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FORMULATION AND EVALUATION OF CONTROLLED RELEASE OSMOTIC TABLET OF GLIPIZIDE

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ABTRACT

Controlled porosity osmotic pump tablets of Glipizide were prepared and final formula is optimized after formulating four formulations by using different polymers, two factors, osmogent ratio and coating percentage are varied and evaluated based on their effects on drug release rate. Tablets of all formulations are prepared by Direct compression method. As the osmogent concentration and pore former increases, drug release increases in the present work, four fomulations are prepared and F3 formulation is optimized.

KEYWORDS: Osmotic drug delivery, osmosis, coating, zero order release.

INTRODUCTION

Oral route is the most commonly used route for drug administration. Osmotic devices are most promising strategy based system for controlled drug delivery. They are among the most reliable controlled drug delivery system and could be employed as oral drug delivery systems or implantable device.[1,2,3] Osmosis is an aristocratic bio phenomenon, which is exploited for development of delivery systems with every desirable property of an ideal controlled drug delivery system. Osmotic system utilizes the principles of osmotic pressure for delivery of drug**.** Chronic diseases such as diabetes, asthma and heart diseases are often treated using multi-drug therapies, which are vulnerable to incidence of side-effects, poor patient compliance and slow improvement of patients.[4,5] Though controlled drug delivery systems have been available separately for these drugs, a system that can deliver these drugs at a prolonged rate may ensure improved patient compliance and reduce the problems associated with the multi-drug therapy.[6] Elementary osmotic pump, [EOP] essentially contains an active agent having suitable osmotic pressure, contained into a tablet coated with a semi

permeable membrane usually of cellulose acetate [CA].[7] A small orifice is drilled through the coating by LASER or high-speed mechanical driller. When exposed to an aqueous environment, the soluble drug within the tablet draws through the semi permeable coating, resulting in the formation of a saturated aqueous drug solution within the device.[8,9] The membrane is non-extensible and increase in volume due to imbibitions of water raises inner hydrostatic pressure, eventually leading to flow of saturated solution of active agent out of the device through the small orifice.[12]

Glipizide is poorly water-insoluble oral hypoglycemic agent belonging to class-II of biopharmaceutical classification system and is one of the most commonly prescribed drugs for the treatment of patients with type-II Diabetes Mellitus.[13,14] It is practically water-insoluble, but its absolute bioavailability is close to and its dissolution is considered to be rate limiting step [i.e., an effective factor] in its absorption from gastro intestinal tract.[15] It also has a relatively short elimination half-life of 2-4 hours, thereby requiring twice daily dosing in large number of patients, which often leads to noncompliance.[16] The present study was aimed towards the development of swellable elementary osmotic pump tablet of a poorly water insoluble drug.[17]

MATERIAL AND METHOD

Glipizide were gift from Lupin research pune india, HPMC, Lactose monohydrate, cellulose acetate, polyethelene glycol 400, Sodium chloride, ethyl cellulose, magnesium stearate, acetone, methanol, potassium dihydrogen phosphate, sodium hydroxide used were of pharmaceutical grade

Formulation and Development

Drug layer composed of glipizide. Lactose, HPMC are weighed accurately and passed through 40#. Pass Sodium chloride through 60# and mixed properly. The mixed powder was lubricated with Magnesium stearate which is passed through 60#. Blend it in a blender for 5 minutes. The prepared blend was placed in die cavity and compressed with hardness 3. 2-4 kp with diameter 3.68 mm by 8 mm round standard concave punches.[18]

Coating of Tablets

Preparation of Coating Solution

The tablet coatings were applied using dip coating process. The tablet was dip coated in polymer solution consisting of Cellulose acetate phthalate (CAP) dissolved in a solution of

Acetone and a non-solvent. Typically, The Polymer-coating solution consisted of 15% CAP and dissolved in acetone [1S9]. After the tablets were coated with polymeric coating solution, they were air dired for 5 sec and then immersed in water bath for 3 min. After removal from the water bath the tablets were then air dired under ambient conditions for at least 12 hrs [20]. Dry tablets are weighed and the average weight was determined. The % of weight gain was calculated by following equation.

% weigh gain = (Wt-Wo/ Wo) *100

Where,

Wt = weight of tablet after coating

W_o = weight of tablet before coating

Evaluation of Prepared Core Tablets

The tablets were evaluated for in process and finished product quality control tests i.e. appearance, thickness, weight variation, hardness, and friability.

Appearance

The core tablets were checked for presence of cracks, depressions, pinholes, uniformity of the color, smooth polish on the surface of tablet etc if any.

Dimensions

Thickness and diameter of core tablets were measured using Verniar calipers. These values were checked and used to adjust the initial stages of compression.

Uniformity of Weight

20 tablets were weighed individually and average weight was calculated from the total weight of 20 tablets. The individual weights were compared with the permissible limits (±5 %). The percent deviation was calculated using the following formula.

$$\text{Percentage Deviation} = \frac{\text{Individual weight} - \text{average weight}}{\text{Average weight}} \times 100$$

Hardness test

Six tablets were randomly selected from each batch and hardness of each tablet was determined by using Pfizer hardness tester.

Friability test

It is the ability of tablets to withstand mechanical shocks during handling and transportations 6.5gm of tablets were picked from each batch and weighed and placed in the Rochae friability test apparatus and operated at rate of 25 RPM for 4 minutes (or up to 100 revolutions), tablets were de-dusted and weighed again. The loss of tablet weight due to abrasion and fracture was measured in terms of % friability (A value of **<1%F** is acceptable).

$$F = \frac{\text{Initial wt} - \text{final wt}}{\text{Initial wt}} \times 100$$

Drug content estimation

The Glipizide tablets were tested for their drug content. Five tablets were finely powdered required quantities of the powder equivalent to 10 mg of Glipizide were accurately weighed and transferred to a 100ml of volumetric flask. The flask was filled with Phosphate buffer (pH 7.5) solution and mixed thoroughly. The solution was made up to volume and filtered. Dilute 10 ml of the resulting solution to 200 ml with Phosphate buffer (pH 7.5) and measure the absorbance of the resulting solution at the λmax 222 nm using a UV spectrophotometer. The linearity equation obtained from calibration curve as described previously was used for estimation of Glipizide in the tablet formulations.

In-vitro Dissolution studies

In vitro drug release studies of the prepared tablets were conducted for a period of 16 hours using an eight station USP type II apparatus (LAB, India) at 37±0.5 ^{0}C the paddle speed was 50 ± 1 rpm. The dissolution medium used in each flask was 900 ml of buffer media pH 7.4 at different intervals, 10 ml of samples were withdrawn and filter through a whatsman filter paper. The equivalent volume of the medium was added to the dissolution flask.

RESULTS AND DISCUSSION

Table 1: Flow properties of Glipizide.

S. no.	Parameter	Value	Type of Flow
1	Bulk density	0.144	----
2	Tapped density	0.263	----
3	Carr`s index	44.07	Very very poor
4	Hausner`s ratio	1.810	Very very poor
5	Angle of repose	42	Very very poor

Table 2: Average values of pre-compressive parameters of tablet blend.

Formula -tion code	Bulk density (g/ml)	Tapped density (g/ml)	Carr`s index (%)	Hausner`s ratio	Angle of repose
F1	0.416	0.463	10.1511	1.112	25
F2	0.403	0.465	13.3333	1.1414	27
F3	0.402	0.448	9.4803	1.114	25
F4	0.430	0.467	7.905	1.086	23

Evaluation of core Tablets

The tablet formulations were subject to various post-compressive evaluation tests, such as, Hardness, Friability and Weight variation, drug content uniformity.

Weight variation test

It was carried out as per official method and the average percentage deviation of all the formulation was found to be within the limit (as per USP standard).

Content uniformity

It also carried out as per official method and it was found that all batches shows good content uniformity. The values for all the formulations were in the ranges from 93.12 to 98.23%.

Hardness test

States that all the formulations were found in the range 8to 10 kp.

Friability test

Compressed tablets have lost less than 1% of their weight is generally considered acceptable. All the formulations have less than 1% friability.

Table 3: Evaluation results of the compressed tablets.

Formula-tion code	Thickness (mm)	Weight variation (mg)	Hardness test (kp)	Friabil -ity test (%)	Content uniformity
F1	4.71± 0.04	340.2 ± 2.47	9.11± 0.26	0.3	94.15 ± 0.48
F2	4.69 ± 0.03	338.7 ± 2.30	9.12± 0.33	0.1	95.03 ± 2.15
F3	4.70 ± 0.01	340.1 ± 2.62	8.82 ± 0.26	0.2	98.23 ± 2.32
F4	4.67 ± 0.01	339.7 ± 3.26	9.18 ± 0.33	0.4	97.4 ± 1.51

The tablets of 4 formulations were tested and analysed for thickness, weight variation, hardness, friability, content uniformity

Table 4: Cumulative % of drug release.

Time (hr)	F1	F2	F3	F4
0	0	0	0	0
1	100	12.12	16.19	19.11
2		14.96	24.96	22.58
4		26.78	36.78	46.12
6		36.79	56.81	52.51
8		58.59	79.14	69.1
10		81.54	99.23	89.23

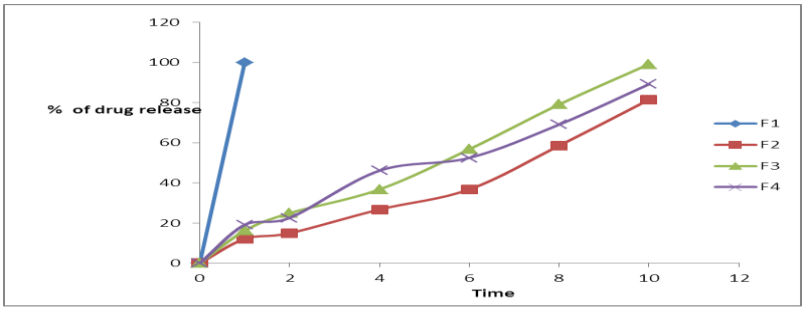

Figure 1: In vitro drug release of all formulations.

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-3 after 30 days. Parameters quantified at various time intervals were shown;

Table 5: Stability Studies of Optimized Formulation.

Formulation Code	Parameters	Initial	1st Month	Limits as per Specifications
F-3	25^0C/60%RH % Release	99.59	99.50	Not less than 85 %
F-3	30^0C/75% RH % Release	99.42	99.52	Not less than 85 %
F-3	40^0C/75% RH % Release	99.60	99.54	Not less than 85 %

Table 6: Results of stability studies of optimized formulation F-3.

S. no.	Time (Hrs)	F-3 1M
1	0	0
2	1	5.71
3	2	7.20
4	3	8.5
5	4	9.60
6	5	10.1
7	6	72.2
8	7	78
9	8	99.60

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