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ORIGINAL RESEARCH ARTICLE

Formulation and Evaluation of Atenolol Floating Tablets Using Different Polymers: Guargum, Sodium Alginate, Hpmc100cps and Carbopol940

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ABSTRACT:

The objective of the present study was to prepare Floating tablets of Atenolol with best polymer. These were developed to prolong the gastric residence time and increase the drug bioavailability .The Tablets were prepared by direct compression technique, using polymers such as Guar gum, Sodium alginate, HPMC-100CPS, Carbopol940, and other standard excipients. Tablets were evaluated for a physical characteristic was evaluated. Hardness, floating capacity, thickness, weight variation and dissolution. Among four polymers studied, Sodium alginate had shown more drug release. Among eight formulations, one (F6) was found to be best of all the trials showing that the drug release matches the brand product.

Key words: Floating Tablets, Gastric Residence Time, Effervescent, Floating Drug Delivery Systems (FDDS)

INTRODUCTION:[1,2]

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs .Different types of dosage forms were developed for oral delivery to over come the problems in the release of drug and stability of the drug in invitro conditions (gastric pH,gastric secretions etc).One such formulation is floating tablets.Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate[3]. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach [4]. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations [5]. Advantages include improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site [6], Delivery of drugs for local action in the stomach. , Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate [7], Treatment of gastrointestinal disorders such as gastro-esophageal reflux. , Simple and conventional equipment for manufacture [8].

Types Of Floating Drug Delivery Systems (Fdds): [9,10]

Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of FDDS which are:

1. Effervescent System:-

Effervescent systems include use of gas generating agents, carbonates (ex. Sodium bicarbonate) and other organic acid (e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide (CO_2) gas, thus reducing the density of the system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporates at body temperature. These effervescent systems further classified into Gas Generating systems and Volatile Liquid/Vacuum Containing Systems.

2. **Non-Effervescent Systems:**

The Non-effervescent FDDS based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as Polycarbonate,

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Polyacrylate, Polymethacrylate, polystyrene as well as bioadhesive polymer such as Chitosan and Carbopol. The various types of this system are Single Layer Floating Tablets, Bilayer Floating Tablets,Alginate Beads and Hollow Microspheres:

Aim of the Work:

Aim of the study is to formulate and evaluate Atenolol floating tablets using different polymers: Guargum, Sodium alginate, HPMC100CPS, Carbopol940 in different ratios.

Objective:

The objective of the present study was to develop floating tablets of Atenolol to prolong gastric residence time and increase drug bioavailability. Atenolol was chosen as a model drug because it is better absorbed in stomach than in lower gastro intestinal tract .It has low elimination half life and basic type of drug.

Plan of Work

1. Preparation of powders
2. Compression of powders into tablets
3. Tablet evaluation
- Thickness
- Hardness
- Friability
- Uniformity of weight
- Drug content
- In vitro dissolution
- In vitro buoyancy studies

Methodology:

1. Formulation of Atenolol floating tablets using different polymers: Guargum, Sodium alginate, Corbopol - 940, HPMC100CPS, and excipients like sodium bicarbonate, Magnesium. State, DCP, Lactose, and talc in different rations.
2. Compression of the powders into floating tablets of Atenolol. [11] Evaluation of floating tablets of Atenolol for physical appearance, hardness, thickness, friability, weight variation, content uniformity test[12], and in-vitro buoyancy studies[13].
3. In vitro dissolution studies for all the formulations of Atenolol floating tablets.

Materials Used:

Atenolol, Guargum, Sodium alginate, HPMC, Corbopol, Sodium bicarbonate, Talc, Mag.stearate, Lactose and Di calcium phosphate.

Table 1: Composition Of Different Formulations (F1,F2,F3,F4,F5,F6,F7&F8)

For.Code	Drug (mg)	Guargum (mg)	Sod. Alginate (mg)	HPMC 100cps(mg)	Corbopol-940 (mg)	Mag.stearate (mg)	Talc (mg)	$NaHCO_3$ (mg)	Lactose (mg)	DCP (mg)
F1	50	100	……	……	…….	3	6	30	…….	111
F2	50	100	……	……	…….	3	3	60	134	…….
F3	50	200	……	……	…….	3.5	3.5	35	…….	58
F4	50	200	……..	……	…….	3.5	3.5	70	23	.....
F5	50	……	200	……	…….	3.5	3.5	70	…….	23
F6	50	……	200	……	…….	3.5	3.5	70	62	…….
F7	50	……	……..	200	…….	3.5	3.5	70	…….	23
F8	50	……	……..	……..	200	3.5	3.5	70	…….	23

Formulation and Preparation of Atenolol Floating Tablets:

All the formulations were prepared by direct compression method[14] using different polymers in various ratios (designated as F-1 to F-8).

Procedure:

1. Atenolol and all other ingredients were individually passed through sieve ≠ 60.
2. All the ingredients were mixed thoroughly for 15 min.
3. The powder mixture was lubricated with talc.
4. The tablets were prepared by using direct compression method.

Table 2 : Quality control parameters of Atenolol floating tablets.

Formulation No:	Avg.Wt mean±SD (n=20)	Hardness Kg/cm^2(n=3)	%Friability (n=20)	%Drug content(n=3)	Buoyancy lag time (min)	Total floating time (hrs)
F_1	297.4±0.5	4.77±0.19	0.111	90.2±2.4	.....	8
F_2	296.7±0.5	7.93±0.10	0.582	103±1.5	29	8
F_3	341.4±0.2	7.7±0.17	0.468	101.0±1.8	8	8
F_4	344.9±0.3	8	0.170	97.2±6.2	15	8
F_5	346.1±0.6	7.70±0.42	0.167	98.2±2.0	4	8
F_6	391.2±0.8	7.87±0.09	0.289	100.1±1.0	3	8
F_7	343.4±0.3	7.72±0.18	0.176	92.87±2.8	30	8
F_8	344.8±0.3	7.92±0.09	0.160	106.20±1.0	30	8

Evaluation of Tablets: [15,16,17,18]

The formulated tablets were evaluated for the following physicochemical characteristics: [19]

General Appearance:

The formulated tablets were assessed for its general appearance and observations were made for shape, color, texture and odor.

Hardness test:

Hardness of the tablet was determined by using the Monsanto hardness tester (n=3or5) the lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

Weight Variation:

20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage. **Friability Test:**

20 previously weighed tablets were placed in the apparatus. Which was given 100 revolutions and the tablets were reweighed. The percentage friability was calculated by using the following formula,

Percentage friability = (initial weight - final weight) / initial weight × 100.

Drug content: [20]

20 tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 100 mg of Atenolol was transferred in to a 100 ml volumetric flask and the volume was made up with0.1N HCl. Further 1ml of the above solution was diluted to 10 ml with 0.1N HCl and absorbance of the resulting solution was observed at 275nm.

***In vitro* Buoyancy studies:**[21]

The in vitro buoyancy was determined by floating lag time, and total floating time. (as per the method described by Rosa et al) The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as the floating lag time (FLT) and the duration of time the tablet constantly floats on the dissolution medium was noted as Total Floating Time respectively (TFT).

***In vitro* Dissolution Studies of Tablets:**[22]

Dissolution parameters:

Apparatus --USP-II, Paddle Method
Dissolution Medium -- 0.1 N HCl (p^H 1.2)
RPM -- 50 rpm
Sampling intervals (hrs) -- 0.5,1,2,3,4,6,8
Temperature -- 37°c ± 0.5°C

Dissolution Study:

As the floating tablets were evaluated for dissolution rate in 0.1 N HCl (pH 1.2).

Procedure:

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°C ± 0.5°C. Tablet was placed in the vessel and the vessel was covered, the apparatus was operated for 8hrs at 50 rpm. At definite time intervals of 5 ml of the dissolution fluid was withdrawn, filtered and again 5ml blank sample was replaced. Suitable dilutions were done with dissolution fluid and analyzed spectrophotometrically at 275 nm using a UV-spectrophotometer (Analytical).

Table 3 : Dissolution Data Of Atenolol Tablets Prepared With Guargum

Cumulative % Drug Dissolved (n=3±SD)		
Time	**F_1**	**F_2**
0.5	19±0.65	45.4±0.84
1	20±0.77	57.3±0.94
2	20.18±0.77	60.9±0.35
3	28.37±0.25	68.9±0.66
4	36.2±0.95	80.5±0.77
6	40.5±0.46	90.3±0.74
8	50.1±0.60	101.5±1.03

Fig 1: Dissolution profile of Atenolol floating tablet (F_1, F2) formulations.

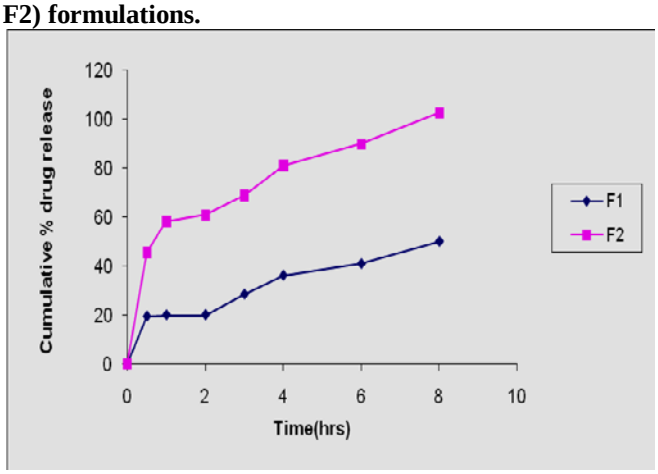

Table 4: Dissolution Data Of Atenolol Tablets Prepared With Guargum

Cumulative % drug dissolved (n=3±SD)		
Time	**F_3**	**F_4**
0.5	40.92±0.46	45.6±0.84
1	42.40±0.89	58.1±0.74
2	59.22±0.74	60.4±0.79
3	66.15±1.00	68.1±0.98
4	74.63±0.52	88.9±1.05
6	88.90±1.05	90.2±0.74
8	89.94±0.95	102.4±1.08

Fig2: Dissolution Profile of Atenolol Floating Tablets (F3, F4) Formulations.

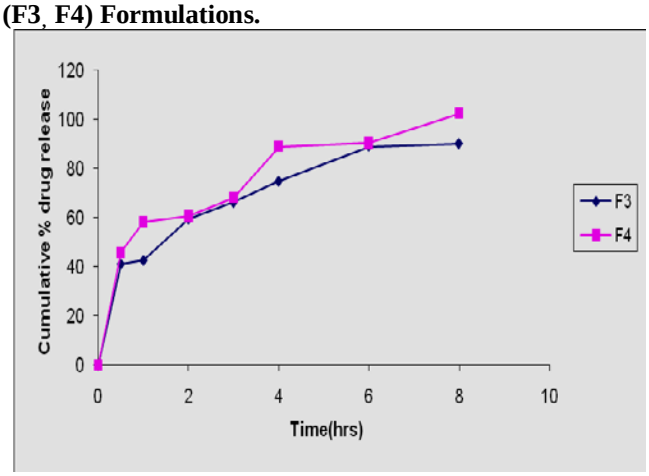

Fig3: Dissolution profile of atenolol floating tablet (F5, F6, Brand)Formulations

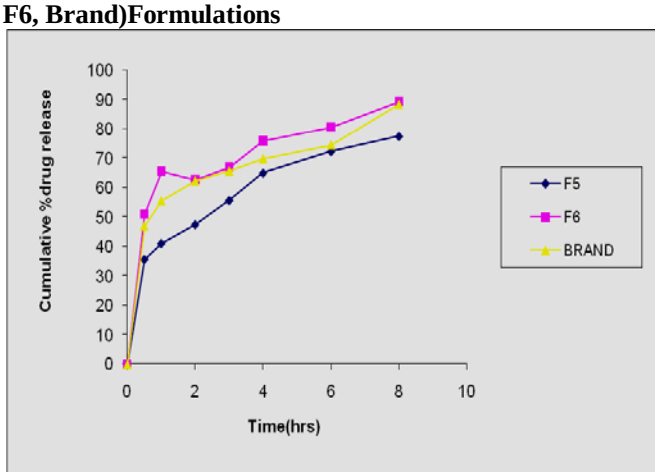

Table 5: Dissolution data of atenolol tablets prepared with Sodiumalginate

Cumulative % drug dissolved (n=3±SD)			
Time (hrs)	**F5**	**F6**	**BRAND**
0.5	35.6±0.62	51.1±0.85	47.2±1.0
1	41.2±0.68	58.7±0.95	55.6±0.74
2	47.5±0.41	62.6±0.8	62.4±0.91
3	55.0±0.72	66.3±0.90	65.74±0.84
4	65.0±0.51	75.8±0.68	69.88±0.90
6	72.3±0.60	80.59±0.80	74.63±0.52
8	77.5±0.80	89.23±0.62	88.45±0.88

Table 6: dissolution data of Atenolol tablets prepared with Hpmc100cps (f_7) & carbopol940(f_8)

Cumulative % drug dissolved (n=3±SD)		
Time	**F_7**	**F_8**
0.5	50.4±0.68	45.38±0.84
1	54.88±0.78	47.04±0.50
2	60.12±0.81	54.32±0.58
3	68.11±0.58	62.31±0.88
4	77.03±1.08	75.25±I.0
6	86.32±0.58	81.05±0.85
8	90.15±0.74	84.19±0.65

Fig 4: Dissolution Profile of Atenolol Floating Tablets (F7, F8) For mulations.

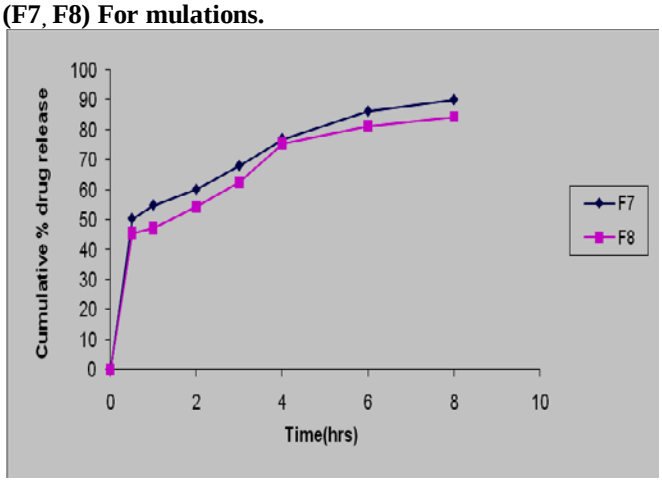

Table 7: Coefficient of correlation (r^2) values of different Formulations of Atenolol floating tablets. [23]

Formulation	Zero order	First order	Higuchi's[5]	Peppa's[6]
F1	0.983	0.984	0.924	0.978
F2	0.985	0.975	0.958	0.985
F3	0.959	0.982	0.985	0.984
F4	0.959	0.969	0.972	0.973
F5	0.975	0.992	0.993	0.987
F6	0.982	0.988	0.996	0.983
F7	0.979	0.994	0.991	0.973
F8	0.968	0.981	0.978	0.965
BRAND	0.974	0.962	0.985	0.986

DISCUSSION:

The objective of the present study was to prepare Floating tablets of Atenolol. These were developed to prolong the gastric residence time[24] and increase the drug bioavailability. Atenolol was chosen as a model drug because it is better absorbed in stomach than the lower gastro intestinal tract. The Tablets were prepared by direct compression technique[25], using polymers such as Guar gum, Sodium alginate, HPMC-100CPS, Carbopol940, and other standard excipients. Tablets were evaluated for a physical characteristic was evaluated. Hardness, floating capacity, thickness and weight variation [26].

Totally eight different formulations of Atenolol were prepared by using four different polymers like Guargum, sodium alginate , HPMC 100CPS ,Corbopol 940, and diluents like lactose, Declaim phosphate in different concentrations. The amount of drug released from all the formulations depends on the concentration of polymer used. [27] Finally the amount of drug released from all the formulations was to be found in the decreasing order.

Sodium Alginate > HPMC100CPS > Corbopol 940 > Guar gum

Among all these formulations the F_6 formulation includes ingredients Sodium alginate with lactose shows the better results (drug content and invitro dissolution studies[28]).The result was compared with branded formulation.The result was satisfactory (Table 5) .

CONCLUSION:

Among eight formulations of floating tablets of Atenolol developed F6 formulation was found to be best of all the trials showing that the drug release matches the brand product. F6 formulation (sodium. Alginate with lactose) can successfully be employed as a controlled release floating drug delivery system.

REFERENCES:

1. Brahmankar D.M, Jaiswal S.B, Biopharmaceutics and Pharmacokinetics a treatise, 1st ed. Vallabh prakashan; New Delhi: (1995) p.64-70.
2. Chein Y.W, Novel Drug DeliverySystems, 2nd ed.: Marcel Dekker; New York: (1992.p.4-56.
3. Gennaro R.A. Remington,The Science and Practice of Pharmacy., 20th ed. New york : Lippincott Williams: (2000) P.1045.
4. Banker G.S, Rhodes C.T, Modern Pharmaceutics. 3rd ed. Marcel Dekker, New York: (1996) P.678-721.
5. Vyas S.P, Khar R.K, Controlled Drug Delivery: Concepts and Advances, 1st ed. Vallabh prakashan, New Delhi: (2002) P.345-376.
6. P.G.Yeole, Floating Drug Delivery System: Need and Development, Ind. J. Pharm Sci., (2005): 67(3); 265-272.
7. Shweta Arora, Floating Drug Delivery: A Review, AAPS Pharmscitech; 47(11); p.268-272. (2005)
8. Libo Yang, A New Intragastric Delivery System for the Treatment of H.Pylori associated with gastric ulcers, Elsevier J. of controlled release., Apr(1999): 34 (5); p. 215-222.
9. Ross and Wilson, Anatomy Physiology and Health Education. 9th ed. Churchil Livingston, p. 295-311. (1998).
10. Wilson K.R.W, Waugh A. Anatomy and physiology in Health and Illness, 9th ed. Churchill Livingstone: London: (1996). P. 342-345.
11. Garima Chawla, Gupta, Pharmaceutical technology; 23(9); p.39-48. July (2003).
12. Desai S, Bolton S. A Floating Controlled Release System: In-vitro and In-vivo evaluation, J. Pharm. Res., p.1321-1325. (1993).
13. Garg S, Sharma S. Gastroretentive Drug Delivery Systems, Pharmatech, p.160-164. (2003).
14. Dr.Jose, Khalid Shah, Gastroretentive Drug Delivery System, Business brief, Pharmtech., p. 165-173.(2003).
15. Deshpande A.A, Shah N.H, Rhodes C.T, Development of a Novel Controlled Release System for Gastric Retention, J. Pharm. Res., 14(6); p. 815-819. (1997).
16. Garima Chawla- A means to address regional variability in intestinal drug absorption: Pharmtech., p.234-238. (2003).
17. David S.S. The effect of density on the gastric emptying on single and multiple unit dosage forms. J. Pharm Res., p.208-213. (1986):3.
18. H.G. Sivakumar, Floating Drug Delivery System for Prolonged Gastric Residence time: A review, Ind. J. Pharm. Edu., p.311-316.oct-dec-2004.
19. B.N.Singh, H.Kim, Floating drug delivery system an approach to control drug delivery via gastric retention, J. Controlled Release., 63(7); p. 235-259. (2000).
20. B.Y.Choi, H.J.Park, Preparation of alginate beads for floating drug delivery system: effect of CO_2 gas forming agent. J. Controlled Release., 25(6); p 488-491. (2000).
21. Timmermans J, Moes A.J. The cut off size for gastric emptying of dosage forms, J. Pharm. Sci.,(82); p. 854. (1993).
22. Bhavana V, Khopade A.J, Jain W.D, Shelly and Jain N.K, Targeted Oral Drug Delivery, Indian drugs., vol (33); p. 365-373. (1996).
23. Roop K. Khar, Controlled Drug Delivery, Gastroretentive systems 4th edn. p. 202-203
24. Hradman J.G, Limbrid, Goodman Gilman's, The Pharmacological Basis of Therapeutics, 10th edn, Newyork: p. 17-65. (2001).
25. Thripati K.D, Essential of Medical Pharmacology, 5th edn, New Delhi: P. 248-49. (2003).

26. Ichikawa M, Watanabe S, Miyake Y, A new multiple-unit oral floating dosage system: Preparation and in-vitro evaluation of floating and sustained-release characteristics, J. Pharm. Sci., (1991): (80); P.1062-1066.
27. Abubakr O. Nur and Jun S. Zhang, Captopril Floating and/or Bioadhesive Tablets: Design and Release Kinetics, Taylor & francis: 26(9); p.965 – 969. (2000).
28. Rouge N, Allemann E, Buoyancy and Drug release patterns of floating mini tablets containing Piretanide and Atenolol as model drugs, Pharm. Dev.Technol., vol (3): P. 3-84. (1998).