CHAPTER I

INTRODUCTION AND OBJECTIVES OF THE INVESTIGATION

Controlled drug delivery is a topic of current interest in pharmaceutical technology and industry. In the last two decades, controlled release dosage forms have made significant progress in terms of clinical efficacy and potential compliance. Controlled release drug delivery systems are those formulations designed to release an active ingredient at rates, which differ significantly from their corresponding conventional dosage forms. The controlled release drug delivery systems are aimed at controlling the rate of drug delivery, sustaining the duration of therapeutic activity and / or targeting the delivery of the drug to a tissue. Drug release from these systems should be at a desired rate, predictable and reproducible.

Polymers which are used as release-retarding materials in the design of controlled release drug delivery systems play a vital role in controlling the delivery of drug from the systems. The success of controlled drug delivery systems depends on how well the polymer regulates the release of drug from the system. Though a wide range of polymers and other release retarding polymers are available, there is a continued need to develop new and more efficient release retarding polymers for controlled release. The major objective of the present study is to develop a new release – retarding and rate controlling polymers for controlled release.

A survey of the literature revealed that modified starches are promising and having good potential as release retardants and rate controlling polymers for
controlled release. The controlled release properties of modified starches generally based on solvent-activation have been intensively investigated. For example, pre-gelatinized starch\textsuperscript{1}, cross linked amylose\textsuperscript{2}, substituted amylose\textsuperscript{3}, short-chained amylose (i.e. amylodextrin)\textsuperscript{4,5} and calcium starch\textsuperscript{6,7}, all have retarded drug release from matrix tablets.

In the present investigation starch acetate, a new chemically modified starch was synthesized and evaluated for its application in controlled release. Starch acetates are novel modified starches that are produced by acetylating native starch. They are reported\textsuperscript{8} to have direct compressible matrix forming properties. Starch acetate is also having good potential for application in coating\textsuperscript{9} because of its film forming properties. Though starch acetate has good film forming properties it has not been investigated thoroughly for controlled release application. Ethylene vinyl acetate copolymer (EVA), a copolymer of ethylene and vinyl acetate, has good film forming properties.\textsuperscript{10,11} In a few reports\textsuperscript{12,13} monolithic systems composed of ethylene vinyl acetate copolymer have been studied for the controlled delivery of macromolecular drugs such as insulin and heparin. In the present investigation, EVA was also evaluated for its application in controlled release.

Glipizide, an effective ant-diabetic drug was selected for formulation into controlled release drug delivery system employing starch acetate and EVA. Glipizide, an effective anti-diabetic requires controlled release formulation owing to its short biological half-life\textsuperscript{14} of 3.4 ± 0.7 h and is rapidly eliminated. Controlled release formulation is needed for glipizide for better control of blood glucose levels to prevent hypoglycemia and enhance clinical efficacy, to reduce
g.i. disturbances and to enhance patient compliance. A few controlled release formulations of glipizide are available commercially.

Among the various approaches, microencapsulation and microcapsules have been widely accepted for controlled release. Polymers and release retarding materials used as a coat play a vital role in controlling the drug release from the microcapsules. Microencapsulation by various polymers and their applications are described in standard text books.\textsuperscript{15,16} Though a variety of polymeric materials are available to serve as release retarding coat materials, there is a continued need to develop new, safe and effective release retarding coat materials for microencapsulation. In the present investigation two new polymers namely (i) Starch Acetate and (ii) EVA were evaluated as microencapsulating agents in the preparation of microcapsules for controlled release.

Preparation of drug embedded matrix tablets is another least complicated techniques for controlled release and is widely used in industry. This technique was also selected for the design of controlled release drug delivery systems employing starch acetate and EVA.

The specific objectives of the investigation are as follows:

1. To prepare and characterize starch acetate, a new chemically modified starch.
2. To evaluate starch acetate as a new microencapsulating agent and to prepare and evaluate starch acetate microcapsules of glipizide for controlled release.
3. To evaluate starch acetate as matrix polymer and to develop starch acetate matrix tablets of glipizide for oral controlled release.
4. To evaluate EVA as a new microencapsulating agent and to prepare and evaluate EVA microcapsules of glipizide for controlled release.

5. To evaluate EVA as matrix polymer and to develop EVA matrix tablets of glipizide for oral controlled release.

6. To design and evaluate controlled release microcapsules and matrix tablets of glipizide for once daily (24 h) administration employing starch acetate and EVA.

7. To characterize the starch acetate and EVA microcapsules and matrix tablets of glipizide and to evaluate the kinetics and mechanism of drug release from these controlled release drug delivery systems of glipizide.


9. To evaluate the stability of release rates of selected controlled release delivery systems developed employing starch acetate and EVA.

Extensive experimentation both in vitro and in vivo has been done to fulfill the objectives of the investigation and the studies carried out and results obtained are described in the subsequent chapters.
REFERENCES


