopic Analysis of Graft Polymer:

The ATR-IR spectra of the grafted surface indicated the absence of the characteristic 1725 cm^{-1} strong band of the C=O group in the plasticizer. It is substituted by the weak doublet at 1710 cm^{-1} characteristic of the carbonyl functions present in PVP) (Figure 3.12). Similarly the 1008 cm^{-1} peak is

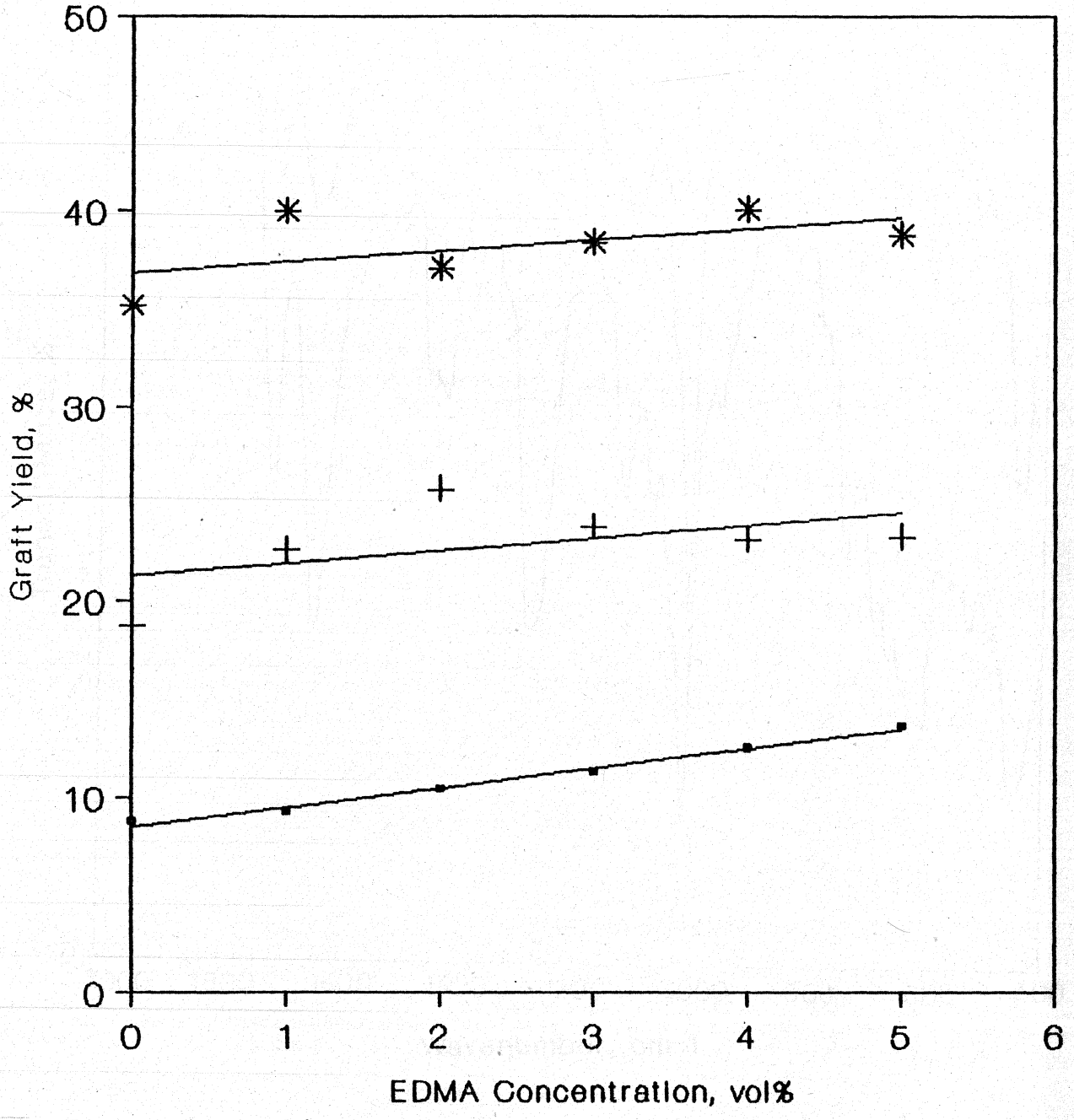


Figure 3.11. Linear regression plots showing variation in graft yield with cross-linker (EDMA) content for NVP system: Figure shows only negligible variation in graft yield with cross-linker (EDMA) content incorporated with 5% NVP (.), 10% NVP (+) and 20% NVP (*) grafted to PVC [0.25 Mrads, 0.005M Cu^{2+}]. S.D. was within $\pm$ 10%.

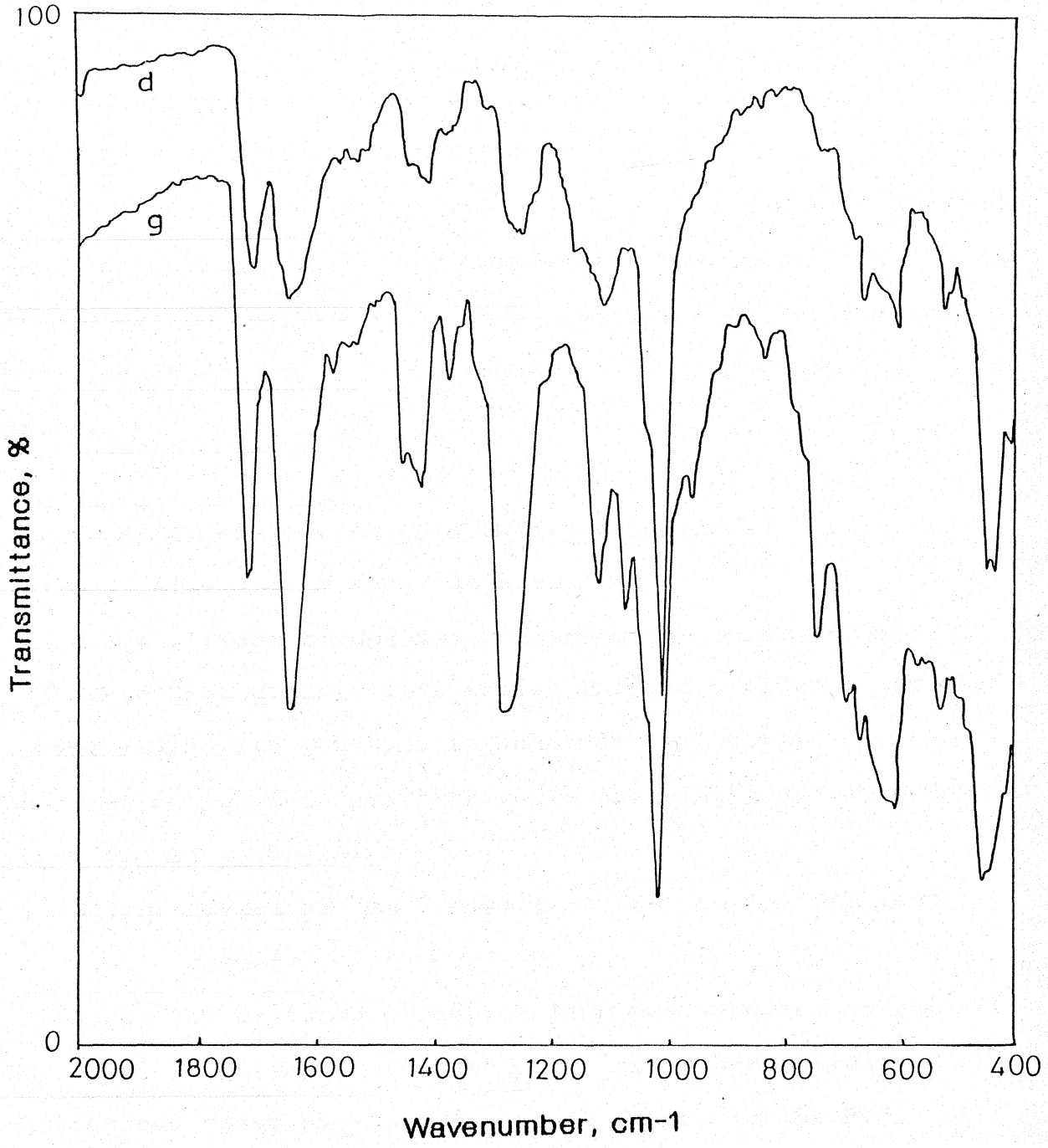


Figure 3.12. ATR-IR spectra of PVC surfaces grafted with NVP: ATR-IR spectra of radiation grafted PVC with 5% NVP with no cross-linker (d) and containing 2% EDMA cross-linker (g) [0.005M Cu^{2+}, 0.25 Mrads].

characteristic of the amide type carbonyl in PVP.

III.1.2.4. Microscopic Evaluation:

It can be seen that the fine layer of graft at the surface alters the surface morphology completely. The optical photomicrograph (Figure 3.13) shows the existance of discoid shaped PVP structure on the surface of the support polymer clearly.

III.1.3. HEMA-Methacrylic Acid (MAA) System:

III.1.3.1. Grafting of HEMA/MAA onto PVC:

III.1.3.1.a. Effect of Monomer Concentration on Graft Yield:

Figure 3.14 clearly illustrates the proportionate increase in graft yield with increase in HEMA:MAA (1:1 vol%) concentration for four grafting media containing varying amounts of Cu^{2+} (0025M to 0.01M) (64).

III.1.3.1.b. Effect of the Presence of Cu^{2+} in the Grafting Medium:

Though the presence of copper ions was expected to prevent homopolymer formation during grafting, heavy homopolymer formation was observed which tended to adhere to the PVC substrate. However, it was found not difficult to remove the homopolymer after the grafting as it peeled off very easily leaving the grafted surface clean.

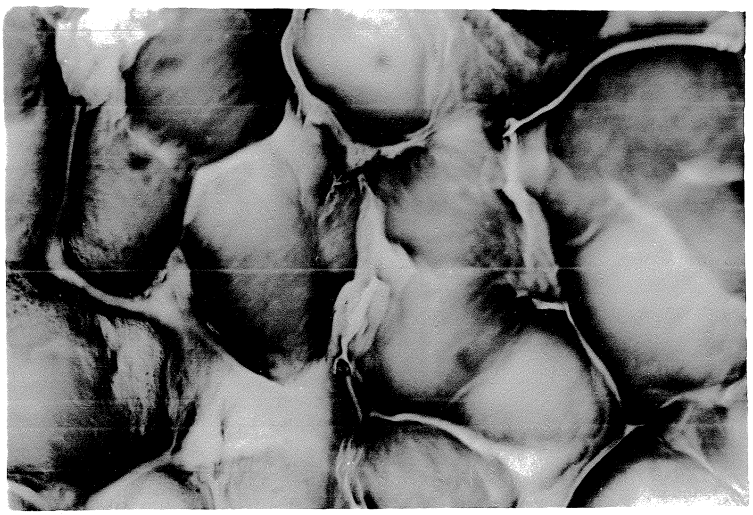


Figure 3.13. Optical photomicrograph of 5% NVP grafted PVC surface [50x, 0.005M Cu^{2+}, 0.25 Mrads].

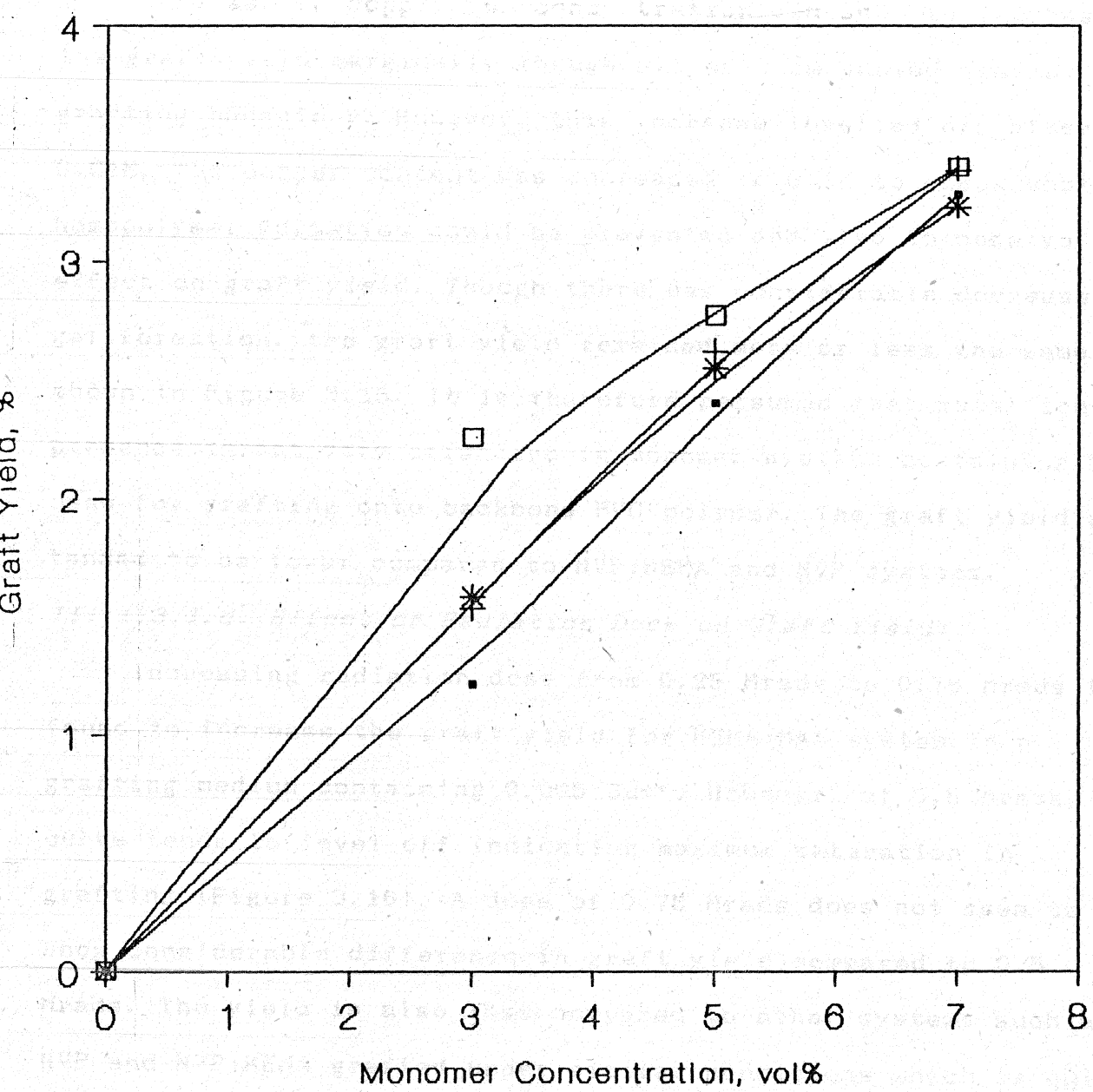


Figure.3.14. Effect of Cu^{2+} ion concentration on graft yield for HEMA50:MAA50 system: Plot shows increase in graft yield with monomer concentration for HEMA50:MAA50 grafted in aqueous media containing 0.0025M (+), 0.005M (*), 0.0075M (□) and 0.01M (x) Cu^{2+} ions [0.25 Mrads]. S.D. was within $\pm$ 5%.

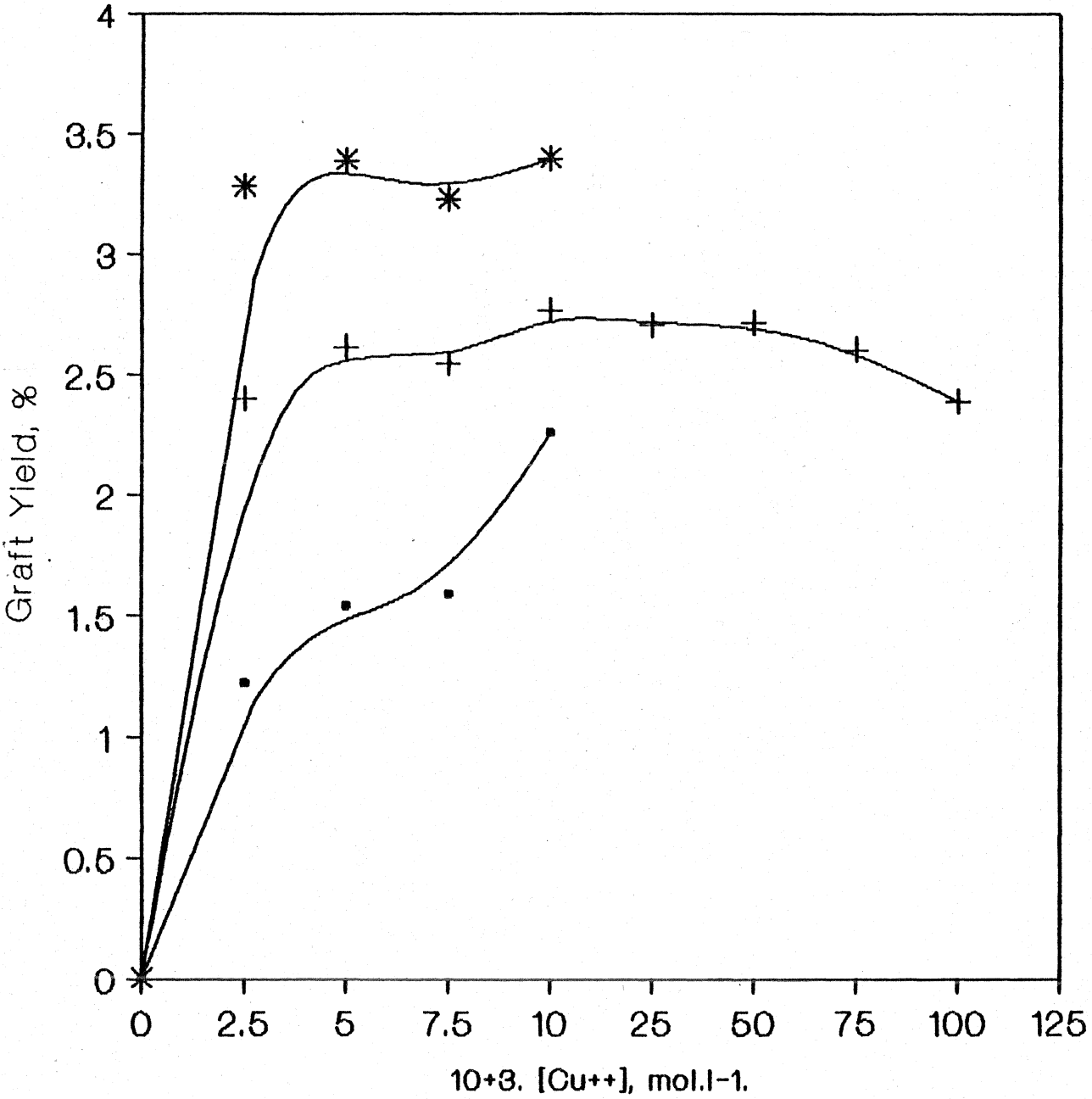


Figure 3.15. Variation in graft yield with increasing Cu^{2+} concentration for HEMA50:MAA50 system: Figure shows lack of effeciency in metal ions in preventing homopolymer formation when 3% (.), 5% (+) and 7% (✳) HEMA50:MAA50 is grafted to PVC. The graft yield does not improve even when high concentrations (0.1M) of Cu^{2+} were used for the 5% monomer system. Heavy white gel formation was observed for all three systems [0.25 Mrads] S.D. was within ± 10%.

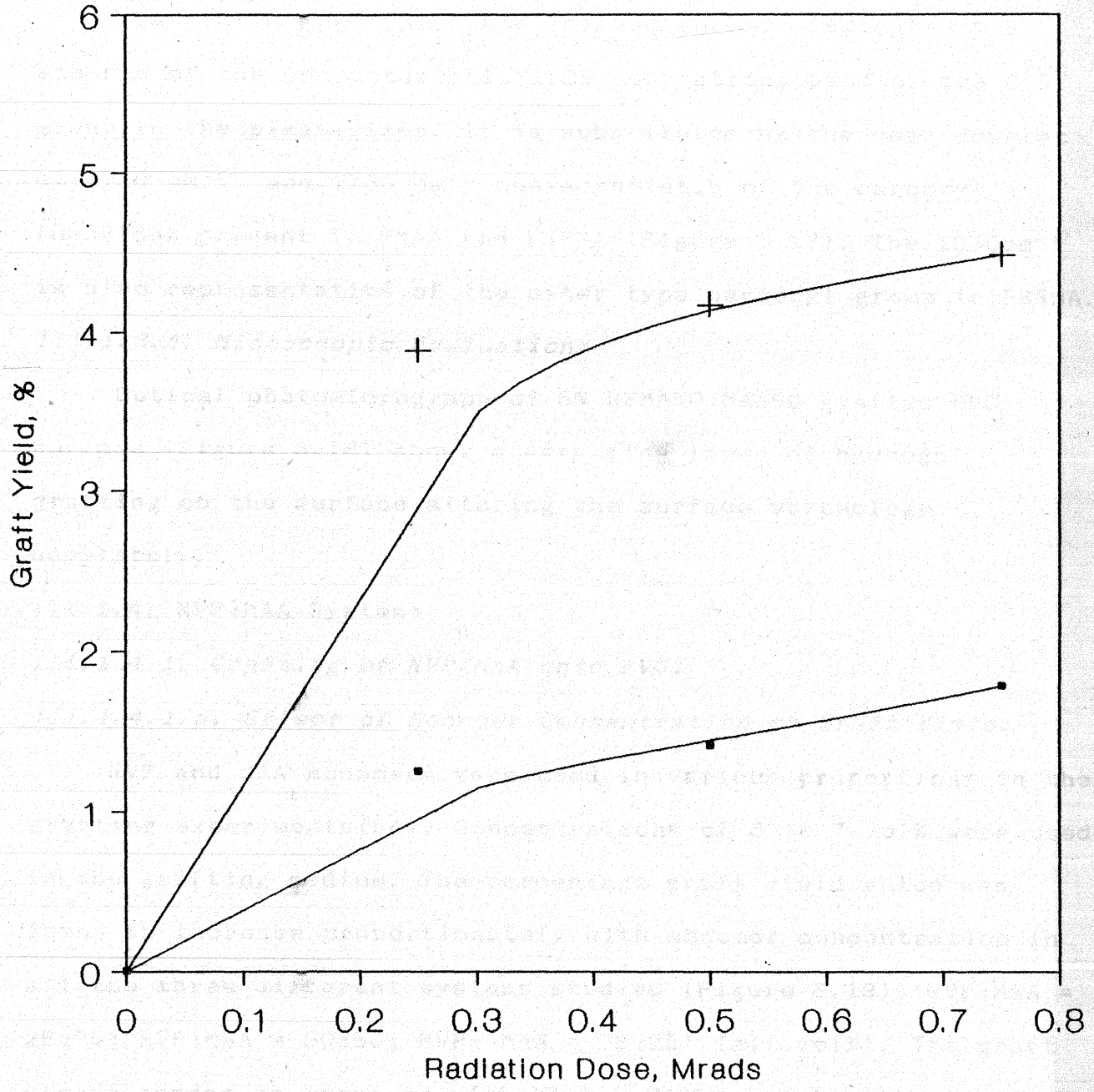


Figure 3.16. Effect of increasing radiation dose on graft yield for HEMA50:MAA50 system: Though graft yield remained low, it is seen to improve with increasing radiation doses when 3% (.) and 5% (+) HEMA50:MAA50 were grafted to PVC [0.005M Cu^{2+}].
S.D. was within $\pm$ 10%.

III.1.3.2. Spectroscopic Analysis of Graft Polymer:

The ATR-IR spectra of the grafted surface indicated the absence of the characteristic 1725 cm^{-1} strong band of the C=O group in the plasticizer. It is substituted by the weak doublet at 1710 cm^{-1} and 1730 cm^{-1} characteristic of the carbonyl functions present in PMAA and PHEMA (Figure 3.17). The 1030cm^{-1} is also representative of the ester type carbonyl group in PHEMA.

III.1.3.4. Microscopic Evaluation:

Optical photomicrograph of 5% HEMA50:MAA50 grafted PVC surface (Figure 3.18) shows a very fine layer of hydrogel grafting on the surface altering the surface morphology completely.

III.1.4. NVP:MAA System:

III.1.4.1. Grafting of NVP/MAA onto PVC:

III.1.4.1.a. Effect of Monomer Concentration on Graft Yield:

NVP and MAA monomers were used in various proportions in the grafting experiments(64). Concentrations of 3 to 7 vol% were used in the grafting medium. The percentage graft yield value was found to increase proportionately with monomer concentration in all the three different systems studied (Figure 3.19) (NVP:MAA = 25:75; NVP:MAA = 50:50; NVP: MAA = 75:25) (all vol%). The graft yields tended to increase with higher MAA concentrations unlike in HEMA:NVP systems where change in concentration of any one monomer did not change the graft yield drastically. Thus, graft

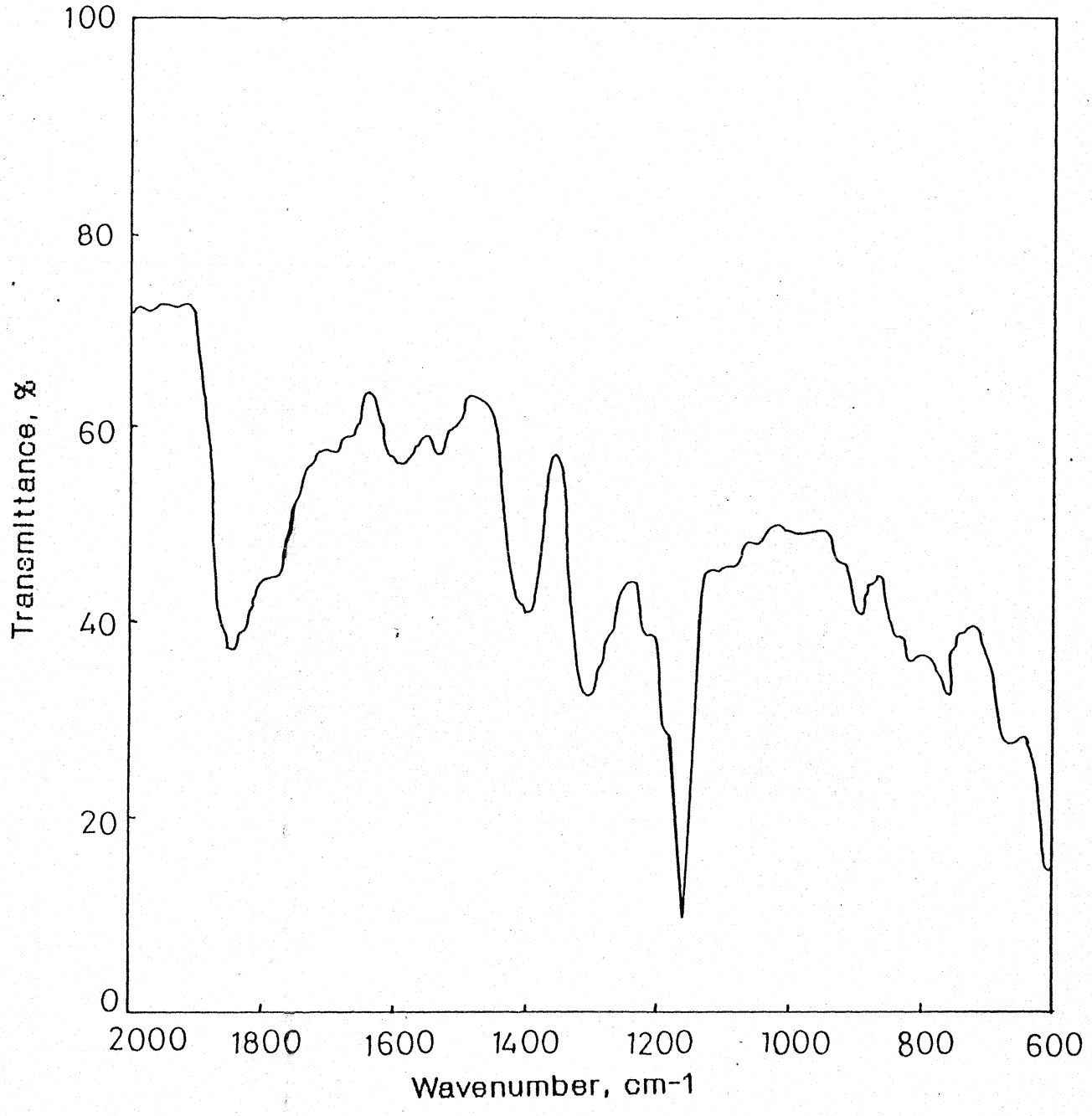


Figure 3.17. ATR-IR spectrum of PVC surface grafted with 5% HEMA50:MAA50 [0.005M Cu^{2+}, 0.25 Mrads].

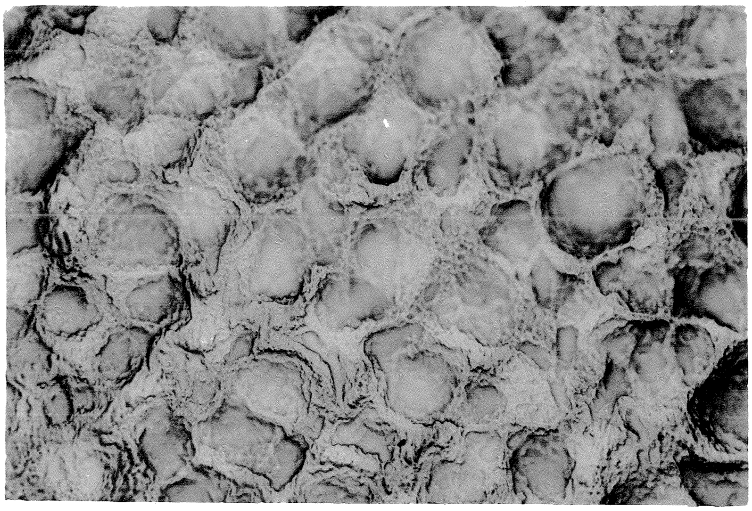


Figure 3.18. Optical photomicrograph of PVC surface grafted with 5% HEMA50:MAA50 [50x, 0.005M Cu^{2+}, 0.25 Mrads].

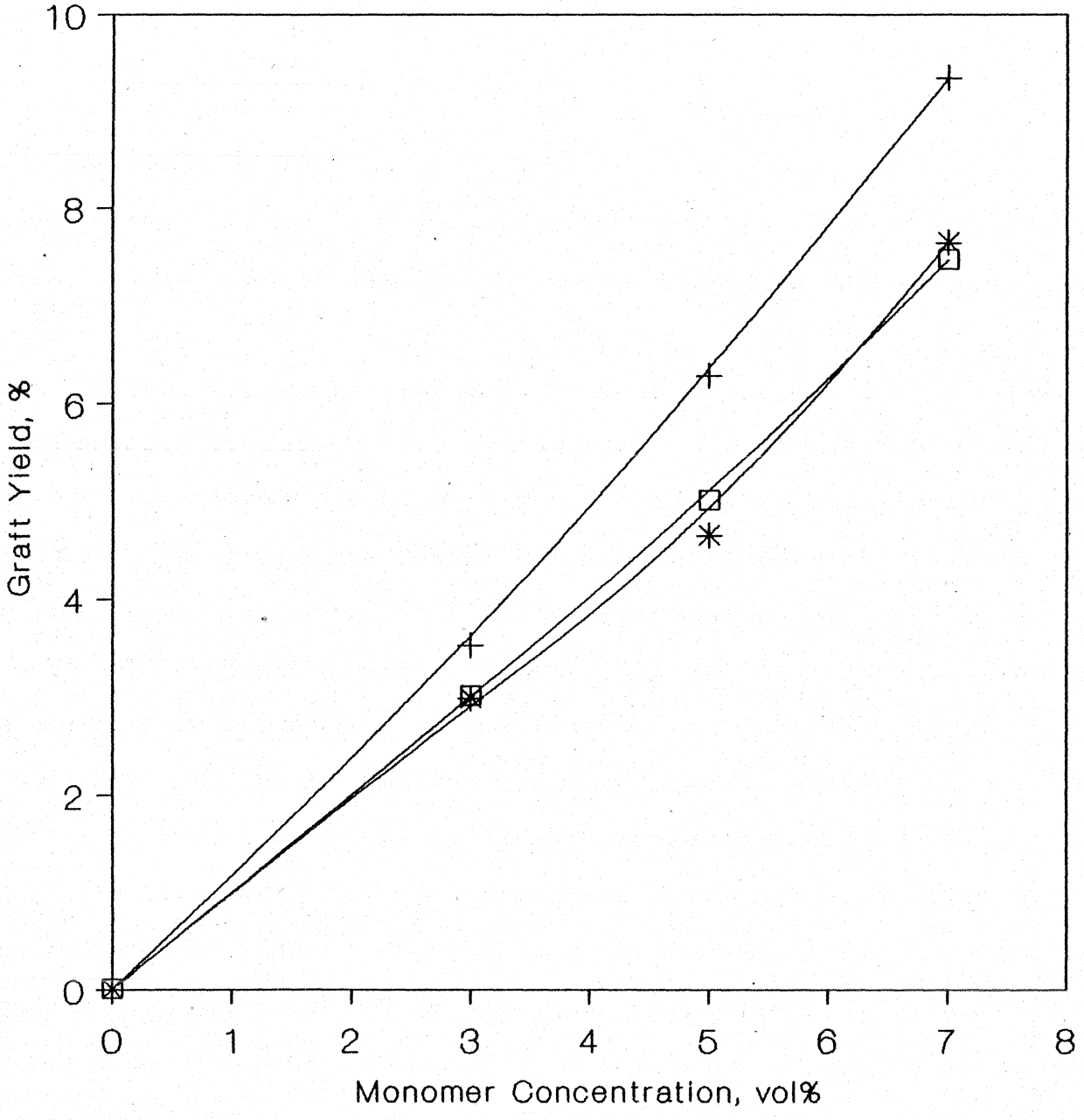


Figure 3.19. Variation in graft yield with monomer concentration for NVP:MAA systems: Figure shows proportionate increase in graft yield with monomer concentration for NVP25:MAA75 (+), NVP50:MAA50 (*) and NVP75:MAA25 (□) systems radiation grafted to PVC [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 5%.

yield values varied in the order N25M75> N50M50 > N75M25.

III.1.4.1.b. Effect of the Presence of Cu^{2+} in the Grafting Medium:

No homopolymerization was observed in any of the above systems studied during grafting due to the presence of cupric ions in the reaction medium unlike in HEMA:MAA systems. This makes the NVP:MAA system comparable with that of NVP:HEMA and NVP systems.

III.1.4.1.c. Effect of Concentration of Cu^{2+} upon Graft Yield:

Molarity of the Cu^{2+} was varied from 0.0025M to 0.01M, while monomer concentrations of 3, 5 and 7 vol% were employed for grafting. The graft yield was found to increase with increase in monomer concentrations for all the systems studied (0.0025M, 0.005M, 0.0075M and 0.01M). However, the graft yield was found to be maximum at 0.005M Cu^{2+} concentration for NVP:MAA system. (Figure 3.20). The homopolymer was found to be present when the Cu^{2+} ion concentration in the grafting medium was 0.0025M. The solutions were all clear and colourless with no trace of any homopolymer in other systems. Thus, the incorporation of cupric ions in the grafting system prevents homopolymerization and facilitates cleaning procedure of the grafted material to a significant extent.

III.1.4.1.d. Effect of Radiation Dose on Graft Yield:

Increasing radiation dose from 0.25 to 0.75 Mrads was also

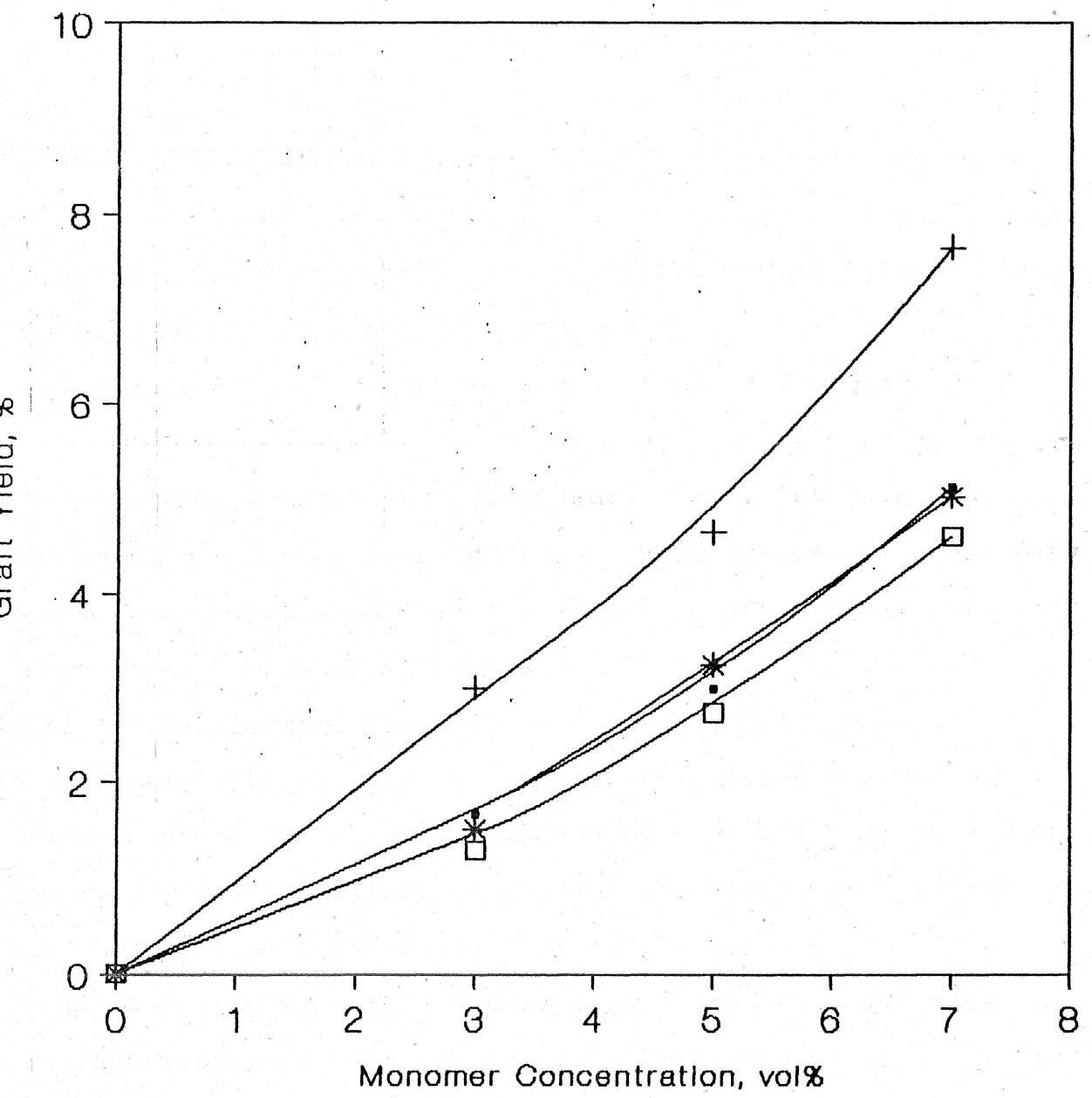


Figure 3.20. Effect of Cu^{2+} ion concentration on graft yield for NVP50:MAA50 system: Figure shows changes in graft yield plotted against monomer concentration for NVP50:MAA50 grafted to PVC in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions [0.25 Mrads].
S.D. was within ± 5%.

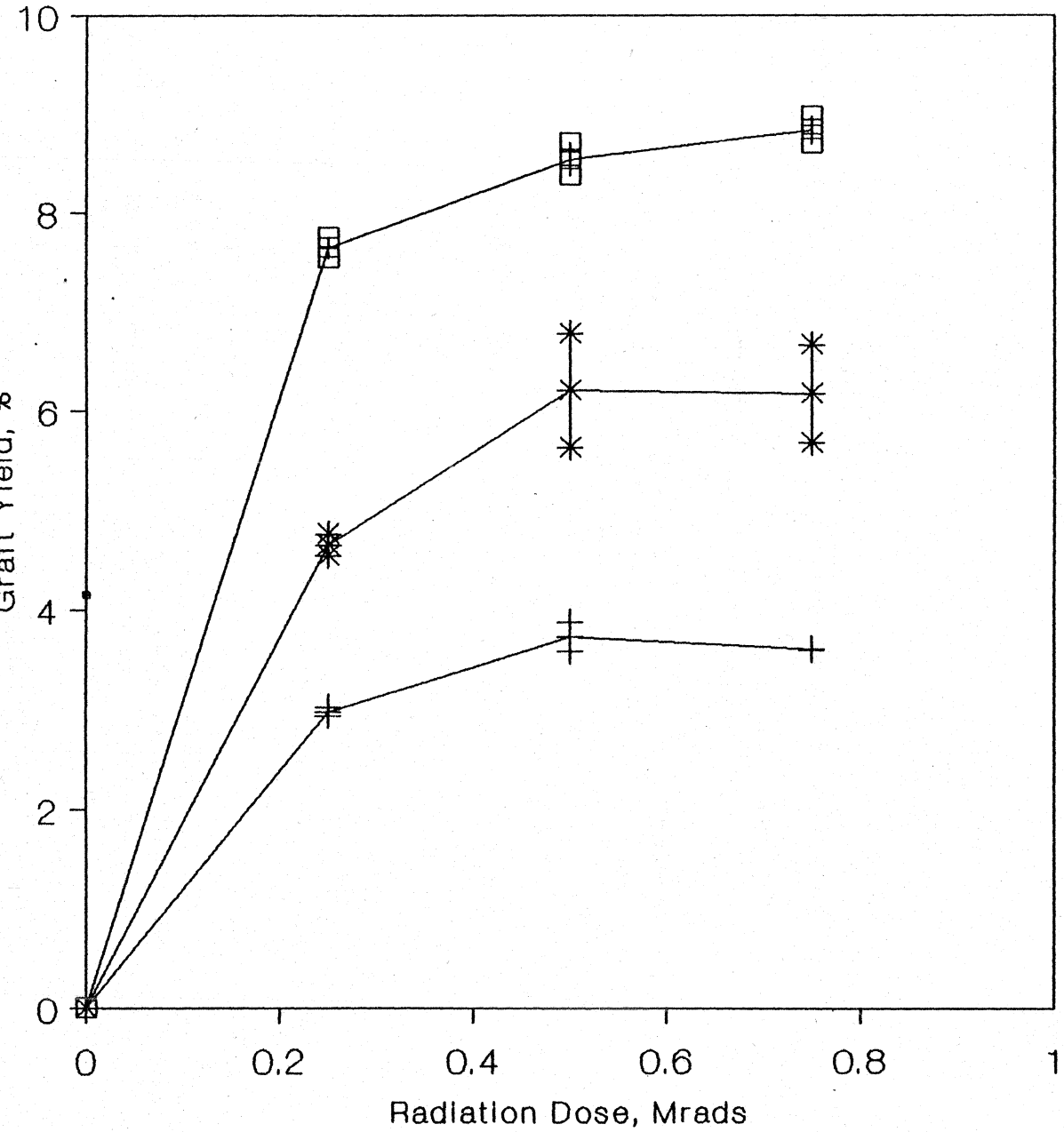


Figure 3.21. Effect of increasing radiation dose on graft yield for NVP50:MAA50 system: Graft yield is seen to attain saturation at about 0.5 Mrads as shown above when it is plotted against high radiation doses for 3% (+), 5% (*) and 7% (□) NVP50:MAA50 monomer systems grafted to PVC [0.005M Cu^{2+}, 0.25 Mrads].

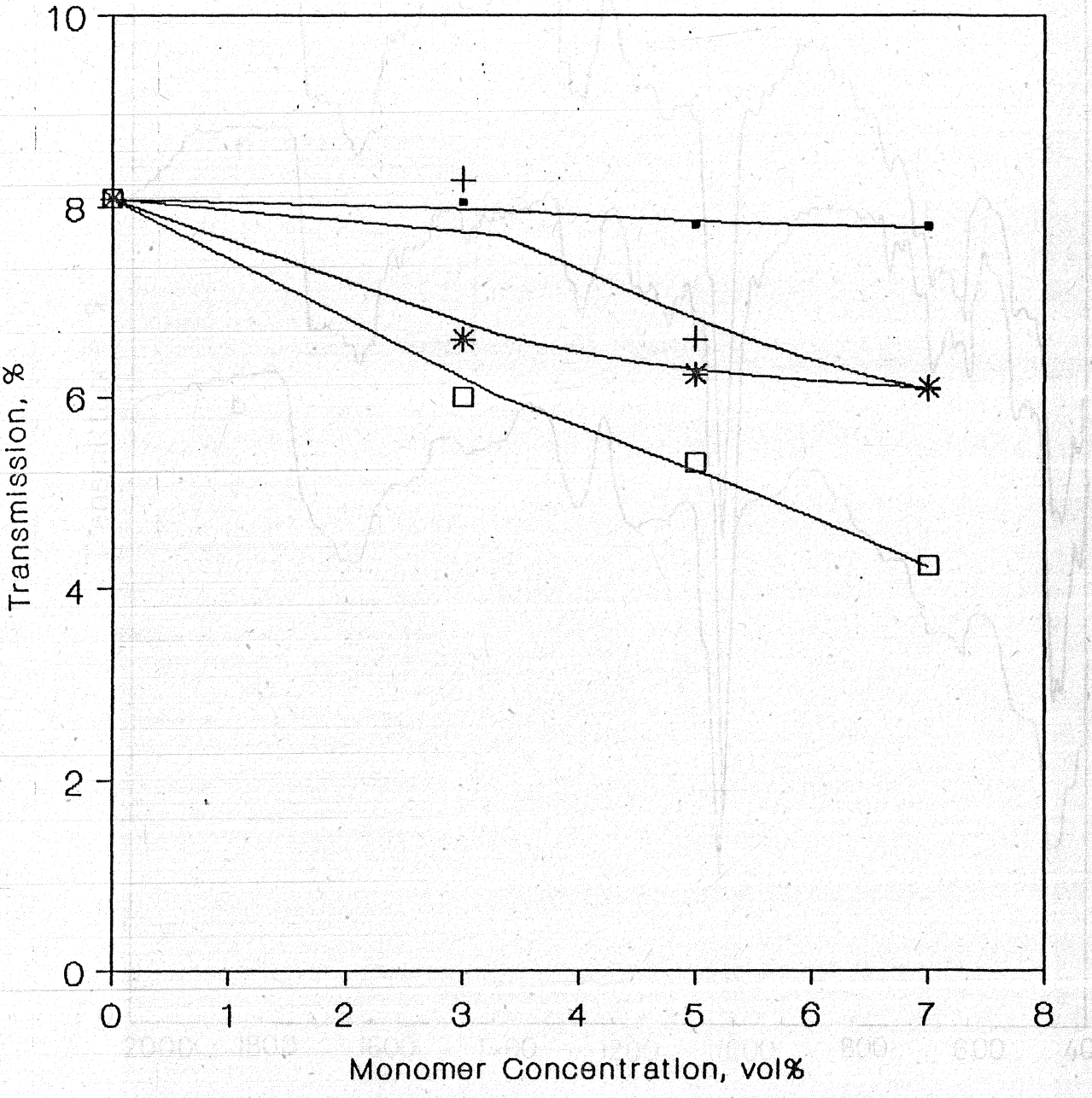


Figure 3.22. Variation in percentage transmission values with increasing monomer concentration for NVP:MAA and MAA grafted PVC systems: Figure shows decrease in transmission values with higher graft monomer contents obtained for NVP25:MAA75 (.), NVP50:MAA50 (+), NVP75:MAA25 (*) and MAA100 (□) systems grafted to PVC and measured at 700 nm in hydrated state [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 10%.

the presence of the grafted layer of the polymer (Figure 3.24) clearly.

III.1.5. MAA System:

III.1.5.1. Grafting of MAA System onto PVC:

III.1.5.1.a. Effect of Monomer Concentration on Graft Yield:

Figure 3.25 clearly illustrates the proportionate increase in graft yield with increase in MAA concentration for the four grafting media containing varying amounts of Cu^{2+}.

III.1.5.1.b. Effect of the Presence of Cu^{2+} in the Grafting Medium:

No homopolymerization was observed while grafting MAA onto PVC due to the presence of cupric ions in the reaction medium as in the case of NVP or NVP/HEMA or NVP/MAA.

III.1.5.1.c. Effect of Concentration of Cu^{2+} upon Graft Yield:

Molarity of the Cu^{2+} was varied from 0.0025M to 0.01M while monomer concentrations of 1, 3, 5 and 7 vol% were employed for grafting. However, samples grafted in the presence of 0.01M copper sulphate showed the highest graft yield values compared to other concentrations in MAA grafted systems(Figure 3.25). This suggests that for every monomer system, there exists an optimum metal ion concentration at which the graft yield reaches a maximum value. Howvever, no trace of homopolymer was found to be present even when the Cu^{2+} ion concentration in the grafting

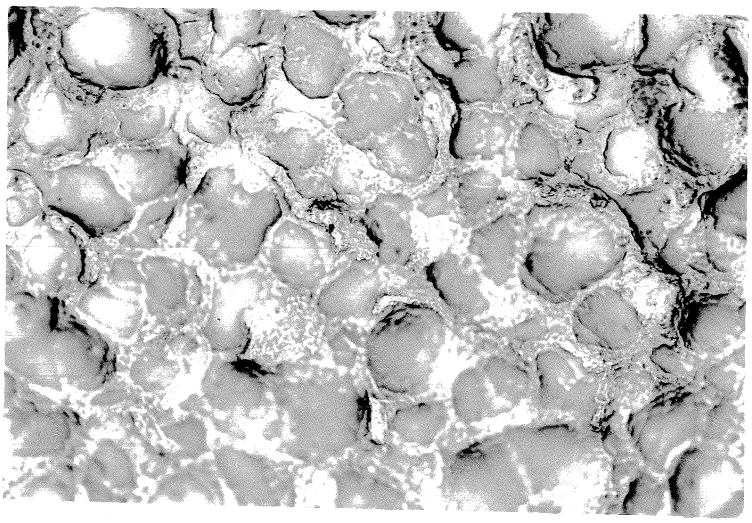


Figure 3.24. Optical photomicrograph of PVC surface grafted with 5% NVP50:MAA50 monomer combination [50x, 0.005M Cu^{2+}, 0.25 Mrads]

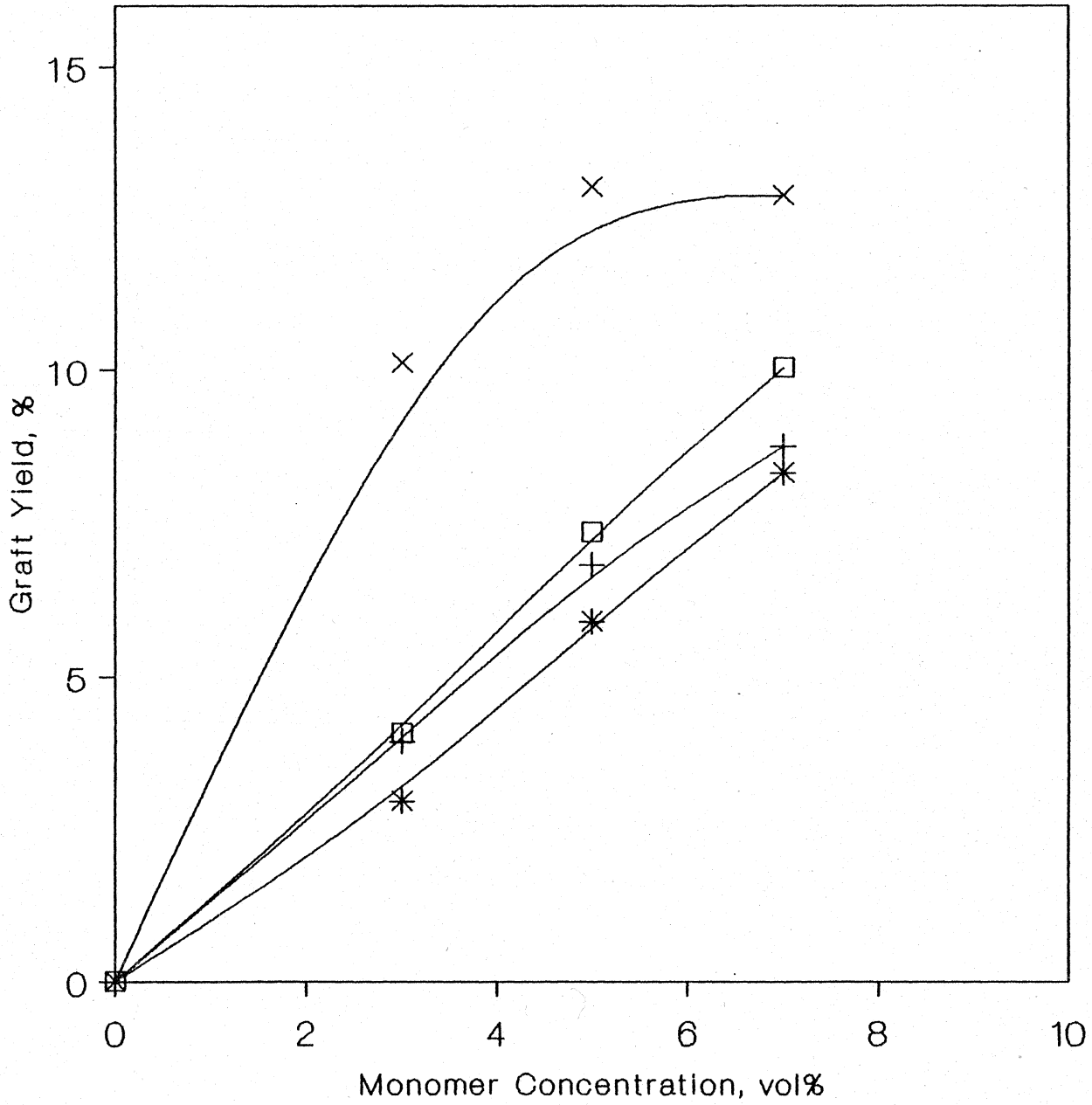


Figure 3.25. Effect of Cu^{2+} ion concentration on graft yield for MAA system: Figure shows increase in graft yield with monomer concentration for MAA grafted PVC system in aqueous media containing 0.0025M (+), 0.005M (*), 0.0075M (□) and 0.01M (x) Cu^{2+} ions [0.25 Mrads]. S.D. was within ± 5%.

medium was 0.0025M. The solutions were all clear and colourless with no trace of any homopolymer.

III.1.5.1.d. Effect of Radiation Dose on Graft Yield:

Increasing radiation dose from 0.25 Mrads to 0.75 Mrads is also found to increase the graft yield substantially for the MAA system for all the four concentrations studied (Figure 3.26). It was observed that sheets tended to become more stiff and rigid at MAA concentrations above 5 vol% when irradiated to a dose of 0.5 Mrads or above.

III.1.5.2. Effect of MAA content on Optical Transparency:

An interesting observation during MAA grafting was that optical clarity (transparency) was excellent and compared similarly with that of control at even high graft yields (Figure 3.22).

III.1.5.3. Spectroscopic Analaysis of Graft Polymer:

The ATR-IR spectra of the grafted surface indicated the absence of the characteristic 1725 cm^{-1} strong band of the C=O group in the plasticizer to be replaced by the 1720 cm^{-1} carbonyl peak of PMAA (Figure 3.27). The weak doublet at 1420 cm^{-1} is also characteristic of the carbonyl functions present in PMAA polymers.

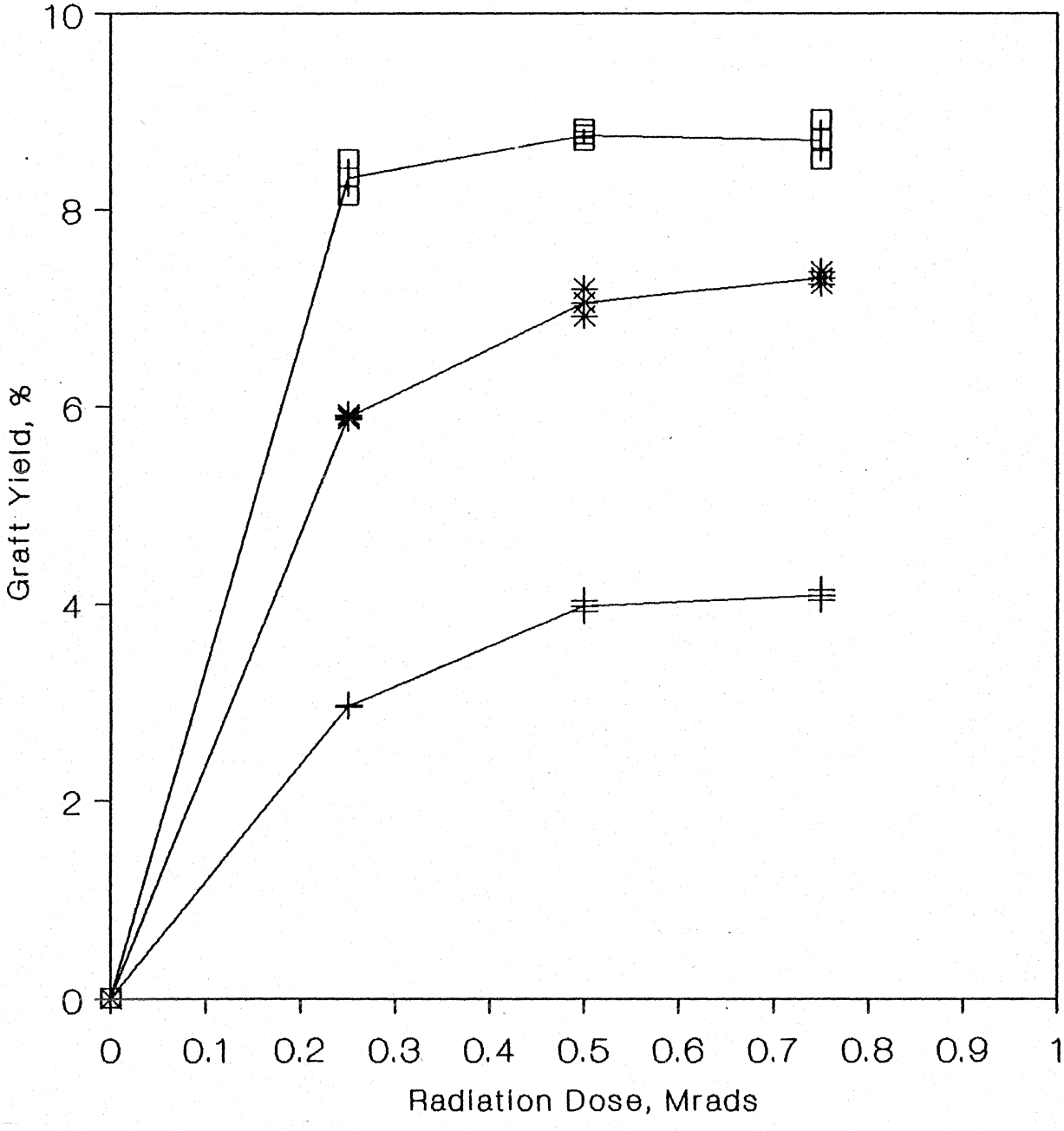


Figure 3.26. Effect of increasing radiation dose on graft yield for MAA system: Figure shows increase in graft yield at higher radiation doses attaining saturation at 0.5 Mrad level for 3% (+), 5% (*) and 7% (□) MAA grafted to PVC [0.005M Cu^{2+}, 0.25 Mrads].

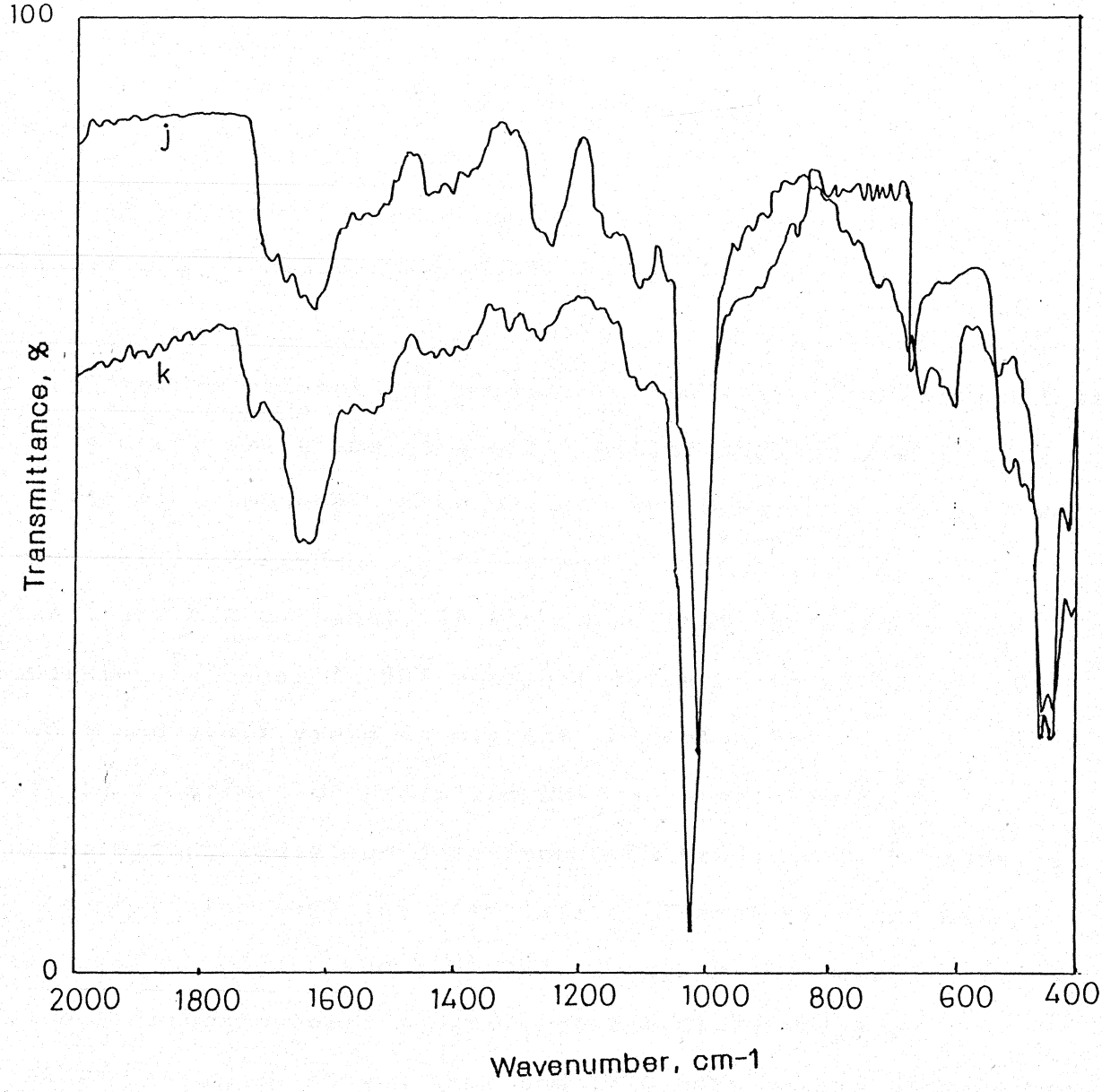


Figure 3.27. ATR-IR spectra of PVC surfaces grafted with MAA: Figure shows spectra of radiation grafted PVC using 5% MAA containing no cross-linker (j) and with 2% EDMA cross-linker (k) [0.005M Cu^{2+}, 0.25 Mrads].

III.1.6. HEMA System:

III.1.6.1. Grafting of HEMA system onto PVC:

III.1.6.1.a. Effect of Monomer Concentration on Graft Yield:

Radiation grafting of HEMA monomer alone was found to be difficult due to heavy homopolymer formation. The presence of cupric ions at very high concentrations in the grafting medium did not seem to prevent gel formation. However, it was found that grafting does take place to a small extent and the yield is proportional to monomer concentration employed. The grafting was carried out in different grafting media such as water, 10% methanol and 50% methanol. It was found that the formation of homopolymer is least in 50% methanol compared to water and 10% methanol and graft yield is highest (Figure 3.28).

III.1.6.1.b. Effect of Radiation Dose on Graft Yield:

Increasing radiation dose from 0.25 Mrads to 0.75 Mrads is also found to increase the graft yield linearly for the HEMA system similar to NVP and HEMA:NVP systems(Figure 3.29).

III.1.6.2. Spectroscopic Analysis of the Graft Polymer:

ATR-IR spectra showed that the 1720 cm^{-1} of the plasticizer is substituted by the 1730 cm^{-1} carbonyl peak in PHEMA. The 1030 cm-1 of PHEMA due to the carbonyl group is also present (Figure 3.30).

III.1.6.3. Microscopic Evaluation:

The optical photomicrograph showed the presence of a fine

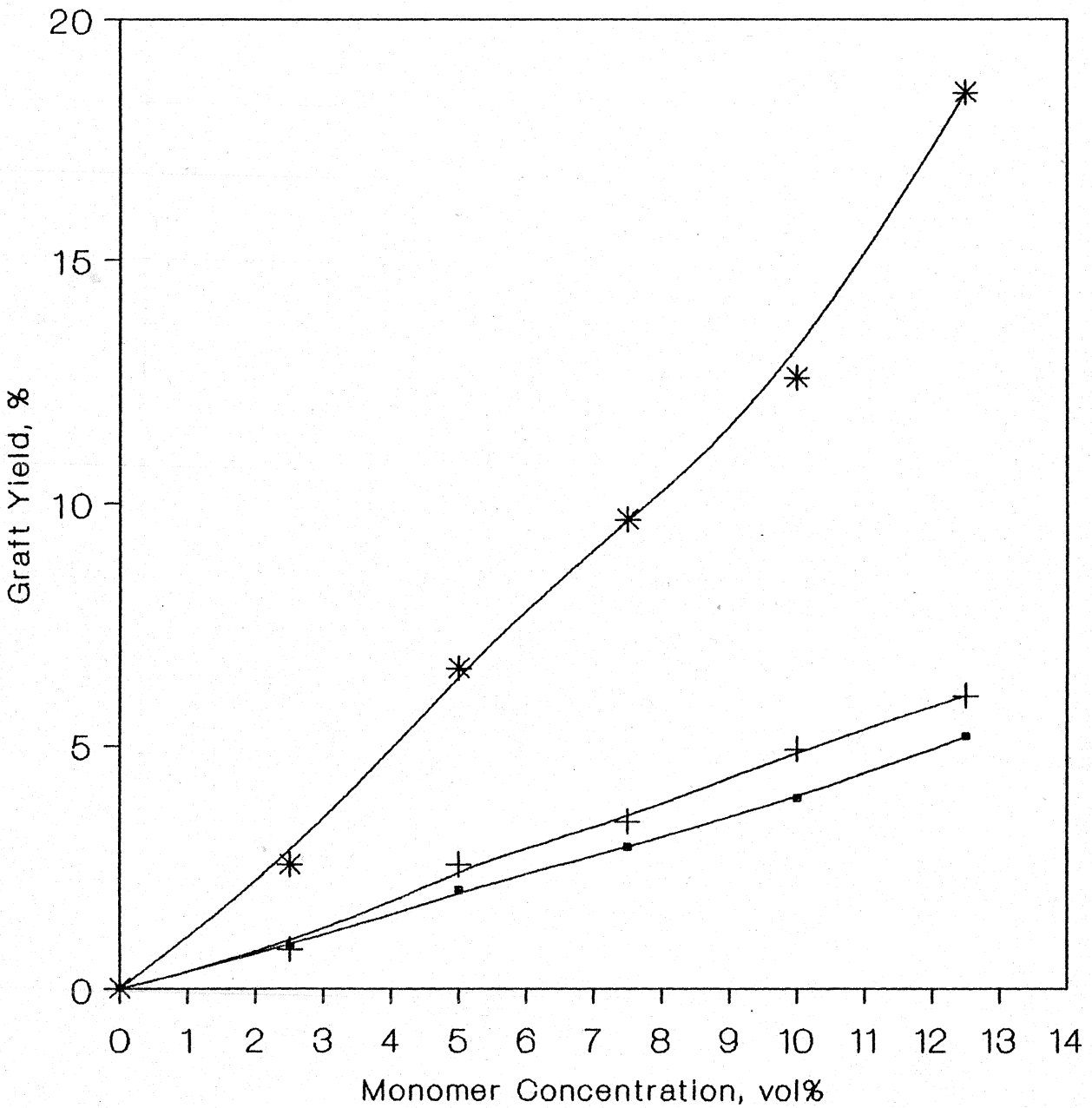


Figure 3.28. Effect of using different grafting media upon graft yield for HEMA system: Figure shows variation in graft yield with monomer concentration for PVC systems grafted using HEMA in different grafting media such as distilled H_2O (.), 10% Methanol (+) and 50% Methanol (*) [0.25 Mrads]. S.D. was within $\pm$ 10%. Heavy gel formation was observed in all systems.

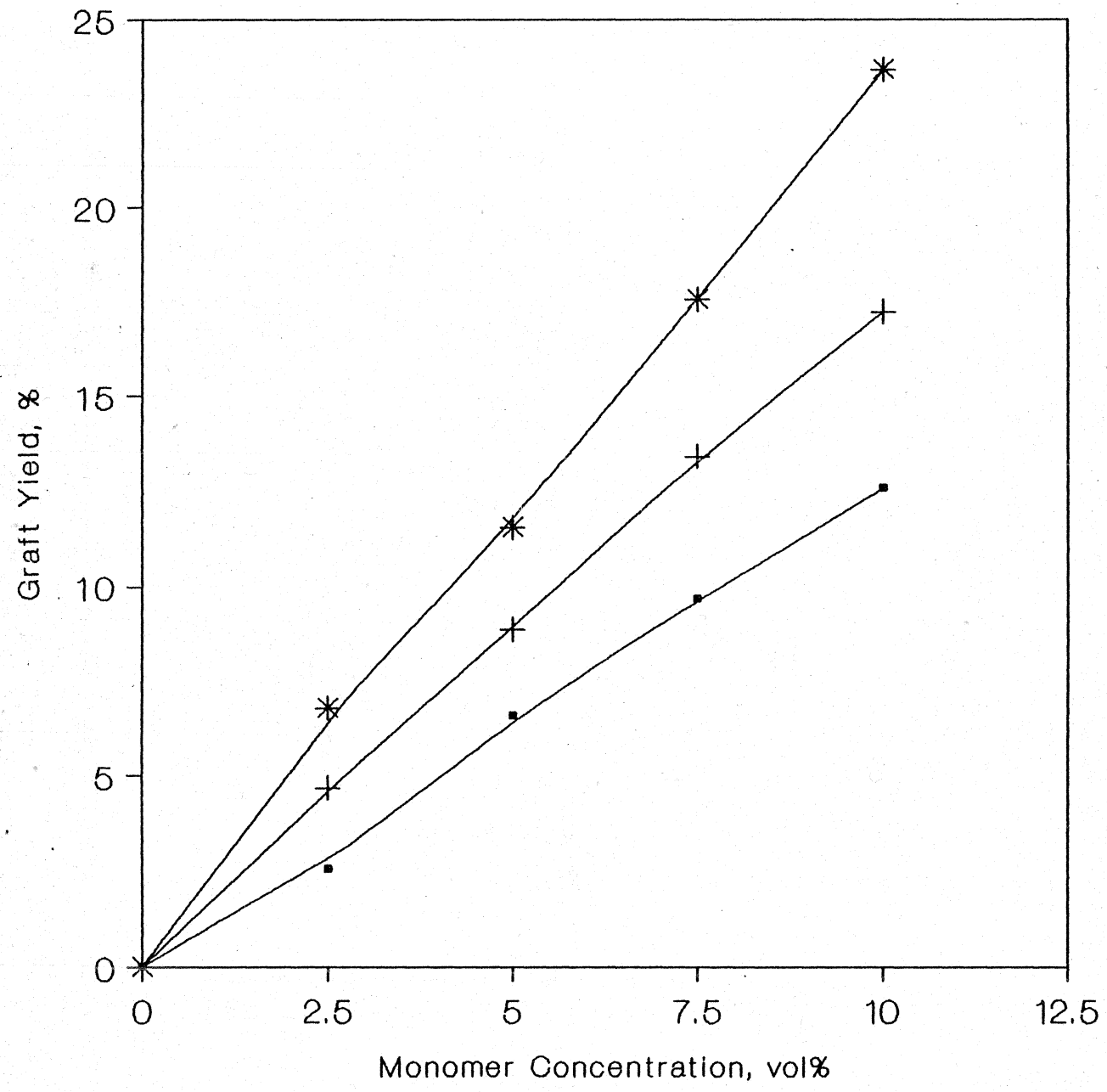


Figure 3.29. Effect of increasing radiation dose on graft yield for HEMA system: Figure shows linear increase in graft yield with increasing HEMA concentration grafted to PVC at 0.25 (.), 0.5 (+) and 0.75 (*) Mrads. 50% Methanol was used as the grafting medium. S.D. was within $\pm$ 10%.

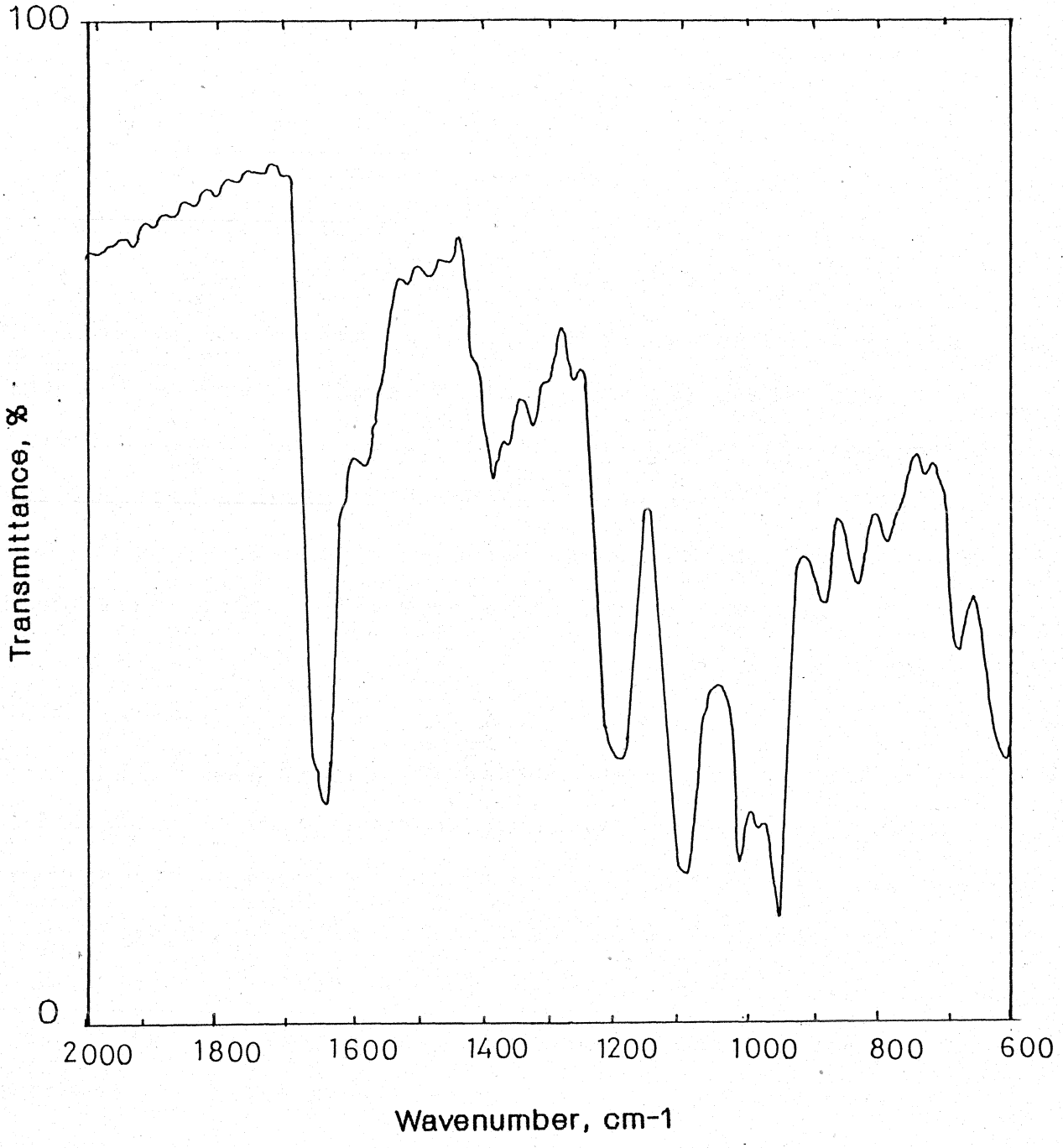


Figure 3.30. ATR-IR spectra of PVC grafted with 5% HEMA [0.25 Mrads].

layer of grafted polymer on the surface of ungrafted PVC (Figure 3.31).

III.2. Effect of Residual Copper Ions in the Graft Polymer:

The atomic absorption estimation of residual copper ion content on the grafted sheets indicated the presence of only 0.25 ppm of Cu^{2+} in the aqueous extract which is well below the acceptable level of 1ppm (Table 3.1). This showed conclusively that the use of this metal ion in solution at the concentrations employed for grafting NVP and HEMA combinations or NVP alone onto PVC are acceptable from a toxicological standpoint to prevent homopolymerization of the monomers during grafting.

III.3. Summary:

Plasticized PVC can be successfully grafted using hydrophilic monomers such as HEMA, NVP or MAA singly or in combination by gamma radiation using a Co^{60} source. The percentage graft yield is found to increase proportionately with increasing monomer content and for most systems with radiation dose. Presence of Cu^{2+} ions in the grafting medium help prevent homopolymerization and increase the graft yield for HEMA/NVP, NVP, NVP/MAA and MAA systems studied. Analysis of the grafted PVC surface using ATR-IR Spectroscopy, SEM and optical microscopy clearly show the presence of grafted polymer on the surface of PVC. PVC grafted

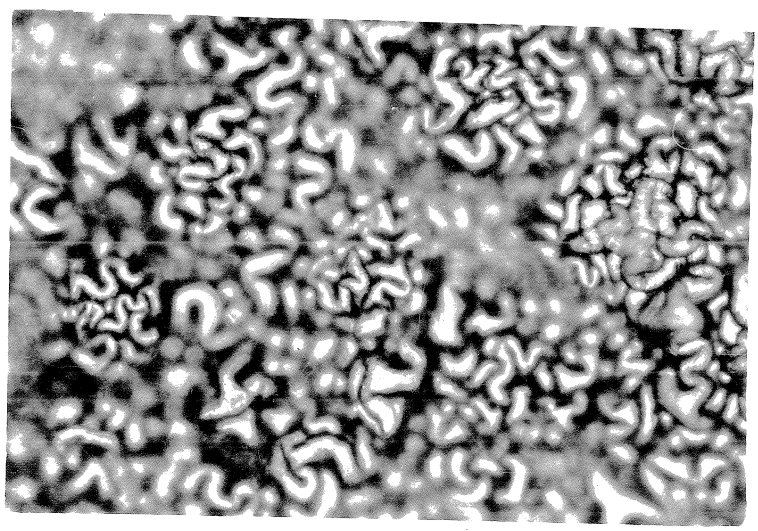


Figure 3.31. Optical photomicrograph of PVC surface grafted with 5% HEMA: [50x, 0.25 Mrads].

Table 3.1.

Atomic absorption spectrophotometric data showing residual cupric ion content in PVC grafted with NVP:HEMA*

	Control	Sample
No.	Mean conc. (µg/ml)	Mean conc. (µg/ml)
1	0.01	0.05
2	0.02	0.05
3	0.02	0.05
4	0.02	0.05
5	0.02	0.06
6	0.02	0.06
7	0.02	0.06
8	0.03	0.05
9	0.03	0.05
10	0.03	0.05

* Calculations are shown in Annexure-A

** Control is triple distilled water used for extraction. Sample is extract of 5% NVP50:HEMA50 graft polymer. All mean values are average of 2 testings.

with NVP and MAA tend to exhibit excellent tranparencies compared to ungrafted material. The residual metal ion content in the grafted polymer has been estimated using atomic absorption technique and found to be within safety limits.

Table 4.1. Surface energy parameters of PVC grafted with NVP:HEMA*

Material	θ_{air}	θ_{oct}	Isw	γ_{sv}^{d}	γ_{sv}^{p}	γ_{sv}	γ_{sw}
Ungrafted PVC	60.6	94.9	54.8	32.1	14.9	46.9	11.6
1 vol%							
N25-H75	29.4	158.7	97.5	16.2	47.1	63.3	0.5
N50-H50	33.1	154.6	96.1	15.3	45.7	61.1	0.7
N75-H25	29.3	152.9	95.5	12.2	45.1	57.3	1.5
3 vol%							
N25-H75	40.3	165.1	99.3	8.9	48.8	57.7	2.8
N50-H50	35.9	162.8	98.8	11.7	48.3	59.9	1.6
N75-H25	32.1	157.6	97.2	15.0	46.8	61.8	0.7
5 vol%							
N25-H75	26.1	139.5	88.9	26.6	39.1	65.7	1.0
N50-H50	22.5	154.1	96.0	21.1	45.6	66.7	0.1
N75-H25	20.3	151.0	94.7	23.4	44.4	67.9	0.2
7 vol%							
N25-H75	19.2	162.1	98.6	20.1	48.1	68.2	0.1
N50-H50	0.0	165.8	99.5	23.0	49.0	72.1	0.0
N75-H25	0.0	180.0	101.0	21.6	50.5	72.1	0.0

*All contact angle values are average of minimum 6 observations.
Standard deviations are within +/- 5%
All units in dynes/cm

IV.1.2. NVP system:

The contact angle values and surface energy parameters of the ungrafted and NVP grafted PVC samples are listed in Table 4.2. The hydrophilic nature of the modified grafted surfaces is indicated by the sharp increase in the polar component of the surface energy (62). Figures 4.1 & 4.2 show the variation in surface energy parameters with increase in EDMA cross-linker concentration for 5 and 10 vol% NVP. With increase in cross-linker content, the hydrophilicity tends to decrease as evidenced by a decrease in polar component and corresponding increase in dispersion component values. However, blood compatibility is not considerably affected as evidenced by the low interfacial energy values shown by all crosslinked samples.

IV.1.3. HEMA:MAA system:

The pattern shown is similar to that of previous systems discussed. The contact angle values and surface energy parameters of the ungrafted and the grafted samples of HEMA:MAA monomer combination(s) onto PVC are listed in Table 4.3. Homopolymer formation took place during grafting as a result of which the yield decreased. However, the hydrophilic nature of the modified grafted surfaces is indicated by the sharp increase in the polar component of surface energy and corresponding decrease in the dispersion component.

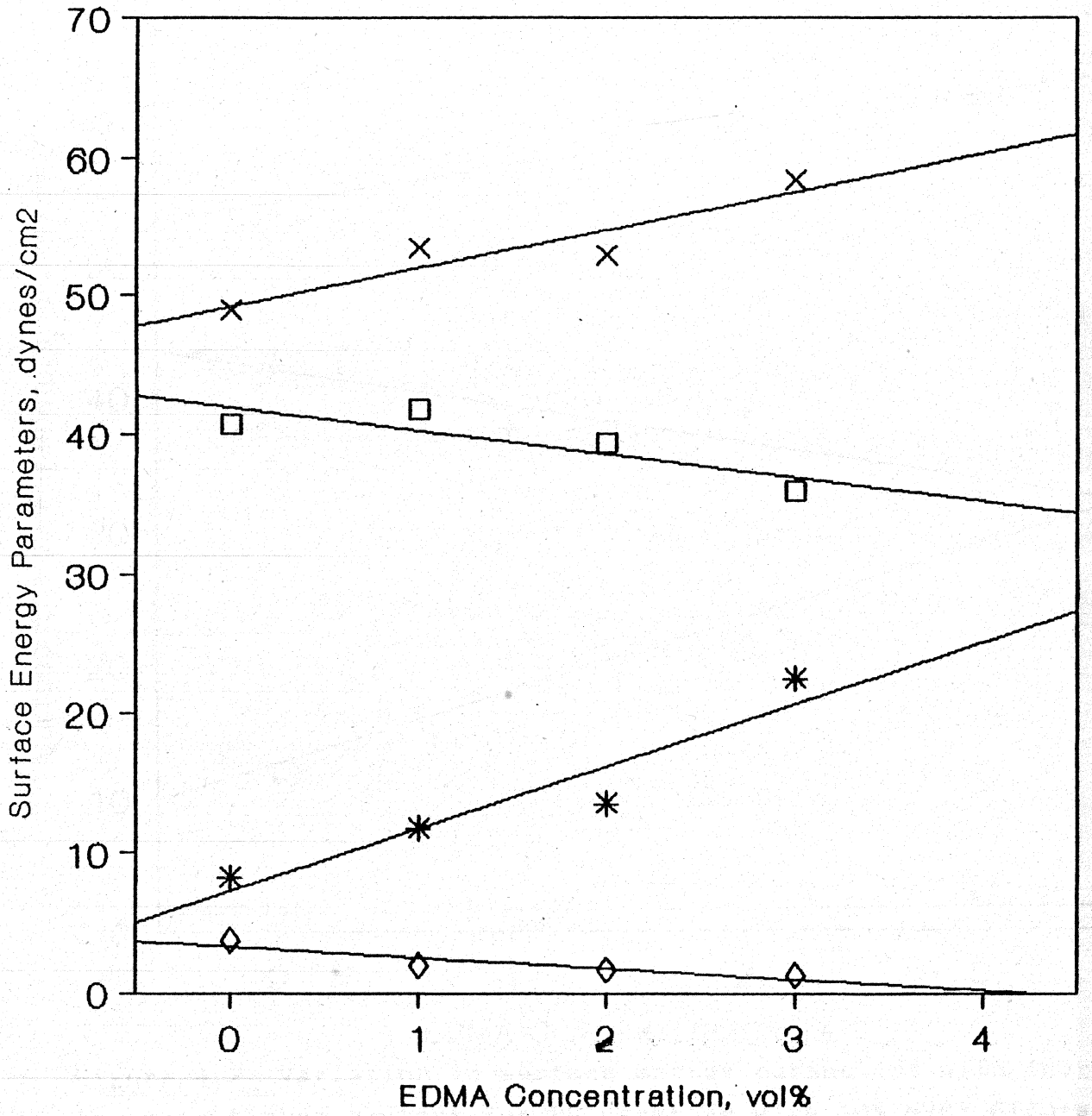


Figure 4.1. Variation in surface energy parameters with increase in cross-linker content for PVC grafted with 5% NVP: Figure shows increase in linear regression values of dispersion component [$\gamma_{s,v}^{d}$] (*) and decrease in polar component [$\gamma_{s,v}^{p}$] (□) with increase in cross-linker [EDMA] content in 5% NVP grafted PVC systems. The total surface energy [$\gamma_{s,v}$] (x) increases whereas the interfacial energy [$\gamma_{s,w}$] (◊) tends to show lower values at higher concentrations of EDMA [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 5%. A minimum of 6 samples was used for each system in all contact angle experiments.

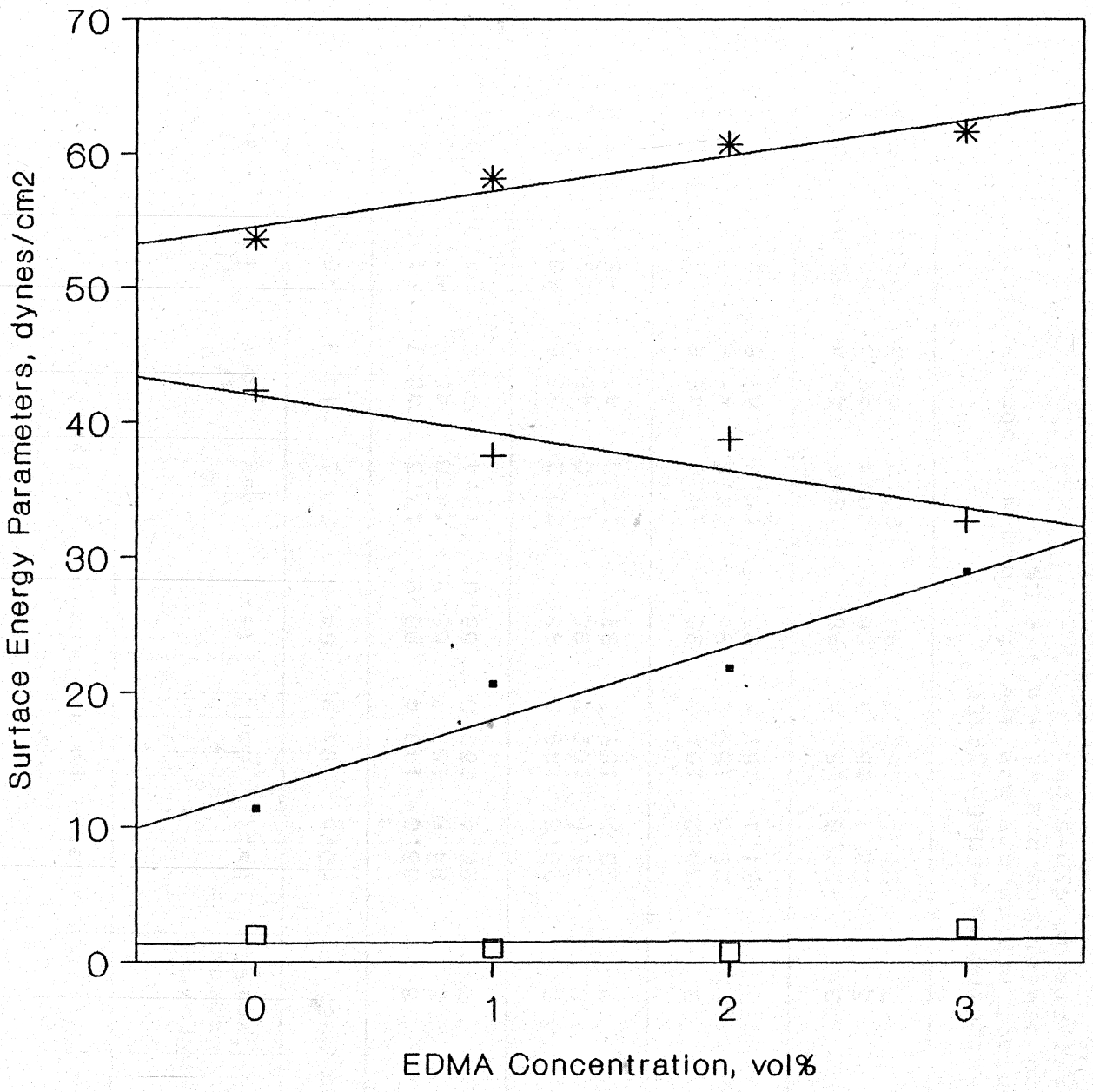


Figure 4.2. Variation in surface energy parameters with increase in cross-linker content for PVC grafted with 10% NVP: Figure shows increase in linear regression values of dispersion component [$\gamma_{s,v}^{d}$] (■) and decrease in polar component [$\gamma_{s,v}^{p}$] (+) with increase in cross-linker [EDMA] content in 10% NVP grafted PVC systems also. The total surface energy [$\gamma_{s,v}$] (✱) increases whereas the interfacial energy [$\gamma_{s,w}$] (◘) tends to show a constant value at higher concentrations of EDMA [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 5%.

Table 4.3. Surface energy parameters of PVC grafted with HEMA:MAA*

Cupric ion conc. (molar)	HEMA/MAA conc. (vol%)	θ_{air}	θ_{oct}	Isw	γ_{sv}^{d}	γ_{sv}^{p}	γ_{sv}	γ_{sw}
Ungrafted PVC		60.6	94.9	54.8	32.1	14.9	46.9	11.6
0.0025	3	33.0	149.4	93.9	17.3	43.7	61.0	0.5
	5	34.6	153.7	95.8	14.8	45.4	60.1	0.8
	7	26.4	160.0	98.0	17.4	47.5	64.9	0.3
0.005	3	28.3	149.0	93.8	20.2	43.5	63.7	0.3
	5	31.8	162.2	98.6	14.0	48.1	62.1	0.9
	7	25.2	158.7	97.5	18.3	47.1	65.4	0.2
0.0075	3	30.2	154.8	96.2	16.9	45.8	62.7	0.4
	5	30.2	155.0	96.3	16.9	45.9	62.7	0.4
	7	21.1	161.1	98.3	19.6	47.8	63.4	0.1
0.01	3	29.8	156.4	96.8	16.6	46.4	63.0	0.4
	5	22.4	156.5	96.8	20.4	46.4	66.8	0.1
	7	21.4	159.2	97.7	20.0	47.3	67.2	0.1

*System studied is HEMA50:MAA50
All contact angles are average of minimum 6 observations.
Standard deviations are within +/- 5%
All units are in dynes/cm

IV.1.4. NVP:MAA system:

The contact angle values and surface energy parameters of the ungrafted and the grafted samples of NVP:MAA monomer combination(s) onto PVC are listed in Table 4.4. Increase in hydrophilic character is seen for all the three sub-systems studied after grafting as indicated by the sharp rise in the polar component value of surface energy and corresponding decrease in dispersion component value.

IV.1.5. MAA system:

The contact angle measurements show that MAA grafted PVC samples also behave similarly like previous systems studied. A sharp increase in hydrophilicity is indicated by the high polar and small dispersion component values compared to ungrafted sheets. (Table 4.5.). The γ_{sw} value also tend to be less than unity indicating lower protein adsorption and better blood compatible properties.

IV.2. Evaluation of Mechanical Properties:

IV.2.1. Tensile Strength and Elongation:

IV.2.1.1. NVP:HEMA system:

The tensile strength and elongation values for PVC sheets grafted on both sides tend to decrease with higher graft content compared with control values in all the three systems studied (63) (Figures 4.3 & 4.4). Higher HEMA content in the graft

Table 4.4. Surface energy parameters of PVC grafted with NVP:MAA*

Cupric ion conc. (molar)	NVP/MAA conc. (vol%)	θ_{air}	θ_{oct}	Isw	γ_{sv}^{d}	γ_{sv}^{p}	γ_{sv}	γ_{sw}
Ungrafted PVC		60.6	94.9	54.8	32.1	14.86	46.93	11.6
0.0025	3	26.1	157.7	97.2	18.2	46.8	65.0	0.2
	5	24.2	156.5	98.5	17.9	48.0	66.0	0.2
	7	20.9	170.0	100.2	17.8	49.7	67.5	0.2
0.005	3	10.0	157.0	97.0	18.2	46.8	65.0	0.2
	5	10.0	170.0	100.2	21.3	49.7	71.0	0.0
	7	16.0	170.0	100.2	19.6	49.7	67.5	0.2
0.0075	3	17.0	157.9	97.3	22.2	46.9	69.0	0.1
	5	22.2	159.0	97.7	19.7	47.2	66.9	0.1
	7	26.3	158.9	97.6	17.7	47.2	64.9	0.3
0.01	3	26.8	162.7	98.7	16.5	48.2	64.7	0.4
	5	15.8	162.3	98.6	21.3	48.1	69.4	0.0
	7	21.3	160.7	98.2	19.6	47.7	67.3	0.1

*System studied is NVP50:MAA50
All contact angles are average of minimum 6 observations.
Standard deviations are within +/- 5%
All units are in dynes/cm.

Table 4.5. Surface energy parameters of PVC grafted with MAA*

Cupric ion conc. (molar)	MAA conc. (vol%)	θ_{air}	θ_{oct}	Isw	γ_{sv}^{d}	γ_{sv}^{p}	γ_{sv}	γ_{sw}
Ungrafted PVC		60.6	94.9	54.8	32.1	14.9	46.9	11.6
0.0025	3	24.1	145.5	92.1	24.3	42.0	66.3	0.5
	5	23.2	152.2	95.2	21.6	44.8	66.4	0.2
	7	21.1	155.1	96.3	21.5	45.9	67.4	0.1
0.005	3	23.2	154.1	95.9	20.9	45.6	66.4	0.1
	5	19.0	156.8	96.9	21.8	46.5	68.3	0.1
	7	14.1	156.9	97.0	23.5	46.5	70.1	0.1
0.0075	3	16.8	162.6	98.7	20.9	48.2	69.1	0.0
	5	14.2	166.9	99.7	20.7	49.2	69.9	0.0
	7	12.1	167.0	99.7	21.3	49.2	70.5	0.0
0.01	3	13.1	170.0	100.2	20.5	49.7	70.2	0.0
	5	12.3	168.2	99.9	21.0	49.4	70.5	0.0
	7	10.0	170.1	100.3	21.3	49.8	71.0	0.0

* All contact angles are average of minimum 6 observations.
Standard deviations are within +/- 5%
All units are in dynes/cm

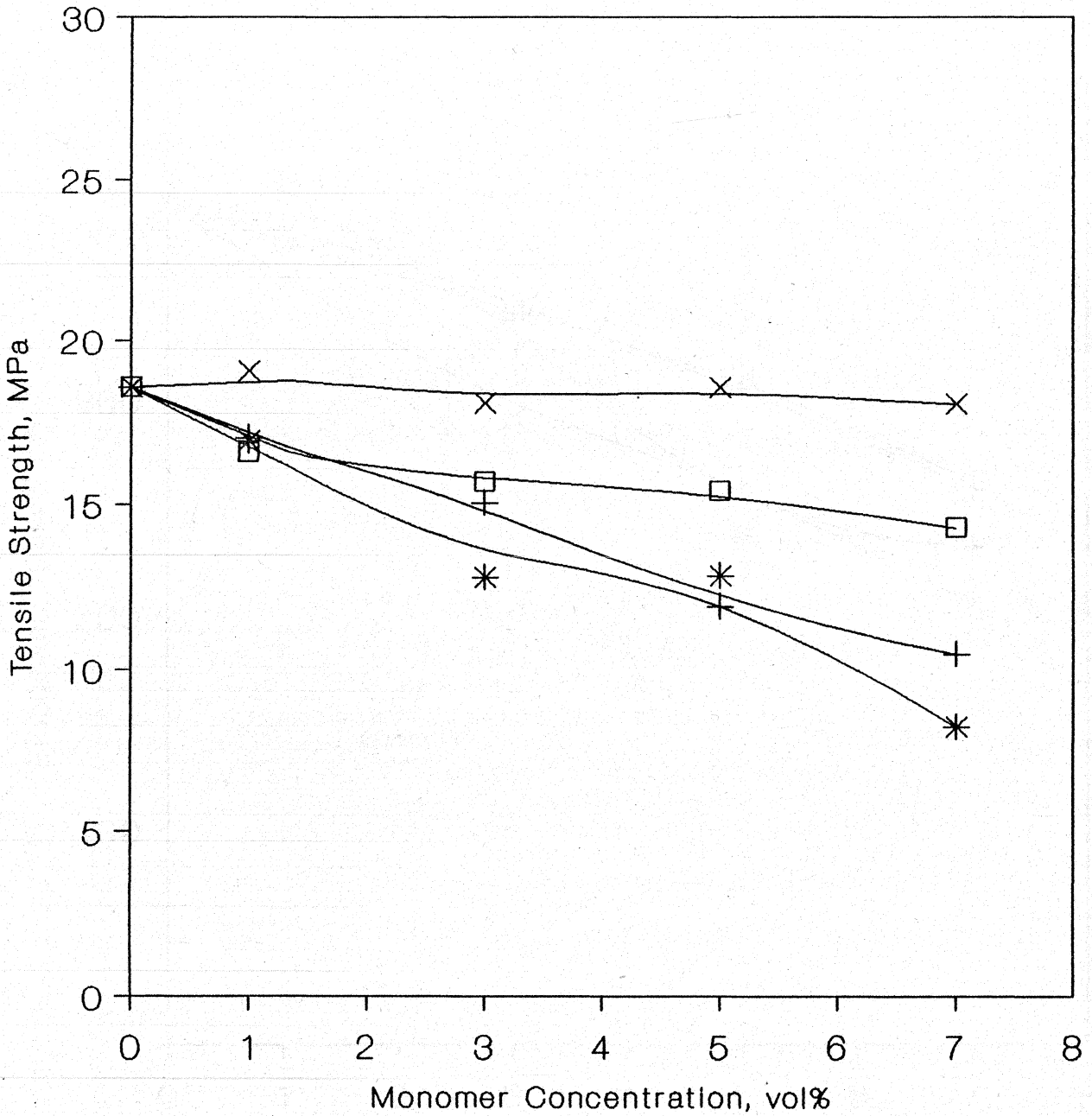


Figure 4.3. Variation of ultimate tensile strength with increasing monomer concentration for NVP:HEMA and NVP grafted PVC systems: Figure shows decrease in tensile strength with increasing monomer content for NVP25:HEMA75 (+), NVP50:HEMA50 (*), NVP75:HEMA25 (□) and NVP100 (x) grafted PVC sheets on both sides [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 10%. A minimum of 6 samples was tested for each system in all mechanical evaluation studies.

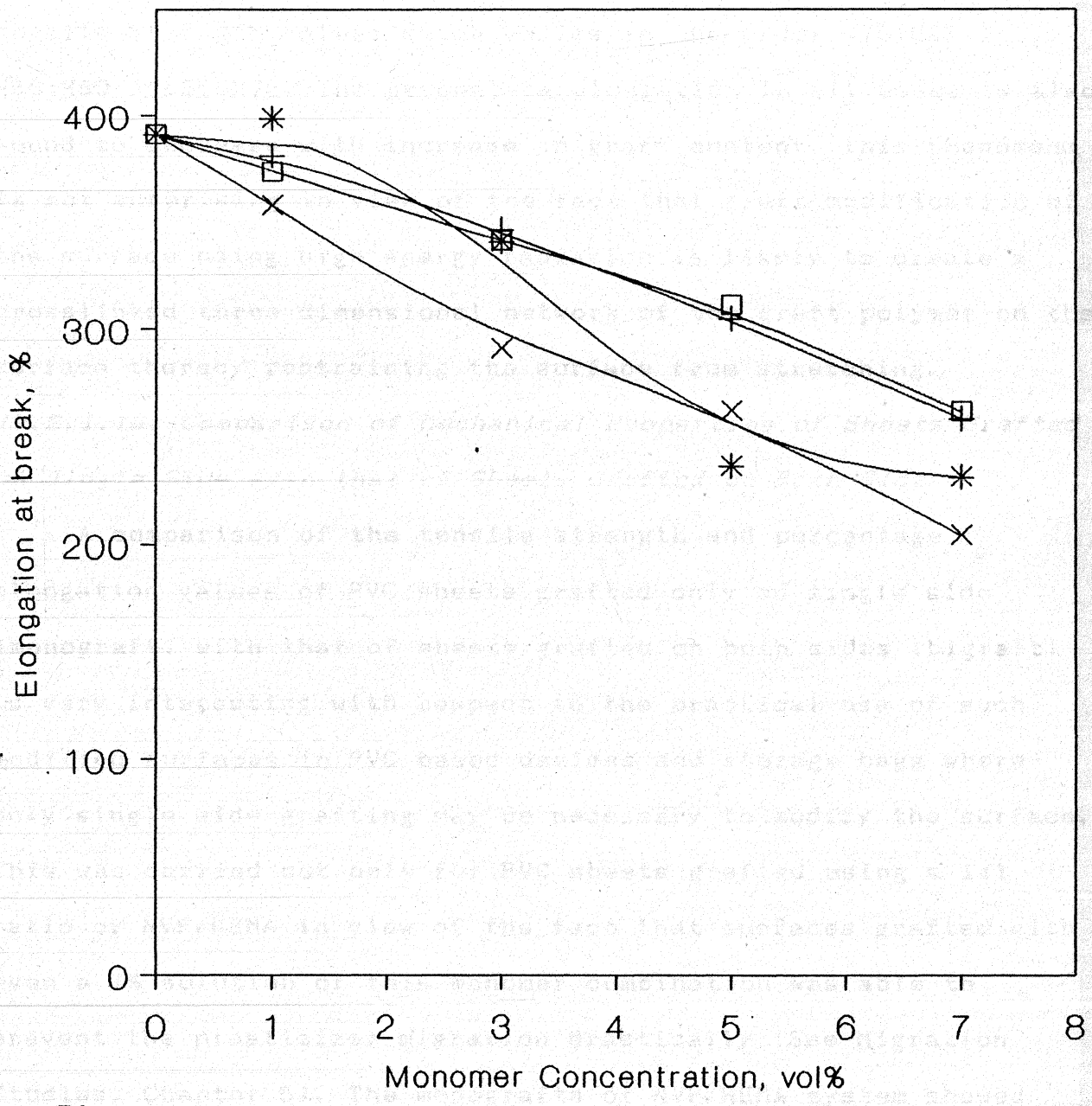


Figure 4.4. Variation in percentage elongation values with increasing monomer concentration for NVP:HEMA and NVP grafted PVC systems: Figure shows changes in elongation with increasing graft monomer content for NVP25:HEMA75 (+), NVP50:HEMA50 (*), NVP75:HEMA25 (□) and NVP100 (x) grafted PVC sheets on both sides [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 15%.

copolymer is found to favour this decrease as evidenced by the tensile strength values which varies in the order N75:H25 > N50:H50 > N25:H75. The percentage elongation in all cases is also found to decrease with increase in graft content. This phenomena is not surprising in view of the fact that graft modification of the surface using high energy radiation is likely to create a crosslinked three dimensional network of the graft polymer on the surface thereby restraining the surface from stretching.

IV.2.1.1a. Comparison of Mechanical Properties of Sheets Grafted on Single Side with that of Sheets Grafted on Both Sides:

A comparison of the tensile strength and percentage elongation values of PVC sheets grafted only on single side (monograft) with that of sheets grafted on both sides (bigraft) is very interesting with respect to the practical use of such modified surfaces in PVC based devices and storage bags where only single side grafting may be necessary to modify the surface. This was carried out only for PVC sheets grafted using a 1:1 ratio of NVP/HEMA in view of the fact that surfaces grafted with even a 1% solution of this monomer combination was able to prevent the plasticizer migration drastically (See Migration Studies, Chapter 5). The monografts of NVP/HEMA system showed drastic improvement in tensile strength compared to bigrafts (for which a steady loss in sterngth was noticed with increasing graft yield) (Figure 4.5). In fact, the tensile strength of monografts

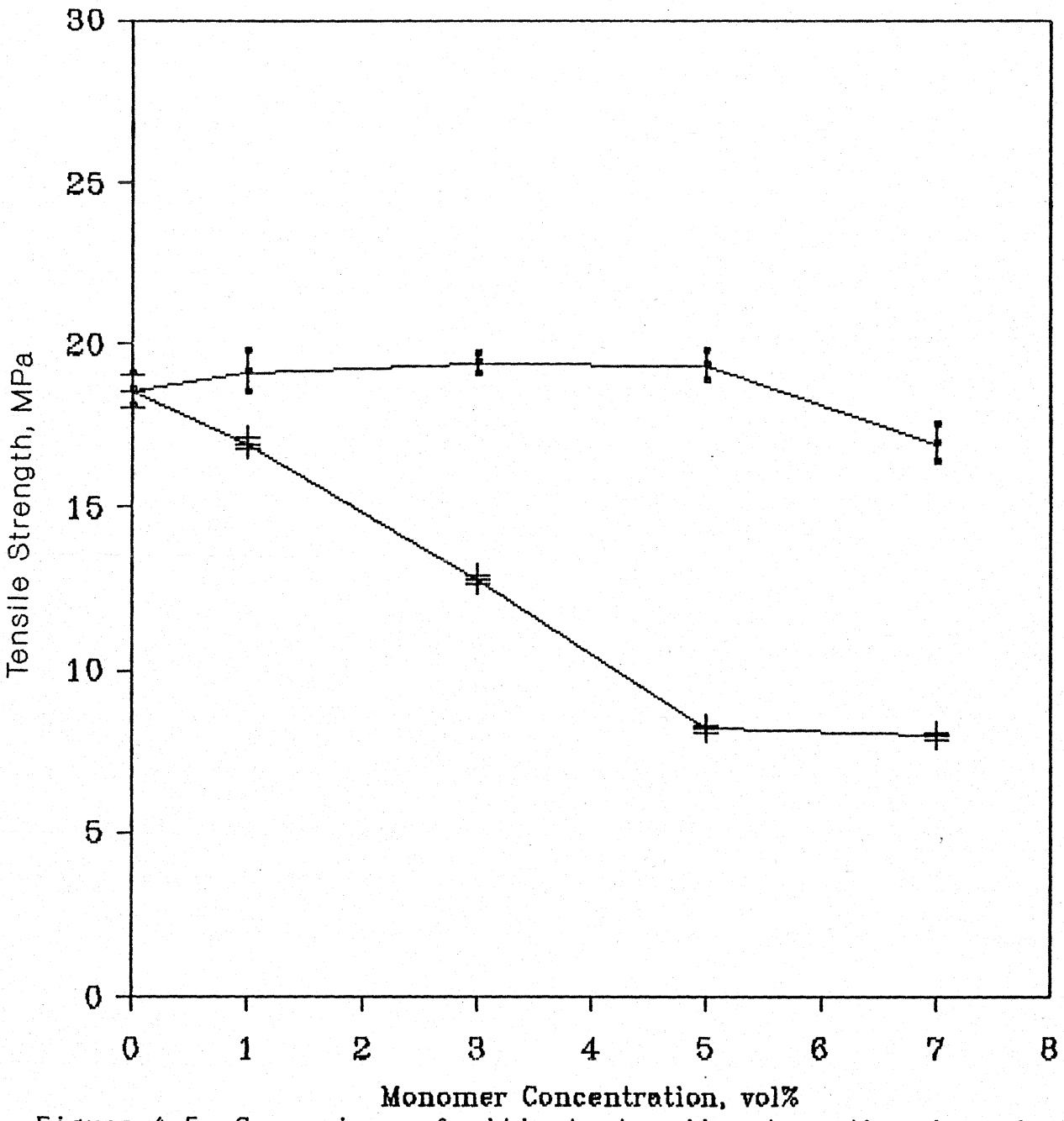


Figure 4.5. Comparison of ultimate tensile strength values for PVC sheets grafted on a single side to sheets grafted on both sides using NVP50:HEMA50 monomer combination: Plot shows drastic improvement in tensile strength values when PVC is grafted with NVP50:HEMA50 on a single side (.) compared to that grafted on both sides (+) [0.25 Mrads, 0.005M Cu^{2+}]. The sheets were hydrated for 24h before testing.

improved with graft yield even when compared to control ungrafted sheets upto 5 vol% monomer concentration after which it showed a slight decrease.

The percentage elongation values of monografts also showed considerable improvement compared to bigrafts (Figure 4.6) (for which a steady loss of elongation values was noticed with increasing graft yield). In fact, the elongation value is observed to rise to nearly 445% when grafted with 1% NVP/HEMA monomer combination from a value of 390% for ungrafted sheets. It remains still higher than control values even at 3% monomer concentration.

IV.2.1.2. NVP System:

In the case of pure NVP grafted sheetings, monografts showed a decreasing trend in their tensile strength values compared to bigrafts with increasing graft yield (Figure 4.7) unlike the behaviour shown by NVP/HEMA combination. The bigrafts, in fact, showed highly comparable values with ungrafted samples and there was very little decrease in strength even at 7% monomer concentration. One reason for this may be due to the highly hydrophilic nature of PVP compared to the grafted copolymers containing PHEMA, where chances of crosslinking due to the presence of traces of EDMA impurity is also likely. However, percentage elongation for NVP system was found to improve considerably in monografts compared to bigrafts (Figure 4.8). At

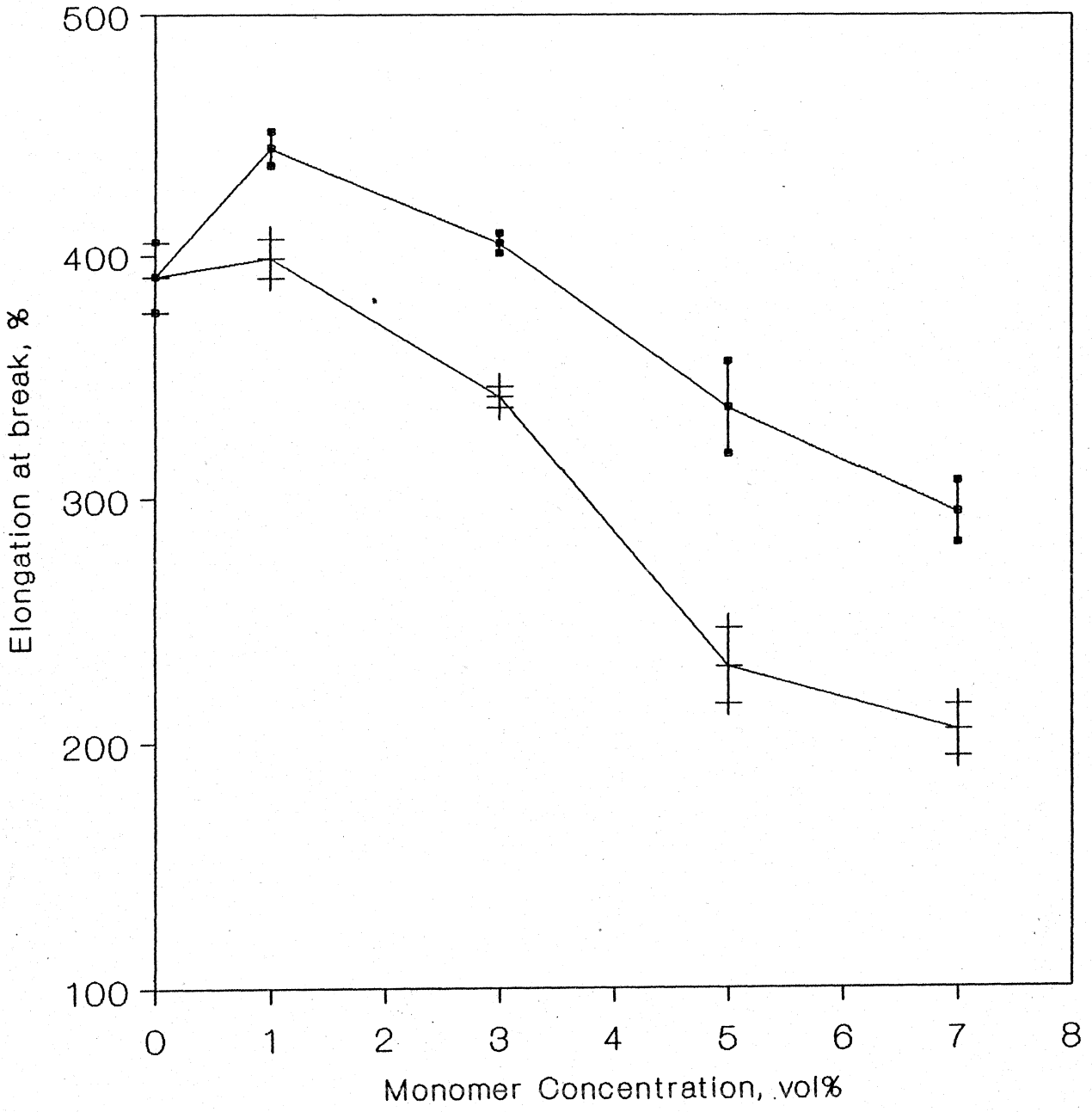


Figure 4.6. Comparison of percentage elongation values for PVC sheets grafted on a single side to sheets grafted on both sides using NVP50:HEMA50 monomer combination: Plot shows drastic improvement in elongation values when PVC is grafted with NVP50:HEMA50 on a single side (.) compared to that grafted on both sides (+) [0.25 Mrads, 0.005M Cu^{2+}]. The sheets were hydrated for 24h before testing.

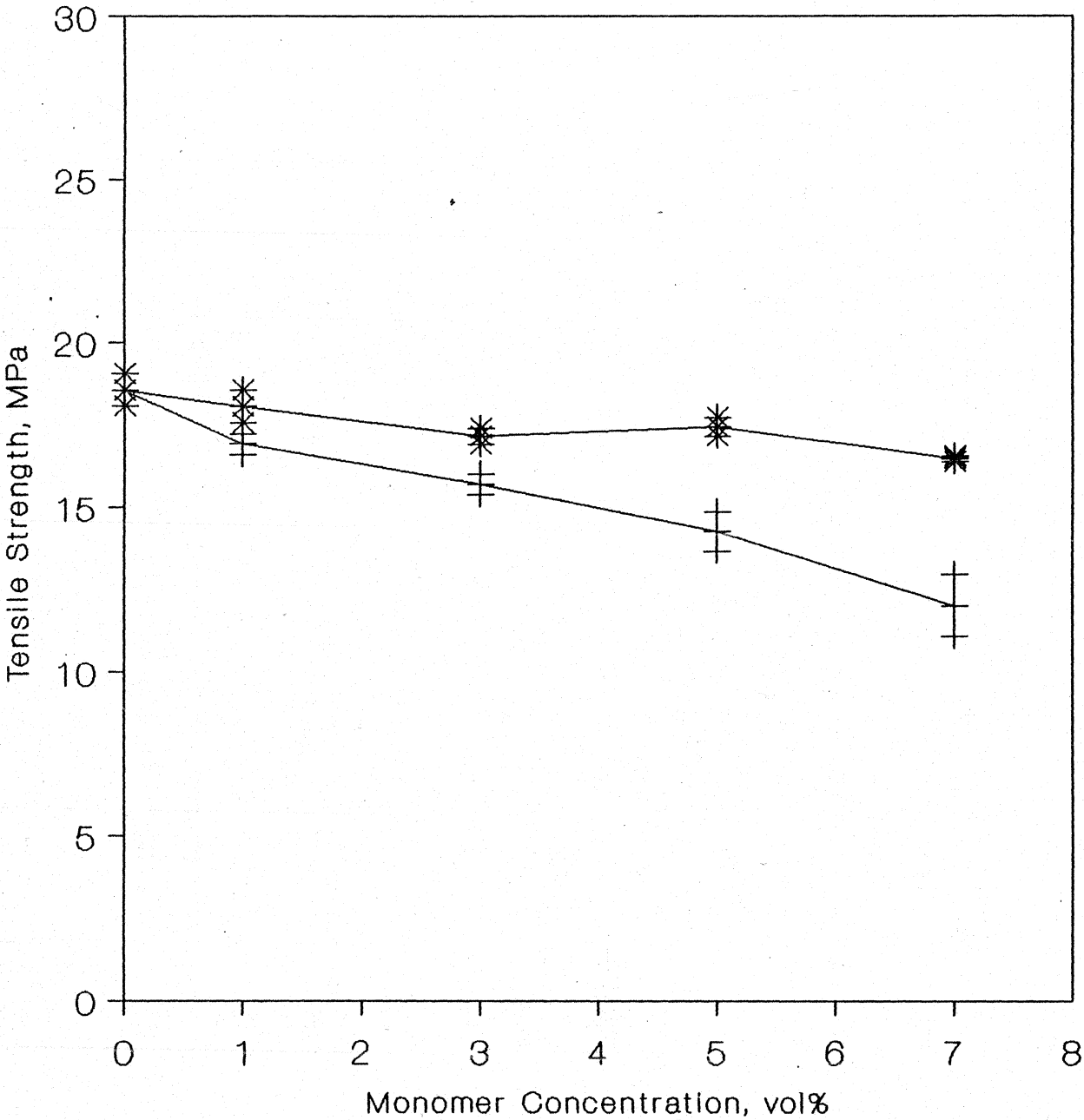


Figure 4.7. Comparison of tensile strength values for PVC sheets grafted on a single side to sheets grafted on both sides using NVP: Figure shows changes in tensile strength with monomer concentration for PVC grafted with NVP on a single side (+) compared to that on both sides (*) [Hydrated, 0.005M Cu^{2+}, 0.25 Mrads].

1% NVP concentration, the value even rose to 450% from 390% observed for control samples and then tended to fall off. This behaviour was very similar to that of NVP/HEMA system.

The fact that monograft properties are better or comparable to control values at monomer concentrations which are pertinent to retard the migration of the plasticizer when grafted is very encouraging since it offers an opportunity to modify the surface of PVC based medical devices to prevent the plasticizer migration without affecting the mechanical properties of the polymer matrix adversely.

IV.2.1.3. NVP:MAA SYSTEM

The tensile strength values show highly comparable values for NVP:MAA grafted samples (monografts only) compared to ungrafted ones (Figure 4.9). The NVP25:MAA75 grafted samples even show a rise in tensile strength compared to control. However, a slight decrease is shown when NVP content goes up as evidenced by NVP50:MAA50 and NVP75:MAA25 grafted samples. Percentage elongation values are not affected compared to ungrafted sheets upto 3 vol% monomer concentration, after which there is a rapid fall (Figure 4.10) for all three NVP:MAA systems studied. The elongation values are found to increase when the MAA content in the monomer system is increased. However all three systems are highly superior in mechanical properties compared to the NVP:HEMA system.

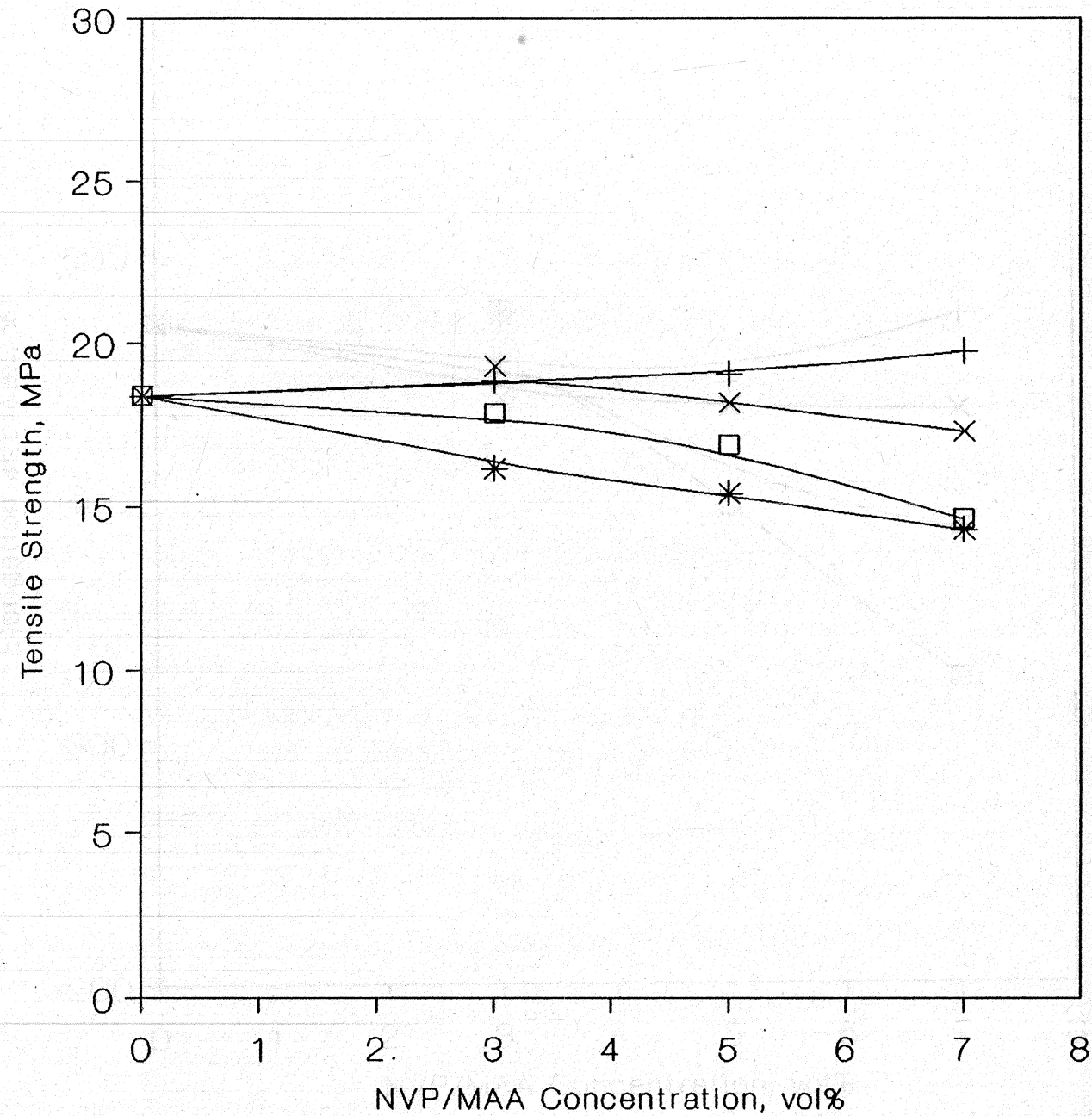


Figure 4.9. Variation of ultimate tensile strength with increasing monomer concentration for NVP:MAA and MAA grafted PVC systems: Figure shows changes in tensile strength with increasing monomer content for NVP25:MAA75 (+), NVP50:MAA50 (*), NVP75:MAA25(□) and MAA100 (x) systems grafted to PVC [Hydrated, 0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 10%.

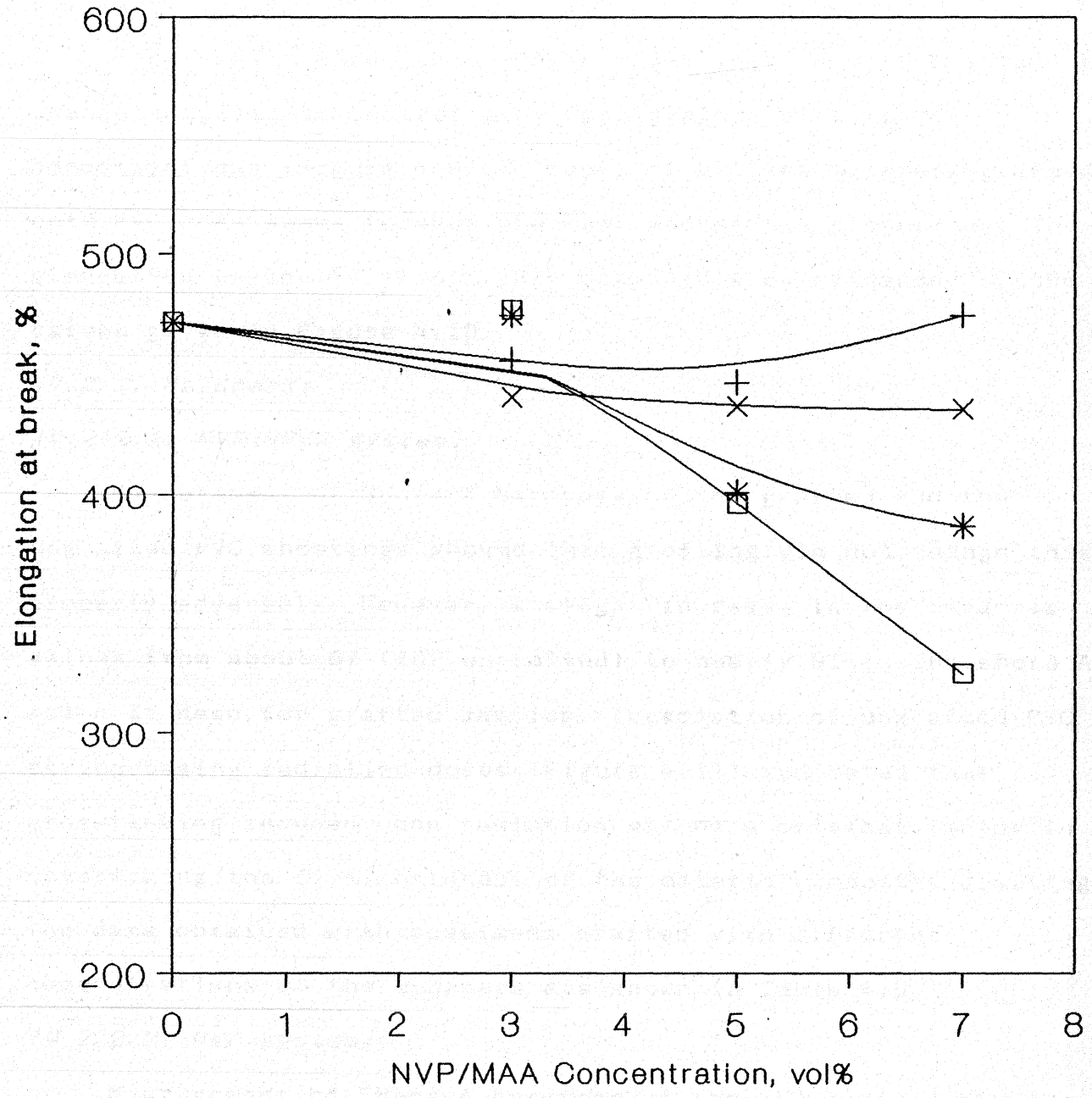


Figure 4.10. Variation of percentage elongation with increasing monomer concentration for NVP:MAA and MAA grafted PVC systems: Figure shows changes in elongation with graft monomer content for NVP25:MAA75 (+), NVP50:MAA50 (*), NVP75:MAA25 (□) and MAA100 (x) systems grafted to PVC [Hydrated, 0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 15%.

IV.2.1.4. MAA system:

The tensile strength of MAA grafted samples do not show any change compared to control even when grafted at high MAA concentrations (Figure 4.9). In fact, of all the monomers grafted onto PVC, MAA seems to show the best mechanical properties. The elongation factor is also highly comparable as evidenced by the values given in Figure 4.10.

IV.2.2. Hardness:

IV.2.2.1. NVP:HEMA system:

Measurement of Shore A hardness of the grafted and the ungrafted PVC sheetings showed that grafting did not change this property adversely. However, a slight increase in the hardness values from about 87 (for ungrafted) to nearly 91 in the shore A scale is seen for grafted samples. Irradiation of ungrafted PVC at increasing radiation doses (Figure 4.11) indicates that crosslinking induced upon radiation may be a critical factor in determining the final hardness of the material than the grafting. The data obtained with specimens grafted with different concentrations of the monomers are shown in Table 4.6.

IV.2.2.2. NVP system:

Measurement of Shore A hardness of the NVP grafted and the ungrafted PVC sheetings showed that grafting did not affect hardness adversely. The data obtained with specimens grafted with different concentrations of the monomers are shown in Table 4.6.

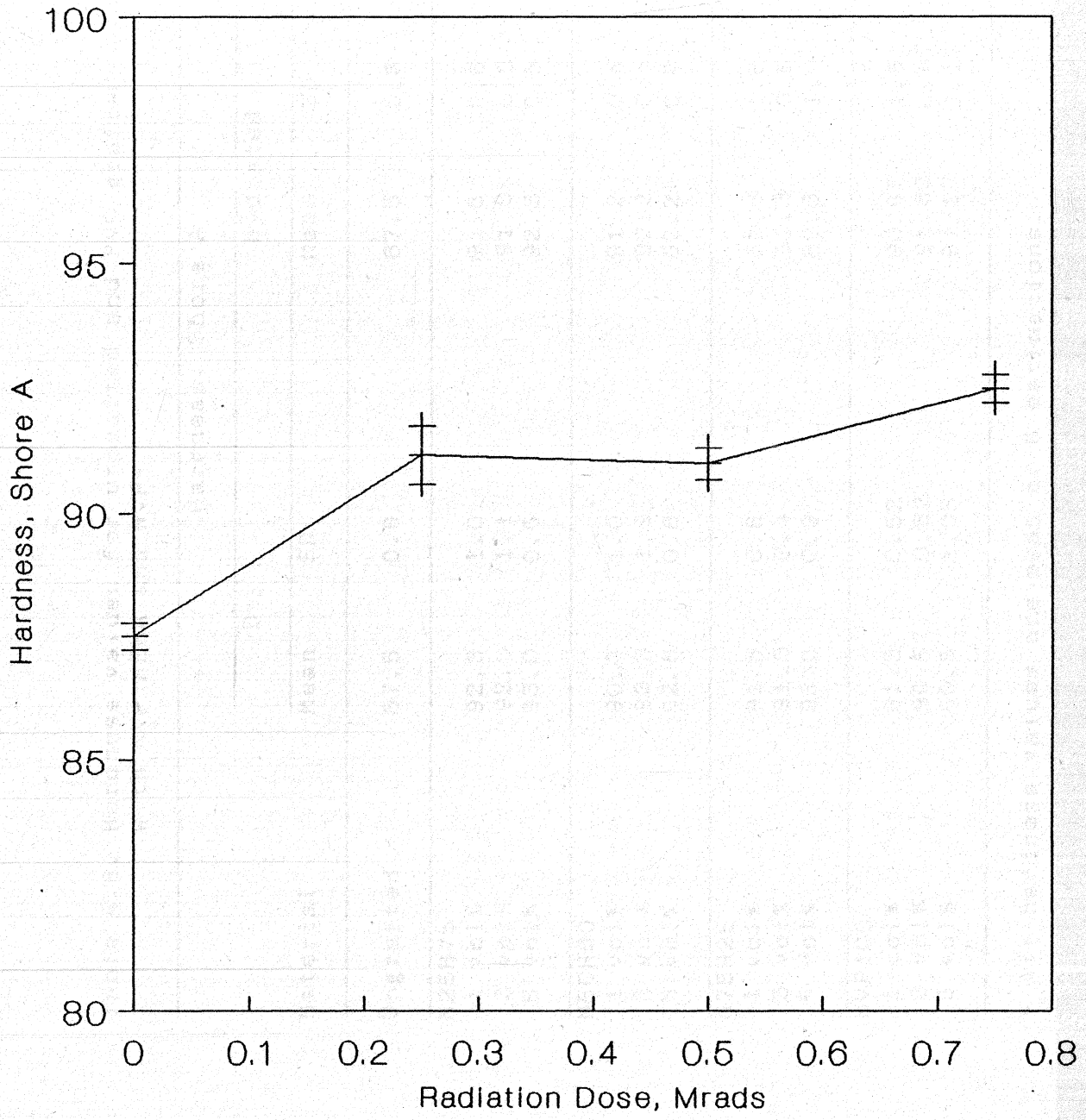


Figure 4.11. Increase in Hardness (Shore A) due to irradiation of ungrafted PVC control at increasing doses (+).

Table 4.6. Hardness values for ungrafted and PVC grafted with NVP:HEMA and NVP*

	Hardness, Shore A			
	Dry		Hydrated	
Material	Mean	SD	Mean	SD
Ungrafted	87.5	0.6	87.5	0.6
N25H75				
1 vol%	92.3	1.0	91.5	0.6
3 vol%	92.0	1.1	91.0	0.9
5 vol%	93.0	0.6	92.3	0.5
N50H50				
1 vol%	90.3	1.0	91.2	0.4
3 vol%	90.3	1.9	92.2	0.4
5 vol%	92.8	0.8	92.2	0.8
N75H25				
1 vol%	91.5	0.6	89.8	1.6
3 vol%	91.8	0.4	91.3	0.5
5 vol%	93.0	0.9	89.8	1.0
NVP100				
1 vol%	91.3	0.52	90.67	1.5
3 vol%	90.67	0.82	91.83	1.47
5 vol%	90.5	1.05	91.13	1.17

* All hardness values are mean of 6 estimations.

IV.3. Water Absorption Characteristics:

IV.3.1. NVP:HEMA system:

The water content in the total polymer, H_2O_{total} was found to increase with increasing monomer concentrations in the grafting medium ie., increasing graft yield, for all the three systems studied irrespective of whether the sheet was grafted only on one side or on both sides (Figure 4.12). The total water content varied proportionately with the NVP content in the monomer combination. This is quite likely due to the higher hydrophilic nature of PVP. The water content present in the graft for PVC, H_2O_{graft}, however tended to decrease with increasing graft content for all the NVP:HEMA systems upto 5 vol% and then level off to a constant value. Figure 4.13. shows this trend. The graft water content in systems containing more NVP (N75H25) showed lower decrease in values compared to systems containing less NVP (N25H75).

IV.3.2. NVP system:

The water content in the total polymer, H_2O_{total} was found to increase with increasing monomer concentrations in the grafting medium for NVP grafted sheets also (Figure 4.14). Varying copper ion concentration during grafting is seen to affect the water content. In fact for the NVP system, 0.0025M copper ion concentration in the grafting medium seem to produce

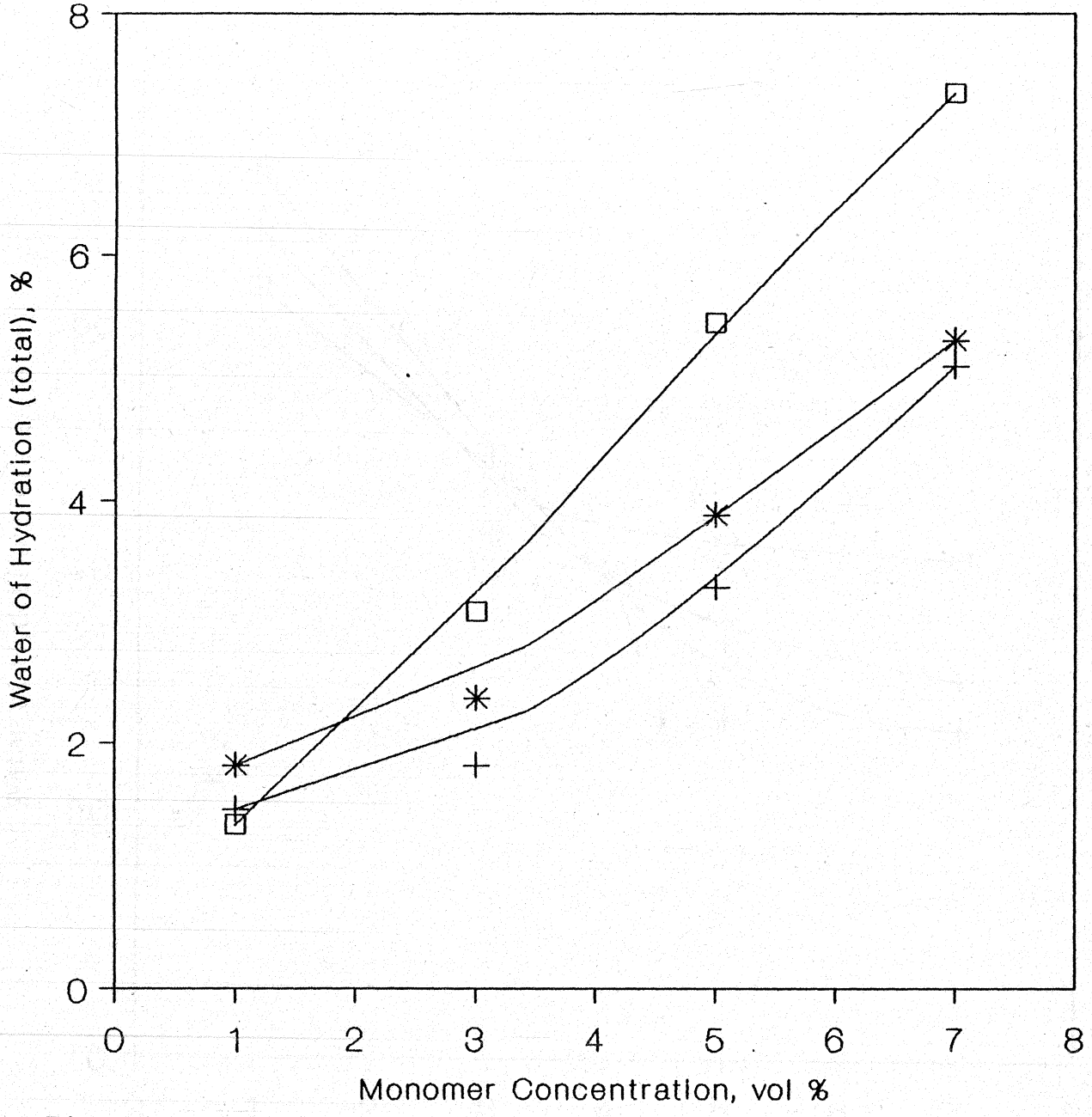


Figure 4.12. Variation in total water content with monomer concentration for PVC grafted with NVP:HEMA monomer combinations: Figure shows increase in total water content with graft monomer concentration for NVP25:HEMA75 (+), NVP50:HEMA50 (*) and NVP75:HEMA25 (□) grafted PVC systems [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 10%. A minimum of 5 samples was used for each system in all hydration experiments.

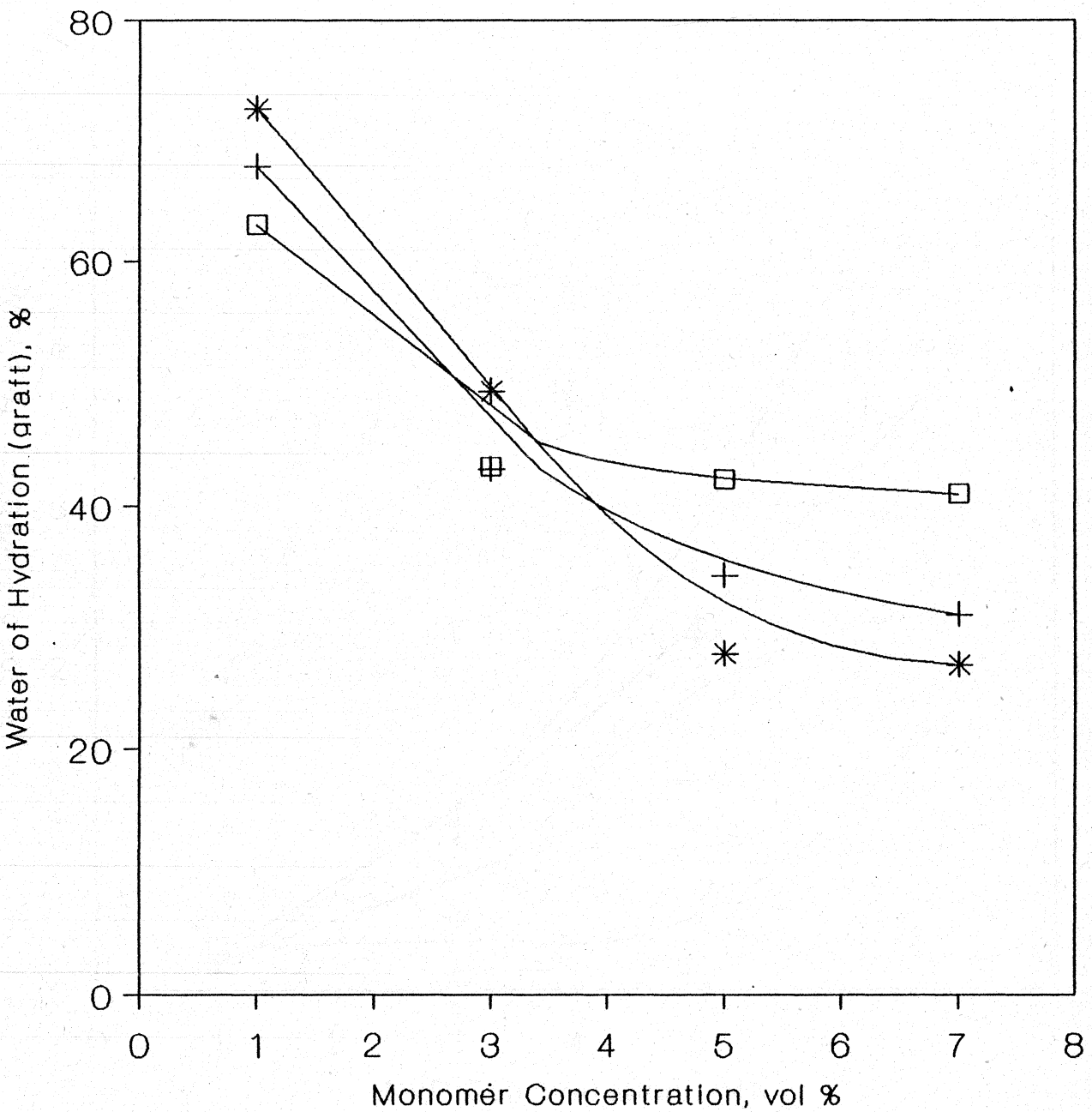


Figure 4.13. Variation in graft water content with monomer concentration for PVC grafted with NVP:HEMA monomer combinations: Figure shows decrease in graft water content with graft monomer concentration for NVP25:HEMA75 (+), NVP50:HEMA50 (*) and NVP75:HEMA25 (□) grafted PVC systems [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within ± 10%.

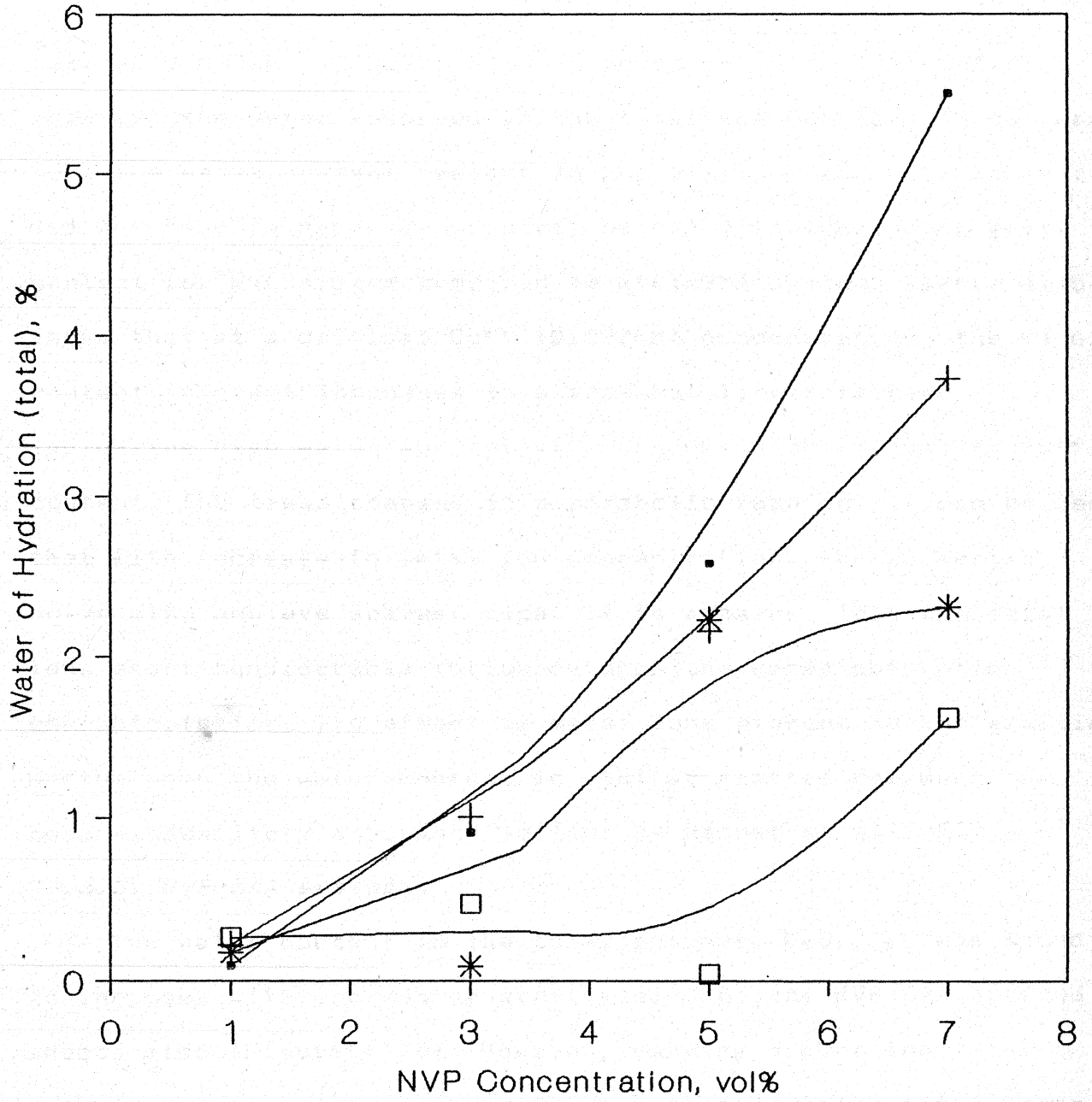


Figure 4.14. Effect of varying Cu^{2+} concentration on total water content for NVP grafted PVC system: Changes in total water content for NVP grafted to PVC in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions are shown above [0.25 Mrads]. S.D. was within ± 10%.

maximum water absorption characteristics. This is expected as the optimum Cu^{2+} ion concentration for NVP system was found to lie between 0.0025M - 0.005M. With increase in metal ion content, however, the water absorbed in the total polymer tend to be less.

The water content present in the graft, H_2O_{graft}, however did not tend to decrease proportionately with increasing graft content for NVP system compared to NVP:HEMA system. Figure 4.15 shows that at a critical Cu^{2+} (0.0025M) concentration, the water content in graft increases in a somewhat linear fashion indicating high water absorptivity whereas with increasing Cu^{2+} content, the trend changes in a parabolic fashion. It can be seen that with increase in metal ion concentration, the parabolic curve also achieve sharper dips. It is apparent that the metal ions exert considerable influence upon the water absorption characteristics. The effect of metal ions present in the grafting medium upon the water content in similar grafted polymers has been exhaustively discussed earlier by Ratner et al(101).

IV.3.3. NVP:MAA system:

The water content in the total polymer, H_2O_{total} was found to increase with increasing graft yield for the NVP:MAA grafted sheets also (Figure 4.16). However, varying copper ion concentration during grafting is seen to affect the total water content as in the case of NVP. Grafting at 0.01M copper ion concentration seem to produce maximum water absorption

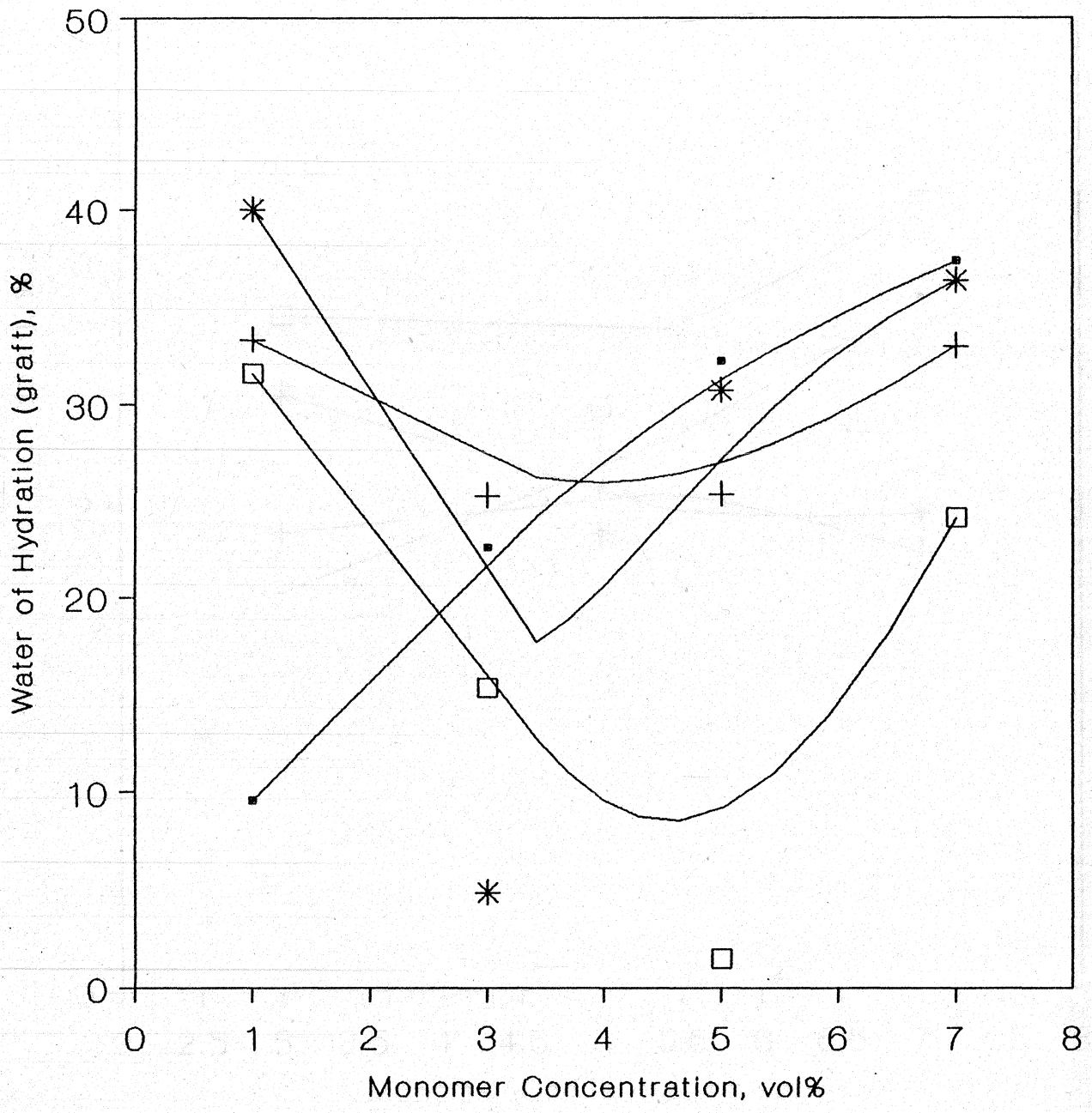


Figure 4.15. Effect of varying Cu^{2+} concentration on graft water content for NVP grafted PVC system: Changes in graft water content for NVP grafted to PVC in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions are shown above [0.25 Mrads]. S.D. was within ± 10%.

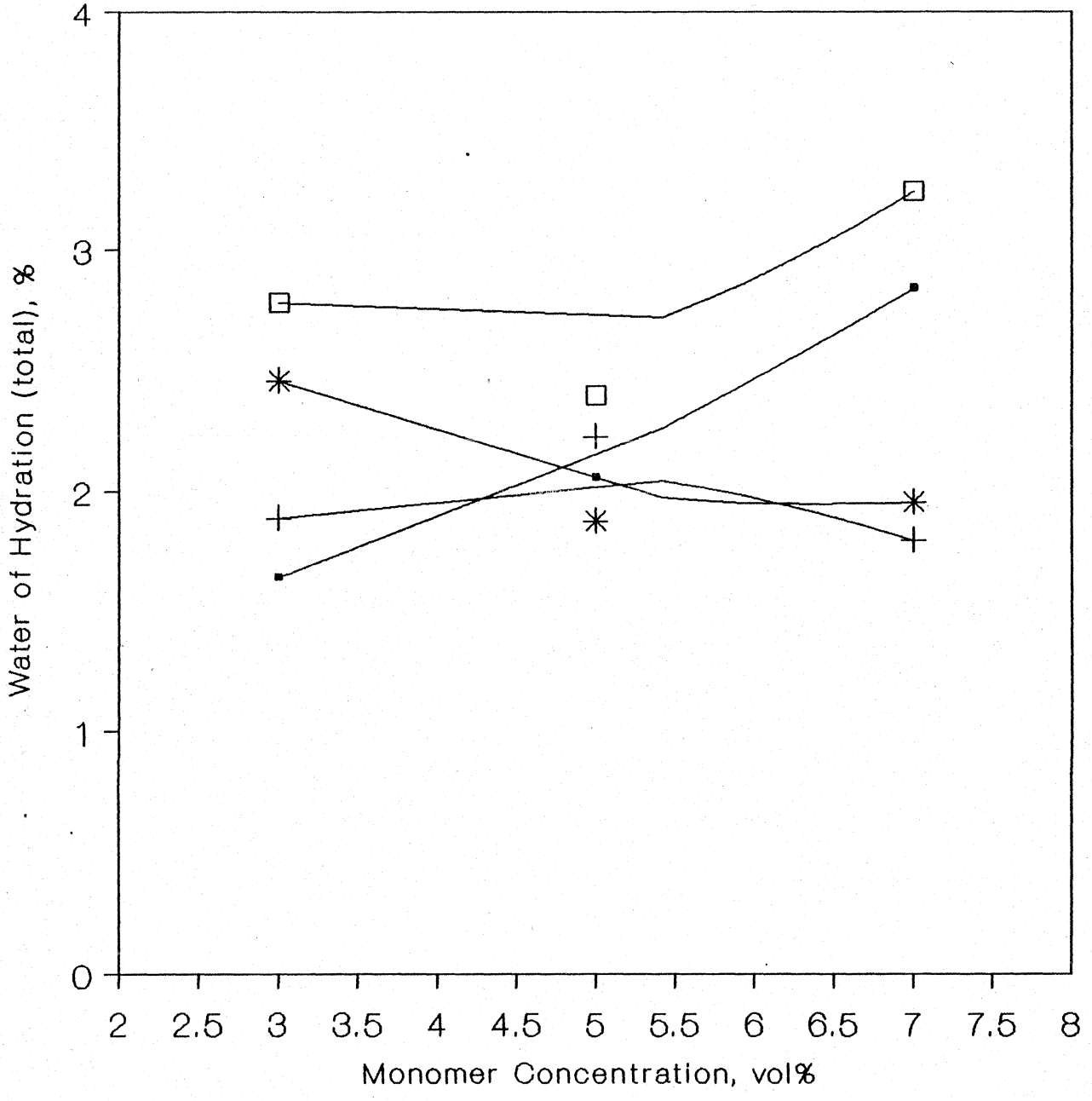


Figure 4.16. Effect of varying Cu^{2+} concentration on total water content for NVP50:MAA50 grafted PVC system: Changes in total water content for NVP50:MAA50 grafted to PVC in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions are shown [0.25 Mrads]. S.D. was within ± 10%.

characteristics for this system. The water content present in the graft, H_2O_{graft}, decreased with increasing graft content for NVP:MAA system, a phenomena similar to the NVP:HEMA system (Figure 4.17)

IV.3.4. MAA system:

Figure 4.18. shows the water absorption trends of MAA grafted sample. The behaviour is similar to that observed in the case of NVP:HEMA and NVP:MAA systems.

IV.4. Estimation of Percentage Transmission:

IV.4.1. NVP:HEMA system:

The transparency measurements at 700 nm show a steady decrease in transparency with increase in graft yield. However this is not likely to affect the final product significantly because the control sample itself was showing only about 8% transmission at this wavelength. The percentage transmission values also do not show considerable change when the samples were subjected to measurements in the dry state and in the hydrated state. Data on the percentage transmission measurements are given in Figure 3.4. and discussed briefly in the previous chapter (III.1.1.2.)

IV.4.2. NVP system:

The transparency measurements at 700 nm for NVP-g-PVC (Figure 3.4) show much better transmission compared to NVP:HEMA

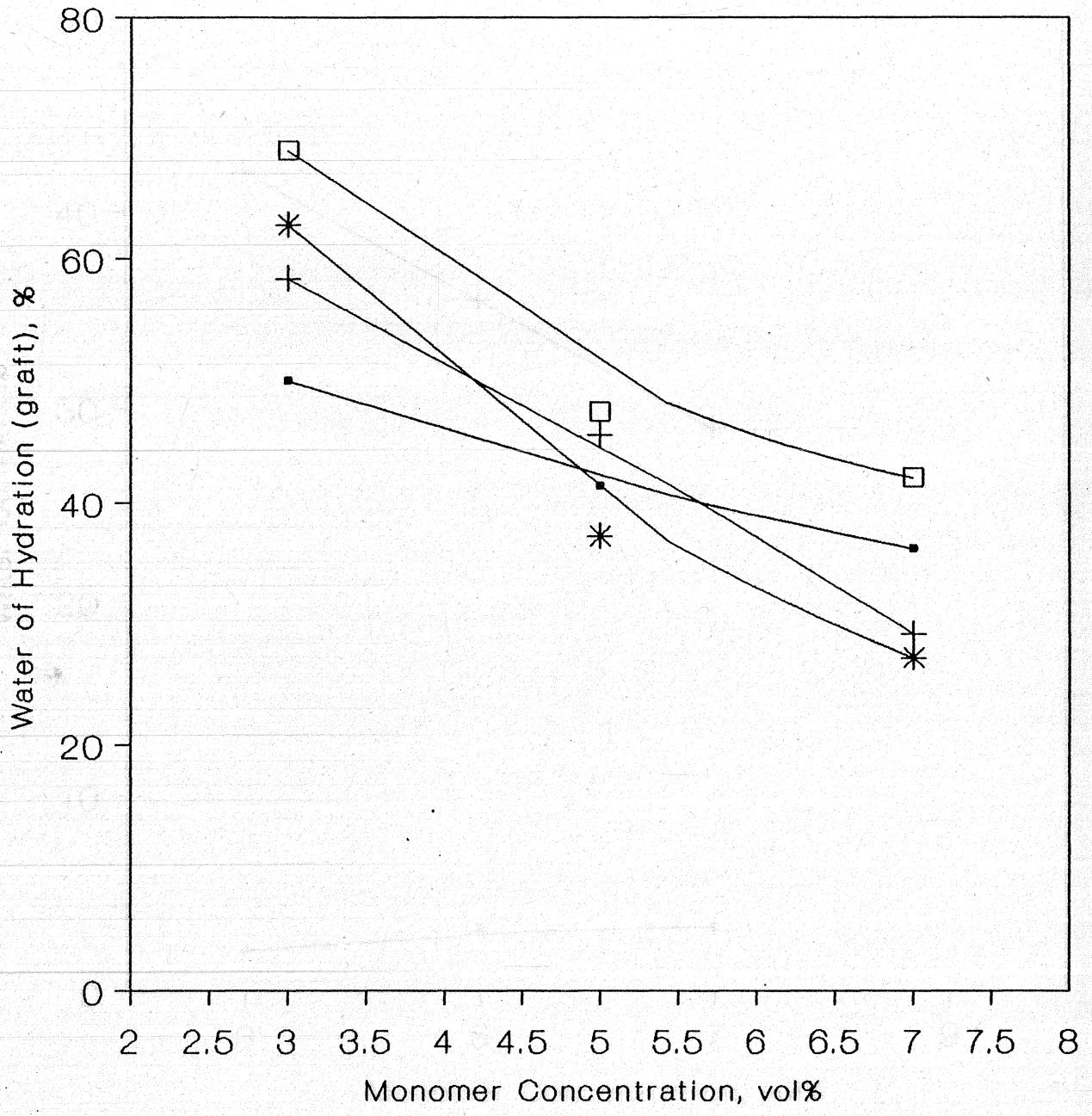


Figure 4.17. Effect of varying Cu^{2+} concentration on graft water content for NVP50:MAA50 grafted PVC system: Changes in graft water content for NVP50:MAA50 grafted to PVC in aqueous media containing 0.0025M (.), 0.005M (+), 0.0075M (*) and 0.01M (□) Cu^{2+} ions are shown [0.25 Mrads]. S.D. was within $\pm$ 10%.

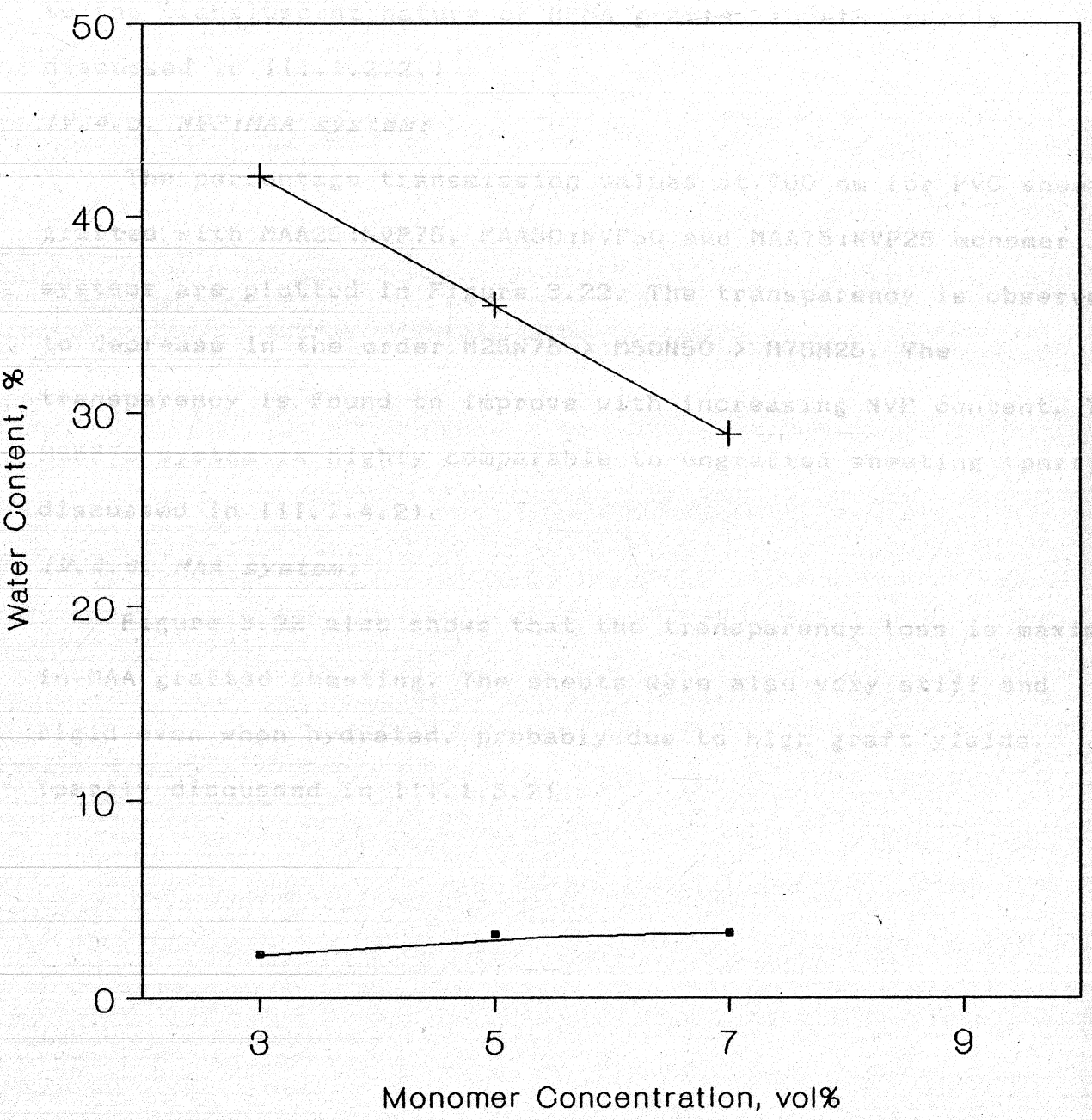


Figure 4.18. Variation in total and graft water contents with increasing monomer concentration for PVC modified with MAA system: Figure shows increase in total water content (.) and decrease in graft water content (+) with increasing monomer concentration for MAA grafted PVC [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 10%.

systems. The grafted sheets are apparently transparent compared to the transluscent nature of HEMA grafted sheets (partly discussed in III.1.2.2.)

IV.4.3. NVP:MAA system:

The percentage transmission values at 700 nm for PVC sheets grafted with MAA25:NVP75, MAA50:NVP50 and MAA75:NVP25 monomer systems are plotted in Figure 3.22. The transparency is observed to decrease in the order M25N75 > M50N50 > M75N25. The transparency is found to improve with increasing NVP content. The M25N75 system is highly comparable to ungrafted sheeting (partly discussed in III.1.4.2).

IV.4.4. MAA system:

Figure 3.22 also shows that the transparency loss is maximum in MAA grafted sheeting. The sheets were also very stiff and rigid even when hydrated, probably due to high graft yields. (partly discussed in III.1.5.2)

CHAPTER V

RESULTS AND DISCUSSION (Contd...)

V.1. Migration Studies:

V.1.1. NVP:HEMA System:

V.1.1.1. Migration into Organic Solvents:

V.1.1.1.a. Migration into n-hexane:

The plasticizer DEHP migrated into organic solvents from modified and unmodified PVC was monitored spectrophotometrically by measuring the absorbance at 274 nm, the characteristic absorption maximum for DEHP. Migration of DEHP into an organic solvent like n-hexane stored in grafted and ungrafted bags show a drastic reduction for NVP25:HEMA75, NVP50:HEMA50 and NVP75:HEMA25 systems studied in this group (Figures 5.1, 5.2 & 5.3). Figure 5.4 shows the U.V. spectrum of the plasticizer migrated into n-hexane at 274 nm at different time intervals. The amount of DEHP migrated in the control ungrafted bag [Control I, Technoport] within five hours is so high (nearly 250 mg) that Fickian behaviour does not hold true for this system as evidenced by Figure 5.5a. While the amount of plasticizer leached out into n-hexane in modified bags for the NVP25:HEMA75 and NVP75:HEMA25 systems is less than 20 mg even after 5h (where grafting concentrations of more than 1 vol% have been used), it was as

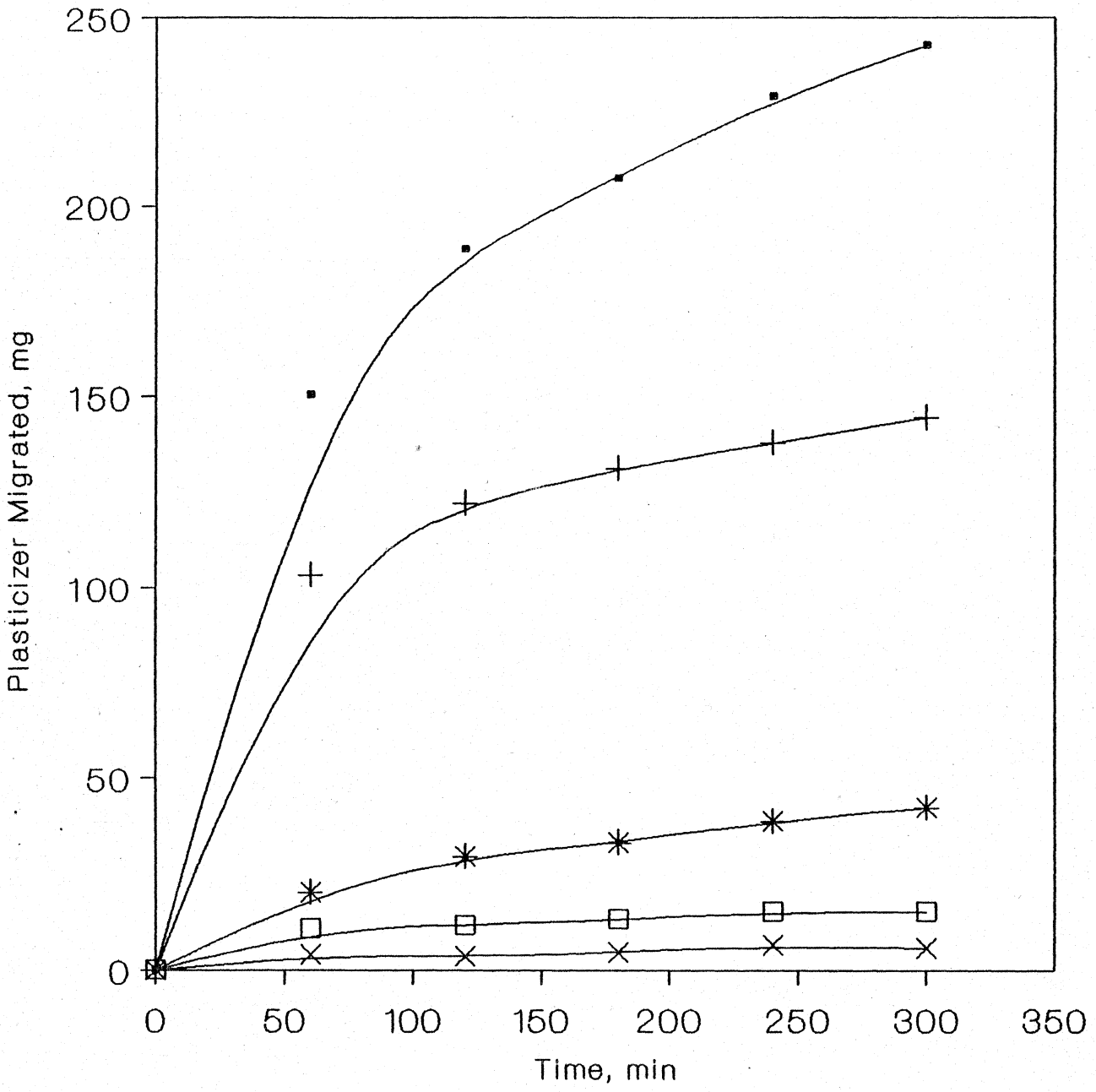


Figure 5.1. Plasticizer migration curves for ungrafted (control) and NVP25:HEMA75 grafted PVC systems in n-hexane: Figure shows amount of DEHP migrated into n-hexane at 30°C plotted against time from ungrafted (.), 1% (+), 3% (*), 5% (□) and 7% (x) (all vol%) NVP25:HEMA75 grafted PVC bags [0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%. A minimum of 3 bags was tested for each system in all migration experiments.

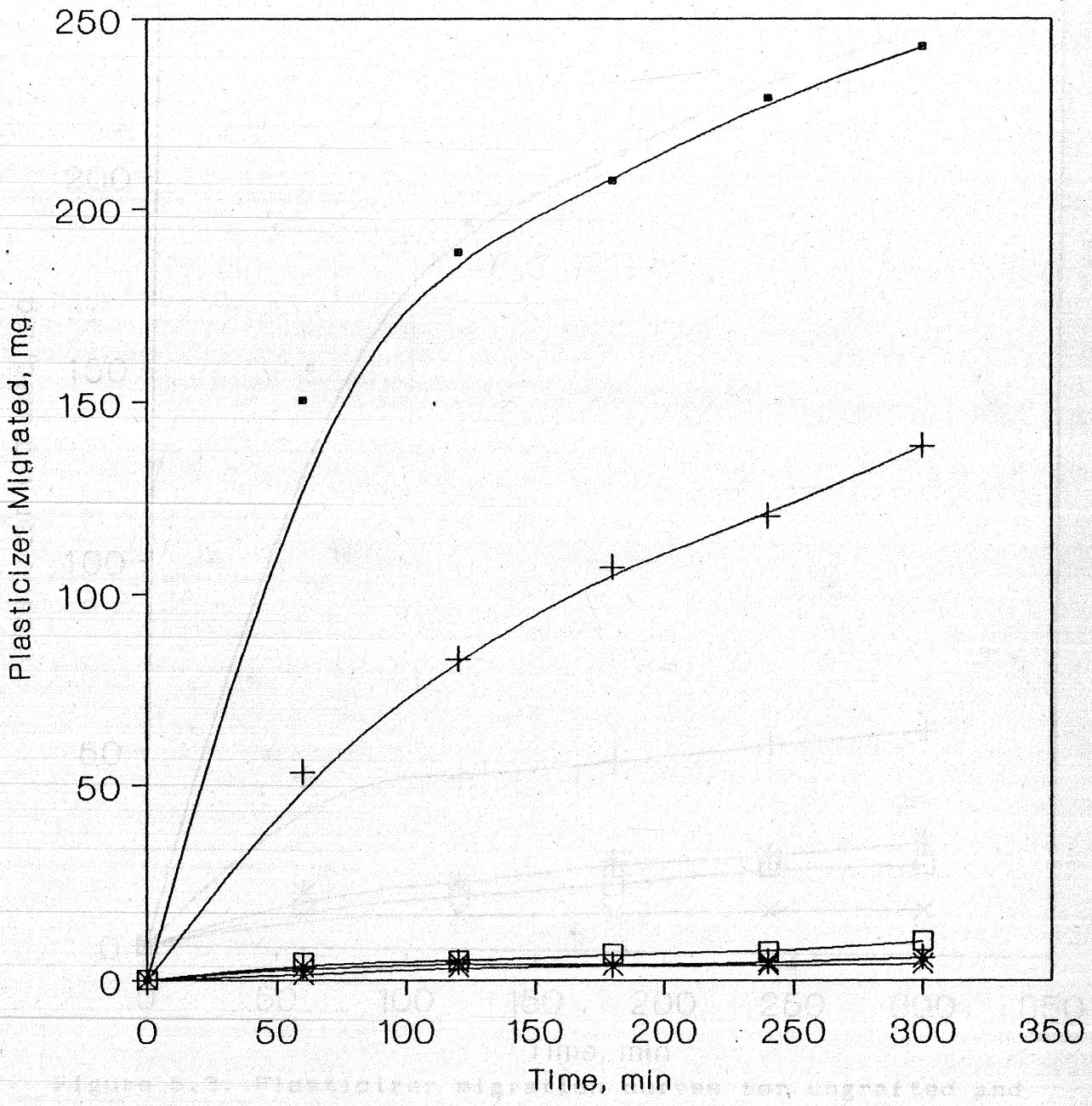


Figure 5.2. Plasticizer migration curves for ungrafted and NVP50:HEMA50 grafted PVC systems in n-hexane: Figure shows amount of DEHP migrated into n-hexane at 30°C plotted against time from ungrafted (.), 1% (+), 3% (*), 5% (□) and 7% (x) (all vol%) NVP50:HEMA50 grafted PVC bags [0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within $\pm$ 5%.

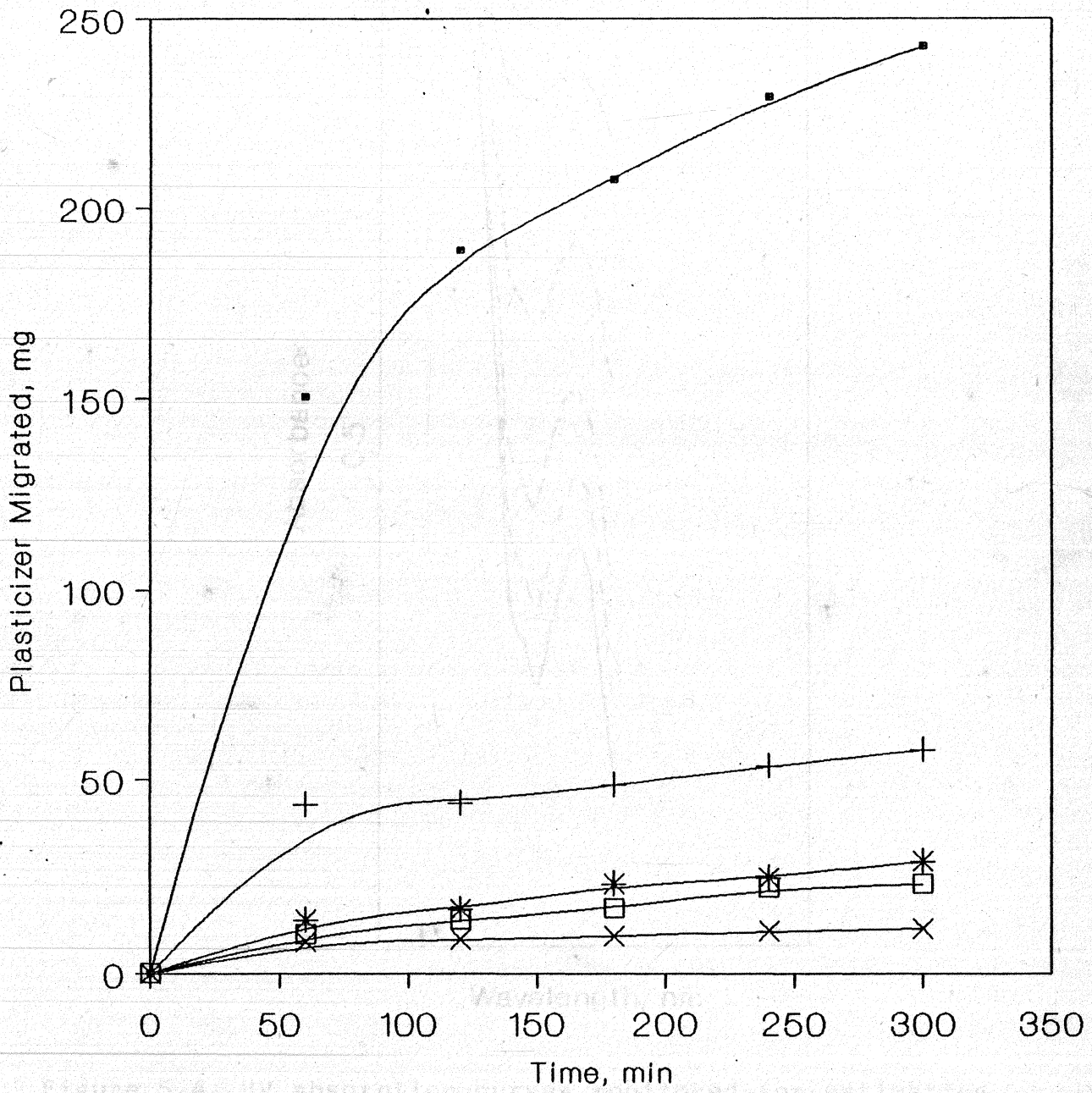


Figure 5.3. Plasticizer migration curves for ungrafted and NVP75:HEMA25 grafted PVC systems in n-hexane: Figure shows amount of DEHP migrated into n-hexane at 30°C plotted against time from ungrafted (.), 1% (+), 3% (*), 5% (□) and 7% (x) (all vol%) NVP75:HEMA25 grafted PVC bags [0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

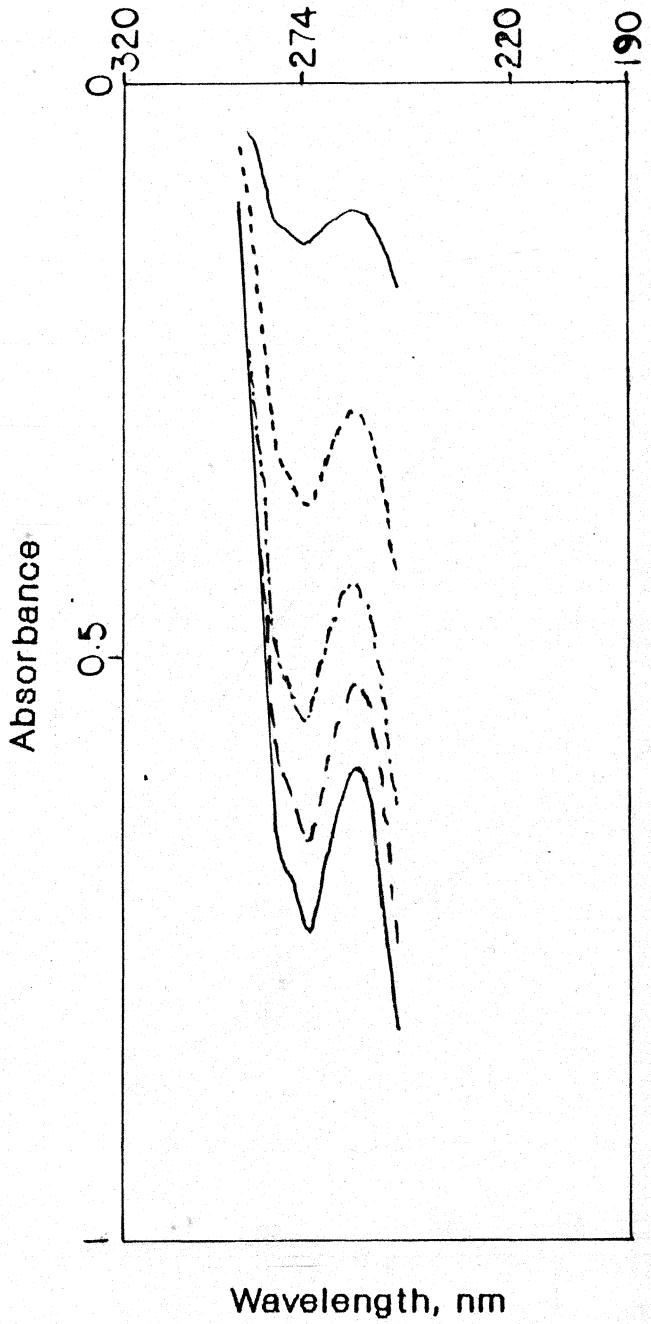


Figure 5.4. UV absorption curves monitored for estimating migrated plasticizer content from NVP:HEMA grafted PVC system: Figure shows the absorption maxima at 274 nm monitored at 1, 2, 3, 4 and 5 hours for estimating quantity of migrated plasticizer DEHP from a NVP50:HEMA50 (5 vol%) grafted PVC bag into n-hexane at 30°C.

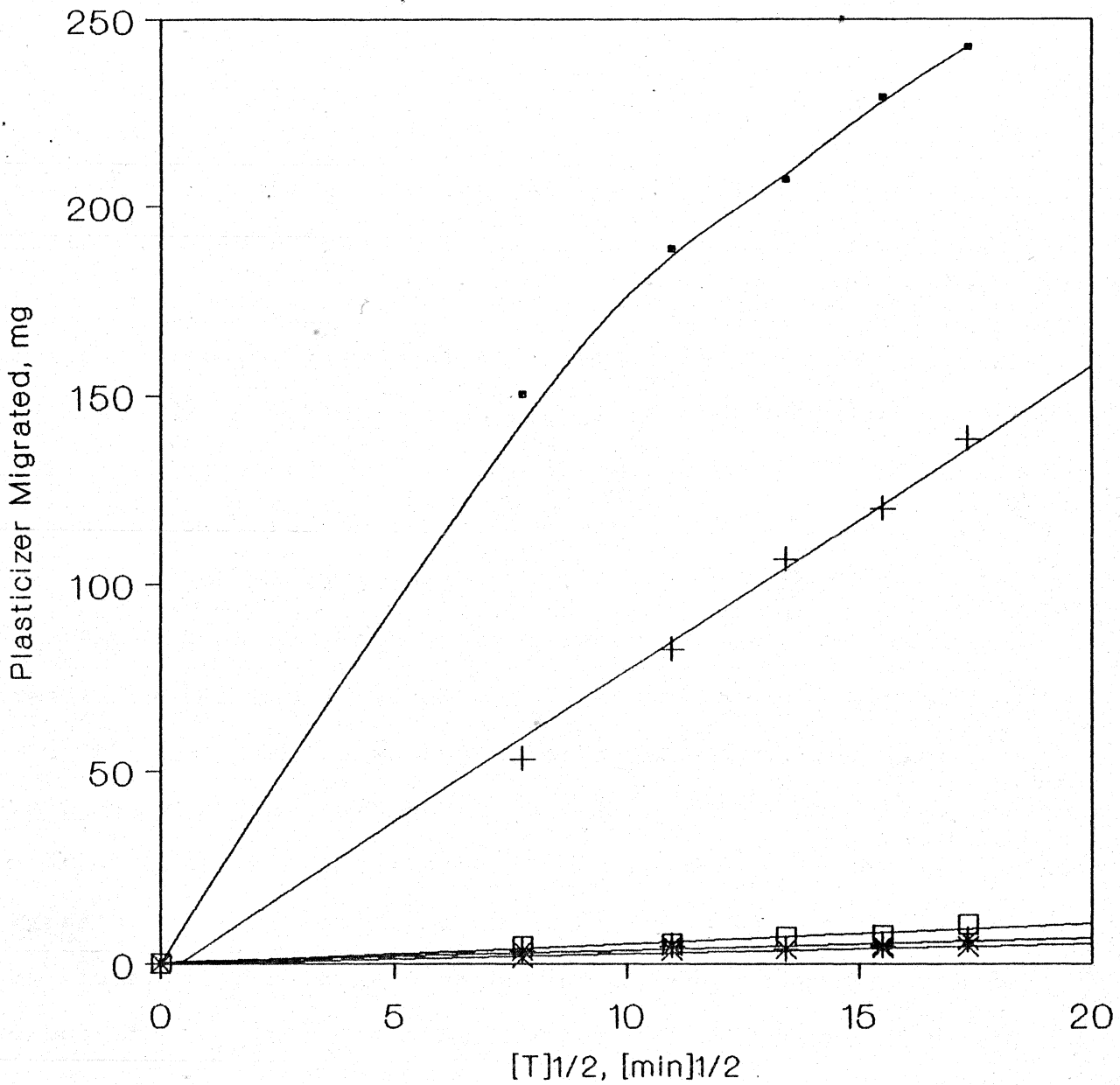


Figure 5.5a. Exhibition of fickian behaviour during DEHP migration from NVP50:HEMA50 grafted PVC system: Figure shows amount of DEHP migrated into n-hexane at 30°C plotted against square root of time showing non-fickian behaviour from ungrafted (.) and fickian behaviour for 1% (+), 3% (*), 5% (□) and 7% (x) (all vol%) NVP50:HEMA50 grafted PVC bags [0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within $\pm$ 5%.

low as 3-10 mg in the case of NVP50:HEMA50 system(61). This is only about 2-4% of the amount of plasticizer migrated from the unmodified bags which is a drastic reduction in the migration amount of DEHP. Reduction in leaching is also observed in bags grafted with 1% monomer but to a slightly lower degree than where higher concentrations of monomer were employed for grafting. Plot of square root of time against amount of plasticizer migrated indicate that all the grafted bags show Fickian behaviour (Figure 5.5b) to a great extent. It can therefore be predicted that the migration is diffusion controlled whereas it is non-Fickian in the case of ungrafted bags.

The reason for this drastic reduction in migration especially for the NVP50:HEMA50 system can be attributed to the fact that in presence of non-polar organic solvents, the hydrophilic network at the surface of PVC tend to shrink and form a very tightly closed network. However, this does not mean that migration will be faster in polar solvents as the migration behaviour is also largely dependent on other factors such as solubility of the plasticizer in the medium, temperature etc.

V.1.1.1.b. Migration into n-heptane:

The NVP50:HEMA50 system was further chosen (due to its low migration in hexane) to study the behaviour of migration of DEHP in other hydrocarbon solvents such as n-heptane and n-octane. The amount of DEHP migrated from NVP50:HEMA50 (5%) grafted PVC

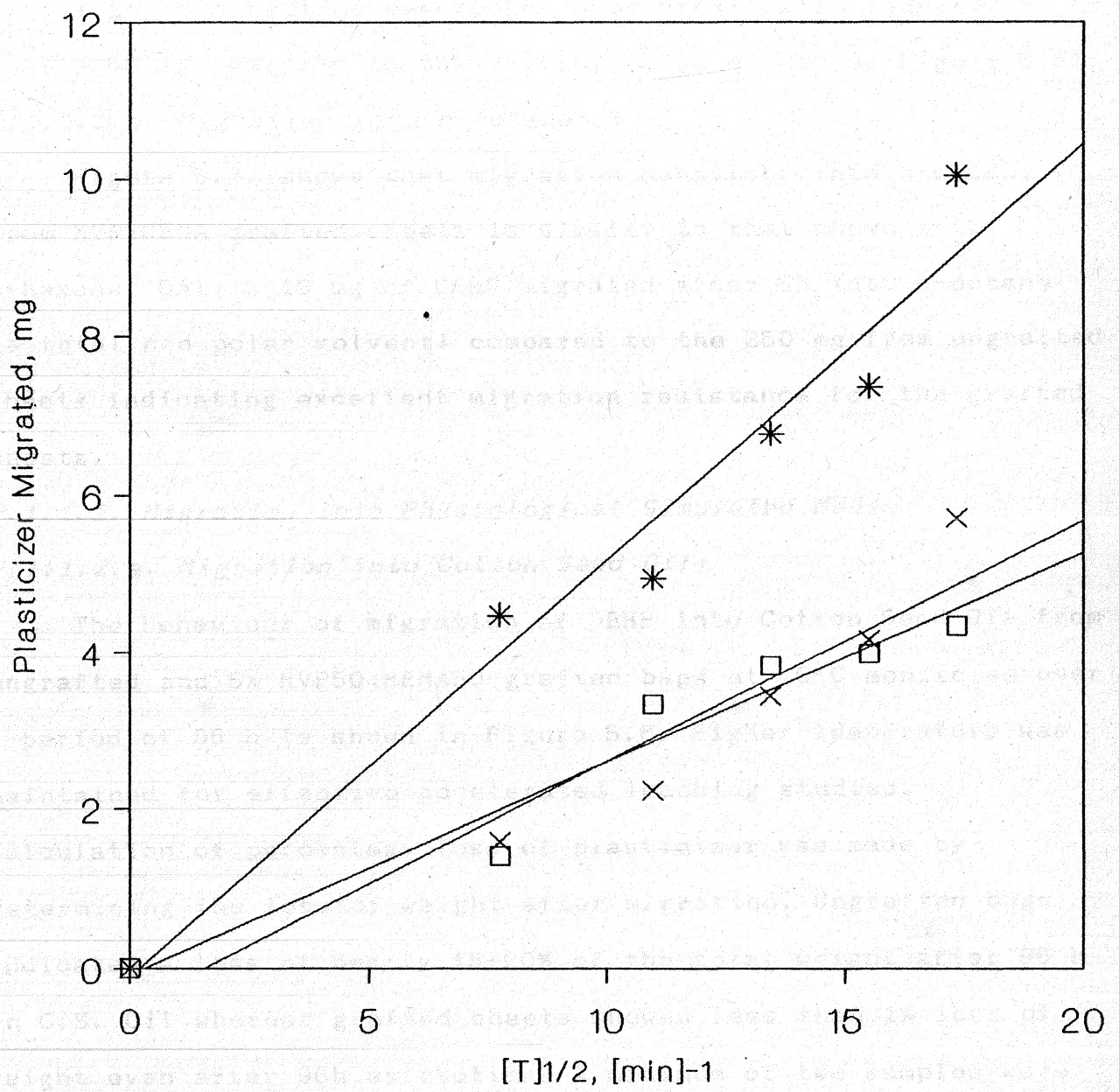


Figure 5.5b. Figure (5.5a) showing the lower part of the graph magnified: Fickian behaviour of PVC grafted with 3% (*), 5% (□) and 7% (x) (all vol%) NVP50:HEMA50 are shown in the figure.

sheetings in n-heptane was found to be drastically reduced to nearly 50 mg compared to the control value of 250 mg(Figure 5.6).

V.1.1.1.c. Migration into n-octane:

Figure 5.7. shows that migration behaviour into n-octane from NVP:HEMA grafted sheets is similar to that shown into n-hexane. Only 5-10 mg of DEHP migrated after 5h into n-octane (a total non-polar solvent) compared to the 250 mg from ungrafted sheets indicating excellent migration resistance for the grafted sheets.

V.1.1.2. Migration into Physiological Simulated Media:

V.1.1.2.a. Migration into Cotton Seed Oil:

The behaviour of migration of DEHP into Cotton Seed Oil from ungrafted and 5% NVP50:HEMA50 grafted bags at 70°C monitored over a period of 96 h is shown in Figure 5.8. Higher temperature was maintained for effective accelerated leaching studies. Calculation of percentage loss of plasticizer was made by determining the loss of weight after migration. Ungrafted bags indicated a loss of nearly 15-20% of the total weight after 96 h in C.S. Oil whereas grafted sheets showed less than 1% loss of weight even after 96h extraction. A minimum of two samples were tested at each time interval but the results were highly reproducible(61).

V.1.1.2.b. Migration into PEG-400:

Grafted sheets tended to show migration in PEG-400 unlike in

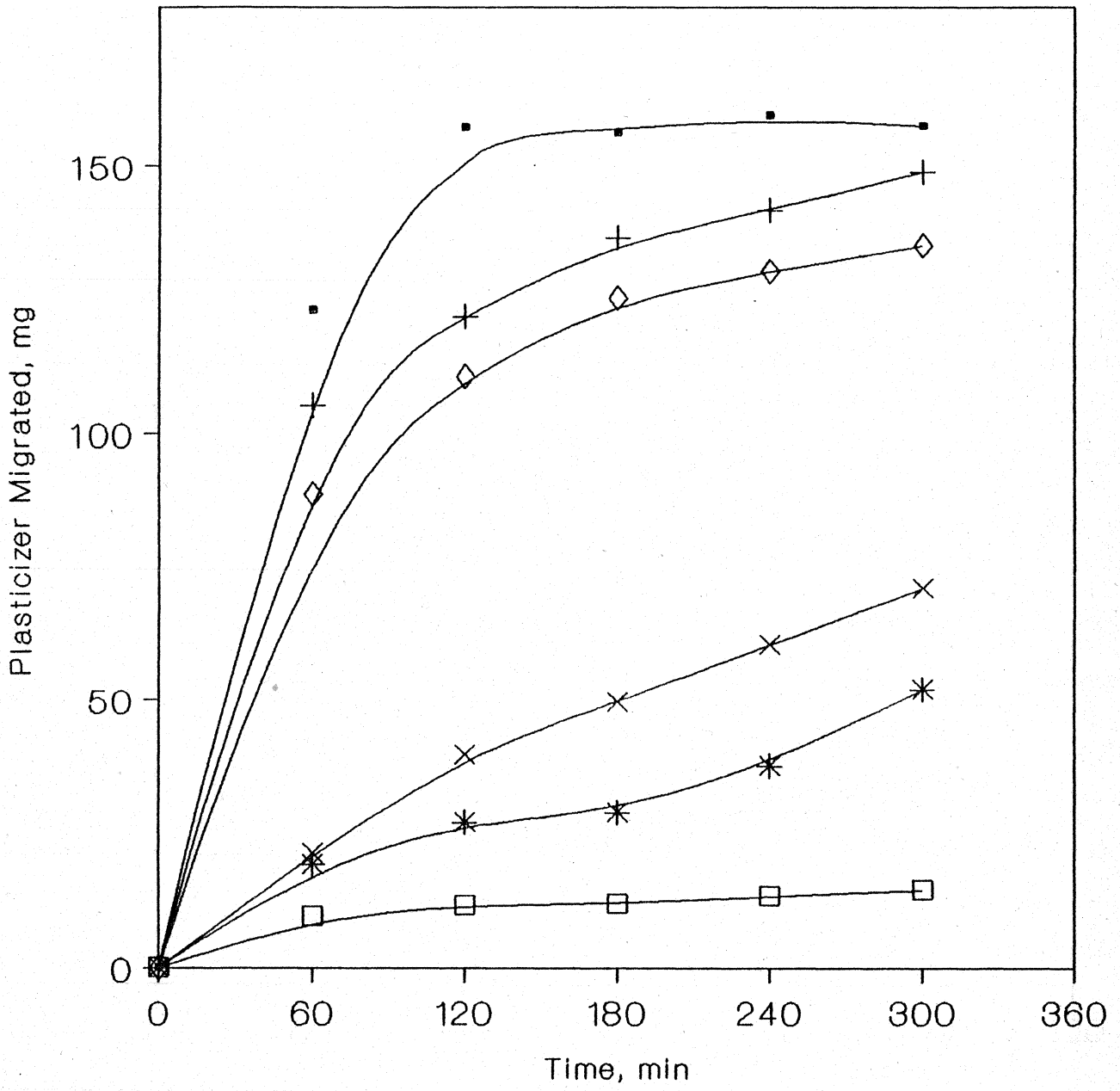


Figure 5.6. Plasticizer migration curves for ungrafted, NVP50:HEMA50, NVP, NVP50:MAA50 and MAA grafted PVC systems in n-heptane: Figure shows amount of migrated DEHP into n-heptane at 30°C against time from Control I [Techno-port] (.), Control II [Terumo] (+), PVC bags grafted with NVP50:HEMA50 (*), NVP (□), NVP50:MAA50 (x) and MAA (◊) [all 5 vol%, 0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

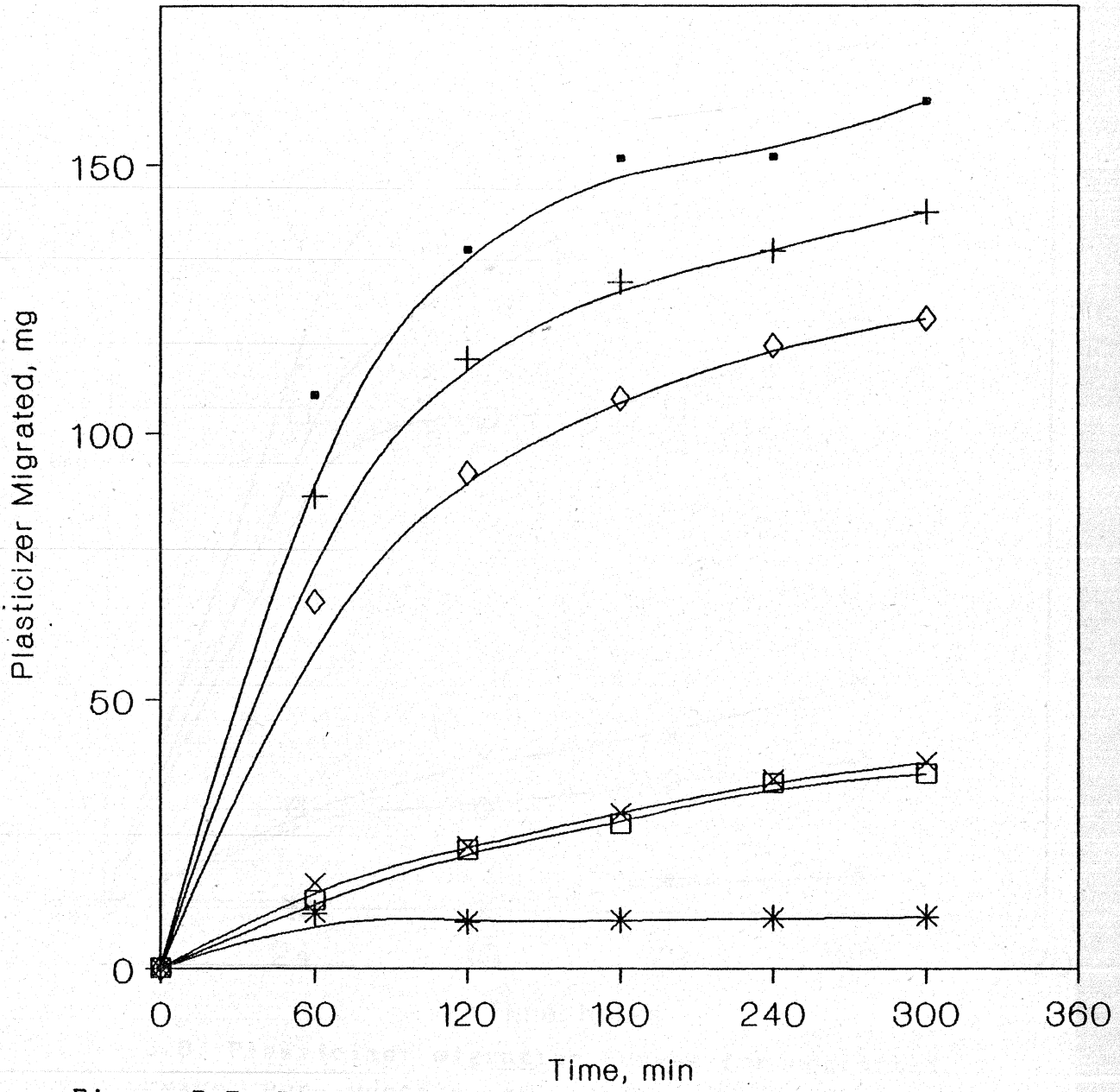


Figure 5.7. Plasticizer migration curves for ungrafted, NVP50:HEMA50, NVP, NVP50:MAA50 and MAA grafted PVC systems in n-octane: Figure shows amount of migrated DEHP into n-octane at 30°C plotted against time from Control I (.), Control II (+), PVC bags grafted with NVP50:HEMA50 (*), NVP (□), NVP50:MAA50 (x) and MAA (◇) [all 5 vol%, 0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

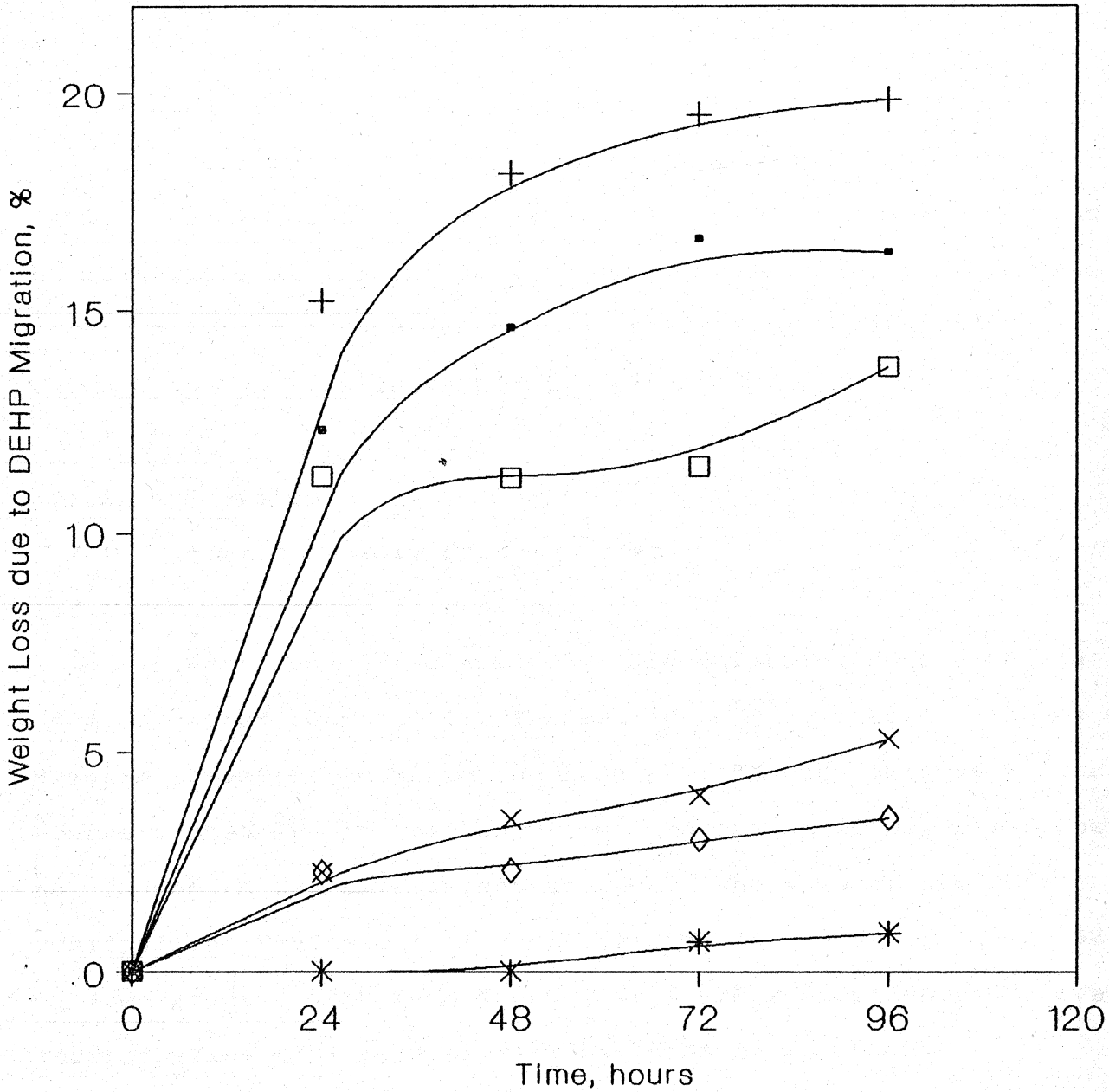


Figure 5.8. Plasticizer migration curves for ungrafted, NVP50:HEMA50, NVP, NVP50:MAA50 and MAA grafted PVC systems in cotton seed oil: Percentage loss of weight due to migrated DEHP into Cotton seed oil at 70°C is plotted against time from Control I (.), Control II (+), PVC bags grafted with NVP50:HEMA50 (*), NVP (□), NVP50:MAA50 (x) and MAA (◊) [all 5 vol%, 0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

cotton seed oil but to a lesser extent than control after 96h (Figure 5.9). The difference in migration shown in different physiological media is interesting and the only reason that can be attributed at present is that PEG-400 being highly polar and highly miscible with DEHP may have relaxed the hydrophilic network at the surface to permit easier migration.

V.1.2. NVP System:

V.1.2.1. Migration into Organic Solvents:

V.1.2.1.a. Migration into n-hexane:

A comparison of the amount of DEHP migrated into n-hexane from ungrafted [Control II, Terumo] and NVP grafted bags shows a drastic reduction in migration from grafted bags (Figure 5.10). However, when NVP is grafted alone, the extent of migration does not reduce to the same extent as was in the case of NVP:HEMA combination. The amount of DEHP migrated is nearly 63 mg and 52 mg when grafted with 5 vol% and 7 vol% NVP respectively. However, incorporation of 1 vol% crosslinker EDMA on the 5% NVP concentration tends to reduce the value to 26 mg. This clearly indicates that grafting helps to reduce the migration considerably for NVP system too and incorporation of crosslinker EDMA enhances its effectiveness. The crosslinking helps to keep the network intact and its hydrophobic nature is basically responsible for the reduction in migration upon crosslinking. NVP

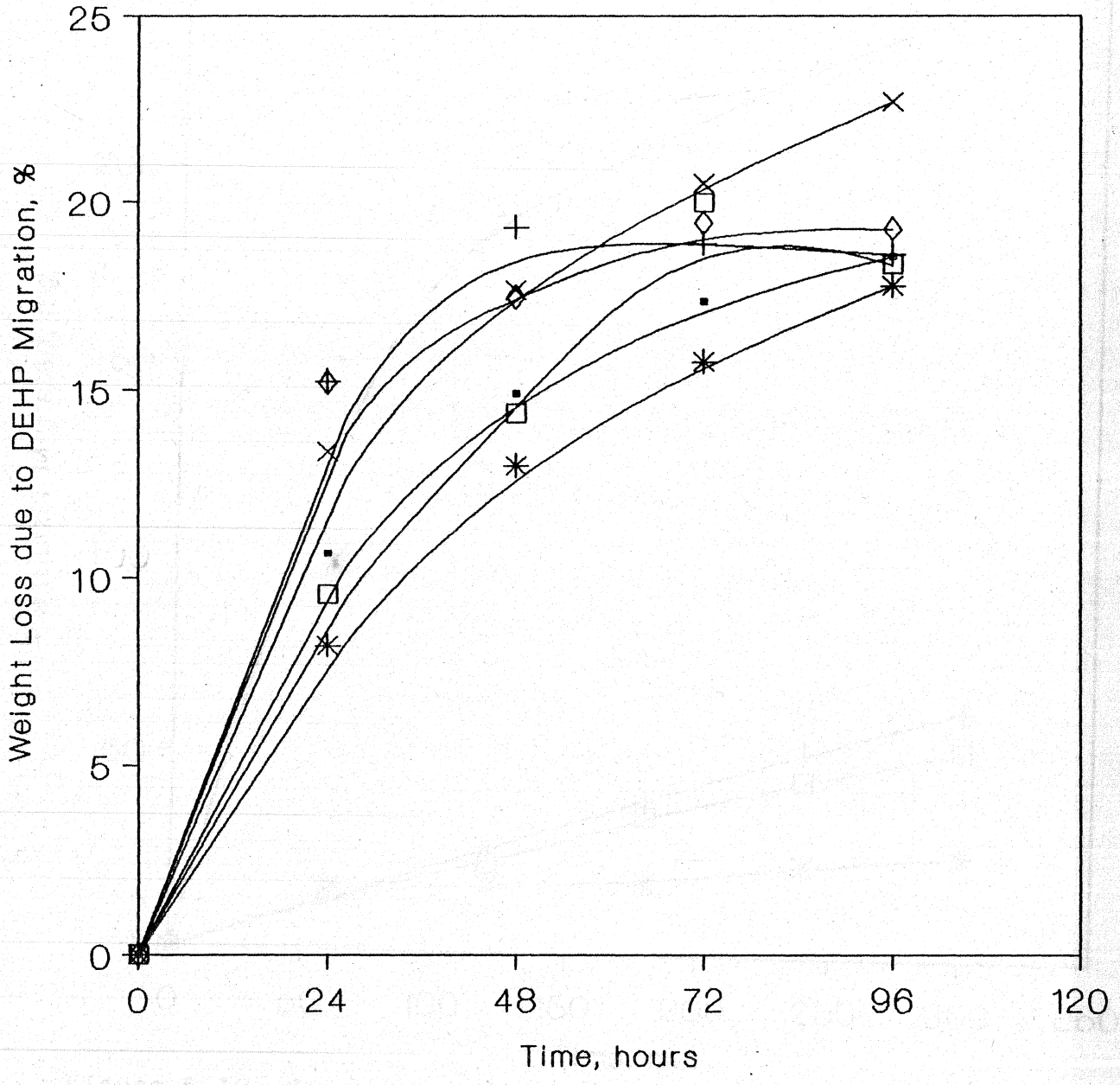


Figure 5.9: Plasticizer migration curves for ungrafted, NVP50:HEMA50, NVP, NVP50:MAA50 and MAA grafted PVC systems in PEG-400: Figure shows percentage loss of weight due to migrated DEHP into PEG-400 at 70°C plotted against time from Control I (.), Control II (+), PVC bags grafted with NVP50:HEMA50 (*), NVP (□), NVP50:MAA50 (x) and MAA (◇) [all 5 vol%, 0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within $\pm$ 5%.

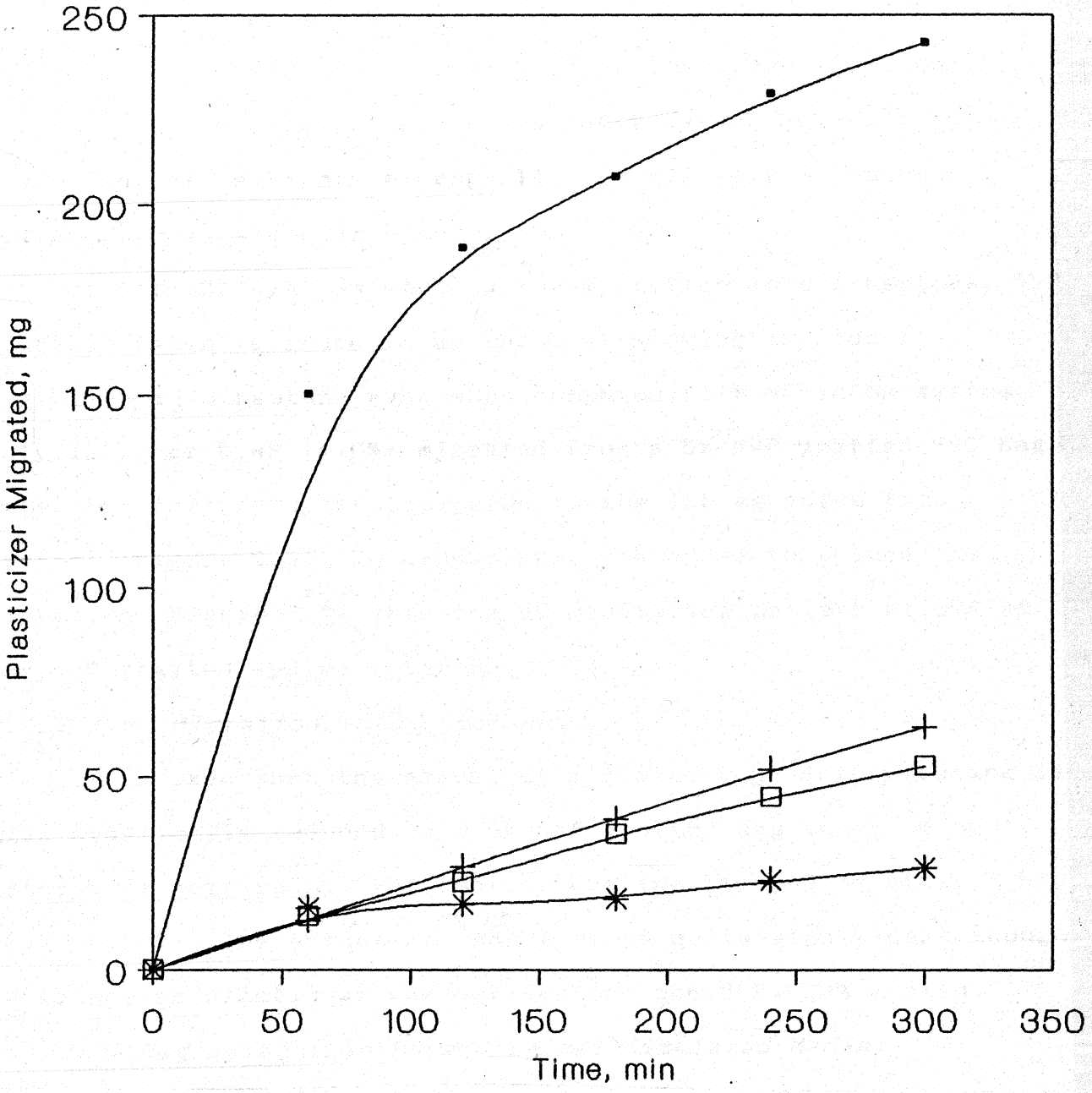


Figure 5.10. Plasticizer migration curves for ungrafted and NVP grafted PVC bags in n-hexane: Figure shows amount of DEHP migrated into n-hexane at 30°C plotted against time from ungrafted (.), 5% NVP (+), 5% NVP + 1% EDMA (*) and 7% NVP (□) (all vol%) grafted onto PVC [0.005 M Cu^{2+}, 0.5 Mrads]. S.D. was within $\pm$ 5%.

grafted PVC is also highly flexible and transparent though it tends to become slightly stiff when dehydrated. However, upon hydration, it is highly hydrophilic and slippery in nature.

V.1.2.1.b. Migration into n-heptane:

Of all the systems studied for migration into n-heptane, NVP grafted system is found to be the best showing the least migration in n-heptane even when compared with NVP:HEMA system. Only 15 mg of DEHP (<10%) migrated from a 5% NVP grafted PVC bag after 5 h into n-heptane compared to the 150 mg value from control (Figure 5.6). No crosslinker was added to reduce the migration. Figure 5.11 show the UV monitoring pattern at 274 nm for NVP grafted system after 5h.

V.1.2.1.c. Migration into n-octane:

It is seen that the amount of migrated DEHP into n-octane is also drastically reduced in a 5% NVP grafted bag (only 36 mg after 5 h) compared to the control bag (nearly 140 mg after 5 h) (Figure 5.7). The extent of reduction is quite significant though it is not as drastic as was noticed for the NVP:HEMA system.

V.1.2.2. Migration into Physiological Simulated Media:

V.1.2.2.a. Migration into Cotton Seed Oil:

Contrary to the observations made for migration from NVP:HEMA grafted sheets in C.S. Oil, the reduction in migration of plasticizer from NVP grafted PVC sheets was not as high as shown by the former system (Figure 5.8). NVP grafted sheets

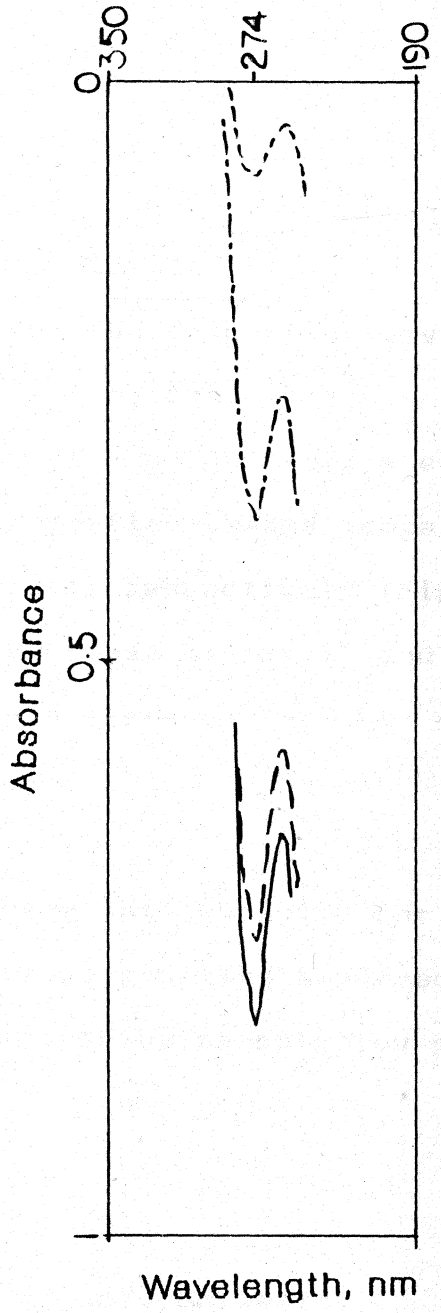


Figure 5.11. UV absorption curves monitored for estimating DEHP migration into n-heptane: UV absorbance spectra showing monitoring of DEHP migration at 274 nm from Control (————), MAA grafted (— — —), NVP50:MAA50 grafted (—·—·—·—) and NVP grafted PVC (————————) into n-heptane at 30°C after 5 hours.

showed nearly 14% loss in weight after 96 h in C.S. Oil compared to negligible loss in weight (<1%) shown by the former.

V.1.2.2.b. Migration into PEG-400:

Migration of DEHP and the resulting loss of weight from NVP grafted sheets was similar to control sheets in PEG-400 in spite of the fact that the quantity of DEHP migrated was only 9.5% and 14.4% at 24 and 48 h for grafted sheets compared to 15.2% and 19.3% for the control sheets respectively (Figure 5.9). However, the values became highly comparable at 72 and 96 h indicating practically no migration resistance for this system in PEG-400.

V.1.3. HEMA:MAA System:

Migration studies were not conducted for HEMA:MAA system as homopolymer formation during grafting hindered graft modification to a considerable extent leading to only low percentage of graft yields.

V.1.4. NVP:MAA System:

V.1.4.1. Migration into Organic Solvents:

V.1.4.1.a. Migration into n-hexane:

A comparison of the amount of DEHP migrated into n-hexane from ungrafted and 5 vol% NVP25:MAA75, NVP50:MAA50 and NVP75:MAA25 grafted PVC bags show (Figure 5.12) that the reduction in the migration of DEHP into NVP/MAA grafted bags even

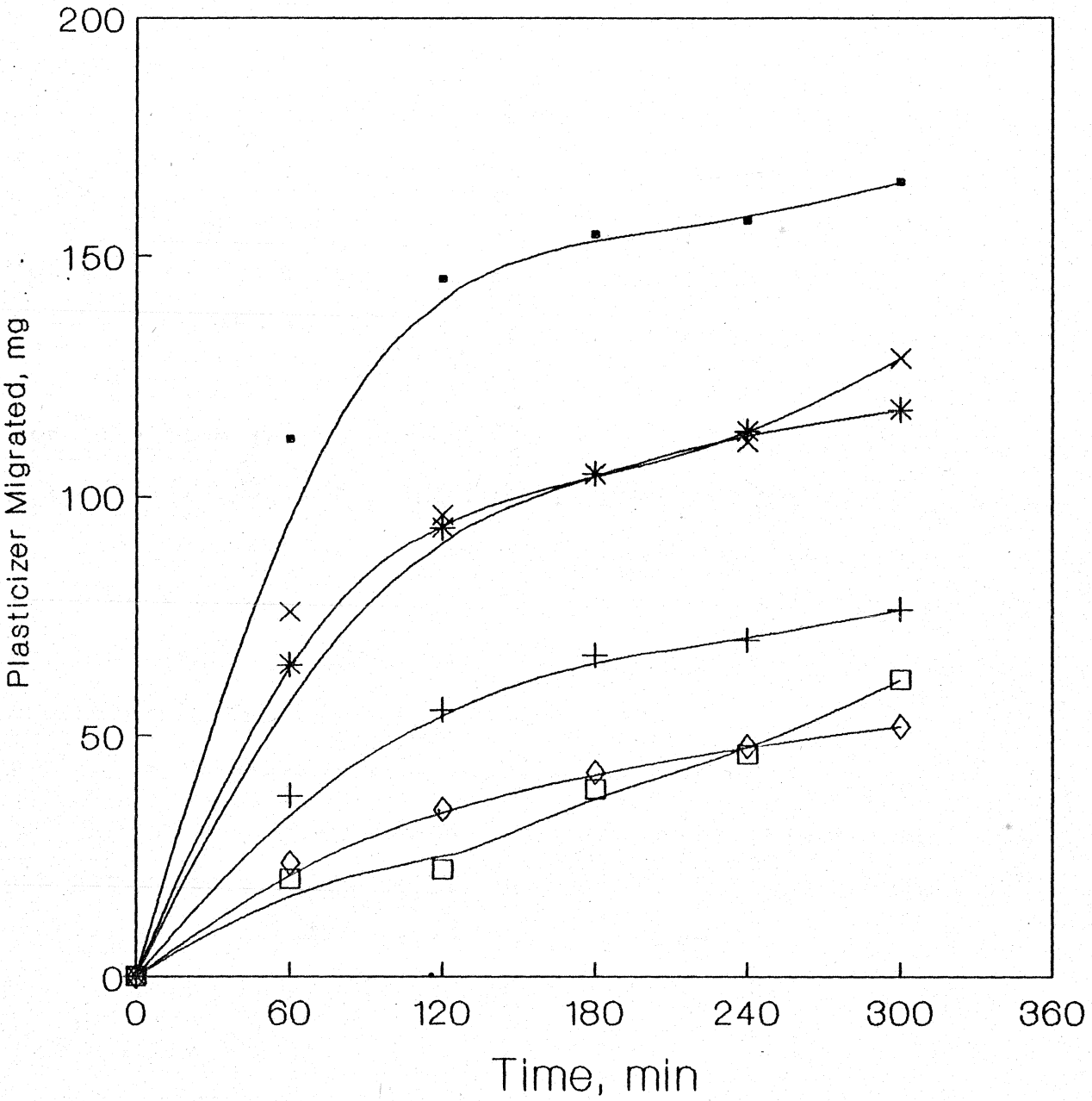


Figure 5.12. Plasticizer migration curves from ungrafted and NVP:MAA grafted PVC bags into n-hexane: Plots showing amount of DEHP migrated into n-hexane at 30°C against time from ungrafted (.), PVC bags grafted with NVP25:MAA75 (+), NVP50:MAA50 (*), NVP75:MAA25 (□) [all 5 vol%], 5% NVP50:MAA50 + 1% EDMA (x) and 5% NVP50:MAA50 + 2%EDMA (◇) [0.005 M Cu^{2+}, 0.5 Mrads] S.D. was within ± 5%.

without crosslinking is quite appreciable compared to control bags [Control II]. It is observed that while approximately 60 and 75 mg leaches after 5h for N25M75 and N75M25 systems respectively, the N50M50 system leaches about 115mg of DEHP compared to about 170 mg for control. Though incorporation of 1 vol% cross-linker EDMA with respect to the monomer(s) concentration in the NVP50:MAA50 system does not reduce the migration appreciably, increase in EDMA concentration to 2 vol% is found to drastically reduce the migration persumably by inducing a higher degree of crosslinking to less than 50 mg. The hydrated NVP/MAA grafted PVC bags are also found to be highly flexible and transparent.

V.1.4.1.b. Migration into n-heptane:

Reduction in migration is observed for this system too but not quite appreciable as was noticed for NVP and NVP:HEMA grafted systems in n-heptane. Nearly 71 mg of DEHP tended to migrate after 5 h and reduction was only about 50% compared to control (Figures 5.6 & 5.11).

V.1.4.1.c. Migration into n-octane:

Good reduction in migration was observed (Figure 5.7) for NVP:MAA grafted system in n-octane, very similar to the migration behaviour of NVP grafted system in n-octane. Less than 25% of the DEHP migrated compared to control.

V.1.4.2. Migration into Physiological Simulated Media:

V.1.4.2.a. Migration into Cotton Seed Oil:

Excellent reduction in migration of DEHP into C.S.Oil is observed from NVP50:MAA50 grafted PVC sheets at accelerated conditions. Only about 5% loss in weight due to migration was noticed in grafted sheets after 92 h compared to nearly 20% loss in weight for control. Though the extent of reduction in migration is not as drastic as was observed for NVP:HEMA system, it is quite significant. Figure 5.8 shows the trend. It can be safely assumed that the presence of PHEMA or PMAA may be the contributing factor for the migration resistance observed for both the systems because PVP grafted sheets did not induce good migration resistance.

V.1.4.2.b. Migration into PEG-400:

Unlike in C.S.Oil, migration resistance was not observed for the grafted sheets into PEG-400 (Figure 5.9). Nearly 22% loss in weight was observed after 96 h. This observation was also similar to that observed for the previous systems studied.

V.1.5. MAA System:

V.1.5.1. Migration into Organic Solvents:

V.1.5.1.a. Migration into n-hexane:

The behaviour of migration from MAA grafted PVC bags was found very similar to that shown by NVP/MAA system. A comparison of the amount of DEHP migrated into n-hexane from ungrafted and

MAA grafted bags (5 vol%) without crosslinking reveal that a reduction in migration does occur in grafted bags (Figure 5.13) compared to control [Control II] but not to a considerable extent. However, when 1% EDMA is added to the monomer in the grafting system, it helps to reduce the migration of DEHP the extent of which becomes drastic when the amount of cross-linker is increased to 2%.

V.1.5.1.b. Migration into n-heptane:

MAA grafting does not seem to induce much migration resistance into n-heptane at 30°C. Only mild reduction in leaching was noticed after 5h (Figures 5.6 & 5.11). This is similar to the migration phenomena observed for MAA grafted sheets in n-hexane.

V.1.5.1.c. Migration into n-octane:

Figure 5.7 shows the migration behaviour of MAA grafted sheets into n-octane. Unlike NVP:HEMA, NVP and NVP:MAA systems studied, MAA grafted sheets do not seem to possess high migration resistance in n-octane. However it was seen in the case of migration to n-hexane that crosslinking with EDMA tended to improve the migration resistance which should hold good in all organic solvents.

V.1.5.2. Migration into Physiological Simulated Media:

V.1.5.2.a. Migration into Cotton Seed Oil:

Excellent migration resistance in C.S. Oil is seen for MAA

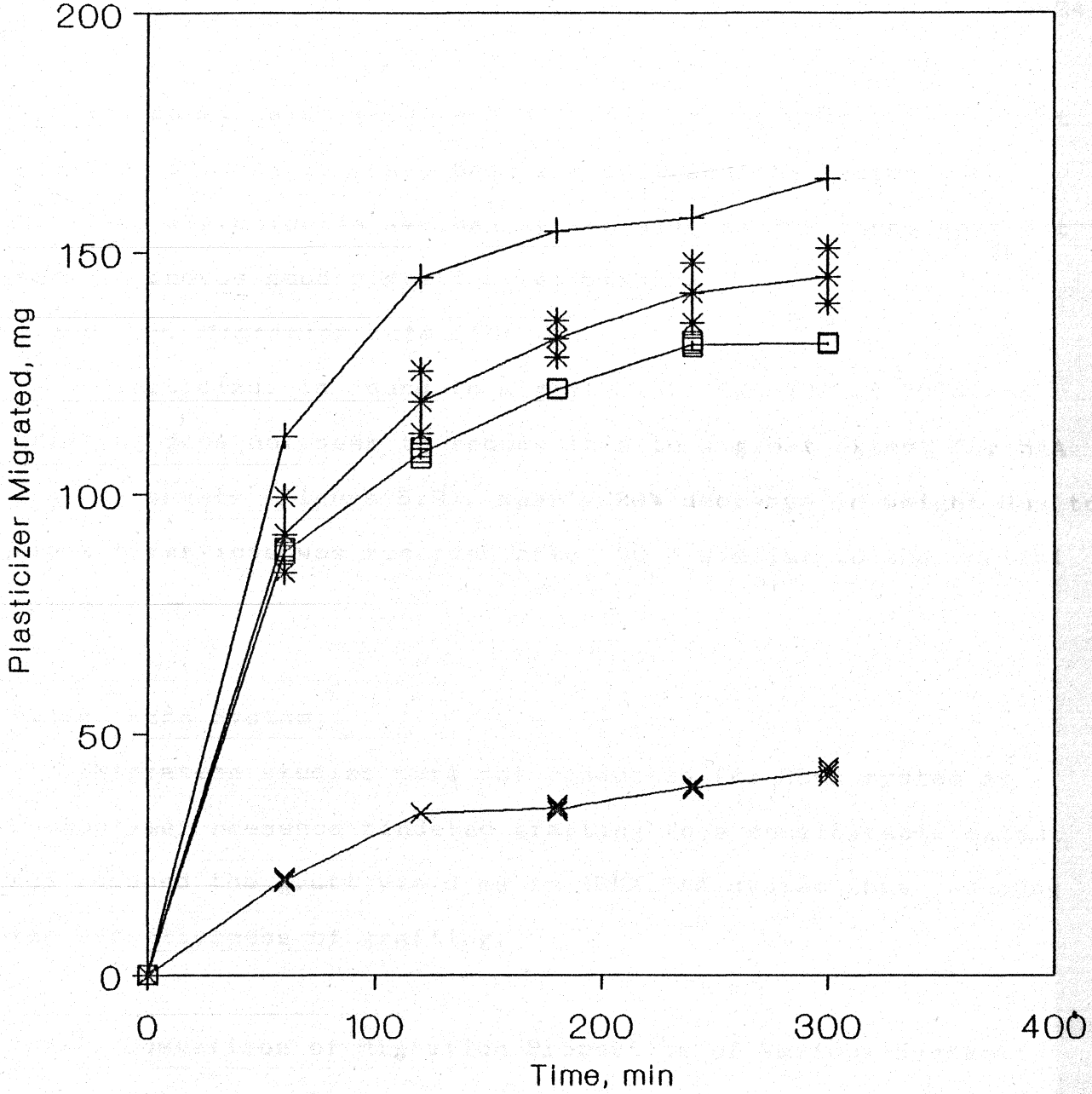


Figure 5.13. Plasticizer migration curves from ungrafted and MAA grafted PVC bags into n-hexane: Plots showing amount of DEHP migrated into n-hexane at 30°C against time for ungrafted (+), PVC bags grafted with 5% MAA (*), 5% MAA + 1% EDMA (□) and 5% MAA + 2% EDMA (x) [0.005 M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

grafted sheets also (Figure 5.8). This proves conclusively that presence of PMAA may have been the contributing factor in reducing migration in NVP:MAA system also as PVP alone does not seem to induce good migration resistance.

V.1.5.2.b. Migration into PEG-400:

Plasticizer is found to migrate into PEG-400 at 70°C and grafting does not seem to reduce this to a great extent for MAA grafted sheets (Figure 5.9). Nearly 20% decrease in weight due to plasticizer loss was recorded after 96 h similar to the control value.

V.1.6. HEMA System:

Migration studies were not conducted for HEMA system as homopolymer presence hindered grafting to a considerable extent and reduced the graft yield as in HEMA:MAA system thus reducing the effectiveness of grafting.

V.1.7. Comparison of Migration Properties of Various Systems Studied in Different Media:

V.1.7.1. Migration into Organic Solvents:

Of all the thirteen grafted (including sub-systems of the four main systems) and two ungrafted control systems studied for migration characteristics into n-hexane, sheets grafted with a 3-5% NVP50:HEMA50 concentration tended to show least migration

which was practically negligible (<10 mg after 5h) compared to control values. An examination of the values of DEHP migrated for different systems shows the order in which grafting helped to reduce migration. The degree of migration resistance varied in the order N50H50 > N25H75 > N75H25 > NVP + 1%CL > MAA + 2% CL > N50:M50 + 2%CL > N75M25 > NVP100 > N25M75 > N50M50 > MAA + 1% CL > MAA100 grafted PVC. Crosslinking certainly seems to improve the migration resistance as is observed for NVP, MAA and N50M50 systems though for N50H50 systems, high migration resistance is achieved without any crosslnking. However, a disadvantage of crosslinking is that it induces stiffness to the grafted sheets.

As far as migration into n-heptane was concerned, the NVP grafted sheets tended to show the best migration resistant properties and was in the order NVP100 > N50H50 > N50M50 > MAA100. No need for any crossslinking was found. The polarity and the dielectric constant of the solvent determines to a great extent the nature of interaction between the modified surface and the medium.

The migration behaviour into n-octane, however shows similar trend as in the case of n-hexane. Systems based on N50H50, NVP and N50M50 systems show minimal migration, in that order. However, MAA grafted systems are found to possess least migration resistance though crosslinking improves this to certain extent.

V.1.7.2. Migration into Physiological Simulated Media:

Three out of four systems (N50H50, N50M50 and MAA) show considerable reduction in migration from grafted sheets into cotton seed oil at accelerated conditions. NVP grafted systems also exhibit reduction though it is not appreciable. The extent of reduction varies in the order N50H50 > MAA > N50M50 > NVP. This is believed to be significant finding as it may have some importance industrially. However, all systems studied without exception showed migration into PEG-400. Though reduction is noticed for most of the systems compared to control, it is insignificant. Therefore it can be seen that the polarity of the medium, solubility of DEHP in the medium, the nature of the grafted surface and its interaction with the medium, all play significant roles in determining the migration resistance from the grafted sheets.

V.2. Effect of Radiation Dose on Migration Behaviour:

It can be seen from Figure 5.14 that with increasing radiation dose used for grafting the hydrophilic monomers onto PVC, the amount of DEHP migrating into n-hexane is reduced further. In fact, for NVP50:HEMA50 system grafted on to PVC, the amount is reduced to nearly 50 mg when irradiated to 0.25 Mrads which in turn reduces further to nearly 10 mg when irradiated to 0.5 Mrad. Irradiation upto 0.75 Mrads does not seem to make

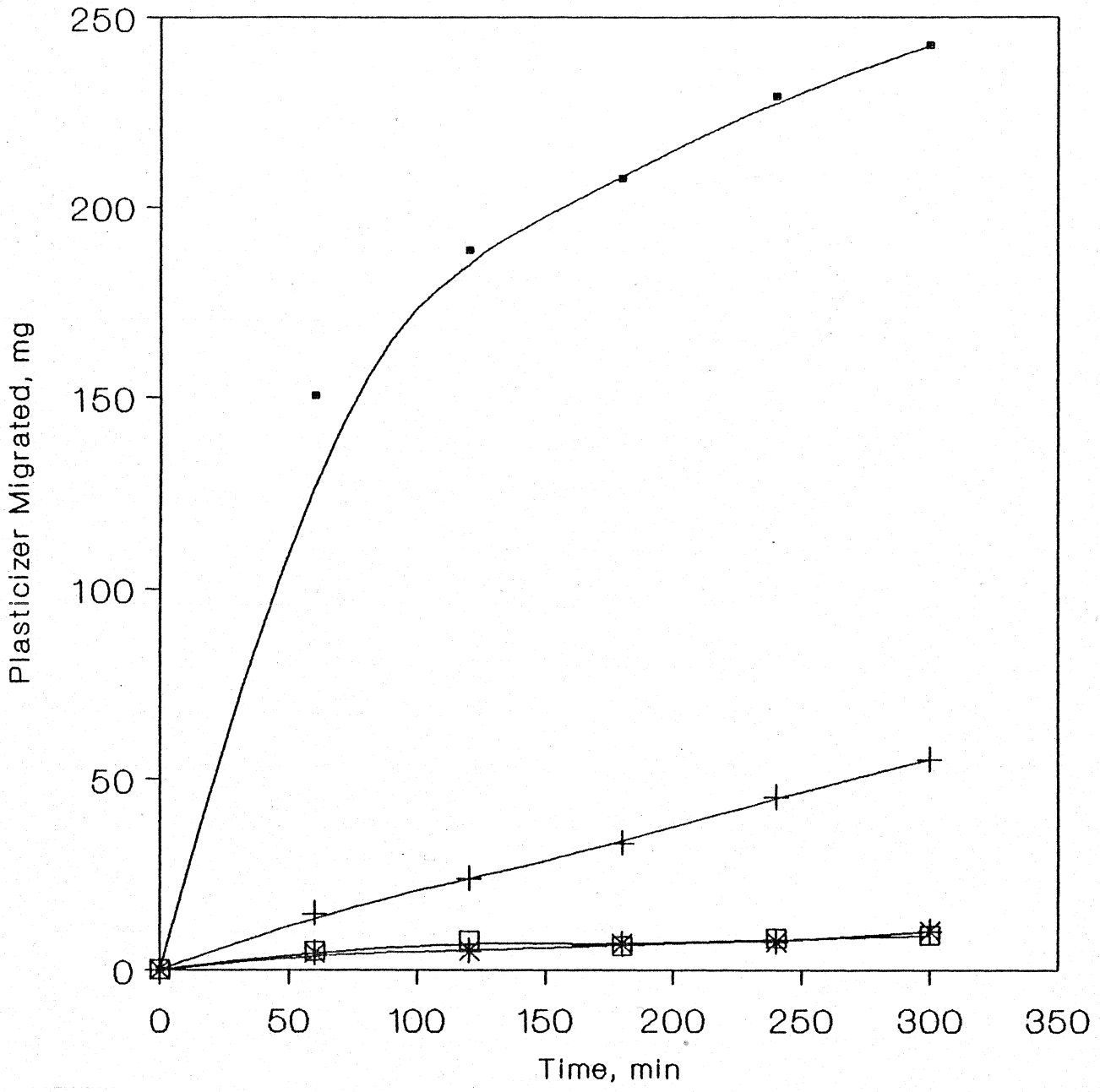


Figure 5.14. Effect of increasing radiation dose during grafting on DEHP migration rate for NVP50:HEMA50 grafted PVC system: Figure shows the amount of migrated DEHP into n-hexane at 30°C plotted against time from PVC bags grafted with 5% NVP50:HEMA50 at radiation doses of 0 (.), 0.25 (+), 0.5 (*) and 0.75 (□) Mrads [0.005M Cu^{2+}]. S.D. was within $\pm$ 5%.

further change. It can therefore be assumed that increasing graft yields and crosslinking induced due to irradiation may be instrumental in reducing the migration. The possibility of a fine hydrophilic network formation in the bulk as well as on the surface of the support polymer also help in enhancing migration resistance. The effect of both these factors together seem to reach a saturation level at about 0.5 Mrads for this system.

V.3. Effect of Sterilization upon Migration into Organic Solvents

The sterilization effect on grafted sheets and its migration properties are of importance because almost all of the medical devices are sterilized by one method or the other prior to use. The conventional methods used are gamma radiation to 2.5 Mrads, steam autoclaving and ethylene oxide sterilization. NVP50:HEMA50 (5 vol%) grafted sheets which showed the least migration were sterilized using all the three methods and the migration into n-hexane studied. The control ungrafted samples were also subjected to same mode of sterilization. Figure 5.15 show that significant migration resistance is retained after all three modes of sterilization. However, gamma radiation seems to be the best as the amount of DEHP migrated was only around 30 mg compared to higher values noticed for autoclaving and ethylene oxide sterilization. Samples sterilized using Ethylene oxide show the maximum migration. However, this seems to be insignificant as this technique is rarely used for PVC due to toxic reasons.

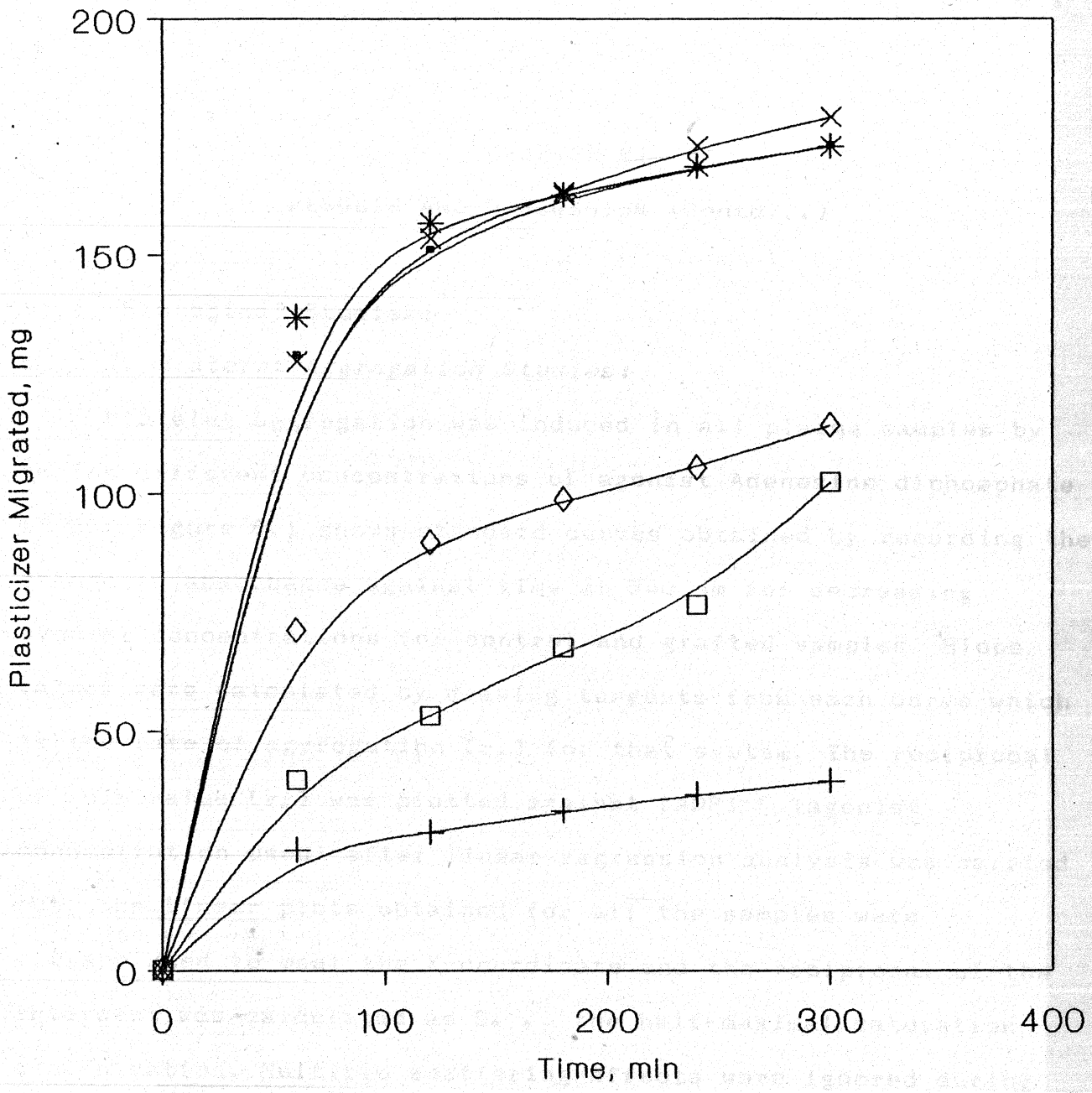


Figure 5.15. Effect of different types of sterilization on DEHP migration rate from control and grafted PVC systems: Figure shows retension in reduction of migration of DEHP into n-hexane in grafted systems even after different modes of sterilization. Plots indicate values for ungrafted control {Irradiated (.), Steam Autoclaved (*), EtO sterilized (x)} and grafted PVC {Irradiated (+), Steam Autoclaved (□), EtO sterilized (◇)} [5 vol%, 0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within ± 5%.

CHAPTER VI

RESULTS AND DISCUSSION (Contd...)

VI.1. Biological Studies:

VI.1.1. Platelet Aggregation Studies:

Platelet aggregation was induced in all plasma samples by adding different concentrations of agonist Adenosine diphosphate [ADP]. Figure 6.1 shows standard curves obtained by recording the change in absorbance against time at 540 nm for decreasing agonist concentrations for control and grafted samples. Slope values were calculated by drawing tangents from each curve which is the rate of aggregation [r_o] for that system. The reciprocal of this value [r_o] was plotted against $[ADP]^{-1}$ (agonist concentration used) after linear regression analysis was carried out. The linear plots obtained for all the samples were extrapolated to meet the X-coordinate and the reciprocal of the intercept was calculated as $S_{0.5}$, the half-maximal saturation concentration. Multiple scattering effects were ignored during the experiment as the platelet concentration used was negligible. The sensitivity was increased further by using a double beam spectrophotometer where the reference beam contained a cuvette containing platelet rich plasma. This procedure is reported to increase the precision of r_o values by compensating for forward

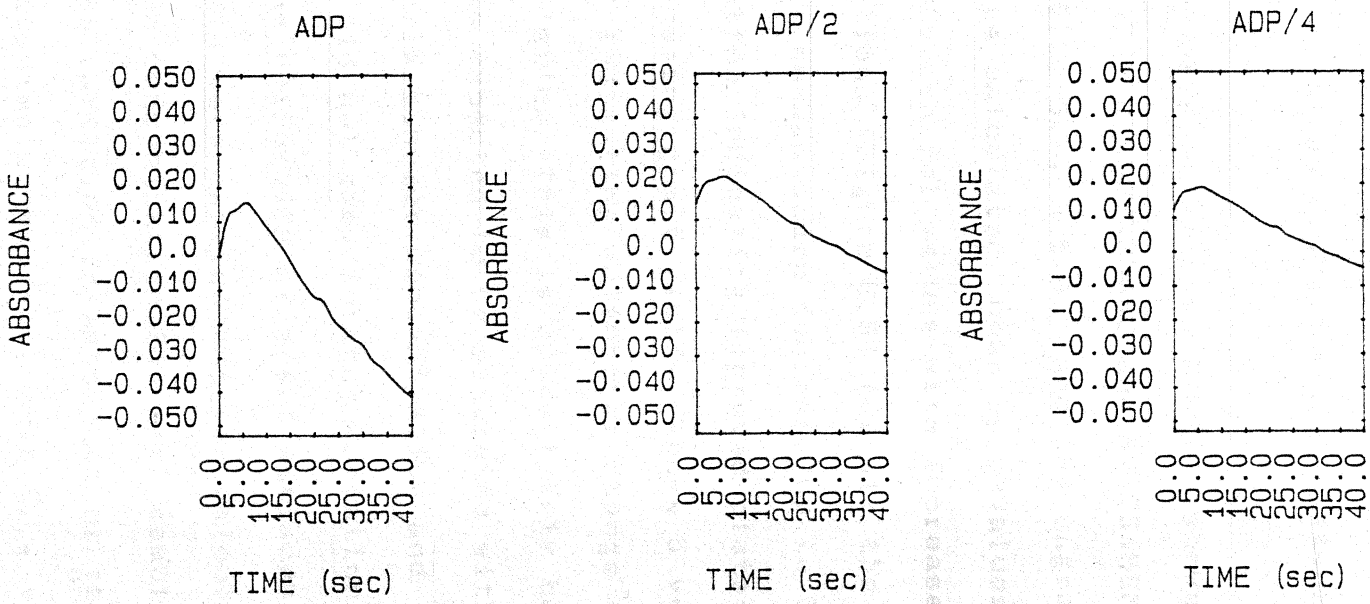


Figure 6.1. Curves indicating variation in slope values with decreasing agonist concentration: Typical curves obtained during spectrophotometric monitoring of change in absorbance values with time at 540 nm during platelet aggregation experiments. Slope values calculated by drawing the tangents to these curves varied with decrease in agonist concentration (right to left) as can be deduced from the curves. A minimum of 6 experiments were conducted for each sample in all platelet experiments.

scattering effects of platelets and their aggregates so that r_o values as small as 0.002 could be measured with reproducibility within 10%.

Plots of r_o^{-1} against $[ADP]^{-1}$ showed linear patterns for NVP25:HEMA75, NVP50:HEMA50 and NVP75:HEMA25 grafted PVC systems (Figures 6.2, 6.3, & 6.4) and the ungrafted control and $S_{o.s}$ values were calculated. Mean $S_{o.s}$ values showed a steady decrease compared to control values with increase in graft monomer concentrations (Figure 6.5) for all the three systems studied. The values showed sharp decrease up to 5 vol% monomer concentration indicating improved platelet aggregation properties with increasing graft yields. Above 5 vol%, the curve tended to level off indicating no further change in aggregation characteristics. This is quite likely because the surface of the polymer is expected to be saturated with the grafted polymer at about 5 vol% monomer concentration and the platelet aggregation property did not show further variation at higher graft levels due to the uniformity of graft surfaces. A minimum of 6 experiments were carried out for calculating the half maximal saturation concentration for each sample. This was necessitated due to the variation in behaviour of the blood samples drawn from different animals. However, mean $S_{o.s}$ values for the three systems did not show much variation with change in monomer ratio as is seen from Figure 6.5.

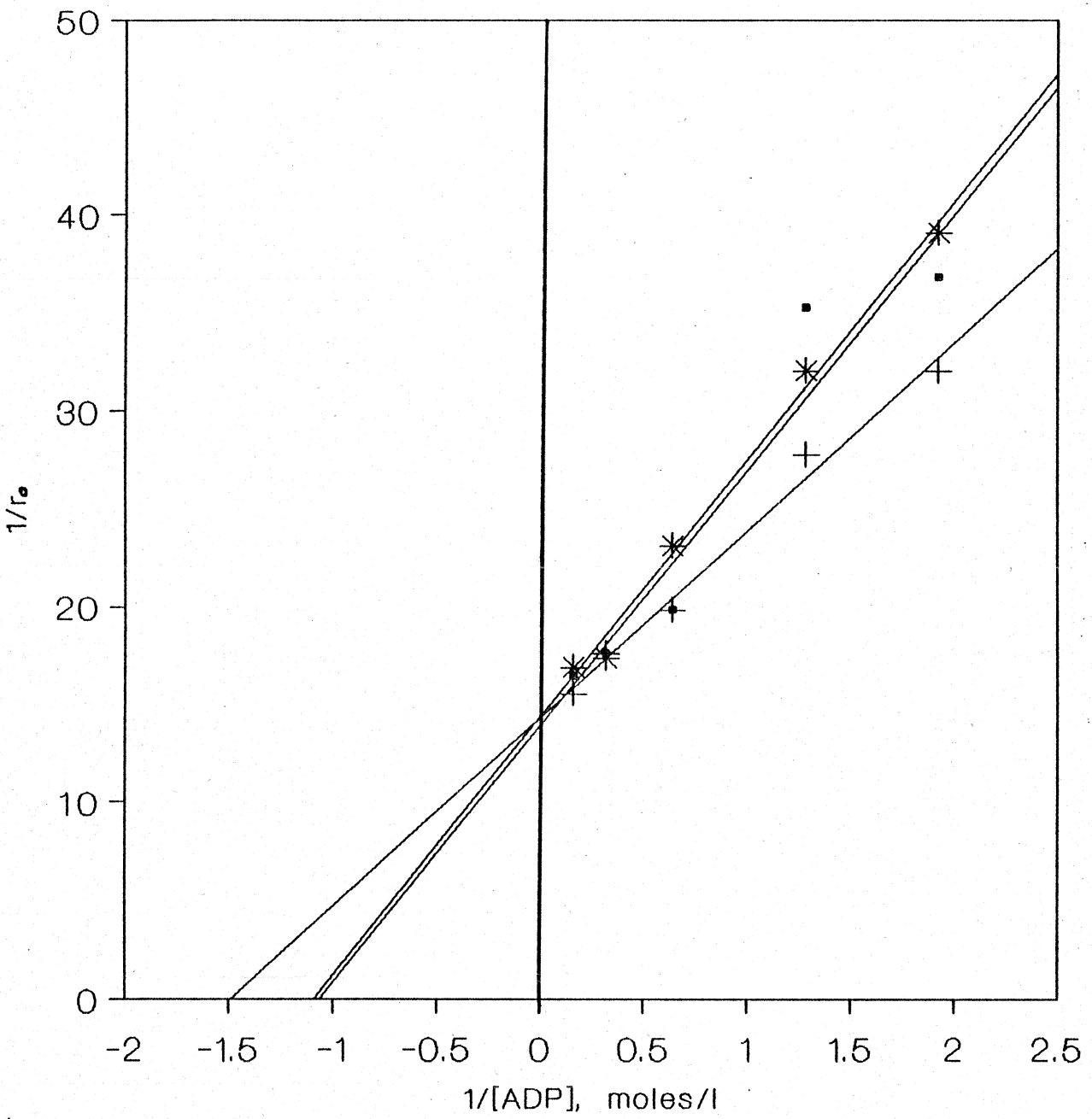


Figure 6.2. Linear regression plots of r_o^{-1} against $[ADP]^{-1}$ for NVP25:HEMA75 grafted PVC system: Figure shows linear regression plots of r_o^{-1} (rate of aggregation) against $[ADP]^{-1}$ (agonist concentration used) extrapolated to X-coordinate to determine $S_{0.5}$ values (reciprocal of the intercept) for PVC sheets grafted with 3% (.), 5% (+) and 7% (*) (all vol%) NVP25:HEMA75 [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 5%.

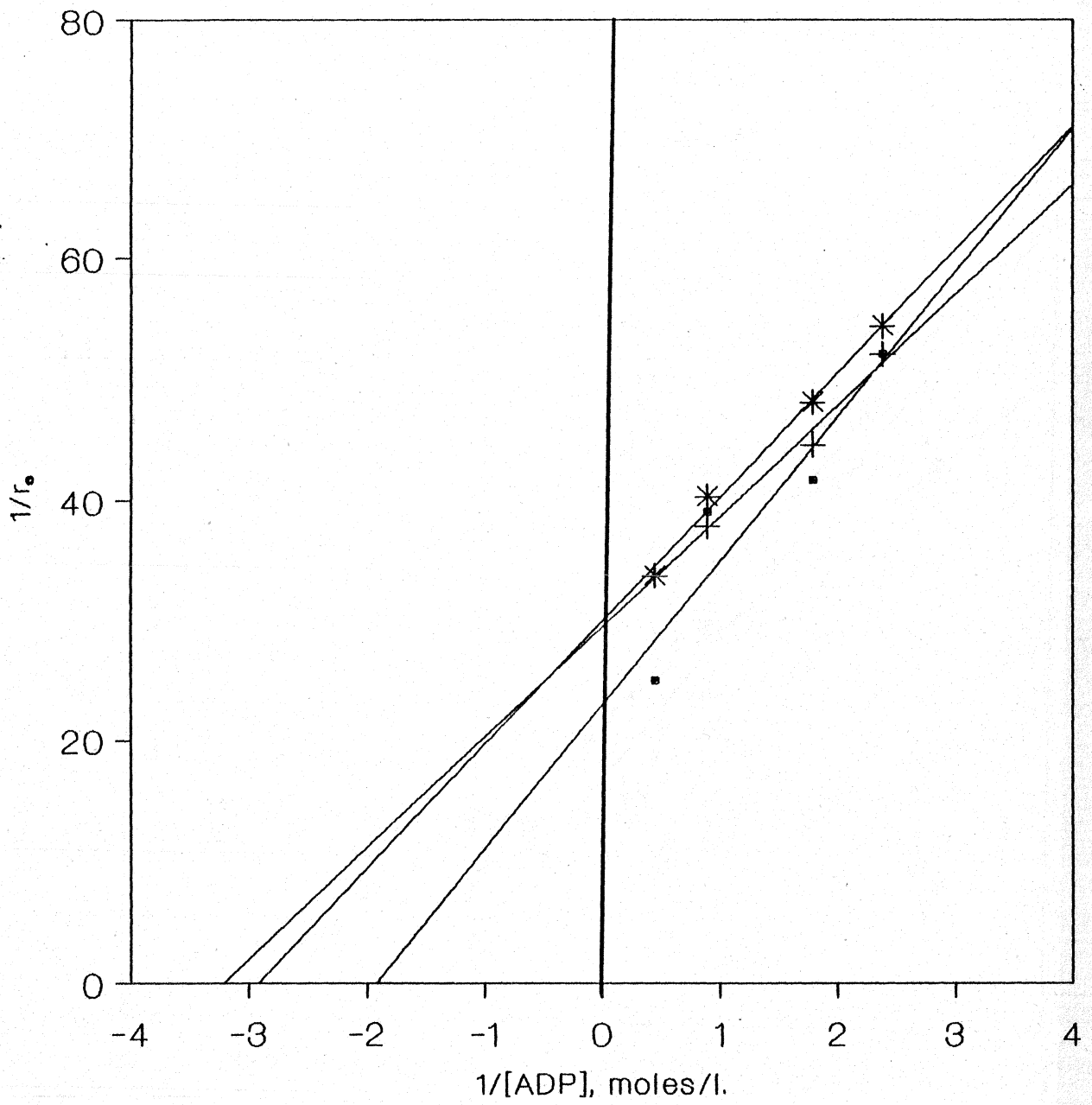


Figure 6.3. Linear regression plots of r_o^{-1} against $[ADP]^{-1}$ for NVP50:HEMA50 grafted PVC system: Figure shows linear regression plots of r_o^{-1} against $[ADP]^{-1}$ extrapolated to X-coordinate to determine $S_{o.s}$ values for PVC sheets grafted with 3% (.), 5% (+) and 7% (*) NVP50:HEMA50 [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 5%.

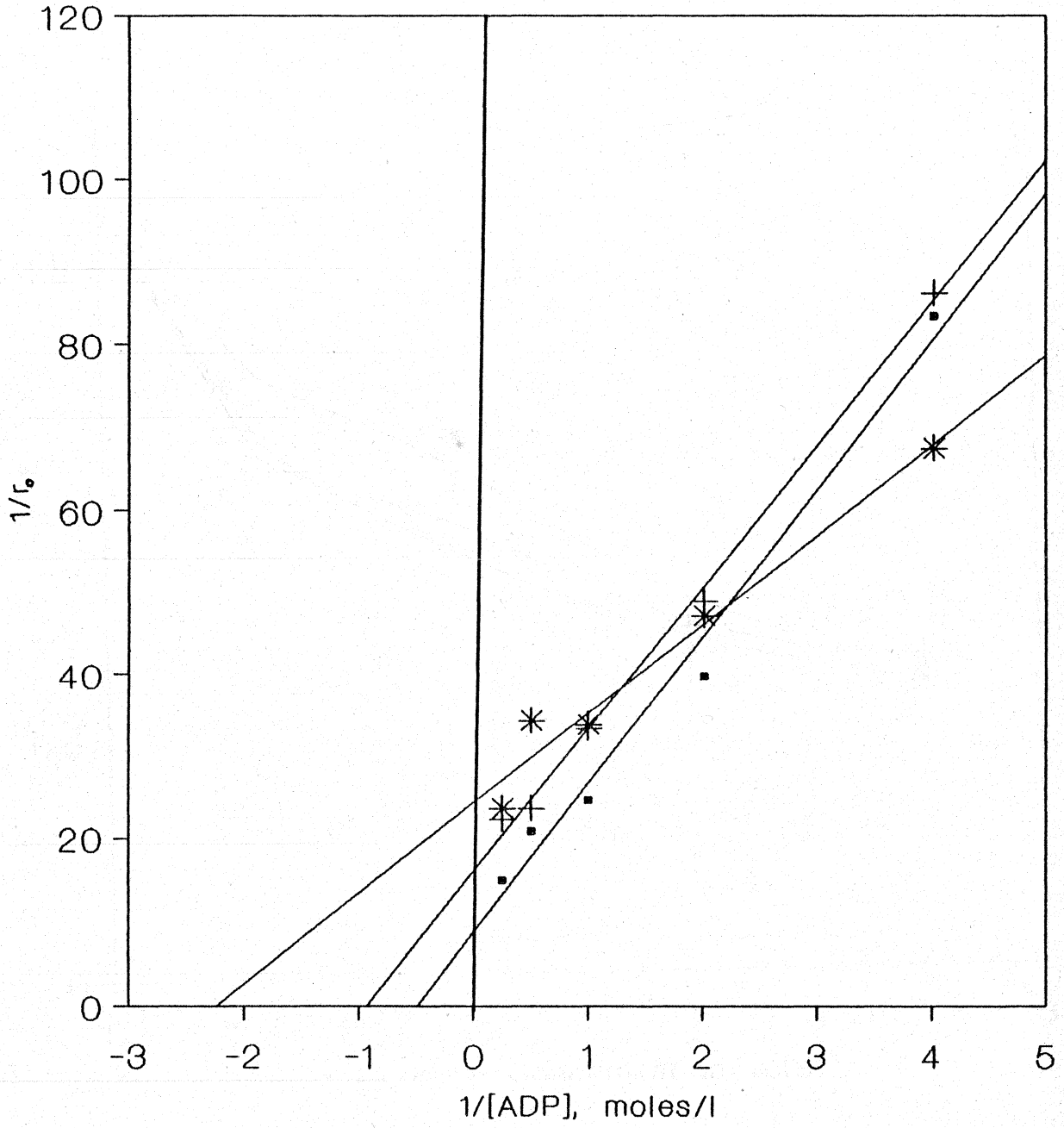


Figure 6.4. Linear regression plots of r_o^{-1} against $[ADP]^{-1}$ for NVP75:HEMA25 grafted PVC system: Figure shows linear regression plots of r_o^{-1} against $[ADP]^{-1}$ extrapolated to X-coordinate to determine $S_{o.s}$ values for PVC sheets grafted with 3% (.), 5% (+) and 7% (*) NVP75:HEMA25 [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 5%.

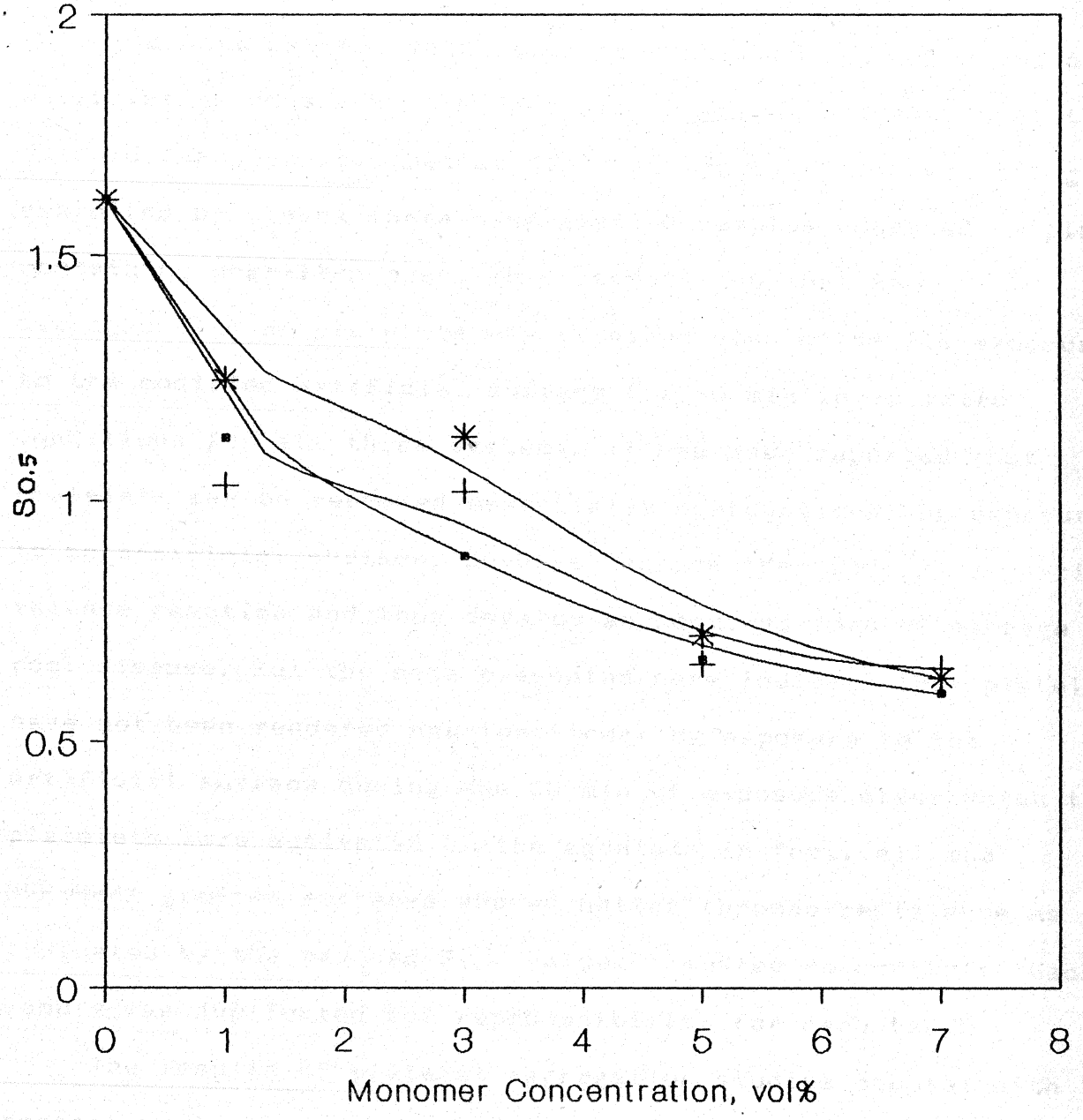


Figure 6.5. Plot showing decrease in $S_{0.5}$ values with graft monomer concentration for NVP:HEMA grafted systems studied: Figure shows sharp decrease in half maximal saturation concentration [$S_{0.5}$] values when plotted against increasing graft monomer concentrations indicating better aggregation tendencies compared to ungrafted sheets for NVP25:HEMA75 (.), NVP50:HEMA50 (+) and NVP75:HEMA25 (*) systems grafted to PVC [0.005M Cu^{2+}, 0.25 Mrads]. S.D. was within $\pm$ 15%.

The half maximal saturation concentration, $S_{0.5}$, being a dissociation constant, its decrease in value indicated that the forward reaction ie., better platelet aggregability was being exhibited by plasma containing grafted samples compared to plasma containing ungrafted ones. This ascertained that the aggregability of platelets was retained even after its exposure to the modified artificial surface for 90 min in *in vitro* conditions for all three systems. It has been reported that platelets may be rendered essentially nonfunctional by exposure to an artificial surface, perhaps because they undergo a partial release reaction and thus develop an acquired form of storage pool disease. But the data presented here indicate that platelets have not been rendered non-functional by exposure to the artificial surface during the 90 min of exposure after which the platelets were activated by the agonist. In fact, all the NVP:HEMA grafted surfaces showed better thrombo-resistance as indicated by the reduced $S_{0.5}$ values compared to controls. Each sample was duplicated for reproducibility for each test.

The results of platelet aggregation studies coupled with the contact angle results tend to show that the blood compatibility of the migration resistant grafted PVC sheets is comparable with that of the control sheeting used in this work.

VI.1.1.1. Effect of Irradiation on Platelet Aggregability:

Ungrafted samples were irradiated upto 0.75 Mrads and $S_{0.8}$ measured. The values showed a steady decrease with increasing radiation dose compared to non-irradiated control. It can therefore be assumed that the platelet aggregation property also improved with increasing radiation dose (Figure 6.6). At least 6 samples were subjected to each test. This justifies the fact that grafting hydrophilic monomers using gamma radiation onto PVC is a technique useful from the blood compatibility point also.

VI.1.2. Migration into Bovine Platelet Rich Plasma:

The DEHP migrated into platelet rich plasma was extracted using the technique adopted by Rock et al. and the amount of DEHP was determined spectrophotometrically by monitoring the absorption maxima of DEHP at 274 nm. The migration of DEHP into PRP was monitored upto 21 days at 4°C. The results indicated a drastic reduction in the migration of the plasticizer into plasma from the grafted bags compared to control ungrafted bags. Figure 6.7 shows the amount of DEHP migrated into unmodified bags as well as bags grafted with a 5% of HEMA/NVP (1:1) at a radiation dose of 0.5 Mrad. In 21 days, the amount migrated from the grafted bags is found to be less than 20% of the amount migrated from the control bags. While there is a sharp decrease in the amount migrating from unmodified bags with respect to time, the migration behaviour assumes an asymptotic character in the case

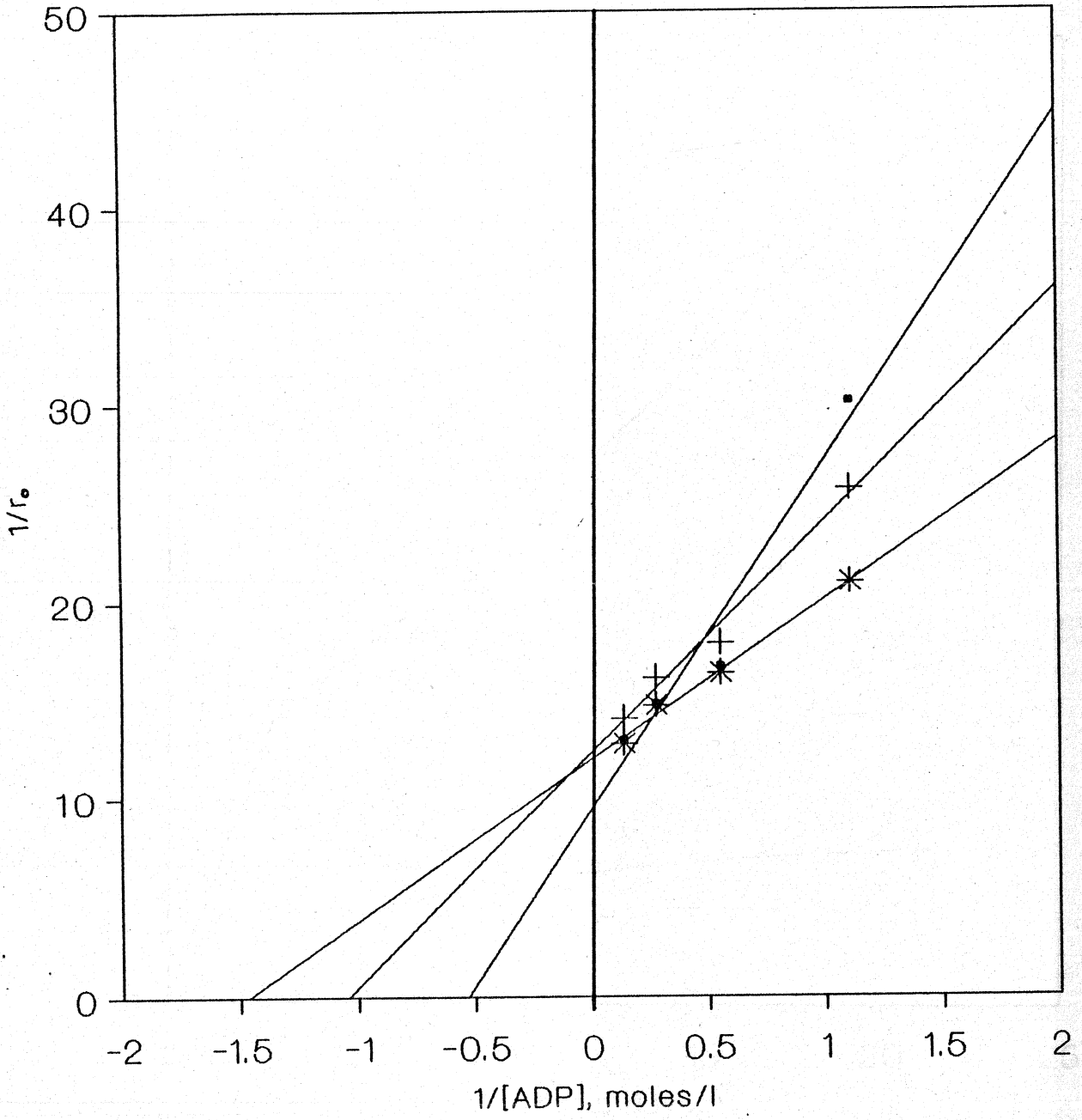


Figure 6.6. Effect of increasing radiation dose on platelet aggregation: Figure shows linear regression plot of r_0^{-1} plotted against $[ADP]^{-1}$ for ungrafted sample showing change in $S_{0.5}$ values with increasing radiation dose. $S_{0.5}$ tends to decrease indicating better platelet aggregation with increase in radiation dose. Unirradiated (.), 0.25 Mrads (+) and 0.75 Mrads (*).

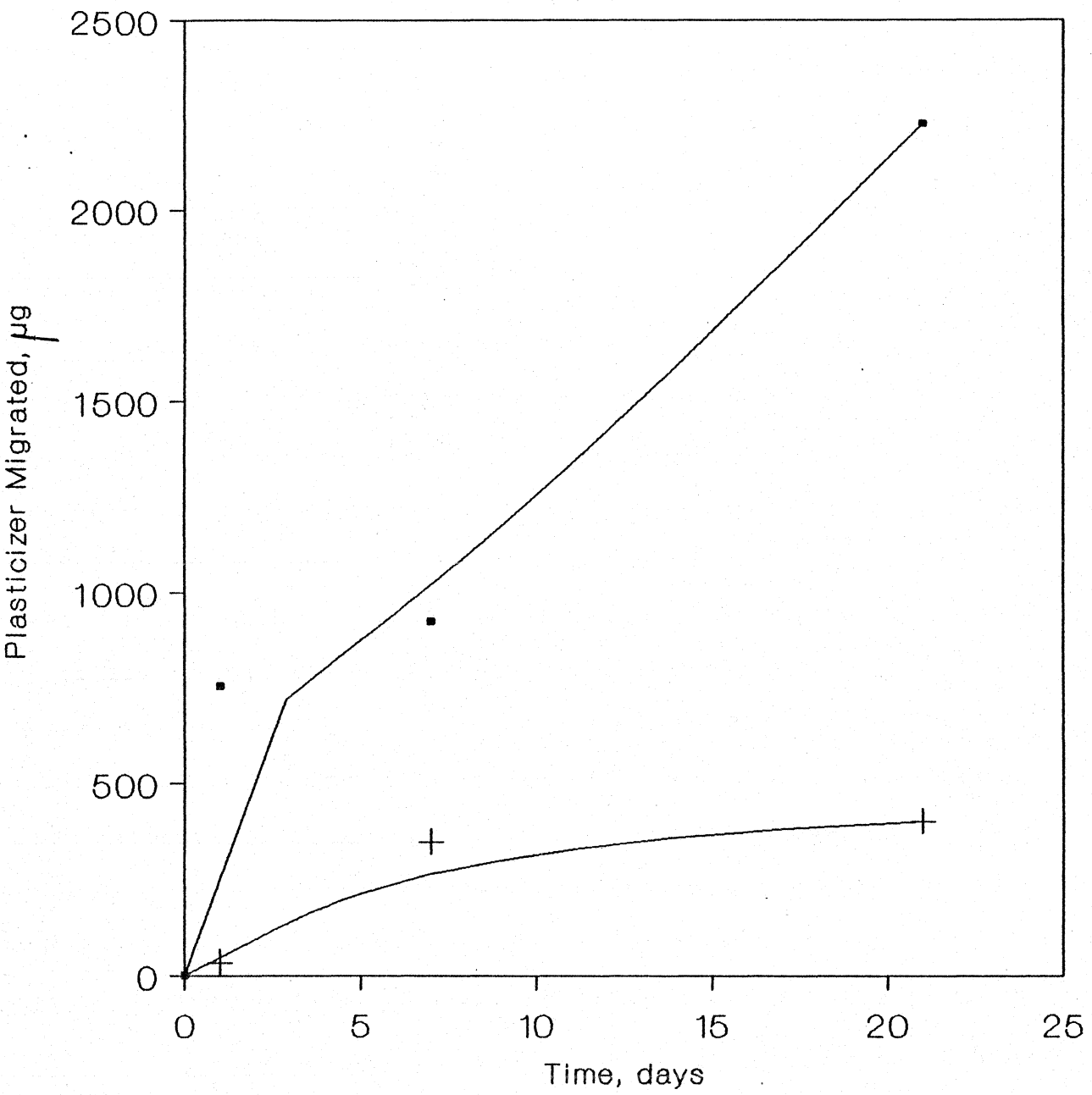


Figure 6.7. Plasticizer migration curves for ungrafted and NVP50:HEMA50 grafted PVC bags in platelet rich plasma: Figure shows sharp reduction in migration of plasticizer DEHP (in micrograms) into platelet rich plasma monitored over a period of 21 days at 4°C from an ungrafted control bag (.) and 5% NVP50:HEMA50 grafted bag (+) [0.005M Cu^{2+}, 0.5 Mrads]. S.D. was within $\pm$ 10%.

of grafted bags. Thus, while there is no considerable variation in the quantity of DEHP migrating from modified bags between 7 and 21 days, during the same period, twice as much DEHP migrated out of unmodified bags. While the reduction in migration undoubtedly seems to be significant, it is not as dramatic as the difference observed between control and grafted bags when non-polar solvents such as n-hexane or n-octane were used as the extractant media. Though n-hexane is one of the most suitable solvents for DEHP, the migration into n-hexane from grafted bags was found to be less than 4% of the value observed for unmodified bags. Though DEHP is insoluble in aqueous solutions, the presence of lipids in the blood has been reported to be responsible for its migration into blood. It can be safely assumed that the network of grafted hydrophilic polymers on the PVC sheet plays a dominant role in reducing the migration into plasma to a great extent. Previous reports have indicated that the rate of migration of plasticizer from PVC is maximum during the first 24 hours. An interesting observation is that, during the first 24 hours, the migration is negligible from the grafted bag compared to control(34 μg compared to 755 μg) whereas there is a tendency for the migration to increase with time in the grafted bag as the time for storage increases. This is evident by comparing the 1, 7 and 21 days values. However, the reduction even at the 21 day limit is quite appreciable. This can be explained by arguing that

the hydrophilic network crosslinked partially with traces of cross-linker present in it tends to swell slowly with time and the network seems to undergo a relaxation facilitating easier migration whereas it is found to be negligible during the first 24 hours. A minimum of 3 experiments were conducted and the standard deviation was found within 10%.

VI.1.3. Migration from Modified Medical Grade Tygon Tubing:

A common medical grade PVC tubing used worldwide is the TYGON® tubing which is also highly plasticized. Modification of the inner surfaces of the tubing using a 3% and 5% NVP50:HEMA50 monomer combination was carried out using the procedure adopted for PVC bags. The migration of plasticizer from the tubing into n-hexane stored in it was monitored spectrophotometrically at 274 nm for different time intervals. The results are plotted in Figure 6.8. It is seen that with increase in monomer concentration used for grafting, the amount of plasticizer migrated decreases and is only less than 10mg for the 5% N50H50 system compared to the high 220 mg for the ungrafted tubing after 4h. This shows that grafting of PVC tubing using hydrophilic monomers is equally effective in increasing its migration resistance as was the case with PVC sheets.

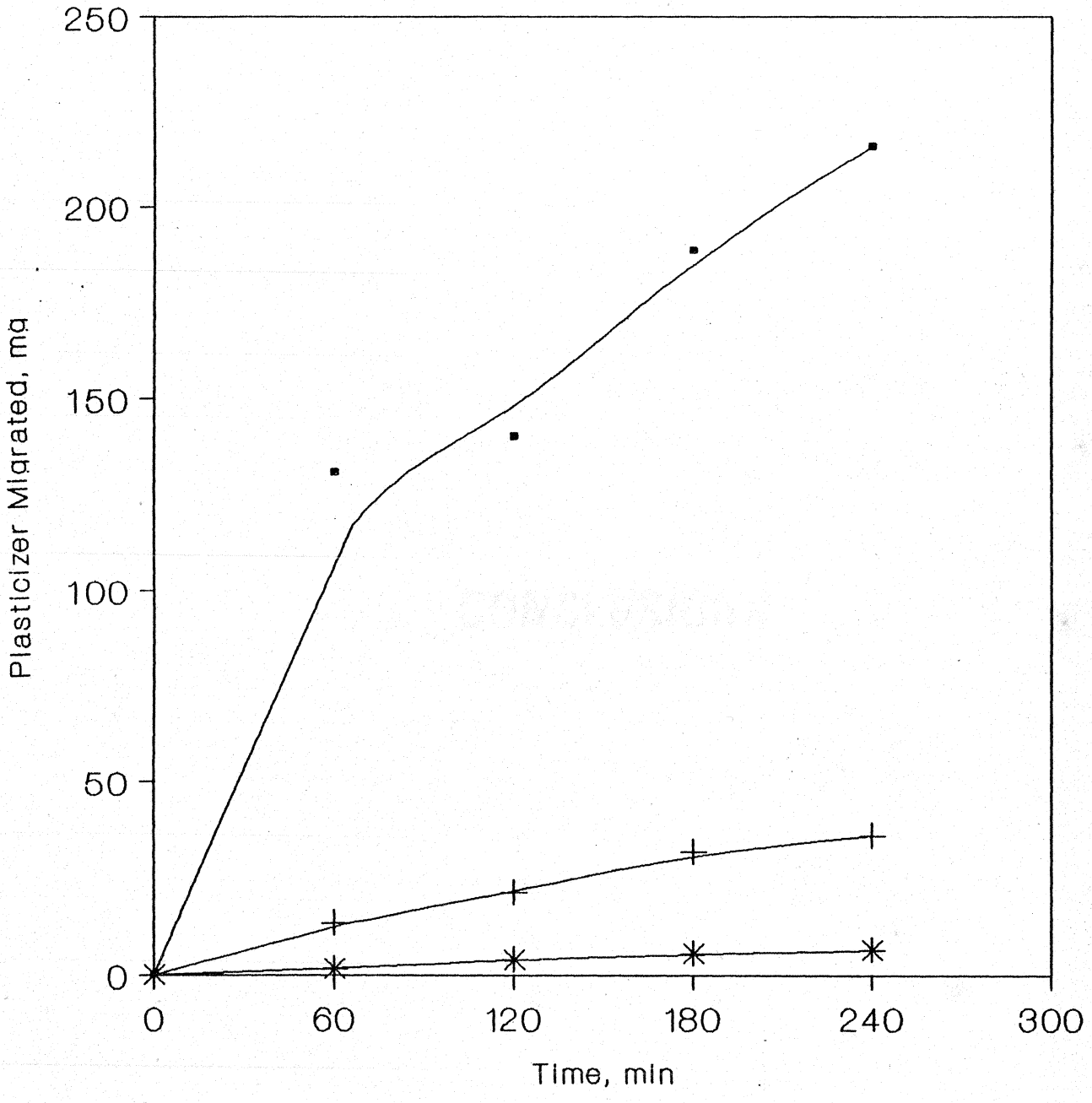


Figure 6.8. Plasticizer migration curves for ungrafted and NVP50:HEMA50 grafted Tygon PVC tubings in n-hexane: Figure shows migration of plasticizer DEHP into n-hexane from unmodified medical grade TYGON tubing (.), tubing grafted with 3% (+) and 5% (+) NVP50:HEMA50 [0.005M Cu^{2+}, 0.5 Mrads]. Drastic reduction in migration is observed for grafted systems. S.D. was within $\pm$ 5%.

CONCLUSIONS

CHAPTER VII

CONCLUSIONS

VII.1. Conclusions

Hydrophilic monomers such as HEMA, NVP and MAA can be conveniently grafted on to plasticized PVC either alone or in combination by using gamma radiation technique. The graft yield is found to increase linearly with monomer concentration for all systems studied. Increasing the radiation dose also helped to improve the graft yield. However, a dose of 0.5 Mrads was found to be the optimum dose for achieving maximum grafting. Incorporation of cross-linker EDMA did not significantly affect the overall graft yield though it helped to improve other properties such as migration resistance.

Grafting hydrophilic monomers in presence of cupric ions at specific concentrations in the aqueous grafting medium prevented homopolymer formation and facilitated the grafting reaction. It also enabled the cleaning of the trunk polymer easier after grafting. Concentrations ranging between 0.0025 M to 0.01 M were found to be optimum for obtaining good graft yields and for preventing homopolymerization in most systems studied. However, PVC sheets grafted with HEMA monomer alone and HEMA:MAA monomer combination showed low graft yields and high homopolymer

formation in spite of increasing the Cu^{2+} ion concentration to 0.1 M. Homopolymer formation was observed in two systems containing HEMA but ironically NVP:HEMA combination did not produce any homopolymerization.

Scanning electron micrographs and optical phase contrast photographs show the existance of fine layers of grafted hydrophilic polymers on the surface of PVC. The nature of the modified surfaces varied with the monomer ratio used for grafting. Attenuated internal total reflectance infra red spectra reveal the characteristic absorption bands indicating modification of the PVC sheets with the hydrophilic polymers. The modified PVC surface assumes hydrophilic character even when grafted with 1 vol% concentration of hydrophilic monomer(s) compared to ungrafted surface as evidenced by the contact angle experiments. The increase in polar component ($\gamma_{s,v}^{p}$) and decrease in dispersion component ($\gamma_{s,v}^{d}$) values of total surface energy ($\gamma_{s,v}$) for all systems studied indicate a sharp rise in hydrophilicity. The interfacial surface energy ($\gamma_{s,w}$) values tend to become very low (~ 0) at higher graft concentrations predicting excellent blood compatible properties according to the hypothesis of Andrade et al..

Tensile strength and elongation properties of the hydrated PVC sheets grafted only on one side are comparable with ungrafted samples. Single side grafting would be ideal in the case in PVC

medical devices used for storage purposes, tranfusion etc. Systems containing MAA and NVP showed better mechanical properties compared to systems containing HEMA, most likely due to their better hydrophilic character. However, grafting on both sides seemed to affect the mechanical properties adversely. Hardness values also showed a slight increase for grafted samples which can be attributed to the effect of irradiation upon them. Optical properties were retained after grafting and were highly comparable with control values for all systems. NVP grafted sheets showed excellent optical properties, even better than control in the hydrated state.

Grafting of hydrophilic monomers onto PVC was found to drastically reduce migration of plasticizer DEHP into organic solvents. Grafting a 3-7 vol% of NVP50:HEMA50 combination was capable of reducing the migration into n-hexane to nearly 2-4% (<10 mg) of the control values. All the thirteen grafted systems studied (including sub-systems) for migration into n-hexane showed improved migration properties of varying degrees compared to ungrafted sheets. NVP50:HEMA50 combination gave the best results. The least migration resistance was observed for MAA grafted sheets. However, crosslinking with EDMA improved the migration resistance considerably when NVP and MAA systems were used alone. All grafted systems showed reduced migration into n-heptane compared to control but in varying degrees. NVP and

NVP:HEMA grafted systems tended to show excellent migration resistance compared to other systems in n-heptane. Migration into n-octane showed similar behaviour as in n-hexane with NVP:HEMA combination giving the best results.

Another important finding of this investigation was the total absence of migration of DEHP from NVP:HEMA grafted sheets into physiologically simulated medium such as cotton seed oil at accelerated conditions. Two other systems, NVP:MAA and MAA grafted sheets also showed excellent migration resistance in cotton seed oil (3-5% loss in total weight) compared to control (20% loss). Though NVP grafted sheets showed migration resistance, it was not significant.

All graft modified PVC sheetings inevitably lost their plasticizer in PEG-400. This suggests that the interaction of the hydrophilic grafted surface with the medium, the relation between solubility parameters of DEHP and the medium, the dielectric constant and polarity of plasticizer and the medium all play important roles in determining the migration.

Migration studies into a biological medium such as platelet rich plasma show that hydrophilic surface modification of PVC may be successfully used to retard DEHP migration in blood storage applications. Migration was reduced to less than 25% in PRP compared to ungrafted bags. Platelet aggregation studies provide valuable insight into the potential use of blood

compatible applications for modified PVC. The retention of aggregability properties of platelets even after PRP was kept in contact with the modified sample for 90 min at 31°C shows that the platelets are not damaged by contact with the foreign surface. The results on platelet agrregation and contact angle studies show that the blood compatible properties of the grafted sheets are comparable to control sheeting.

It can be said in conclusion that grafting of hydrophilic monomers selectively onto PVC trunk polymer using gamma radiation is capable of reducing the migration of DEHP without drastically affecting other properties of such PVC sheetings. It also provides a clean, economical and industrially viable process to surface modify medical grade PVC to mitigate the threat posed by migration of DEHP from PVC to a great extent.

VII.2. Future Lines of Reasearch:

This work can never be said as complete. Migration phenomena of plasticizer is quite complex and is governed by a number of parameters of which only a few have been dealt with in this work. The migration aspects of plasticizer into the human body is yet to be fully understood. The difficulty in isolating, identifying and estimating the plasticizer levels in humans undergoing transfusion of blood or blood products stored in PVC packs itself poses great hinderance. The blood compatible aspects of

modified PVC sheets is an area yet to be studied completely. The hydrophilic nature of the surface and the low interfacial surface energy obtained by grafting indicates a better non-thrombogenic surface. PVC has never been successful as an implant due to its complex nature. However, the investigations reported in this thesis suggest that hydrophilic surface modification of plasticized PVC sheetings can be said to effectively retard the migration of plasticizer DEHP to a significant extent. To the best of our knowledge, this is the first time it has been shown that gamma radiation grafting of hydrophilic polymers onto PVC can retard plasticizer migration and at the same time improve the blood compatibility of the PVC surface. Very simple, routinely used hydrophilic monomers have been employed in this work to surface modify PVC. Many more hydrophilic monomers have been reported in the literature which find applications in the biomaterials area. Future work should therefore focus upon the effect of grafting novel hydrophilic monomers or even a combination of hydrophilic and hydrophobic monomers to optimise the hydrophobicity/hydrophilicity of the grafted surface. The use of multifunctional hydrophilic monomers for grafting to provide a highly crosslinked surface may also be a key to retard the plasticizer migration from PVC to a greater extent. The investigation reported here is therefore only a beginning in the direction of such efforts.

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APPENDICES

APPENDIX A

i) Acid Citrate Dextrose:

Trisodium Citrate, 2 H_2O	2.2 g
Citric Acid	0.8 g
Dextrose	2.5 g

Made upto 100 ml with double distilled water (pH = 5.0-5.1).

ii) Tris Buffer:

Dextrose	1.0 g
Calcium Chloride	5.5 mg
Magnesium Chloride	0.199 g
Potassium Chloride	0.402 g
Sodium Chloride	8.12 g
Trizma Base	1.756 g

Dissolved in 900 ml distilled water, pH was adjusted to 7.4 with dil. HCl and made upto 1 l with distilled water.

iii) Grafting Medium (0.01M Cu^{2+}):

Copper sulphate, $2H_2O$	2.4968 g
Distilled Water (double distilled)	1000 ml

Copper sulphate was dissolved in double distilled water and made upto 1 litre. This solution was further diluted to prepare lower concentrations of grafting medium (0.0025M, 0.005M and 0.0075M).

iv) Calculation of residual cupric ion content in PVC grafted with NVP:HEMA using atomic absorption spectrophotometry*:

Net resultant curpic ions present
in the grafted sample = 0.05 - 0.03
= 0.02 µg/ml or ppm.

The total volume of the extract was 12.5 ml before testing.

Concentration of cupric ions
in the total extract = 0.02 x 12.5
= 0.25 µg/ml or ppm.
==========

which is less than 1 ppm and acceptable as per DHSS standards.

[* Table 3.1.]

APPENDIX-B

Abbreviations used are:

ACD	-	Acid citrate dextrose
ADP	-	Adenosine diphosphate
ATR-IR	-	Attenuated total reflectance-infra red
CL	-	Cross-linker
C.S.Oil	-	Cotton seed oil
Cu^{2+}	-	Cupric ion
DEHP	-	di-(2-ethylhexyl) phthalate
EDMA	-	Ethyleneglycol dimethacrylate
HEMA	-	2-(hydroxyethyl) methacrylate
HPLC	-	High performance liquid chromatography
H_2O_{total}	-	Water of hydration in the total polymer.
H_2O_{graft}	-	Water of hydration in the graft polymer.
Isw	-	Polar interaction at the surface/ water interface
M	-	Molar
MAA	-	Methacrylic acid

Mrads	-	Megarads
NVP	-	N-(vinyl pyrrolidone)
N25:H75	-	NVP:HEMA = 25:75
N50:H50	-	NVP:HEMA = 50:50
N75:H25	-	NVP:HEMA = 75:25
N25:M75	-	NVP:MAA = 25:75
N50:M50	-	NVP:MAA = 50:50
N75:M25	-	NVP:MAA = 75:25
$\emptyset$	-	Air-in-water contact angle
$\not{\emptyset}$	-	Octane-in-water contact angle
PVC	-	Poly(vinyl chloride)
PEG-400	-	Polyethylene glycol
PRP	-	Platelet rich plasma
γ_o	-	Rate of aggregation
$\gamma_{s.v}$	-	Surface energy
$\gamma_{s.v}^p$	-	Polar component of surface energy
$\gamma_{s.v}^d$	-	Dispersion component of surface energy
$\gamma_{s.w}$	-	Interfacial free energy at surface/water interface
S.D.	-	Standard deviation
$S_{o.s}$	-	Half maximal saturation concentration
Tris	-	Tris (hydroxy methyl) amino methane
vol%	-	Volume percent