



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम, तिरुवनन्तपुरम - 695 011, केरल, भारत
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
THIRUVANANTHAPURAM - 695 011, KERALA, INDIA
(एक राष्ट्रीय महत्त्व का संस्थान, विज्ञान और प्रौद्योगिकी विभाग, भारत सरकार)
(An Institution of National Importance, Department of Science and Technology, Government of India)
टेलीफोन नं./Telephone No.: 0471-2443152 फैक्स/Fax: 0471-2446433, 2550728
ई-मेल/E-mail: sct@sctimst.ac.in वेबसाइट/Website: www.sctimst.ac.in

PROJECT COMPLETION REPORT

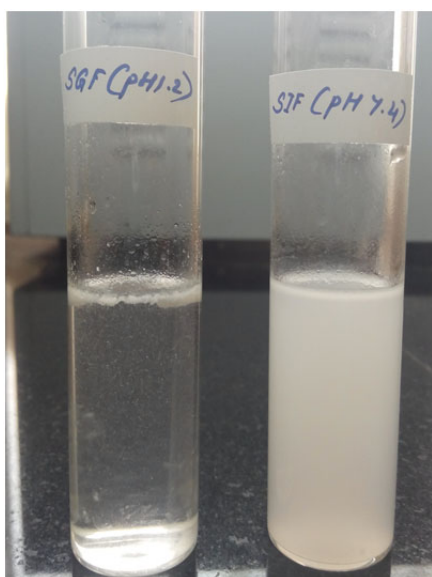
1. **Project Number** : 8154
2. **Title of the Project** : Oral Insulin Delivery System
3. **Funding Agency Name** : TRC, SCTIMST
4. **Project Reference Number provided by the Funding Agency:**
5. **Principal Investigator (Name & Address)** : Dr. Rekha M.R.
Scientist G
Division of Biosurface Technology
BMT Wing, SCTIMST
6. **Co-Investigators (Name & Address):**
 - i.
7. **Implementing Institution** :
SCTIMST
8. **Collaborating Institutions** : None
9. **Date of Commencement** :
10. **Duration** : 3 Years
11. **Date of Completion** :
12. **Objectives as approved :**
13. **Deviation made from original objectives if any, while implementing the project and**

reasons thereof :

14. **Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :**

pH sensitive nanoparticles

Insulin loaded nanoparticle are pH sensitive, that is these particles shrink at gastric pH (acidic) and gets dispersed at intestinal pH



15. **Detailed analysis of results :**

16. **Summary sheet of not more than 2 pages under following heads : (Title, Introduction, Rationale, Objectives, Methodology, Results, Translational Potential)**

Oral Insulin Delivery System

Oral insulin has advantages over other forms of insulin delivery as it follows the normal physiological pathway, i.e., via hepatic portal circulation it first reaches liver and then the peripheral tissues.

Diabetic mellitus is a common endocrine disorder, which poses a serious healthcare challenge. The global prevalence of diabetes is estimated to increase from 4% in 1995 to 5.4% by the year 2025. The WHO predicted that the major burden would occur in the developing countries. There will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million in the developing countries. Countries

with the largest number of diabetic people now are and will be India, China and United States in the year 2025. Diabetes mellitus is a heterogeneous disorder characterized by varying degrees of insulin resistance and insulin deficiency, which leads to disturbance in glucose homeostasis. The disease if uncontrolled, is characterized by high blood glucose levels, polydipsia, polyuria, polyphagia, feeling of tiredness, blurred vision and weight gain or weight loss. Diabetes mellitus is classified into two major forms; Type I (IDDM) characterized by insulin deficiency resulting from pancreatic beta-cell destruction mediated by autoimmune disorder and Type II (NIDDM) is generally characterized by peripheral insulin resistance and relative insulin deficiency, which may range from predominant insulin secretory defect with insulin resistance.

Insulin is the most important drug for diabetic therapy and insulin administration is the treatment for all Type-I diabetic patients and many Type II diabetic patients. Especially for type I diabetic patients the only treatment currently available is taking exogenous insulin injections.

In normal persons during each meal there is pulsatile release of insulin which amounts upto 50-60 μ IU/ml at the peak and is independent of the calorie intake. During a day of 24 hours, BGL in diabetic patients remains elevated throughout with excessive glycemic excursions after each meal. In diabetic patients there is no secretion of insulin or is minimal. Insulin is produced and secreted by the pancreas as and when the need arises. In healthy persons insulin reaches first in liver and then only it reaches the peripheral tissues. Liver is the primary site of action of insulin and hence exposed to higher concentration of insulin.

Deficiencies in the current way of insulin administration

- Insulin is administered in a non-physiological way
- Majority of the subcutaneously administered insulin is reaching the wrong targets i.e muscles and kidney.
- The insulin effect reaches a plateau, presumably because of the prevailing insulin resistance in muscle.
- The pharmacodynamics do not replicate the normal dynamics of its endogenous release.

Advantages of oral insulin

- Injection and as well as other routes namely pulmonary, nasal or buccal delivers insulin into systemic circulation. Hence only a small percentage of insulin reaches

liver which is the primary site of action according to normal physiology.

- Oral insulin has advantages over other forms of insulin delivery as it follows the normal physiological pathway, i.e., via hepatic portal circulation it first reaches liver and then the peripheral tissues.

Efforts for developing oral insulin delivery system are one of the most active research areas for the past many decades. At present the diabetic patients who are dependent on insulin for normal life have to take multiple subcutaneous injections a day, which is a painful ordeal. Moreover daily injections can lead to infections and thereby other related complications. So many efforts are being taken worldwide to realize an alternative insulin delivery route other than parenteral. Being protein insulin cannot be given orally which is the most accepted route of drug intake. The major hurdles in getting insulin into the systemic circulation orally are digestive acids, enzymes and poor absorption via the intestinal wall. Packaging the drugs along with protease inhibitors or giving protective coating could enable protein-based drugs to survive the intestinal conditions, but it cannot aid them in crossing the gut lining. To overcome these obstacles various polymers are tried for developing micro and nanoparticles as oral peptide carriers. It is reported that nanoparticles can easily reach the systemic circulation from the intestine via Peyer's patches.

In view of the above facts we have developed a polymeric nanoparticle based oral insulin formulation, which takes care of both the hurdles faced in oral protein delivery. The polymer that is encapsulating the insulin is pH sensitive. This nanoparticles has shown to have sustained — release property.

- pH sensitive nanoparticles for oral insulin delivery.
- The polymer that is encapsulating the insulin is pH sensitive. The lipid-polymer complex protects the insulin from the harsh gastro-intestinal environment.
- Its nanomeric size helps to cross the intestinal barrier efficiently.
- These nanoparticles have controlled — release property. Preliminary studies demonstrated the efficacy in diabetic animals.
- Using gelatin capsules is the most suitable way of delivering this OINP formulation
- By TGA analysis - nanoparticles have aqueous content and these OINP particles were successfully converted into free flowing powder formulation for the ease of packaging and delivering.
- The biological activity of insulin in the powder formulation was evaluated and was found to be intact even after one year storage.

17. Contributions made towards increasing the state of knowledge in the subject :
18. Conclusions summarising the achievements and indication of scope for future work :
19. Science and Technology benefits accrued :
- a. List of research publications with complete details :
 - b. Manpower trained on the project :
 - i. Research Scientists or Research Fellows : Two
 - ii. No. of PhD's produced :
 - iii. Other Technical Personnel trained :
 - c. Patents taken, if any : One
 - d. Products developed, if any : One (to be translated)

20. Abstract: (In 300 words for possible publication in Bulletin):

- a. Background:
- b. Materials:
- c. Results:
- d. Conclusion:

21. Procurement/Usage of Equipment:

a. Details of Equipment:

Sl. No.	Name of Equipment	Make/ Model	Cost (Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdown

b. Suggestions for disposal of equipment(s):

Dr. Rekha M.R.
(Name and Signature of PIs with date)

Routing: Signed copy of "Project completion Report" by PI → root@sctimst.ac.in, rpc@sctimst.ac.in