Journal of Pharmacreations

PharmaCreations

Pharmacreations | Vol.3 | Issue 4 | Oct - Dec- 2016
Journal Home page: www.pharmacreations.com

Research article ***Open Access***

Formulation and evaluation of floating tablets with different polymers

G. Anuhya Goud, Vadala Triveni, G. Venkataih, Dr.A.Yasodha*[1], A.Sivakumar[2]

[1]*Dhanvanthri College of Pharmaceutical Sciences, Mahabubnagar- 509002, Telangana, India.*
[2]*AurobindoPharma Limited, Unit –VII, Jadcherla, Hyderabad.*

***Corresponding author: Dr.A.Yasodha**
Email: yyasodhasivakumar@gmail.com

ABSTRACT

Oral route of administration gets the highest priority for the delivery of drug as well as better patient compliance. Floating tablet is selected for achieving a prolonged and predictable drug delivery profile in the gastrointestinal tract to control the gastric residence time using a gastro retentive dosage forms that will provide as with new and important therapeutic options. Biguanide is also used prokinetic agent for treatment of upper gastrointestinal motility disorders. After Oral administration, Biguanide is rapidly absorbed from the stomach and the upper part of the GIT with fewer side effects. It is weak base with good solubility in acidic pH but significantly reduced solubility in alkaline medium. Such weak base, formulated as an oral controlled release dosage form is exposed to environments of increasing pH with subsequent precipitation of poorly soluble free base with in the formulation that is no longer capable of being released from the formulation. Thus, prolonging the gastric retention of Biguanide beneficial by improving bioavailability, therapeutic efficacy by possible reduction of dose.

Hence in the present study an attempt will be made to develop floating tablets of Biguanide in order to sustain its release in the stomach and the upper part of the GIT.

Keywords: Grastroretentive drug delivery, Biguanide, Sustained release

INTRODUCTION

From many decades, conventional dosage forms, which are of prompt releasing nature, are used for treatment of acute and chronic diseases [1]. The conventional dosage forms provide no control over release of drug. To maintain the drug concentration within the therapeutically effective range, it is often necessary to take this type of conventional dosage forms several times a day [2]. This results in significant fluctuations in drug levels. With many drugs the basic goal of therapy is to achieve a steady state blood level that is therapeutically effective and nontoxic for an extended period of time [3].

The design of proper dosage regimens is an important element in accomplishing the goal [4]. A basic objective in dosage form design is to optimize the delivery of the medication so as to achieve a measure of control of the therapeutic effect in the face of uncertain fluctuations in the *in vivo* environment in which the term 'Sustained Release' is known to have existed in the medical and pharmaceutical literature for many decades [5]. Sustain release has been constantly used to retard

the release of therapeutic agent such that its appearance in the circulation is delayed and/or prolonged and its plasma profile is sustained in duration [6-9].

The onset of its pharmacological action is often delayed and duration of therapeutic action is sustained. The object of sustained release of drug, in a general way is to modify the normal behaviour of drug molecule in a physiological environment. It can lead to the following [10-11].

1. Sustaining drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with minimization of desirable side effects.
2. Localization of drug action by spatial placement of a controlled release system usually rate controlled adjacent to or in the diseased tissue of organ.
3. Targeting drug action by using carriers of chemical derivatives to deliver drug to particular target cell type.

This is usually accomplished by maximizing drug availability, i.e; by attempting to attain a maximum rate and extent of drug absorption; however, controlled of drug action through formulations also implies controlling bioavailability to reduce drug absorption rates.

Classification of Sustained Release Drug Delivery System

Sustained Release drug delivery system can be classified into following categories.

A. Rate programmed drug development system
B. Activation modulated drug development system.
C. Feed base modulated drug development system.
D. Site targeting drug development system.

All categories consist of the following common structure features

1. Drug reservoir compartment.
2. Rate-controlling elements.
3. Energy sour

The aim of the study is to formulate and evaluate Biguanide floating tablets using different polymers HPMCK4M, HPMC15M, HPMC K100M, and Sodium. Bicarbonate, Magnesium Stearate, Sodium CMC. Ethyl cellulose, & Talc in different ratios.

In order to optimize the therapy research efforts have been focused on the development of oral sustained release (SR) preparations as well as controlled release gastro retentive dosage forms. A conventional oral SR formulation releases most of the drug content at colon, thus requiring that the drug will be absorbed from colon. The above drawbacks provide a rationale for developing Biguanide as a gastro retentive dosage form, which is retained in the stomach and produces a constant input of drug to the absorption.

MATERIALS AND EQUIPMENT

Materials used

Table 1: Materials used for the formulation development

S.NO	MATERIALS USED	COMPANY	
1	BIGUANIDES	Sreepathi Pharmaceuticals ltd.	Pharmaceutical grade
2	GUAR GUM	SD Fine Chemicals Ltd., Mumbai	Pharmaceutical grade
3	SODIUM ALGINATE	SD Fine Chemicals Ltd., Mumbai	Pharmaceutical grade
4	CARBOPOL	SD Fine Chemicals Ltd., Mumbai	Pharmaceutical grade
5	MAGNESIUM STEARATE	Ranbaxy pharmaceuticals, Delhi	Pharmaceutical grade
6	TALC	SD Fine Chemicals Ltd., Mumbai	Pharmaceutical grade

Equipment's used

Table 2: Equipment used for the process

S.No.	Name of the Equipment	Manufactured by
1	8 bowl Dissolution apparatus	Electro Lab
2	Single stage tablet punching machine	Cad mach
3	U.V. Spectrophotometer	Analytical
4	Analytical Balance	Adair Dutt Instruments Pvt. Ltd., AD50B
5	Friability Apparatus	Electro Lab
6	Hardness tester	Ketan
7	Tapped density tester	Electro Lab

METHODOLOGY

Formulation and preparation of biguanides

Floating tablets

Various ratios (designated as F-1 to F-20).

Procedure

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

Compressibility Index

Weighed API was transferred to 100ml-graduated cylinder and subjected to 500,750&1250 taps in tap density tester (Electro lab). The difference between two taps should be less than 2%. The %of compressibility index calculated using formula **CI =v_i – v_t/ v_i*100**

S.No	Compressibility index	flow
1	5-12	Free flow
2	12-16	Good flow
3	18-21	Fair
4	23-25	Poor
5	33-38	Very poor
6	>40	Extremely poor

RESULT AND DISCUSSION

Calibration curve of biguanide

Table 3: Calibration curve

S.NO	Concentration	ABSORBANCE
1	2	0.013
2	4	0.03
3	6	0.041
4	8	0.043
5	10	0.055
6	15	0.078
7	20	0.125
8	30	0.158

9	40	0.205
10	50	0.257
11	60	0.302
12	70	0.358
13	80	0.411
14	90	0.456
15	100	0.503

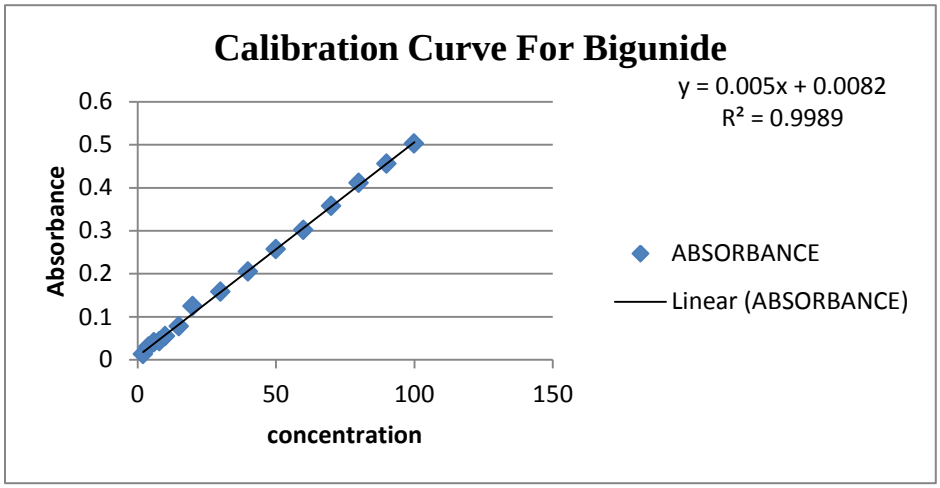

Figure 16: Calibration curve of Biguanide in 0.1 N HCl

IR studies

From the infrared spectra it is clearly evident that there were no interactions of the drug. IR Spectrum of the pure drug shows the characteristic peaks at 3345.87cm-1 and 463.50cm-1. The IR Spectrum of Drug and polymer exhibited peaks at 3345.26cm-1 and 644.69cm-1. This confirms the undisturbed structure of the drug in the formulation. This proves the fact that there is no potential incompatibility of the drug with the polymers used in the formulations. Hence, the formula for preparing Biguanide: Floating Tablets can be reproduced in the industrial scale without any apprehension of possible drug-polymer interactions.

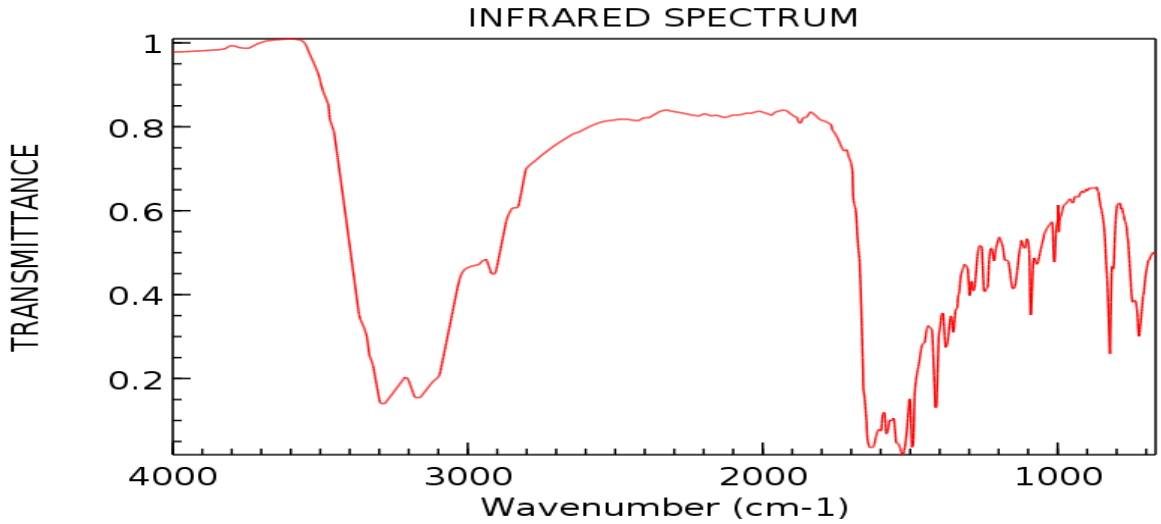

Fig 17: IR-Spectrum for Biguanide

Table 10: Data for IR Spectra of Biguanide

Functional Group	Frequency (cm^{-1})
C-H Aromatic (stretching)	3017.49
c=c Aromatic (stretching)	1404.72
C-N (stretching)	1161.78
C-H (stretching)	2860.92
CH_2 (bending)	1437.05
O-H (stretching)	3345.87

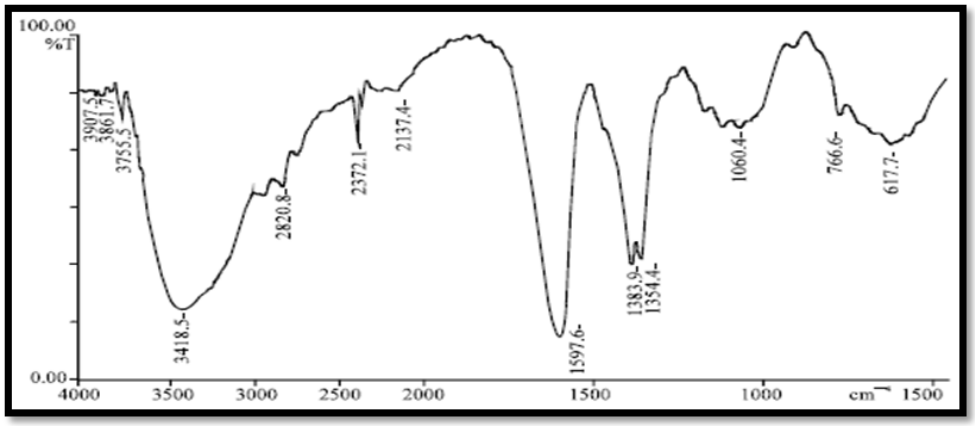

Fig18: IR-Spectrum for Sodium Alginate

Plan of work for different formulations

Formu Lation No.	Biguanides (mg)	HPMC K4M (mg)	HPMC K15M (mg)	HPMC K100M (mg)	Ethyl Cellulose (mg)	SodimCMC (mg)	$NaHCO_3$ (mg)	Mag. Stearate (mg)	Talc (mg)
F_1	100	100	-----	-----	-----	-----	30	12	08
F_2	100	150	-----	-----	-----	-----	40	15	10
F_3	100	200	-----	-----	-----	-----	50	18	12
F_4	100	-----	100	-----	-----	-----	30	12	08
F_5	100	-----	150	-----	-----	-----	40	15	10
F_6	100	-----	200	-----	-----	-----	50	18	12
F_7	100	-----	-----	100	-----	-----	30	12	08
F_8	100	-----	-----	150	-----	-----	40	15	10
F_9	100	-----	-----	200	-----	-----	50	18	12
F_{10}	100	-----	-----	-----	100	-----	30	12	08
F_{11}	100	-----	-----	-----	150	-----	40	15	10
F_{12}	100	-----	-----	-----	200	-----	50	18	12
F_{13}	100	-----	-----	-----	-----	100	30	12	08
F_{14}	100	-----	-----	-----	-----	150	50	18	12
F_{15}	100	100	-----	-----	100	-----	50	18	12
F_{16}	100	100	-----	-----	200	-----	70	20	12
F_{17}	100	-----	100	-----	100	-----	50	18	12
F_{18}	100	-----	100	-----	200	-----	70	20	12
F_{19}	100	-----	-----	100	100	-----	50	18	12
F_{20}	100	-----	-----	100	200	-----	70	20	12

Dissolution data of Biguanide Tablets prepared with HPMC K4M in different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)		
	F1	F2	F3
0.5	21.73±0.77	20.52±0.77	19.53±0.65
1	32.78±0.55	27.38±0.5	28.97±0.25
2	44.94±0.69	37.47±0.84	35.89±0.62
3	59.23±0.99	48.89±0.96	45.70±0.85
4	64.88±0.77	59.93±0.55	54.38±0.78
5	70.67±0.95	65.85±0.52	61.25±0.85
6	76.45±1.25	70.81±0.95	67.06±0.95
7	84.94±0.95	77.54±1.25	72.52±0.58
8	90.873±1.08	82.878±0.99	77.88±1.05

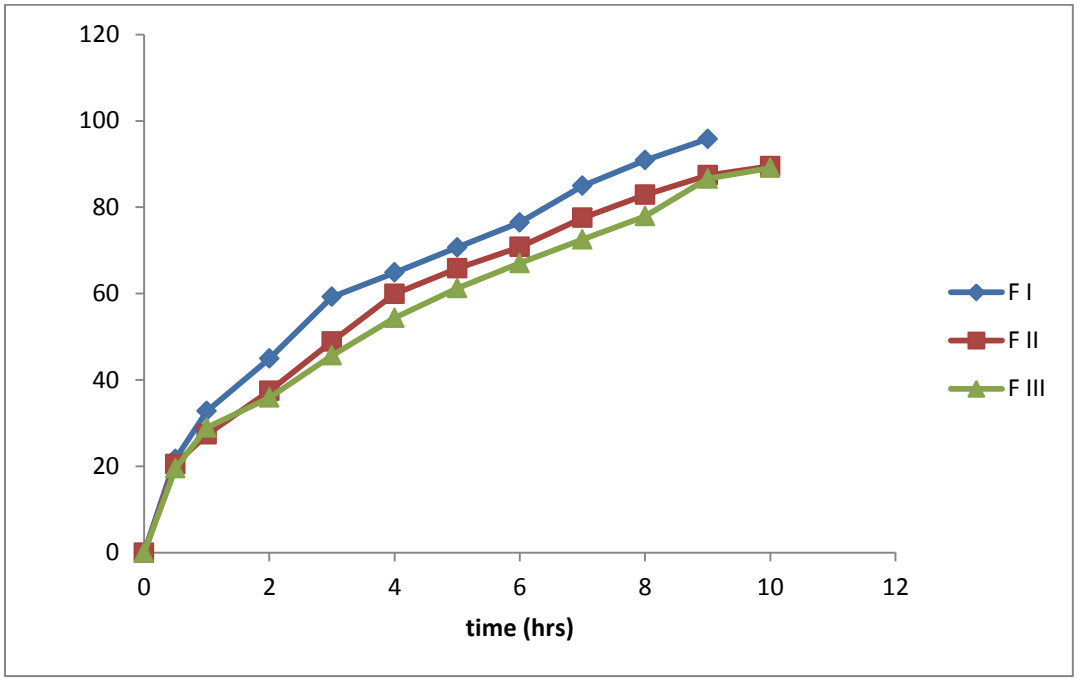

Fig 19: Dissolution profile of Biguanide floating tablets (F1, F2, F3 formulations).

Dissolution Data of Biguanide Tablets Prepared with hpmc k 15M IN Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)		
	F4	F5	F6
0.5	18.45±0.88	18.42±0.98	19.62±0.77
1	29.81±0.58	27.73±1.20	27.86±0.65
2	36.26±0.95	35.63±1.58	36.35±0.44
3	43.78±0.58	42.04±0.25	41.45±0.58
4	52.16±0.77	49.79±0.52	47.80±0.51
5	59.56±0.84	57.25±0.88	55.25±0.72

6	65.20±0.51	64.33±08	60.24±0.81
7	70.01±0.65	69.64±0.95	66.73±0.25
8	76.80±1.05	75.41±1.0	71.34±0.42
9	83.97±0.54	81.44±0.85	78.52±1.00
10	87.26±0.28	83.84±0.77	80.17±0.77
11	93.10±0.85	92.80±0.65	91.33±0.89
12	-	-	88.75±0.22

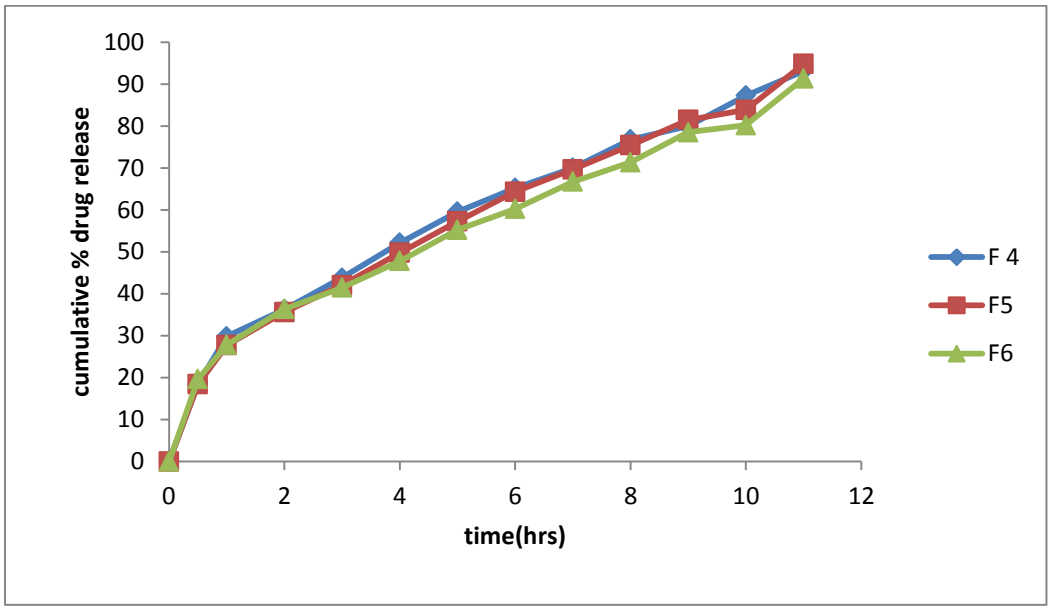

Fig20: Dissolution profile of Biguanide floating tablets (F4, F5, F6 formulations).

Dissolution Data of Biguanide Tablets Prepared with HPMC K100M IN Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)		
	F7	F8	F9
0.5	18.81±0.77	19.89±0.55	14.21±0.88
1	29.02±0.52	28.04±0.66	18.87±0.54
2	35.70±0.84	35.43±0.95	27.19±0.65
3	43.32±0.66	41.65±0.58	35.66±0.98
4	49.25±0.61	47.18±0.39	43.32±0.58
5	55.28±0.59	53.81±0.89	51.06±0.85
6	60.92±0.35	58.89±0.94	57.13±0.69
7	66.08±0.92	64.53±0.88	63.63±0.58
8	70.44±0.94	69.43±0.90	69.71±0.85
9	77.22±1.08	72.83±0.85	73.34±0.69
10	80.90±1.02	79.98±0.44	79.27±0.84
11	87.83±0.55	83.52±0.68	82.86±0.58
12	91.90±0.98	90.65±0.74	87.97±0.55

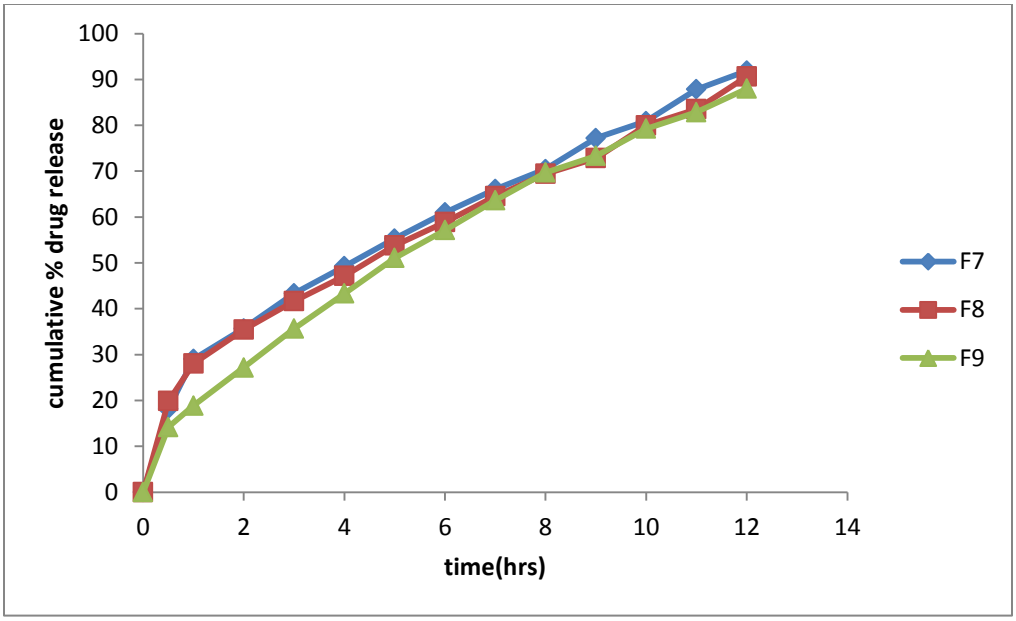

Fig21: Dissolution profile of Biguanide floating tablets (F7, F8, F9 formulations).

Dissolution Data of Biguanide Tablets Prepared with ethyl cellulose in Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)		
	F10	F11	F12
0.5	27.981±0.58	23.085±0.58	22.319±0.36
1	37.26±0.65	33.69±0.77	35.89±0.980.88
2	44.09±0.59	41.56±0.69	40.61±0.46
3	56.11±0.58	53.35±0.25	52.24±0.58
4	64.93±0.58	60.96±0.89	61.93±0.88
5	76.36±0.58	68.79±0.58	65.27±0.85
6	85.24±1.00	83.97±0.98	78.46±0.88
7	88.1343±0.88	86.319±0.58	85.26±0.85
8	95.2854±0.54	93.1921±0.65	94.72±0.89

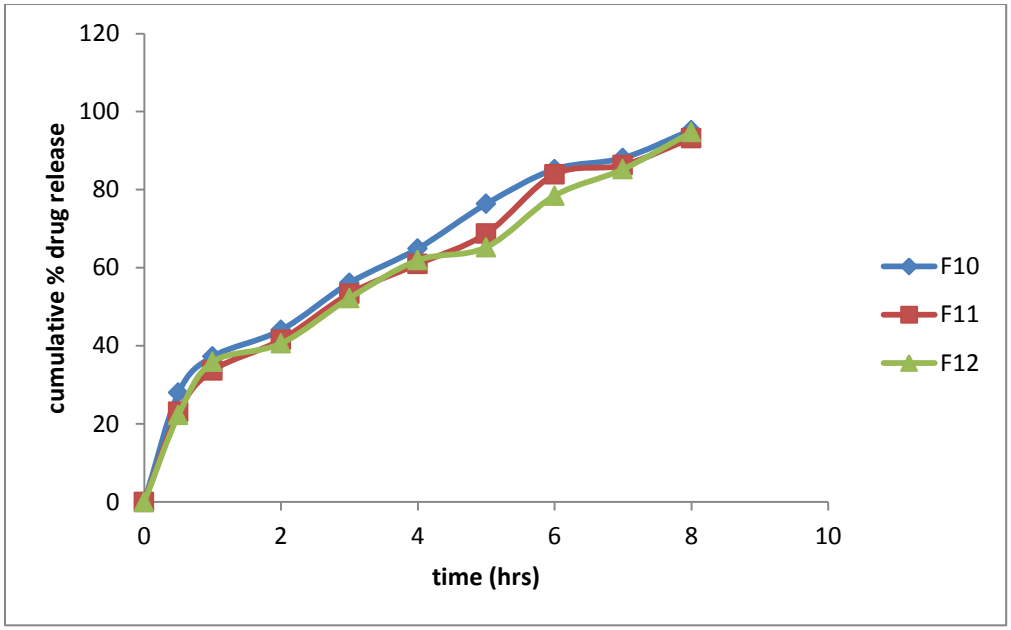

Fig22: Dissolution profile of Biguanide floating tablets (F10, F11, F12 formulations).

Dissolution Data of Biguanide Tablets Prepared with Sodium CMC in Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)	
	F13	F14
0.5	26.62±0.58	28.70±0.58
1	39.80±0.54	42.53±0.89
2	48.66±0.66	53.81±0.87
3	64.11±0.77	65.09±0.84
4	81.70±0.85	87.84±0.77
5	97.53±0.67	99.56±0.95

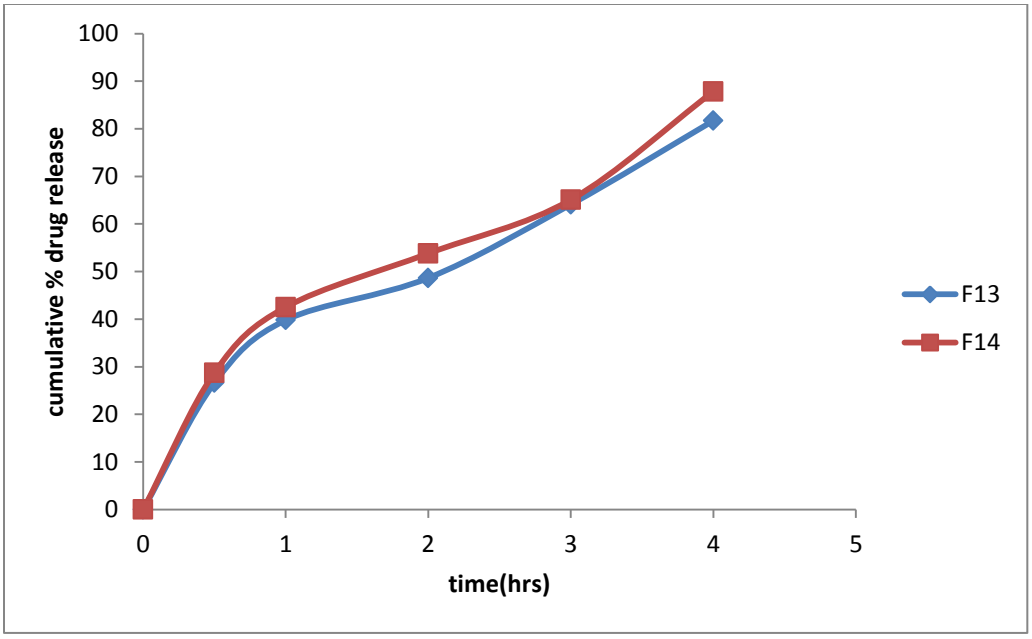

Fig23: Dissolution profile of Biguanide floating tablets (F13, F14 formulations).

Dissolution Data of Biguanide tablets prepared with HPMC k4m+ethyl cellulose in Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)	
	F15	F16
0.5	21.42±0.44	19.539±0.84
1	26.49±0.68	28.97±0.68
2	39.27±0.98	35.89±0.57
3	55.22±0.55	45.70±0.84
4	61.82±0.84	54.38±0.58
5	66.86±0.67	61.25±0.95
6	74.53±0.52	67.06±0.58
7	83.82±0.86	72.52±0.84
8	88.50±1.05	77.88±0.66
9	93.09±0.85	86.60±0.75
10	99.82±0.67	88.19±0.85
11		94.85±1.00

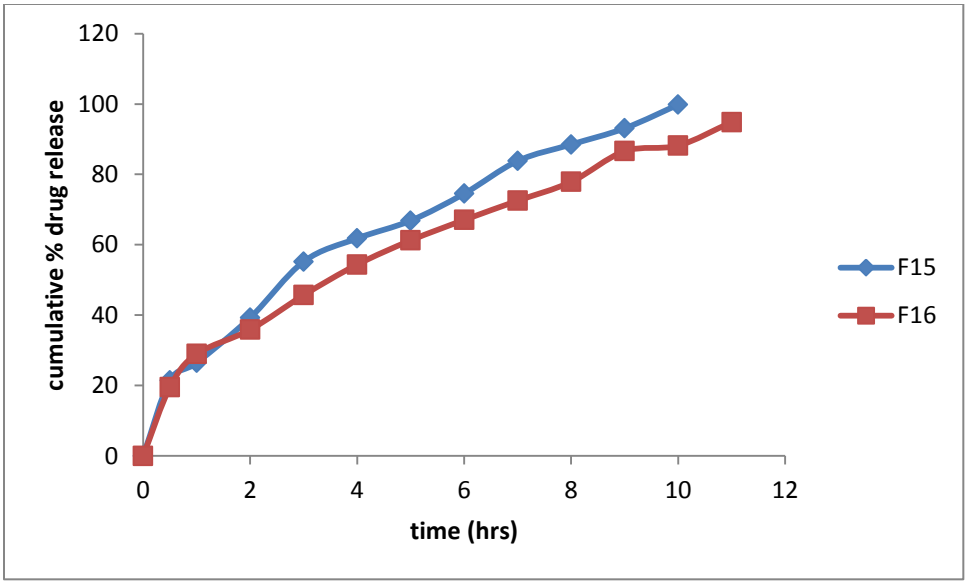

Fig 24: Dissolution profile of Biguanide floating tablets (F15, F16 formulations).

Dissolution Data of Biguanide Tablets Prepared with hpmc k15m+ethyl cellulose in Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)	
	F17	F18
0.5	18.09±0.66	18.13±0.52
1	26.53±0.84	26.76±0.85
2	34.61±0.64	36.06±0.56
3	38.80±0.71	38.44±0.85
4	46.21±0.75	44.07±0.58
5	53.92±0.68	50.31±0.65
6	60.80±0.95	56.69±0.95
7	66.18±1.00	63.77±0.85
8	73.06±0.84	70.66±0.65
9	79.12±0.98	75.08±0.68
10	81.82±0.65	77.35±0.85
11	89.86±0.66	84.43±0.68
12	92.68±0.58	88.78±0.98

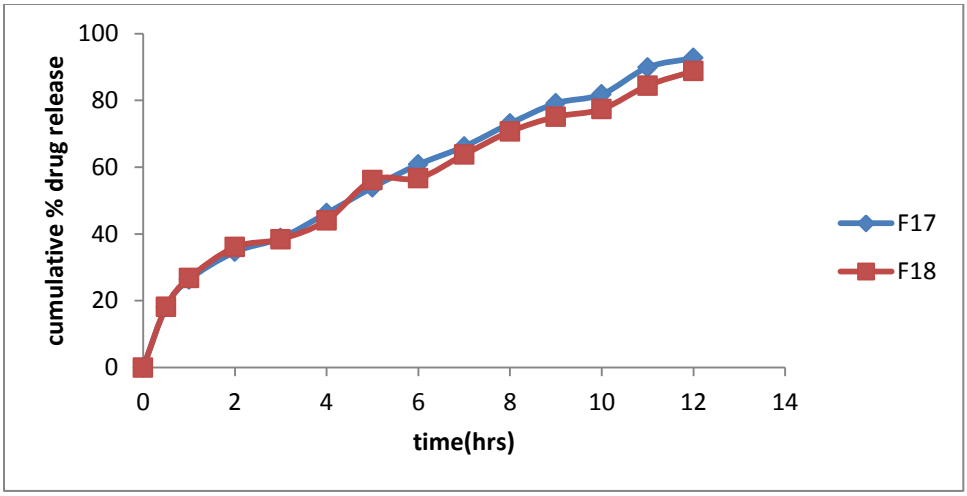

Fig25: Dissolution profile of Biguanide floating tablets (F17, F18 formulations).

Dissolution Data of Biguanide Tablets Prepared with HPMC k100m+ethyl cellulose in Different concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED (n=3±SD)	
	F19	F20
0.5	12.15±0.56	12.81±0.88
1	18.31±0.66	18.81±0.59
2	27.29±0.84	27.13±0.69
3	34.85±0.66	32.90±0.77
4	41.57±0.67	40.11±0.84
5	47.69±0.66	42.03±0.98
6	51.73±0.54	47.19±1.0
7	55.05±0.74	51.77±0.66
8	63.37±0.58	59.52±0.74
9	68.54±0.66	65.89±0.68
10	71.65±0.65	67.67±0.84
11	80.23±0.89	76.88±0.88
12	83.76±0.84	81.31±0.57

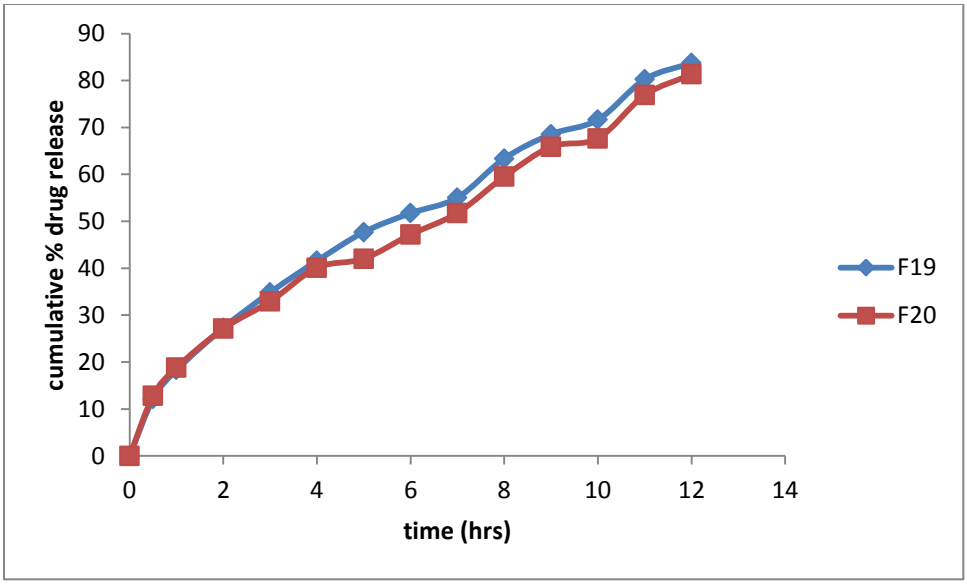

Fig 26: Dissolution profile of Biguanide floating tablets (F19, F20 formulations).

Release kinetics: Coefficient of correlation (r) values of different batches of Biguanide floating tablets

Formulation	Zero order	First order	Higuchi's	Peppa's
F_1	0.920	0.946	0.997	0.996
F_2	0.931	0.936	0.997	0.996
F_3	0.948	0.957	0.996	0.994
F_4	0.949	0.958	0.995	0.991
F_5	0.957	0.964	0.996	0.993
F_6	0.950	0.958	0.994	0.990
F_7	0.937	0.968	0.993	0.992
F_8	0.947	0.957	0.994	0.992
F_9	0.963	0.972	0.991	0.992
F_{10}	0.932	0.941	0.992	0.981
F_{11}	0.944	0.953	0.990	0.988
F_{12}	0.942	0.955	0.992	0.984
F_{13}	0.957	0.913	0.983	0.978
F_{14}	0.923	0.917	0.981	0.974
F_{15}	0.940	0.971	0.995	0.990
F_{16}	0.944	0.976	0.996	0.994

F_{17}	0.952	0.979	0.990	0.987
F_{18}	0.950	0.960	0.988	0.983
F_{19}	0.961	0.974	0.997	0.997
F_{20}	0.961	0.975	0.983	0.985

Dissolution Parameters of Biguanide Tablets

Formulation	Dissolution Parameters					
	N	K_0	K_1	T_{50}	T_{75}	T_{90}
F_1	0.507	9.375	0.301	2.5	5.8	8.0
F_2	0.514	7.775	0.248	3.6	6.8	10.0
F_3	0.507	7.604	0.223	3.5	7.5	10.1
F_4	0.505	7.424	0.204	3.8	7.5	10.2
F_5	0.507	7.268	0.186	4.0	8.1	10.5
F_6	0.479	6.593	0.175	4.5	8.5	11.1
F_7	0.479	5.861	0.151	4.0	8.5	11.2
F_8	0.483	6.563	0.175	4.5	9.3	12.0
F_9	0.610	6.762	0.179	5.1	9.1	>12
F_{10}	0.459	10.6	0.354	5	9.5	11.9
F_{11}	0.500	10.43	0.299	2.6	4.8	7.2
F_{12}	0.486	10.32	0.299	2.8	5.5	7.8
F_{13}	0.530	16.94	0.502	2.1	3.5	4.8
F_{14}	0.495	18.92	0.453	2.0	3.8	4.9
F_{15}	0.535	9.431	0.267	2.5	6.0	8.5
F_{16}	0.503	7.895	0.199	3.8	7.5	10.5
F_{17}	0.510	6.817	0.181	4.5	8.2	11.0
F_{18}	0.487	6.421	0.149	5.0	9.1	>12
F_{19}	0.604	6.188	0.142	6.1	10.2	>12
F_{20}	0.617	5.867	0.122	6.3	11.2	>12

Stability dissolution profile of F17 for 1st and 2nd month

S.No	Time (in minutes)	F5 1st Month	F5 2nd Month
1	**0**	0	0
2	**10**	71.62	70.88
3	**15**	82.26	82.59
4	**20**	90.82	91.78

5	**30**	96.05	96.33
6	**45**	97.59	97.94

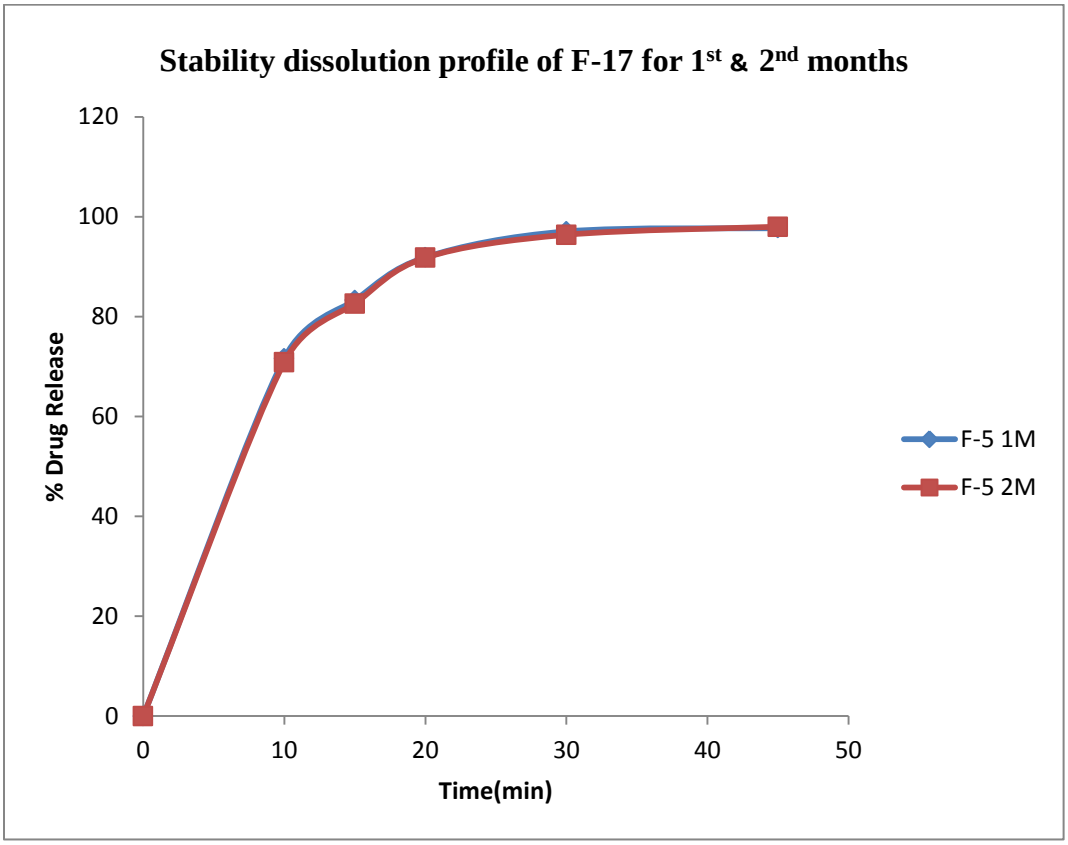

Fig 27: Stability Dissolution Profile of F-17 for 1st & 2nd months

CONCLUSION

The objective of the present study is to develop a Floating matrix tablet of Biguanide. In this present study an attempt was made to increase the GI residence time of Biguanide, as the drug is having less gastric residence time, by formulating in to Floating tablets.

Systematic studies were conducted using different concentration of rate releasing polymer HPMC k15m, ethyl cellulose, HPMC k100m, sodium CMC for attending the drug release in upper GIT. All the prepared systems were evaluated for the different properties. Before the preparation of tablets, preformulation studies were conducted like drug- excipient stability studies to find out the interaction, micromeritic properties to assess flowability, compressibility properties and solubility studies. And all the formulations gave good results for above preformulation studies. Formulated tablets gave satisfactory results for various physical tablet evaluation parameters like tablet dimensions, hardness, friability, weight variation, buoyancy, content uniformity, *in-vitro* study all the formulations were found within the permissible range. Formulation 17 has shown better dissolution profile over a long period up to 12 hours.

Among these all formulations (F1-F20), it was observed that formulation 17 contain HPMC k15m, ethyl cellulose in different concentration has shown better dissolution profile, which compete with other formulation. So Formulation 17 was found to be the best formulation among others.

REFERENCES

[1]. Leon Lachman, Herbert A. Liberman, the Theory and Practice of Industrial Pharmacy 293-302.
[2]. Robinson Jr, Lee V.H.L, Marcel Dekker, Controlled drug delivery, Fundamentals and Applications, New York 2, 1978, 24-36.
[3]. Brahmankar D.M, Jaiswal S.B, Vallabh prakashan Biopharmaceutics and Pharmacokinetics a treatise, New Delhi, 1, 1995, 64-70.
[4]. Chein Y.W, Marcel Dekker, Novel Drug Delivery Systems, New York, 2, 1992, 4-56.
[5]. Ansel, Pharmaceutical Dosage form and Drug Delivery System, Lipincott 7, 553.
[6]. Gennaro R.A. Remington, Lippincott Williams the Science and Practice of Pharmacy, New York, 20, 2000, 1045.
[7]. Banker G.S, Rhodes C.T, Marcel Dekker Modern Pharmaceutics. New York, 3, 1996, 678-721.
[8]. Vyas S.P, Khar R.K, Vallabh prakashan, Controlled Drug Delivery, Concepts and Advances, 1st ed., New Delhi, P.345-376, 2002.
[9]. P.G.Yeole, Floating Drug Delivery System: Need and Development, *Ind. J. Pharm Sci.*, 67(3), 2005, 265-272.
[10]. Shweta Arora, Floating Drug Delivery: A Review, AAPS Pharmscitech., 47(11), 2005, 268-272.
[11]. Ross and Wilson, Anatomy Physiology and Health Education, Churchil Livingston, 9, 295-311.