CHAPTER - 1

INTRODUCTION
Cancer has become one of the major causes of death since 1960's. There are three main approaches to deal with established cancer. They are -

a) surgical excision
b) irradiation
c) chemotherapy

The role of each of these depend on the type of tumour and stage of its development. The chemotherapy of cancer has been under vigorous investigation and important gains have been made in the treatment of some neoplasms. Chemotherapy with cytotoxic drugs is the main method of treatment for only a few relatively rare cancers but it is increasingly used as an adjuvant to surgery or irradiation in a range of common types of tumour(1). The major problems in cancer chemotherapy are -

a) toxic drug effects on normal cells,
b) rapid clearance of the drug from tumour tissues.

Although anticancer drugs come from many different classes of chemicals and act by different mechanisms, they are toxic

(1)
specifically to actively proliferating cells, regardless of whether they are malignant or normal, and rapidly eliminated from circulating blood by enzymatic degradation or urinary excretion. In many cases, the toxic drug effects on normal cells are more profound and long-lasting than any therapeutic effect on tumor cells. Efforts have been, therefore, directed towards increasing the drug selectivity by means of selective drug administration into the tumor feeding arteries (2,3), optimized dose schedule based on cell cycle specificity (4) or multimodal chemotherapy in combination with various kinds of drugs.

There are at least two options in pursuing optimal drug action: pharmacological and pharmaceutical. In the case of the former, the development of a new drug which exclusively attacks tumor cells is conventional and particularly important in this respect. Unfortunately, however, the results with the drugs available at present and the prospect in pharmacology do not necessarily warrant any optimism. This may be attributable to either the lack or the ambiguity of biochemical differences between tumor and normal cells in terms of quality. Recent advances in colloid and polymer chemistry indicate the possibility that certain modification of dosage form provide a targeted delivery system maximizing the efficiency of cancer chemotherapy. That is if an anticancer drug were associated with an appropriate carrier material, the drug carrier complex would accumulate or retain at its desired site of action and/or release the drug in an active form at a suitable rate. This pharmaceutical route seems simpler more practical and attractive, and this is expected to play a crucial role in cancer chemotherapy.
Drug targeting is a specific form of drug delivery where the pharmacological agent is directed selectively to its site of action, that is, organ or cell. Drug goes to the site where it is needed and other tissues are not exposed to possible harm. So it leads to reduction of side effects and adverse reactions. Drug targeting can be achieved with a wide variety of different approaches including chemical modification (prodrugs), implants and by using specific carrier systems.

In the present study an attempt has been made to formulate and prepare various colloidal drug delivery systems of 5-fluorouracil which could be used to achieve targeting. The different colloidal drug delivery systems containing 5-fluorouracil prepared include:

a) Niosomes prepared from various Span group of surfactants
b) Polyterephalamide microspheres
c) Microspheres using copolymers of acrylic and methacrylic acid esters.

After optimization of formulation conditions these systems were characterised for particle size and size distribution, drug entrapment efficiency, in vitro leaching rate and in vivo drug distribution in different organs like kidney, lung, liver and intestine of rat.