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Research Article

DESIGN AND CHARACTERIZATION OF FLOATING TABLETS OF ANTI-DIABETIC DRUG

M Seth*, DS Goswami, H Dhaliwal, N Uppal, S Kashyap and KD Sharma

S.D. College of Pharmacy, Barnala, 148101, Punjab, India.

ABSTRACT

The objective of the study is to formulate and evaluate floating tablet of Pioglitazone employing guar gum, a natural gum in comparison to gellan gum which is also a natural polymer. Sodium bicarbonate was added as gas generating agent, produced carbon dioxide in the gastric acid environment which helps to maintain the buoyancy. Addition of bees wax has significantly enhanced the buoyancy of the tablets formulated with both the two polymers. Gelatin which is used as binder provides strength to the tablet. The floating tablets of Pioglitazone were prepared by direct compression method. The prepared tablets evaluated in terms of pre-compression parameters, physical characteristics, *in vitro* drug release, floating duration and floating lag time. The formulation optimized for different concentration of guar gum and gellan gum. The results of *in vitro* drug release studies showed that optimized formulation (F13) could release the drug (98%) for more than 12 hrs and remain buoyant for more than 12 hrs.

Keywords: Anti-diabetic drug, floating tablet, guar gum, gellan gum.

INTRODUCTION

Oral route is the most convenient and extensively used route for drug administration. Over the years the oral dosage forms have become sophisticated with development of controlled release drug delivery system (CRDDS).[1]

In the development of oral controlled drug delivery system other main challenge is to modify the GI transit time. Prolong gastric retention increases the duration of drug release, improves bioavailability and also beneficial for local action.[2]

The prolongation of the gastric residence time of delivery devices could be achieved by preventing their passage through the pylorus or by maintaining them in buoyant fashion in gastric juice. Floating drug delivery system (FDDS) is most widely used system to prolong the GRT to obtain sufficient drug bioavailability.[3]

Pioglitazone is an effective oral anti-diabetic agent that belongs to the thiazolidonediones drug class and is widely prescribed in the management of non-insulin dependent (Type II) diabetes mellitus. It is poorly soluble in aqueous fluids and is majorly absorbed from stomach. Dosage forms that are retained in the stomach would increase its oral bioavailability and efficacy. Pioglitazone has a short biological half-life of 3-6 hrs and is eliminated rapidly. So the sustained release floating tablet formulations are needed for Pioglitazone to prolong its duration of action and to increase its oral bioavailability and to improve patient compliance.[4]

Therefore, in the present study it was aimed to design gastroretentive floating tablets of Pioglitazone by using various natural and synthetic polymers as tablet matrix formers, sodium bicarbonate as gas generating agent, bees wax as floating enhancer.

MATERIALS AND METHODS

Materials

Pioglitazone hydrochloride was purchased from Balaji drug, Gujrat, guar gum was purchased from Central Drug House (P) Ltd. New Delhi, gellan gum was purchased from Sanjay Biological Museum, Amritsar and sodium bicarbonate ($NaHCO_3$), bees wax, gelatin, talc, mg. stearate, Di-basic calcium

phosphate were also purchased from Central Drug House (P) Ltd., New Delhi.

Methods

Flow properties of powder blend

Angle of repose

The angle of repose of powder blend was determined by the funnel method. Accurately weighed powder blend was taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation[5]

$$\tan \theta = h/r$$
$$\theta = \tan^{-1} (h/r)$$

Where, H = height of the pile, R = radius of the base of pile

Bulk density and tapped density

Both bulk density (BD) and tapped density (TD) was determined. A quantity of 2 gm of blend powder previously shaken to break any agglomerates formed was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm
at second intervals. Tapping was continued until no further change in volume was noted. The bulk density and tapped density were calculated using the following formula:

$$\text{Bulk density} = W / V_0$$
$$\text{Tapped density} = W / V_f$$

Where, W = weight of the powder, V_0 = initial volume, V_f = final volume

Compressibility index

The Compressibility index of the powder blend was determined by Carr's compressibility index. The formula for Carr's Index is as below[6]

Carr's Index (%) = [(TD-BD) x100]/TD

Formulation of Pioglitazone floating matrix tablets

Initially, different floating matrix tablets containing 30 mg of Pioglitazone hydrochloride were prepared by direct compression of different homogenous blends containing guar gum (natural gum) and gellan gum (natural gum) in different ratios individually in order to achieve the desire drug release profile. Sodium bicarbonate was used as gas generating agent at 34% strength in each case. Bees wax was used as floating enhancer at 6% and gelatin was used as binder at 10% concentration respectively in each formulation. All the ingredients were passed through # 60 mesh sieves separately. The drug, polymer and diluents were mixed according to the formula given in table no.1 to get a uniform mixture. Then add Mg. stearate and talc as glident and lubricant and thoroughly blended for 3 mins. Finally the mixture was compressed using rotary punching machine (Rimek, Karnavati, India) using a 11mm punch. Compression force of machine was adjusted to obtain the hardness for each formulation.

Evaluation parameters of the tablet

Physical characterization

Shape of tablets

The Compressed tablets were examined under the magnifying lens for check the shape.

Tablet dimentions

Thickness and diameter were measured using a calliberated vernier caliper. Five tablets of each formulation were taken randomly and thickness was measured individually.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Five tablets were randomly picked and hardness of the tablet was determined.

Weight variation test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. Twenty tablets were selected randomly and weighed individually to check for weight variation. The following percentage deviation in weight variation was allowed show in the table[7]

Percentage (%) deviations can be check by the given below

%Maximum positive deviations = $(W_H - A/A) \times 100$
%Minimum negative deviations = $(A - W_L/A) \times 100$

Where, W_H = Highest wt. in mg, W_L = Lowest wt. in mg, A = Average wt. of tablet

Friability Test

The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed (w_0 initial) and transferred into friabilator was operated at 25 rpm for 4 mins or run up to 100 revolutions. After that the tablets were weighed again (w).[5]

The % loss in weight was then calculated by:-

% Loss in weight = 100 (1-w/w_0)

Tablet density

Tablet density is an important parameter for floating tablets. The tablet will float when its density less than 0.1(N) HCl. The density was determined using following formula[8]

$$V = \pi r^2 h$$

$$d = m/v$$

V = volume of the tablet (cc)
r = radius of the tablet (cm)
h = crown thickness of the tablet (cm)
m = mass of the tablet (mg)

Determination of swelling index

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in 100 ml beaker of 0.1 (N) HCl and after 1, 2, 4, 6 and 8 hrs each beaker containing tablet was withdrawn, blotted with tissue paper to remove the excess water and weighed on the analytical balance. The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula.[9]

Swelling index = [(weight of wet tablet–weight of dry tablet) /Dry weight of tablet] x100

***In vitro* buoyancy study**

The *in vitro* buoyancy was carried out by determining floating lag time. The tablets were placed in a 100 ml glass beaker containing 0.1(N) HCl. The time required for the matrix tablet to rise from bottom to the surface of the glass beaker and float on surface was determined. Total floating time was measured as buoyancy lag time during *in vitro* dissolution studies.

***In vitro* drug release study**

In vitro drug release studies for all the formulations were carried out using dissolution apparatus USP II type (paddle method). The dissolution media used 900ml 0.1(N) HCl, maintained at 37±0.5°C and the media was rotated at 50 rpm. Aliquots were withdrawn at different time intervals, filtered and analyzed spectrophotometrically at 269 nm for cumulative drug release. The dissolution studies were conducted in triplicate and the mean values were plotted against time.[10]

RESULTS AND DISCUSSIONS

As the flow property of the powder mixture is important for the uniformity of the mass of the tablets, therefore bulk density, tapped density, angle of repose and compressibility of the powder were analyzed before compression of the tablets. Angle of repose and compressibility index ranged 26.5±0.52^0 to 27.8±0.66^0 and 11.11±0.44 to 20±0.08% respectively. The results of bulk density and tapped density also ranged from 0.56±0.21 to 0.68±0.10 gm/cm^3 and 0.67±0.16 to 0.83±0.09 gm/cm^3 respectively. All these data indicate that the flow property of powder blends was satisfactory (Table no.2).

The hardness of all the formulations were in the range of 4.37±0.03 to 6±0.03 (kg/cm^2) and %weight loss in the friability test was found to be in the range of 0.31±0.04 to 0.55±0.01% this indicates sufficient hardness and has good mechanical resistance of the tablets. Thickness and diameter of formulated tablets were of 2.87±0.024 to 4±0.034 mm and 9.01±0.28 to 11.03±0.33 mm respectively. The variations in weight were within the range of -0.204±1.21 to 0.534±1.2% complying with pharmacopoeial specifications (±7.5%). The drug content varied between 96.16-98.48% in all tablets with low standard deviation indicating content uniformity of the prepared batches. All the physical properties are within the pharmacopoeial specifications and the above parameters are given in the Table no.3. The swelling index of all the formulations given in the Fig no.1 to 3.

All the tablets were prepared by effervescent approach. Sodium bicarbonate was added as a gas generating agent. $NaHCO_3$ induced carbon dioxide generation in the presence of dissolution medium [0.1(N) HCl, pH 1.2]. Bees wax used as floating enhancer in the formulation. The combination of sodium bicarbonate and bees wax provided desired floating ability. Floating lag time and duration was described in the below table no.4. Tablet density was found to be less than 1. It was observed that tablets prepared with gellan gum shows better floating behavior as compare with guar gum.

The results of the *in vitro* drug release studies of Pioglitazone hydrochloride floating tablets in 0.1(N) HCl graphically shown in Fig no.4 and 5. All formulations (F1-F14) contained same amount of Pioglitazone and varying the polymers in different concentrations. By comparing the values of *in vitro* dissolution studies (Fig no. 4 and 5) the higher drug release was shown by F7 and F13 (containing equal amount i.e 1:7) within 12 hrs but the highest drug release was shown by F13 i.e 97.111%. A significantly higher rate and extent of drug release was observed from the batches based on guar gum. The release was found to be more controlled in the tablets with higher grade and higher proportions of the polymer at a definite level.

Table 1: Composition of floating tablet of Pioglitazone hydrochloride

Ingredients	Formulation code													
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14
Pioglitazone hydrochloride	30	30	30	30	30	30	30	30	30	30	30	30	30	30
Guar gum	60	90	120	150	180	210	240	---	---	---	---	---	---	---
Gellan gum	---	---	---	---	---	---	---	60	90	120	150	180	210	240
Gelatin	35	35	35	35	35	35	35	35	35	35	35	35	35	35
Sodium Bicarbonate	120	120	120	120	120	120	120	120	120	120	120	120	120	120
Bees Wax	21	21	21	21	21	21	21	21	21	21	21	21	21	21
DCP	80	50	20	---	---	---	---	80	50	20	---	---	---	---
Mg.Stearate	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2	2	2

Table 2: Flow properties of the powder blend

Formulation Code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of repose (θ)	Compressibility Index (%)
F1-F7	0.56±0.21-0.67±0.11	0.67±0.16-0.80±0.38	26.5±0.52-27.5±0.94	11.11±0.44-20±0.08
F8-F14	0.60±0.07-0.68±0.10	0.69±0.11-0.83±0.09	26.7±0.58-27.8±0.66	11.50±.1.54-18.07±0.06

Table 3: Evaluation parameters of the tablets of Pioglitazone hydrochloride

Formulation Code	Diameter (mm)	Thickness (mm)	Hardness (kg/cm^2)	%Loss in wt.	%Weight variation	Drug content (%)
F1	9.01±0.28	3.32±0.021	4.44±0.04	0.31±0.04	0.534±1.2	98.48±0.007
F2	9.57±0.29	3.39±0.034	4.37±0.03	0.34±0.03	0.231±2.11	98.37±0.005
F3	9.79±0.02	3.32±0.032	4.89±0.05	0.48±0.07	0.324±1.02	98.28±0.006
F4	9.89±0.56	3.42±0.023	5.11±0.05	0.52±0.04	0.431±1.03	97.87±0.001
F5	9.66±0.66	3.62±0.045	5.27±0.07	0.51±0.07	0.45±2.03	97.47±0.006
F6	10.55±0.89	3.07±0.12	5.88±0.04	0.45±0.04	0.251±2.03	97.77±0.007
F7	11.01±0.56	2.98±0.032	6±0.03	0.46±0.07	0.221±3.02	97.27±0.003
F8	9.07±0.21	3.39±0.21	4.55±0.13	0.37±0.06	-0.204±1.21	98.18±0.006
F9	9.1±0.11	3.42±0.034	4.59±0.24	0.45±0.04	-0.245±1.34	97.77±0.005
F10	9.27±0.23	3.47±0.043	4.66±0.05	0.44±0.03	0.289±2.11	98.08±0.010
F11	9.25±0.13	4±0.034	4.42±0.09	0.42±0.04	0.278±1.22	97.27±0.003
F12	9.22±0.12	3.88±0.012	4.86±0.23	0.64±0.07	0.345±1.09	97.07±0.004
F13	10.88±0.15	3±0.034	5.57±0.05	0.54±0.02	0.311±1.08	96.76±0.003
F14	11.03±0.33	2.87±0.024	5.66±0.04	0.55±0.02	0.276±1.22	96.16±0.005

Table 4: In vitro buoyancy study of floating tablet of formulations F1-F14

S. No.	Formulation Code	Tablet density	Floating lag time (min)	Floating duration (hrs)
1	F1	0.98±0.01	15	<12
2	F2	0.98±0.01	15	<12
3	F3	0.97±0.01	13	<12
4	F4	0.94±0.02	11	<12
5	F5	0.90±0.03	10	<12
6	F6	0.89±0.03	9	>12
7	F7	0.92±0.02	10	>12
8	F8	0.97±0.08	15	<12
9	F9	0.94±0.05	14	<12
10	F10	0.95±0.03	13	<12
11	F11	0.96±0.03	10	<12
12	F12	0.98±0.02	9	>12
13	F13	0.96±0.01	8	>12
14	F14	0.94±0.03	9	>12

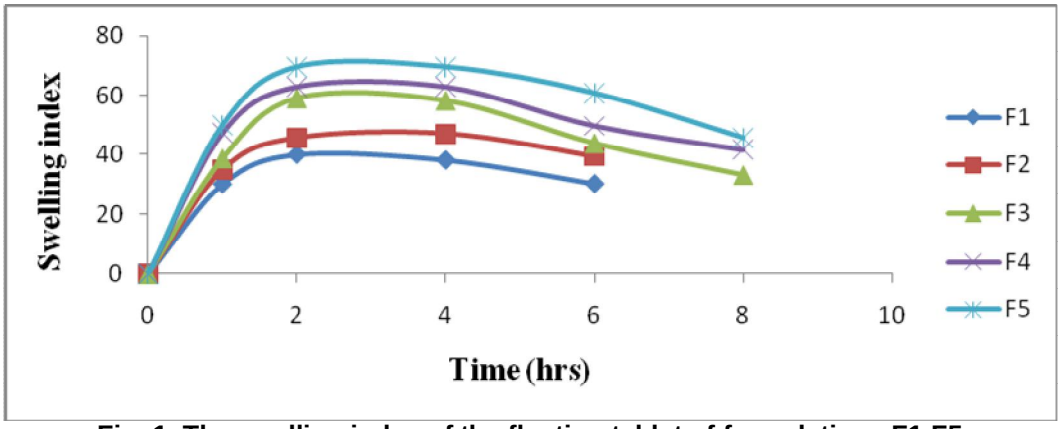

Fig .1: The swelling index of the floating tablet of formulations F1-F5

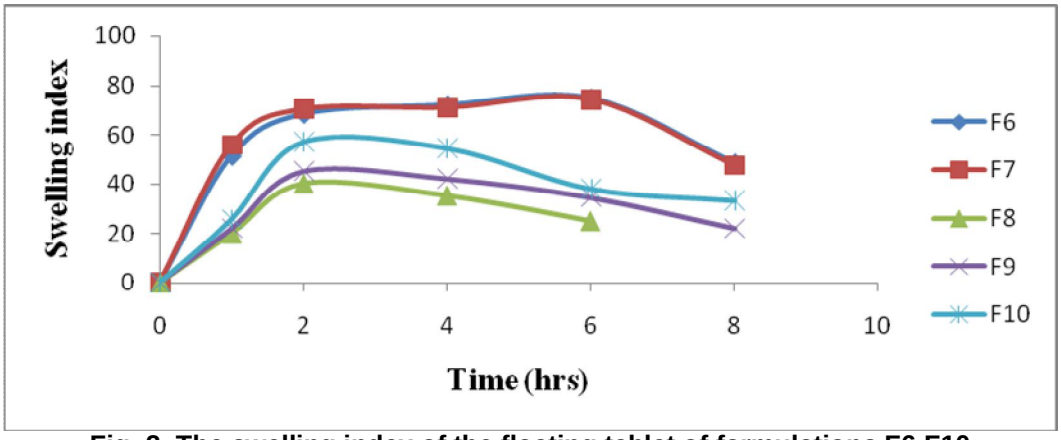

Fig. 2: The swelling index of the floating tablet of formulations F6-F10

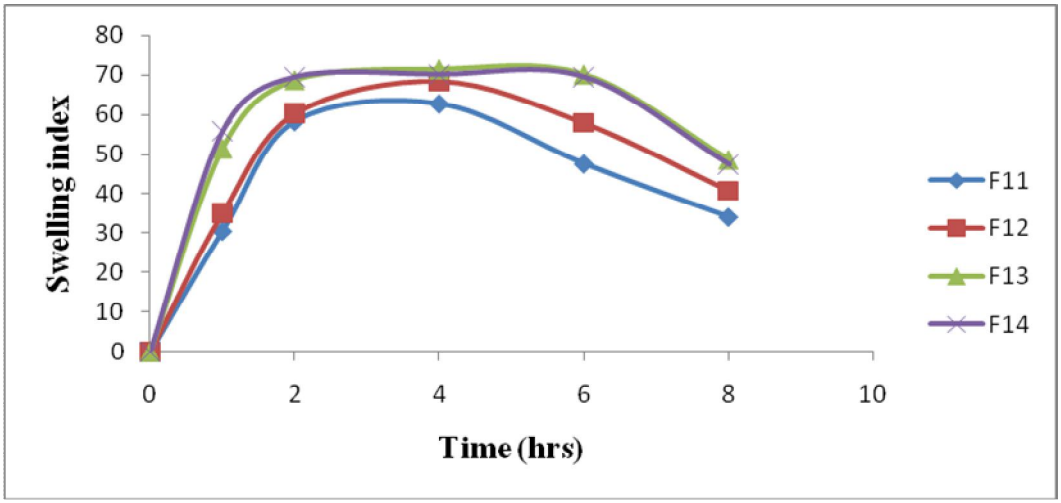

Fig. 3: The swelling index of the floating tablet of formulations F11-F14

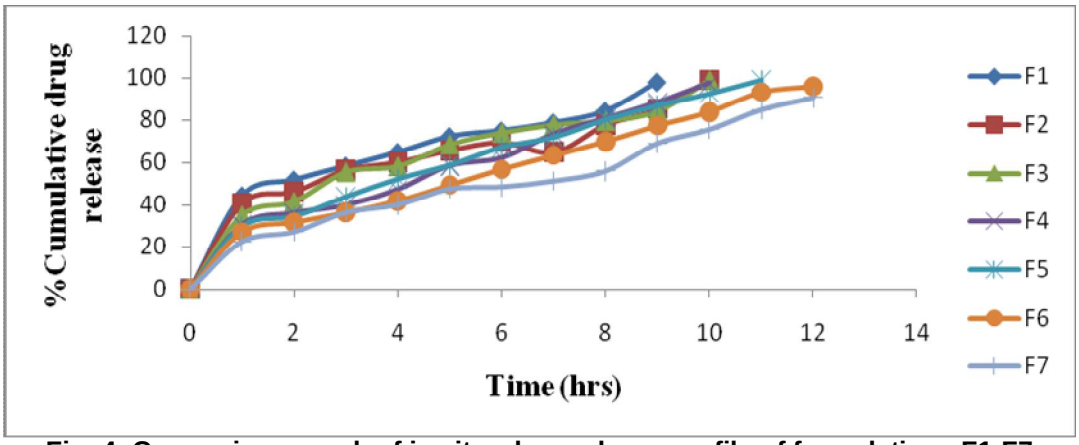

Fig. 4: Comparison graph of in vitro drug release profile of formulations F1-F7

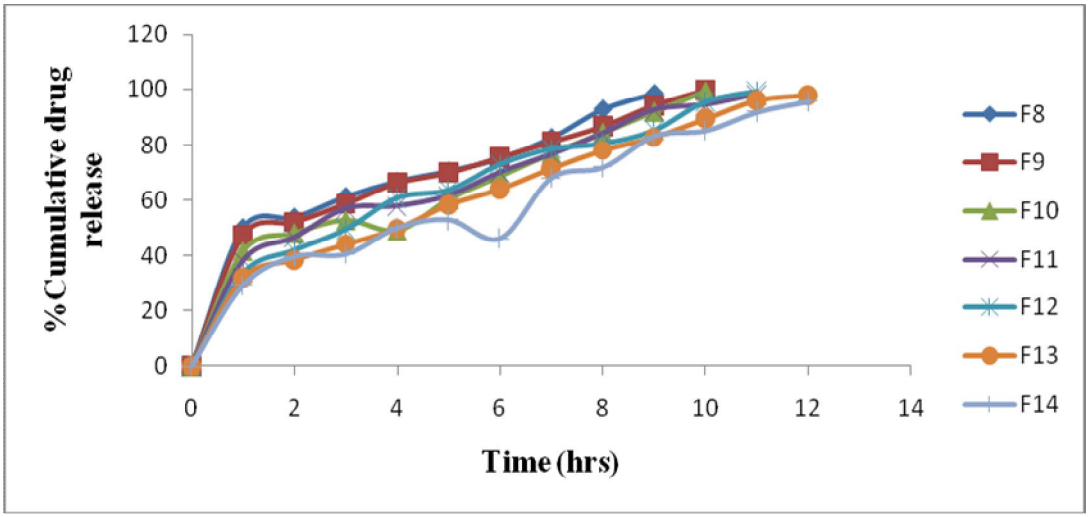

Fig. 5: Comparison graph of in vitro drug release profile of formulations F8-F14

CONCLUSION

In the present study Pioglitazone floating tablets by direct compression method using polymers like guar gum and gellan gum was developed. Formulation F13 containing gellan gum showed controlled drug release for more than 12 hrs, emerging as best formulation.

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