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Formulation and *In-Vitro* characterization of glimipride loaded mucoadhesive gelatin microspheres

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ABSTRACT

Mucoadhesion is defined as the adhesion of synthetic or biological macromolecules to the biological surface, which can be epithelial tissue or the mucus membrane on the surface of tissue or other parts. The mucoadhesive microspheres of Glimipride were prepared by Emulsion cross linking method using natural polymer Gelatin utilizing temperature change and cross linking agent glutaraldehyde was able to sustain the drug release efficacy. The stability study results shows that the formulation F5 was stable at temperature 40 ± 2˚C/75% RH at the end of 3 months.

The comparative study with the marketed SR formulation results showed that the F5 microsphere formulation had a sustained and prolonged drug release at the end of 24 h than the marketed glimipride SR formulation.

The results of the study revealed that the use of natural polymer Gelatin is an effective strategy for the designing and development of glimipride loaded mucoadhesive microspheres for easy, reproducible and effective oral controlled drug delivery for the treatment of type II Diabetes mellitus.

Keywords: Glimipride, Mucoadhesion, Cross Linking, Gelatin

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INTRODUCTION

Mucoadhesion is defined as the adhesion of synthetic or biological macromolecules to the biological surface, which can be epithelial tissue or the mucus membrane on the surface of tissue or other parts.[1,2] Microspheres are spherical solid particles ranging in size from 1-1000 µm. They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. Microsphere carrier systems made from the naturally occurring biodegradable polymers have attracted considerable attention for several years in sustained drug delivery (Bentia S., 1984) which can precisely control the release rates and target drugs to a specific body site with enormous impact in formulation and development of novel drug delivery systems. Microspheres from an important part of such delivery systems[3,4] (Woo et al., 2001, Capan et al., 2003, Gohel et al., 1988) they have varied applications and are prepared using various polymers. However, the success of these microspheres is limited due to their short residence time at the site of absorption.

Diabetes mellitus is a group of metabolic diseases characterized by elevated blood glucose levels (hyperglycemia) resulting from defects in insulin secretion, insulin action or both. Insulin is a hormone manufactured by the beta cells of the pancreas, which is required to utilize glucose from digested food as an energy source. [5, 6]

The main objective of present study is to provide is to provide needed therapy for the treatment of NIDDM because, among the people who are suffering from long term disorders, the major were categorized under the people who are suffering from diabetes. A special dosage form is needed for them that can provide continuous therapy with high margin of safety.

MATERIALS & METHODS [7, 8]

Glimipride was obtained as a gift sample from Arvindo Remedies, Chennai. Gelatin was obtained from Bafna Pharma, Chennai. Other recipients were obtained from Merck Laboratories, Mumbai.

Preparation of mucoadhesive gelatin microspheres:

Gelatin microspheres were prepared by an emulsification cross linking method. 10 ml of 15% (w/v) aqueous gelatin solution preheated to 60˚C.[9] The specified quantity of

Glimipride was dissolved in phosphate buffer pH 7.4 preheated to 60˚C. Then the mixture was added drop wise to 50 ml of liquid paraffin with 1% w/v span 80 preheated to 60˚C and emulsified by stirring with magnetic stirrer at rpm 1000. Then the stabilized emulsion is allowed to cool and cross linking agent glutaraldehyde was added and the stirring was continued at room temperature for 6 hours.[10] The cross linked microspheres were cooled and washed with Petroleum benzene to remove unreacted glutaraldehyde and liquid paraffin. After washing, the microspheres were dried at room temperature and stored in desiccators.[11-12]

Table 1: Formulation of Glimipride Mucoadhesive Microspheres

Batch	Amount of Ingredients			
	Glimipride (mg)	Gelatin (gm)	Liquid paraffin (ml)	Glutarylaldehyde (ml)
F1	100 mg	2.0	50	0.5
F2	100 mg	1.5	50	0.5
F3	100 mg	1.0	50	0.5
F4	100 mg	0.75	50	0.5
F5	100 mg	0.5	50	0.5
F6	100 mg	0.5	50	0.5

RESULT & DISCUSSION

Percentage yield: The total amount of dried microcapsules was weighed and the percentage yield was calculated by taking into consideration the total weight of the drug and polymer used for preparation of microspheres.

$$\text{Percentage Yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

Table 2: Percentage yield of Glimipride Mucoadhesive Microspheres

Formulation	Theoretical yield (gm)	Practical yield (g)	Percentage yield (%)
F1	2.11	1.960	92.84
F2	1.21	1.448	90.44
F3	1.11	1.059	96.08
F4	0.85	0.799	93.75
F5	0.61	0.577	96
F6	0.36	0.281	80.15

Drug Content: 100 mg of microspheres was weighed and suspended in phosphate buffer pH 7.4. The suspension was suitably diluted with phosphate buffer pH 7.4 in 100 ml standard flasks and filtered to separate the fragments. Drug content was analyzed after suitable dilution by UV spectrophotometer at a wavelength of 225 nm against phosphate buffer pH 7.4 as blank. All the studies were carried out in triplicate.

Table 3: Drug content of Glimipride Mucoadhesive Microspheres

Formulation	Drug content (%) w/w
F1	81.74
F2	85.78
F3	87
F4	83.22
F5	87.36
F6	82.88

Entrapment Efficiency: 50 mg of microspheres were powdered and dissolved in phosphate buffer pH 7.4 in 50 ml volumetric flask and made up to the volume. The solution was kept for 1 hour with occasional shaking. Further 1 ml solution was diluted up to 50 ml with phosphate buffer pH 7.4. The content was analyzed spectrophotometrically at 225 nm against phosphate buffer pH 7.4 as blank. The % EE of each formulation was calculated using the following equation

$$\%\ EE = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Table 4: Entrapment efficiency of Glimipride Mucoadhesive Microspheres

Formulation	Entrapment Efficiency (%)
F1	81
F2	86.28
F3	87
F4	83.24
F5	87.52
F6	82

Drug Loading Capacity: Drug loaded microspheres were digested with phosphate buffer pH 7.4 at room temperature for 12 h. After filtration and suitable dilution, Glimipride present in the solution was determined.

$$\text{Drug loading (\%)} = \frac{\text{Actual drug content in weighed quantity of powder} \times 100}{\text{Weighed quantity of the microspheres}}$$

Table 5: Drug loading Capacity of Glimipride Mucoadhesive Microspheres

Formulation	Drug loading Capacity (%)
F1	3.893
F2	5.358
F3	7.56
F4	10.23
F5	17.56
F6	12.39

Mean Particle Size by Microscopy: Particle size analysis was carried out by using optical microscopy. About 200 microspheres were selected and their size was determined by using optical microscope fitted with standard micrometer scales. All the studies were carried out in triplicate.

In Vitro Release Study: In-vitro drug release studies were performed using USP dissolution test apparatus I (basket type). The dissolution studies were performed in 900 ml dissolution medium (Phosphate buffer pH 7.4), at 50 rpm maintained at 37 ± 0.5ºC. At predetermined time intervals an aliquot of 10 ml was withdrawn and replenished with fresh medium. Amount of drug in each aliquot was determined using a UV-Spectrophotometer (UV-1800, Shimadzu, Japan) at 225 nm using a suitable blank. All trials were conducted in triplicate and the average (± SD) reading was noted.

Table 6: Mean Particle size of Glimipride Mucoadhesive Microspheres

Formulation	Mean Particle Size (µm)
F1	588
F2	572
F3	645
F4	694
F5	754
F6	526

Table 7: Cumulative percentage drug release of Formulation F1 to F6

Time (hrs)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	9.88	5.89	9.74	7.29	9.24	9.24
2	18.24	12.1	13.81	15.18	14.55	17.8
3	24.51	17.88	20.2	21.21	24.47	23.21
4	31.51	23.41	27.22	27.85	30.6	31.29
5	37.72	27.86	30.92	36.72	36.8	38.25
6	45.72	34.3	39.75	42.99	45.01	41.56
7	52.07	38.22	44.15	49.29	48.75	52.01
8	79.32	44.9	50.86	57	58.39	58.3
9	86.25	50.67	59.33	61.52	63.57	65.55
10	93.03	55.59	63.89	71.94	71.4	69.94
11	100.75	67.37	67.37	76.6	75.06	74.77
24	----	74.22	89.65	98.88	100.3	97.7

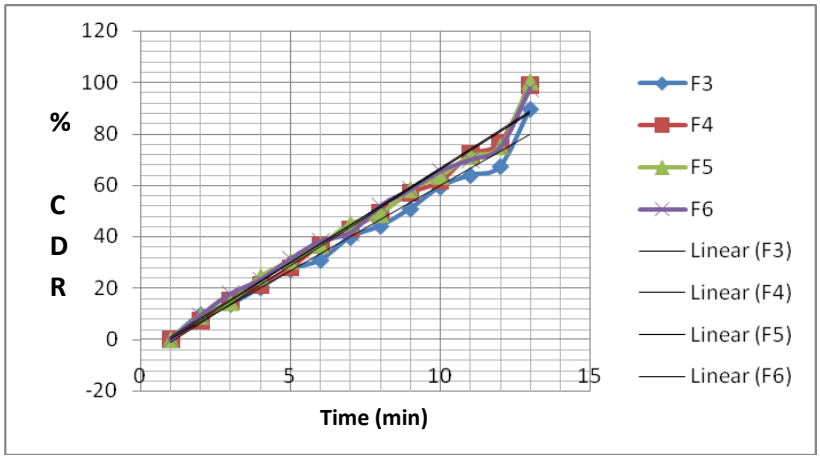

Figure 1: Cumulative percentage drug release of Formulation F1 to F6

CONCLUSION

The Mucoadhesive microspheres of Glimipride were prepared by Emulsion cross linking method using natural polymer Gelatin utilizing temperature change and cross linking agent glutaraldehyde was able to sustain the drug release efficacy.

The evaluation parameters like morphological analysis, drug content, and entrapment efficiency, drug loading capacity, swelling ratio, in vitro mucoadhesion studies and *invitro* drug release studies was done for the microspheres and found to be satisfactory.

The stability study results shows that the formulation F5 was stable at temperature 40 ± 2°C/75% RH at the end of 3 months. The comparative study with the marketed SR formulation results showed that the F5 microsphere formulation had a sustained and prolonged drug release at the end of 24 h than the marketed glimipride SR formulation.

The results of the study revealed that the use of natural polymer Gelatin is an effective strategy for the designing and development of glimipride loaded mucoadhesive microspheres for easy, reproducible and effective oral controlled drug delivery for the treatment of type II Diabetes mellitus.

REFERENCES

1. Saravanan M, Bhaskar K, Gomathinayagam Maharajan, Kalathil Sadasivan Pillai, Development of gelatin microspheres loaded with diclofenac sodium for intra-articular administration. Journal of Drug Targeting, 2011; 19(2):96-103.
2. Ulubayram K, Evoglu I, Hasvici N, Gelatin microspheres and sponges for delivery of macromolecules. Journal of Biomater Applications, 2002; 16:227-41.
3. Bentia S. Microcapsules, New applications and characterization. Lab. Pharma. Prob. Tech, 1984; 32(2):694-701.
4. Gohel MC, Amin AF, Formulation optimization of controlled release diclofenac sodium microspheres using factorial design, Journal of Control Release, 1998; 51:115-22.
5. Sudha Talasila, Senthil kumar KL, Ezhilmuthu and Yamini Pendyala, Formulation and *in vitro* characterization of gelatin microspheres loaded with Lisinopril dehydrate, International Journal of Pharmacology and Clinical Sciences, 2012; 1(2):613-22.
6. Behera BC, Sahoo SK, Dhal S, Barik BB, Characterization of glipizide - loaded polymethacrylate microspheres prepared by an emulsion solvent evaporation method. Tropical Journal of Pharmaceutical Research, 2008; (1):851–879.
7. Mukul Sengupta, Srinivasa Rao SK, Formulation and evaluation of ethyl cellulose microsphere of glipizide, International Journal of Pharmaceutical Research and Bioscience, 2012; 1(3):391-95.
8. Arora Neha, Khattar Himanshi, Parashar Deepa, Arora Nageen, Evaluation of entrapment efficiency of glipizide microsphere, IOSR Journal of Pharmacy, 2012; 2(2):180-81.
9. Shailesh Lokhande, Aruna Birajdar, Amir Quazi, Atul Akunt, Design and Evaluation of glipizide containing micro balloons for floating controlled drug delivery system, Iranian Journal of Pharmaceutical Research, 2012; 2(8):43-50.
10. Gaikwad Abhijit, Pathode Parag, Pawar Amol. Formulation and evaluation of glipizide pellets by using fluid bed coating method. International Journal of Research & Pharmaceutical Science, 2011: 2(2):359-365.
11. Sarode SM, Mittal M, Magar RM, Shelke AD, Formulation and evaluation of floating microsphere of glipizide, Journal of Chemical and Pharmaceutical Research, 2011; 3(3):775-83.
12. Suja C Jayan, Sandeep AV, Mohammed Rifash, Mareema CM, Design and *in vitro* evaluation of gelatin microspheres of Salbutamol sulphate, Hygeia journal of Drugs and Medicines, 2009; 1(1):17-20.