DEVELOPMENT OF INTERPENETRATING POLYMER NETWORK
MICRO PARTICULATE DRUG FORMULATIONS AND THEIR
CONTROLLED RELEASE CHARACTERISTICS

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SYNOPSIS OF THE Ph.D.THESES

Development of drug delivery systems is of much interest to the pharmaceutical scientists as these systems provide prolonged duration of action of drugs having short biological half-life, and reduce dose-related toxicity, dosing frequency, and patient non-compliance. Among the various sustained release drug delivery systems, pharmaceutical industries prefer sustained release tablet dosage form because of the ease of production using the existing tablet manufacturing infrastructure; Biopolymers have received increased attention to formulate tablets for controlled release of drugs.

The controlled release of pharmacologically active agents to the specific site of actions (viz., colon) therapeutically most favorable rate and dose treatment has been the major goal in the designing such devices. Two objectives of our carried research work i.e., first one is preparation of micro particulates and their chemical analysis and second one is drug delivery applications of the developed micro systems. In order to pursue research in this area we developed novel polymeric matrices in the form of microspheres/micro beads as drug delivery systems for anti-malarial and anti-cancer drugs. These research works are presented in seven chapters of this thesis.

**Chapter I** covers the recent developments of micro particulates as drug delivery carriers for biomedical applications. The various synthetic methodologies for the preparation of micro beads and microspheres as controlled drug delivery systems viz., polymeric particulates, pH sensitive and thermo responsive properties have been included in this chapter. Different methods of drug loading and in vitro drug release details including the aim of the work and brief survey of literature pertaining to the present study is also given in this chapter.

**Chapter II** discuss the details on materials and experimental procedures used throughout this research. Several characterization techniques such as UV-visible spectrophotometer, Fourier transform infrared (FTIR) spectroscopy, differential scanning calorimetry (DSC), thermo gravimetric analysis, scanning electron microscope (SEM),
dynamic light scattering (DLS) and X-ray diffraction studies (X-RD) have been employed. These methods were employed the prepared different types of micro particulates for using drug delivery and in-vitro release studies are also given in this chapter.

Chapter III describes the development of microspheres from carbohydrate polymers, such as Chitosan (CS) and Guar Gum-g-poly (Acrylamide) [GG-g-PAm]. And these microspheres were characterized by DSC, SEM and particle size distribution. DSC thermograms have confirmed the uniform molecular distribution of the drug molecules in the microspheres. SEM micrographs exhibited a spherical morphology of the prepared microspheres. The swelling studies of microspheres have shown that an increasing amount of GG-g-PAm in the microspheres, water uptake has increased. This effect is correlated with the release rates of the 5-Flourouracil (5-FU) though the microspheres containing different amount of GG-g-PAm. The microspheres could be retained in the gastric environment for more than 10 hours it is due to the pH sensitive nature of microspheres which would help to improve the bioavailability of 5-FU.

Chapter IV represented the preparation of pH sensitive 5-FU loaded Pectin-poly (vinyl pyrrolidone) (PC-PVP) based micro beads. FTIR, DSC and X-RD studies confirmed the molecular level dispersion of drug in the beads. SEM pictures have shown the good compatibility of PC and PVP compositions present in the beads with smooth surface. The encapsulation efficiency of 5-FU was found to vary from 69% to 82% depending upon the blend composition, cross-linking and the amount of drug loading. Drug release studies indicated controlled release of 5-FU for more than 10 h and potentially used for colon cancer drug delivery.

Chapter V deals with Pyronaridine loaded NaAlg-g-(LSA-co-PAm) semi-IPN micro beads for controlled release of pyronaridine, DSC and XRD studies confirmed the molecular level dispersion of drug in the micro beads. SEM pictures have shown the good compatibility of NaAlg and LSA compositions present in the micro beads with smooth surface. The encapsulation efficiency was found to vary between 59 and 68% depending upon the blend
composition, cross-linking and the amount of drug loading. Drug release studies indicated controlled release of pyronaridine for more than 10 h and potentially used for drug delivery.

Pyranaridine drug was loaded into these microbeads via blending method. Various formulations were prepared by varying ratios of LSA/AAm/NaAlg, crosslinker and % of pyronaridine loading. Microbeads were characterized by DSC, XRD, SEM and FTIR. DSC and X-RD studies were performed to understand the crystalline nature of drug after encapsulation into semi IPN microbeads. SEM images gave the beads with smooth surface. FTIR spectroscopy of microbeads shown the confirmed the formation of co-polymerization and grafting between the polymers.

In Chapter VI we had explored the possibility of the preparation of novel biopolymeric microspheres from Lignosulphonic acid (LSA) and gelatine (GT) blends. And the novelty of the present study lies in using of LSA as cheap and low cost material. It was also seen that LSA obtained could be successfully used for preparation of biopolymeric microspheres. An anti-malarial drug pyronaridine loaded blends microspheres were prepared by using glutaraldehyde (GA) as a crosslinker; XRD studies confirmed the molecular level dispersion of drug in the microspheres. SEM pictures have shown the good compatibility of GT and LSA compositions present in the microspheres with smooth surface. The encapsulation efficiency was found to vary from 47.4% to 61.09% depending upon the blend composition, cross-linking and the amount of drug loading. In vitro release profile of pyronaridine implied decreased drug release rate with increased GA. Summary of the thesis are presented in Chapter VII.

In conclusion, the study demonstrates successful development of pH responsive carbohydorate based microspheres/microbeads for controlled release of an anti-cancer drug 5-Fluorouracil and anti-malarial drug pyronaridine. The developed micro systems will be useful for specific colon, and breast cancer drug delivery applications. The microspheres and microbeads had been developed which were useful for production of size and shape controlled selected drugs. The developed micro particles showed good releasing studies at gastrointestinal conditions. Hence we conclude that the prepared micro particles shown the excellent potential for medical applications of cancer and malaria.
LIST OF PUBLICATIONS

A) PAPERS IN JOURNALS

1. E. Chandra Sekhar¹, K.S.V. Krishna Rao² and R. Ramesh Raju¹*,
   “Chitosan/guar gum-g-Acrylamide semi IPN microspheres for controlled release
   studies of 5-Fluorouracil” *Journal of Applied Pharmaceutical Science.* 01 (08);
   2011: 199-204.

2. E. Chandra Sekhar¹, P. Rama Subba Reddy², K.S.V. Krishna Rao²* and
   R. RameshRaju¹*, “Development of Pectin-Poly (Vinyl Pyrrolidone) Blend Micro
   (Accepted).

3. Chandra Sekhar Espenti¹, K. Madhusudana Rao³, Krishna Rao KSV*² and
   R. Ramesh Raju*¹, “Synthesis and characterization of Sodium
   alginate/(Lignosulfonicacid-g-Acrylamide) interpenetrating micro beads for
   controlled release of an anti-malarial drug pyronaridine”. *Indian Journal of

4. Chandra Sekhar Espenti¹, K. Madhu Sudana Rao³, S. Eswaramma², Krishna Rao
   KSV*² and R. Ramesh Raju*¹, “Development of Lignosulfonicacid-co-Gelatin Inter
   Penetrating Network microspheres for Controlled Release of an Anti-Malarial Drug
   (Pyronaridine)”. *Wulfenia.* (Accepted).
B) PAPERS IN CONFERENCES


