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RESEARCH ARTICLE

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A Path for Horizing Your Innovative Work

FORMULATION AND EVALUATION OF ETHYL CELLULOSE MICROSPHERE OF GLIPIZIDE

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Abstract: In the present study an attempt was made to develop a new sustained drug delivery for Glipizide microspheres by using polymer Ethyl cellulose to improve patient compliance and safety. It is possible to prepare microspheres containing Glipizide by solvent evaporation method, to prolong activity with increased stability without losing its therapeutic activity. Use of this approach has the potential not only to improve the therapeutic effectiveness of the drug but also to allow a reduction in the total drug needed and minimizing toxic side effects. Microspheres are one of the devices that have been used for the delivery of drugs to affected area. Microspheres are relatively non-toxic and non-immunogenic preparations made to reduce the gap between the sustained release preparations and controlled release preparations.

Keywords: Glipizide, Microspheres, Ethyl cellulose, solvent evaporation method.

INTRODUCTION

For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms. Immediate release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. Microsphere carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery.[1]

Microspheres can be defined as solid, approximately spherical particles ranging from 1 to 1000µm. They are made of polymeric, waxy or other protective materials, that is, biodegradable synthetic polymers and modified natural products such as starches, gums, proteins, fats and waxes. The rate of release of drug from microspheres dictates their therapeutic action. Release is governed by the molecular structure of the drug and the polymer, the resistance of the polymer to degradation, and the surface area and the porosity of the microspheres.[1, 2]

The aim of this work is to investigate the possibility of obtaining a prolonged, relatively constant effective level of Glipizide from the ethyl cellulose microsphere formulations using ethyl cellulose as Ethyl cellulose is a non-biodegradable, biocompatible, non-toxic, cellulose polymer having good film forming properties, which has been used as bio-material and in the controlled delivery of the drugs.

Although the drug is highly effective, it suffers from the major drawbacks, such as

1. Bitter in taste.
2. Incidence of side effects because of frequent doses.
3. Low biological half life.

Glipizide was selected for this project to minimize the above drawbacks and to prepare a better formulation.

MATERIALS AND METHODS

Glipizide, Ethyl Cellulose and HPMC Methocel k100M CR Premium was obtained as gift samples from Dey's Medical Pvt. Ltd. And Chloroform was a gift sample from East India Chemical works. All chemicals used were laboratory grade.

Method of preparation

EC polymer (2gm) was dissolved in chloroform (100ml) to form a homogeneous polymer solution core material Glipizide (0.8gm) was added to the polymer solution (10ml) and mixed thoroughly. The resulting mixture was then added in a thin stream to 200ml of aqueous mucilage of SCMC (0.5%) contained in a 450ml beaker, while stirring at 1000 rpm to emulsify the added dispersion as fine droplets. A Remimake medium duty stirrer with speed meter (model RQT124) was used for stirring. The solvent was then removed by continuous stirring at room temperature (28º) for 3 hours to produce spherical microspheres. The microspheres were collected by vacuum filtration and washed repeatedly with water. The product was then air dried up to obtain discrete microspheres. Different proportions of core to coat materials namely 9:1(MC1), 8:2(MC2) and 7:3 (MC3) were used to prepare microspheres with varying thickness.[3]

***In vitro* Drug Release**

Release of Glipizide from the microspheres of size 20/35 and 35/60 was studied in phosphate buffer of pH 7.4(900ml) using an USPXXIII three station dissolution rate test apparatus with rotating paddle at 50 rpm and 37±1ºC as prescribed for Glipizide tablets in USPXXIV. A sample of microspheres equivalent to 10mg of Glipizide was used in each test samples were withdrawn through a filter (0.45µ) at different time intervals over a period of 24 hours and were assayed at 223nm for Glipizide using Shimadzu UV-150 double beam spectrophotometer. Drug releases were conducted in triplicate.[3]

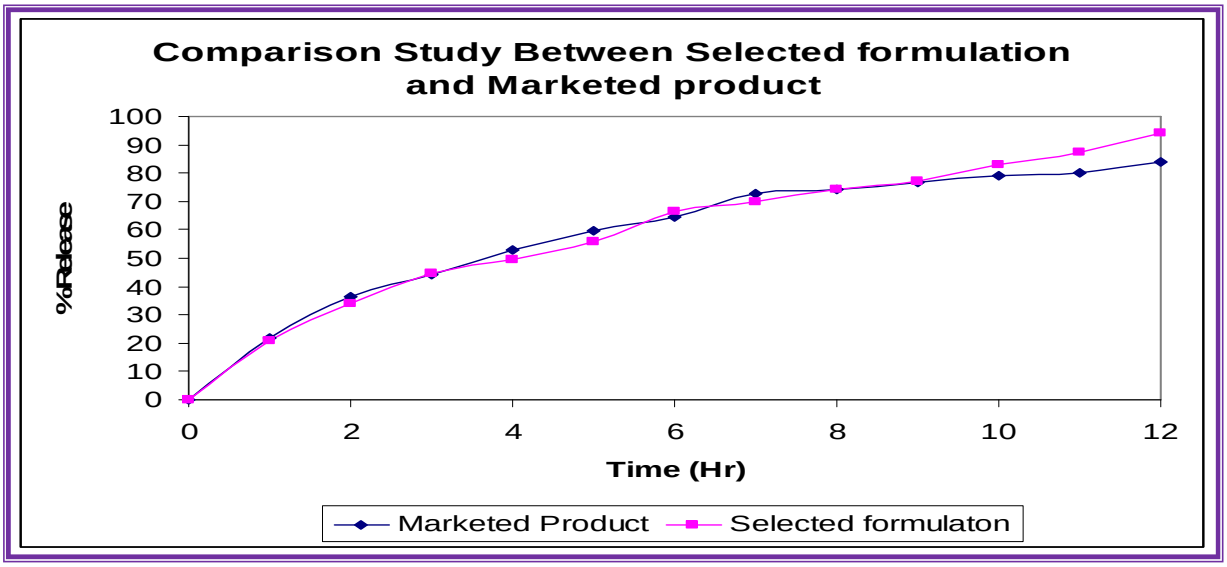

Figure 1 Comparison study between Selected Formulation and Marketed Product.

Percent of entrapment: The percent of entrapment was determined for all the batches and it was shown in TABLE (1). The encapsulation efficiency was in the range of 77-84% with various batches. Drug content of the microspheres was found to be nearly same in all the batches.

Scanning electron microscopic study:

The microspheres were observed under a scanning electron microscope. The instrument used for this study was Hitachi S-450 scanning electron microscope.

Micromeritics:

Micromeritic investigations such as bulk density, true density, porosity[4], angle of repose and consolidation index[5] were carried on Glipizide microspheres in order to standardize the product and to optimize the pilot production of dosage forms.

STABILITY STUDIES

Physical stability and effect of aging on the drug release were studied in the control as well as microspheres. All microsphere formulations were kept in a small air tight glass containers and stored at different temperatures of 4±1º C in a refrigerator and 45±2º C in the oven and in a dessicator containing saturated solution of conc. H_2SO_4 (13.1 ml to 100 ml with distilled water) to obtain 85% RH, effect of aging on their release characteristics was studied after 4th week using dissolution method.

Table No 4 shows the stability of microsphere formulation at various temperatures like 4ºC, room temperature (32ºC), 45ºC and 85% RH. There was no significant change in the release pattern when it was stored at 4ºC, room temperature and at 45ºC. The release rate was little bit affected when it was stored at 85% RH.[3]

CONCLUSION

The microspheres were prepared by solvent evaporation method and characterized by using scanning electron microscope. Sustained release formulation of Glipizide in the form of microspheres was developed to a satisfactory level in term of drug release, content uniformity and Micromeritics properties. Future work is required to stabilize the product, in vivo studies, estimate the amount of drug present in the various organs with disposition kinetics and establish appropriate dosage regimens to gauge the significant changes in the metabolism of the drug before studies in the clinic.

Table 1

Percentage of Entrapment

Sr **No.**	**Formulation**	**Encapsulation Efficiency (%)**
1	MC1	77.2
2	MC2	79.6
3	MC3	83.9

Table 2

The Arithmetic Mean Sizes of Microspheres of Glipizide

Sr No	**Formulation**	**Particle size ± SEM (µm)**
1	MC1	372.8 ± 9.7
2	MC2	488.6 ± 10.5
3	MC3	667.5 ± 12.9

Table 3

Micromeritic Parameters

Sr **No**	**Formulation**	**Bulk Density**	**Porosity (%)**	**Angle of Repose**	**Consolidation Index (%)**
1	MC1	0.79	18.22	15.3	13.4
2	MC2	0.83	16.72	16.6	12.2
3	MC3	0.91	15.16	17.3	10.5

Table 4

Stability of Different Microsphere formulation

Formulation	**At 4ºC**	**At Room Temperature**	**At 45 ºC**	**85 % RH**
MC1	94.34	94.26	88.24	85.26
MC2	97.10	95.32	87.69	84.91
MC3	96.68	95.23	85.14	85.74

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