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Research Article

DESIGN AND IN-VITRO COMPARATIVE STUDIES OF GLIPIZIDE MICROCAPSULES PREPARED BY DIFFERENT POLYMERS

LATHEESHJLAL L*, DR. S SATYANAND, MEHUL VAIDYA

Department of Pharmaceutics, Karpagam University, Coimbatore, Tamilnadu, India. latheesh18@yahoo.co.in, latheesh185@gmail.com

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ABSTRACT

The main objective of the present study was to prepare and evaluate the mucoadhesive microcapsules of Glipizide by using different mucoadhesive polymer. Glipizide is a second- generation sulfonylurea derivative used for the treatment of type II diabetes. Its short biological half-life [0.3 ± 0.7 h] necessitates the need to be administered in two or three doses of 2.5-10 mg per day and the mucoadhesive microcapsule dosage forms exhibit a prolonged residence time at the site of application and thus contribute to improved or better therapeutic performance of drug. The Glipizide microcapsules were prepared by Ionic Gelation process by using different mucoadhesive polymers with different ratios. Evaluation studies shows, the microcapsules were found to be discrete, spherical, free flowing and the microcapsules were in the size range of 845µ. The microcapsules were exhibited good mucoadhesive properties in an in-vitro wash off test and the in-vitro release studies of Glipizide microcapsules shows significant difference in their release rate. Based on the evaluation studies it was concluded that the microcapsules prepared by mucoadhesive polymer Alginate-Gum Kondagogu [3:1] ratio showed slow and controlled release over extended period of time when compared to other mucoadhesive polymer and the Drug release was diffusion controlled and followed zero-order kinetics.

Keywords: Ionic Gelation process, Glipizide, Gum kondagogu, Gum Karaya, HPMC, Carbopol.

INTRODUCTION

The GI tract is the most preferred and commonly used route for the delivery of drugs. Micro encapsulation has been accepted as a process to achieve controlled release and drug targeting and Mucoadhesion has been a topic of interest in the design of drug delivery system to prolong the residence time of the dosage form at the site of application or absorption and to facilitate intimate contact of the dosage form with underlying absorption surface to improve and enhance the bioavailability of drugs. The objective of this study is to develop, characterize, and evaluate Mucoadhesive microcapsules of glipizide employing various Mucoadhesive polymers for prolonged gastrointestinal absorption. Glipizide is a second generation oral ant diabetic drug in type 2 diabetes, which can actually lower the blood glucose level in humans by stimulating the release of insulin from the pancreas.

MATERIALS AND METHODS

Glipizide was obtained as gift sample from madras pharmaceuticals, carbopol and HPMC were obtained from central drug house, Mumbai, Gum Kondagogu, Gum Karaya were obtained from cooperative corporation ltd, Visakapatnam, all the other reagents used were analytical grade.

Preparation of mucoadhesive microcapsules by Ionic gelation method

Sodium alginate and mucoadhesive polymer was dissolved in purified water to form homogeneous polymer dispersion. 2 gm of glipizide was added to polymer dispersion and mixed thoroughly with stirrer and this dispersion was added drop wise into a calcium chloride solution by using syringe no 18. The added droplets were retained in the calcium chloride solution for 15min to complete the curing reaction and to produce spherical rigid microcapsules having coat: core ratio 1:1[MC1]. Similarly microcapsules with core coat ratio 2:1[MC2], 3:1[MC3] were also prepared and the same different ratios was prepared by using different mucoadhesive polymer [formulation code MC1, MC2, MC3 were prepared by gum karaya, MC4, MC5, MC6 were prepared by gum kondagogu, MC7, MC8,MC9 were prepared by HPMC and MC10, MC11, MC12 were prepared by carbopol]

Characterization and Evaluation of mucoadhesive microcapsules

A] Size distribution and size analysis

For size distribution analysis, different samples in batch were separated by sieving, using a range of standard sieves .The amount retained on different sieves was weighed and the mean particle size of microcapsules was calculated.

B] Flowabilty of microcapsules

The angle of repose was measured according to the fixed funnel and free standing cone method. The bulk density of the microcapsules was calculated by determining the hausner's ratio and carr's index from the pored and tapped bulk densities of a known weight of sample using a measuring cylinder.

C] Drug content evaluation

Glipizide content in the microcapsules was estimated by a UV spectrophotometric method based on the measurement of absorbance at (223nm) in phosphate buffer (pH 7.4)

D] Scanning electron microscopy (SEM)

The samples for the SEM analysis were prepared by sprinkling the gel beads on one side of double adhesive stub. The stub was then coated with fine gold dust. The get beads were then observed with the scanning electron microscope.

E] Micro encapsulation efficiency

Micro encapsulation efficiency was calculated using the following formula.

$$\text{Microencapsulation Efficiency} = \frac{\text{Estimated Percentage Drug Content}}{\text{Theoretical Percentage Drug Content}} X100$$

F] Mucoadhesion evaluation

The Mucoadhesive property of the microcapsules was evaluated by an in vitro adhesion testing method known as the wash-off test.

G] Infrared spectroscopic studies

Compatibility between the drug and the different polymers were studied using Perkin Elmer 2000 FT-IR system.

H] In vitro release studies

Dissolution studies of microcapsules were performed according to USP XXIII 8-station dissolution rate test apparatus in phosphate buffer. The temperature was maintained at 37±1°C and the rotation speed was 50 rpm. The samples were withdrawn at various time intervals and analysed spectrophotometrically.

RESULTS AND DISCUSSION

Mucoadhesive Microcapsules of Glipizide were prepared by *Ionic Gelation process* and the prepared microcapsules were found to be discrete spherical and free flowing. The microcapsules were in the size range of 845µ shown in Table 1. The SEM photograph indicates that the microcapsules were spherical and completely covered with the polymer which is shown in Fig 1. Low coefficient of variation [<2.0%] in percentage drug content indicated uniformity of drug content in each batch of microcapsules. IR studies showed that there is no chemical incompatibility between the drug and the polymer. Glipizide release from the microcapsules was slow and spread over extended period of time, and the release was depended on the coat: core ratio. The microspheres prepared by 3:1 coat: core ratio was found to be more sustained release as it yield slow release of drugs. Based on the *in-vitro* studies, Microcapsules formulated by 3:1 core: coat ratio of all polymers was subjected to comparative studies and in-vitro wash off studies which is shown in Table 2 and Table 3. In vitro wash off test showed that the mucoadhesive potential of gum kondagogu was relatively high and the Comparative studies showed significant difference in their release rate.

The Microcapsules prepared by Gum kondgogu offered much slower release to drug when compared to other polymer which is given in Table 3. And the drug release followed zero order kinetics and controlled by Non-Fickian Diffusion in each cases.

Table 1: Physical properties of microcapsules prepared by Ionic Gelation method

Formulation	Angle of repose	Bulk Density	Carr's Index	Hausner Ratio	Average particle size	% Encapsulation Efficiency	Swelling Index [%]
MC1	21.06	0.49	14.95	1.13	826.83	92.67	57
MC2	22.08	0.59	13.79	1.09	850.15	93.55	98
MC3	24.14	0.65	12.24	1.04	862.78	94.29	124
MC4	22.86	0.45	19.45	1.22	791.35	90.37	66
MC5	23.08	0.51	17.36	1.16	844.12	92.30	115
MC6	25.94	0.60	16.10	1.10	864.48	94.38	141
MC7	20.06	0.49	13.95	1.10	821.76	93.71	55
MC8	21.98	0.52	12.89	1.07	842.66	93.98	94
MC9	23.16	0.61	12.34	1.02	863.56	94.02	120
MC10	21.15	0.48	19.25	1.20	827.34	90.44	56
MC11	22.29	0.52	16.96	1.14	840.22	91.30	100
MC12	24.94	0.59	16.65	1.08	869.58	92.98	122

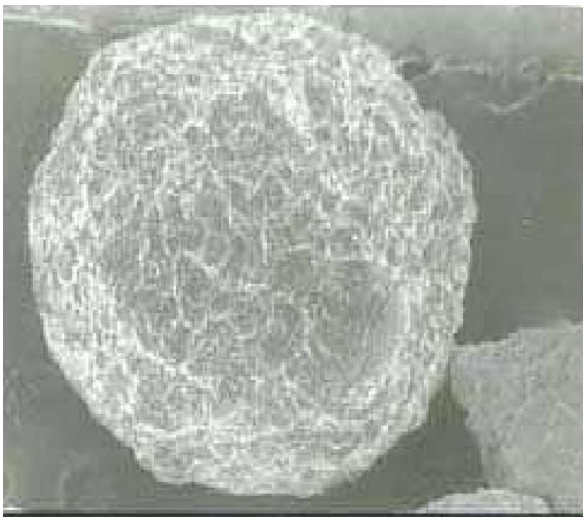

Fig. 1: SEM of Glipizede microcapsules [F6]

Table 2: In-vitro comparative release of Glipizide Microcapsules

Formulation	Percent Glipizide released at times [h]					
	1	2	4	6	8	10
F3	10.06	23.55	47.55	68.89	98.98	-------
F6	07.46	17.22	35.28	58.17	79.56	99.04
F9	14.56	30.09	55.15	72.05	99.56	---------
F12	11.06	25.66	49.12	69.88	99.25	--------

Table 3: In vitro wash-off test

Formulation	Percentage of alginate beads adhering to tissue									
	0.1N HCL, pH1.2					Phosphate buffer pH7.4				
MC3	89	68	52	28	04	90	80	62	56	40
MC6	94	78	60	49	30	97	93	84	76	70
MC9	86	65	50	25	---	85	75	58	50	30
MC12	87	66	51	27	02	88	78	60	52	35

CONCLUSION

The mucoadhesive microcapsules with coat consisting of alginate and mucoadhesive polymers were prepared by Ionic Gelation process. The microcapsules exhibited good mucoadhesive properties in an in-vitro wash off test and the in-vitro release studies of Glipizide microcapsules shows significant difference in their release rate. The microcapsules prepared by mucoadhesive polymer Alginate-Gum Kondagogu [3:1] showed slow and controlled release over extended period of time when compared to other mucoadhesive polymer. And the Drug release was diffusion controlled and followed zero-order kinetics.

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