International Journal of Pharmacy and Industrial Research (IJPIR)

ISSN:2231-6567

IJPIR |Volume 13 | Issue 1 | Jan - Mar - 2023
Available online at: www.ijpir.com

Research article Pharmacy

Formulation and in vitro evaluation of effervescent floating tablets of Flurbiprofen

K. Revathi, Dr. Hemalatha*, Dr. Jyothi penta

Holy Mary Institute of Technology and Science (HITS), College of Pharmacy Keesara, Hyderabad – 501301, India

***Corresponding Author: Hemalatha**

ABSTRACT

The present study was to develop floating tablets of Flurbiprofen to achieve prolong gastric residence time, leading to an increase in drug bioavailability and patient compliance floating tablets were prepared direct compression. The Tablet prepared and characterized for bulk density, Tapped density, Carr's index, Hausner's ratio and angle of repose. Developed formulations were evaluated for weight variation, thickness, hardness, friability, drug content, *in vitro* drug release. All the formulations exhibited acceptable physical properties and best formulation was F9 was selected based on the *in vitro* characteristics was released 98.31 %

Keywords: Flurbiprofen, Gum Copal, Gum Damar, Psyllium Husk, Floating Tablets.

INTRODUCTION

Oral delivery of drugs is the most preferable route of drug delivery. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient compliance and flexibility in formulation and cost effective manufacturing process[1]. Many of the drug delivery systems, available in the market are oral drug delivery type systems Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as:

1. Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
2. A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3. The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the C_{SS} values fall or rise beyond the therapeutic range.
4. The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever overmedication occurs.[2]

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize method of medication and provide a number of therapeutic benefits.[3]

The aim of the present work is to formulate & evaluate gastro retentive floating tablets of Flurbiprofen using various polymers.

The gastro retentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability.

Flurbiprofen is a member of the phenylalkanoic acid derivative family of nonsteroidal anti- inflammatory drugs

(NSAIDs). It is primarily indicated as a pre-operative anti-miotic (in an ophthalmic solution) as well as orally for arthritis or dental pain. Side effects are analogous to those of ibuprofen. In the present investigation floating tablets of Flurbiprofen were prepared by direct compression using various polymers. An orally administered controlled drug delivery system encounters a wide range of highly variable conditions, such as pH, agitation intensity, and composition of the gastrointestinal fluids as it passes down the G.I tract. Considerable efforts have been made to design oral controlled drug delivery systems that produce more predictable and increased bioavailability of drugs. However, the development process is precluded by several physiological difficulties, like inability to retain and localize the drug delivery system within desired regions of the G.I tract and highly variable nature of the gastric emptying process. An important factor, which may adversely affect the performance of an oral controlled drug delivery system, is the G.I transit time. The time for absorption in the G.I transit in humans, estimated to be 8-10 hr from mouth to colon, is relatively brief with considerable fluctuation. G.I transit times vary widely between individuals, and depend up on the physical properties of the object ingested and the physiological conditions of the gut. This variability may lead to predictable bioavaialability and times to achieve peak plasma levels. One of the important determinants of G.I transit is the residence time in the stomach.[8]

Majority of the drugs are well absorbed from all the regions of the G.I tract while some are absorbed only from specific areas, principally due to their low permeability or solubility in the intestinal tract, their chemical instability, the binding of the drug to the gut contents, as well as to the degradation of the drug by the microorganisms present in the colon. Therefore, in instances where the drug is not absorbed uniformly over the G.I tract, the rate of drug absorption may not be constant in spite of the drug delivery system delivering the drugs at a constant rate into the G.I fluids. More particularly, in instances where a drug has a clear cut absorption window, i.e., the drug is absorbed only from specific regions of the stomach or upper parts of the small intestine; it may not be completely absorbed when administered in the form of a typical oral controlled drug delivery system. It is due to the relatively brief gastric emptying in humans, which normally averages 2-3 hrs through the major absorption zone. It may cause incomplete drug release from the dosage form at absorption sites leading to diminished efficacy of the administered dose. It is apparent that for a drug having such an absorption window, an effective oral controlled drug delivery system should be designed not only to deliver the drug at a controlled rate, but also to retain the drug in the stomach for a long period of time. For this drug, increased or more predictable availability would result if controlled release systems could be retained in the stomach for extended periods of time. [9,10]

It is suggested that compounding narrow absorption window drugs in a unique pharmaceutical dosage form with gastro retentive properties would enable an extended absorption phase of these drugs. After oral administration, such a dosage form would be retained in the stomach and release the drug there in a controlled and prolonged manner, so that the drug could be supplied continuously to its absorption sites in the upper gastrointestinal tract. This mode of administration would best achieve the known pharmacokinetic and pharmacodynamic advantages of controlled release dosage form for these drugs.

METHODOLOGY

Formulation development of floating Tablets

For optimization of sodium bicarbonate concentration, granules were prepared by direct compression method.

Procedure for direct compression method

1. Drug and all other ingredients were individually passed through sieve no 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 by using 10 mm punch.

Table 1: Formulation composition for Floating tablets

	FORMULATION CHART											
Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Flurbiprofen	50	50	50	50	50	50	50	50	50	50	50	50
Gum Copal	30	60	90	120	-	-	-	-	-	-	-	-
Gum Damar	-	-	-	-	40	80	120	160	-	-	-	-
Psylliu Husk	-	-	-	-	-	-	-	-	20	40	60	80
Sodium bicarbonate	30	30	30	30	30	30	30	30	30	30	30	30
Aerosil	4	4	4	4	4	4	4	4	4	4	4	4
Mg.Stearate	5	5	5	5	5	5	5	5	5	5	5	5
Lactose	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total												

All the quantities were in mg

RESULTS AND DISCUSSIONS

Analytical Method

Determination of absorption maxima

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 235 nm.

Calibration curve

Graphs of Flurbiprofen was taken in 0.1N HCL (pH 1.2)

Table 2: Observations for graph of Flurbiprofen in 0.1N HCl

Conc [µg/mL]	Abs
0	0
2	0.122
4	0.236
6	0.341
8	0.459
10	0.571

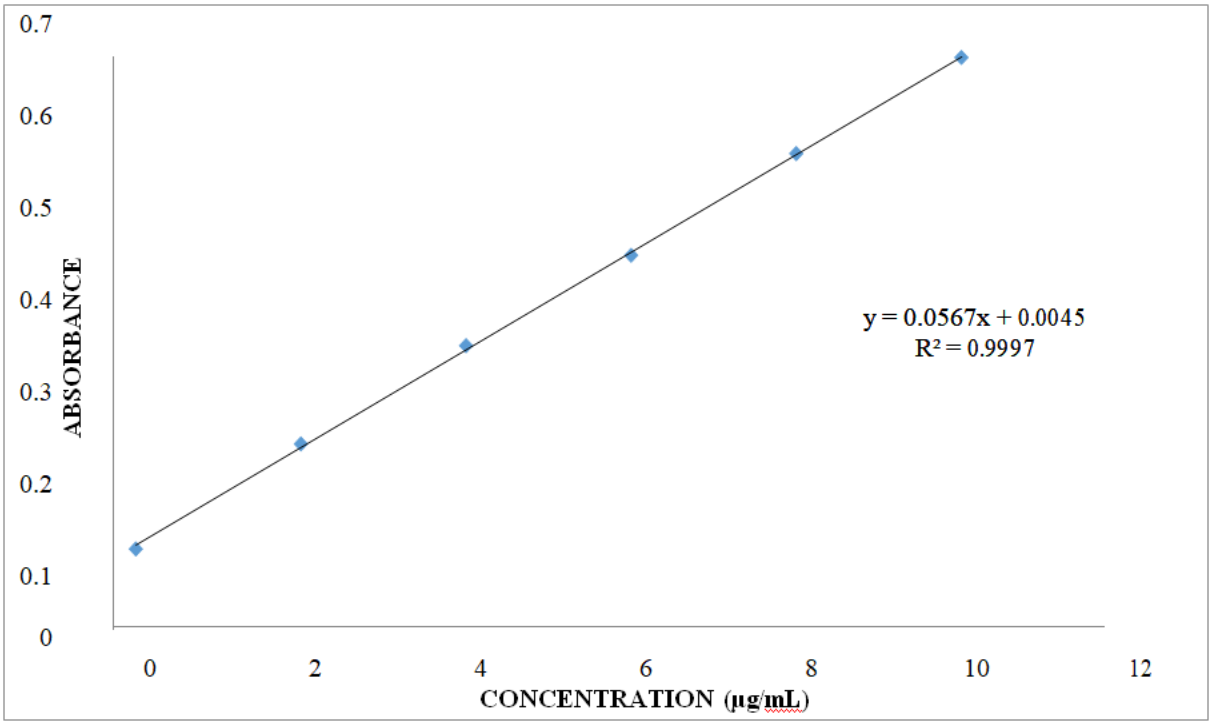

Fig 1: Standard graph of Flurbiprofen in 0.1N HCL

Standard graph of Flurbiprofen was plotted as per the procedure in experimental method and its linearity is shown in Table 2 and Fig 1. The standard graph of Flurbiprofen showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Preformulation parameters of powder blend

Table 3: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's Ratio
F1	24.2	0.419	0.486	13.95	1.162
F2	24.5	0.409	0.485	15.68	1.186
F3	25.2	0.409	0.480	14.77	1.173
F4	27.8	0.429	0.488	12.14	1.138
F5	27.2	0.450	0.501	10.25	1.114
F6	26.4	0.462	0.522	11.54	1.130
F7	30.2	0.450	0.507	11.25	1.127
F8	29.3	0.439	0.504	12.93	1.148
F9	28.5	0.462	0.526	12.31	1.140
F10	28.0	0.450	0.500	10.00	1.111
F11	27.5	0.439	0.496	11.46	1.129
F12	28.3	0.429	0.493	13.10	1.151

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.409 to 0.462 (gm/ml) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.480 to 0.526 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 19.85 which show that the powder has good flow properties. All the formulations has shown the hausners ratio ranging between 1.111 to 1.186 indicating the powder has good flow properties.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

In vitro quality control parameters

Formulation codes	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (sec)	Total Floating Time(Hrs)
F1	499.26	4.3	0.63	4.45	96.59	35	10
F2	500.29	4.5	0.56	4.96	98.35	25	11
F3	498.03	4.9	0.24	4.10	95.52	15	10
F4	496..75	4.0	0.52	4.32	99.29	56	9
F5	499.89	4.5	0.40	4.16	100.06	42	8
F6	496.92	4.6	0.19	4.57	98.56	30	10
F7	498.57	4.2	0.58	4.14	96.15	28	9
F8	495.38	4.1	0.33	4.89	97.33	57	10
F9	497.22	4.5	0.25	4.77	99.78	45	11
F10	500.09	4.7	0.37	4.50	98.42	32	8
F11	496.37	4.4	0.22	4.15	99.83	28	10
F12	498.88	5.1	0.37	4.93	98.92	24	8

All the parameters such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

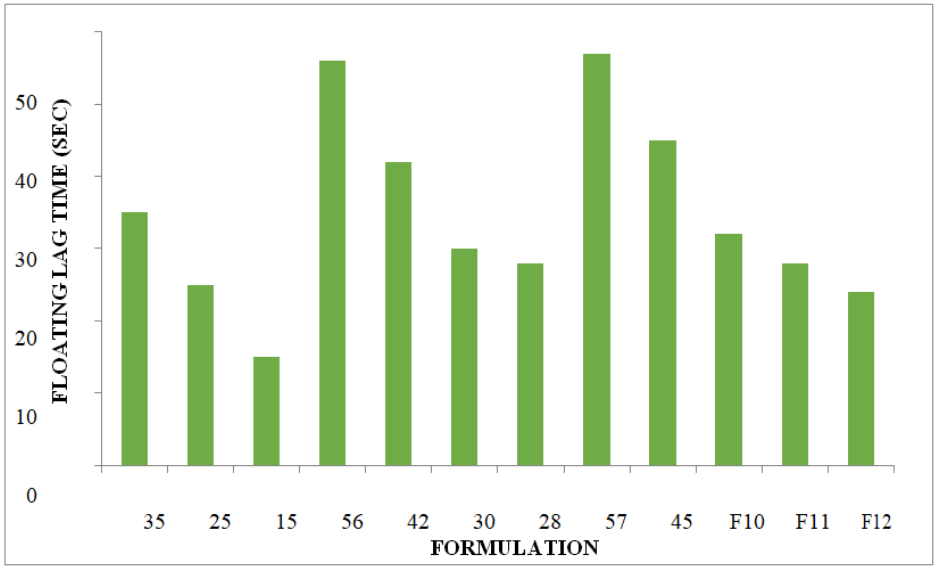

Fig 2: Floating lag time (sec)

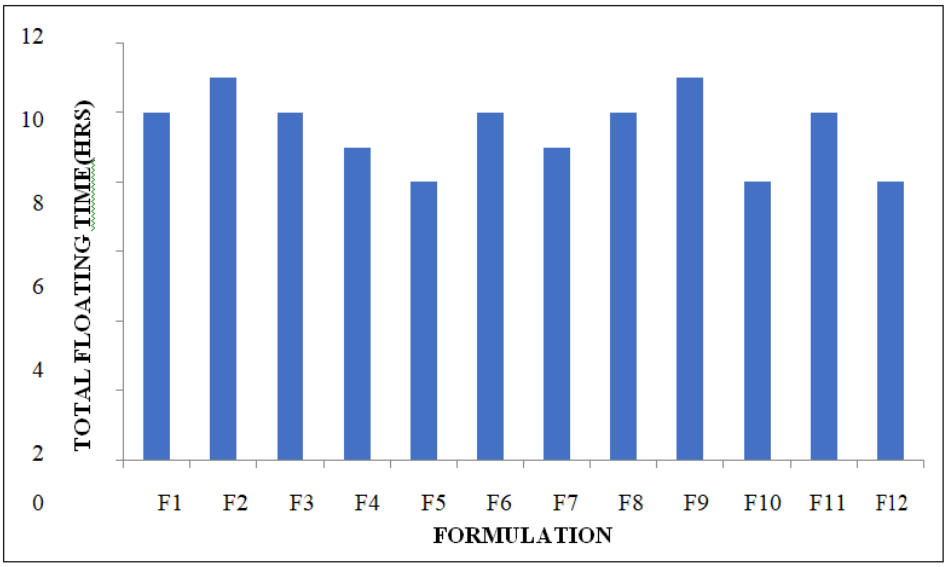

Fig 3: Total Floating Time (Hrs)

In Vitro Drug Release Studies

Table 4: Dissolution data of Floating Tablets

Tim	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	5.89	12.8	18.9	15.3	10.4	12.1	10.5	8.80	20.1	13.8	16.9	13.7
1	10.4	16.7	23.6	19.9	17.8	18.6	14.0	12.5	24.3	18.1	20.4	18.4
2	18.7	23.8	28.7	28.4	27.4	29.7	18.6	18.9	28.7	23.2	23.8	21.7
3	25.9	28.3	33.1	36.2	38.1	34.2	23.4	26.8	41.5	30.8	30.7	28.9
4	31.2	35.1	40.3	42.9	43.5	39.9	26.8	33.3	49.9	34.7	38.1	35.1
5	39.5	42.8	47.6	48.2	50.2	48.6	31.5	38.1	56.8	40.6	41.5	39.7
6	46.1	50.1	50.9	56.9	57.9	53.1	36.8	49.5	64.9	47.1	55.2	48.1

7	50.1	56.8	59.1	64.3	67.7	58.3	39.4	55.7	71.8	62.5	58.7	53.1
8	54.6	62.9	66.5	71.8	74.2	62.8	45.3	59.0	78.4	73.8	62.1	59.3
9	59.1	71.3	70.7	76.9	78.9	67.9	51.1	64.4	83.1	75.3	73.5	66.2
1	63.9	77.5	86.5	82.1	86.2	73.2	54.5	67.5	90.2	80.9	80.4	75.6
1	69.4	82.7	91.5	87.1	93.4	78.7	67.2	70.4	94.6	85.3	83.2	79.8
1	73.6	88.1	99.2	92.7	97.8	85.1	78.1	73.6	98.3	90.1	87.0	83.5

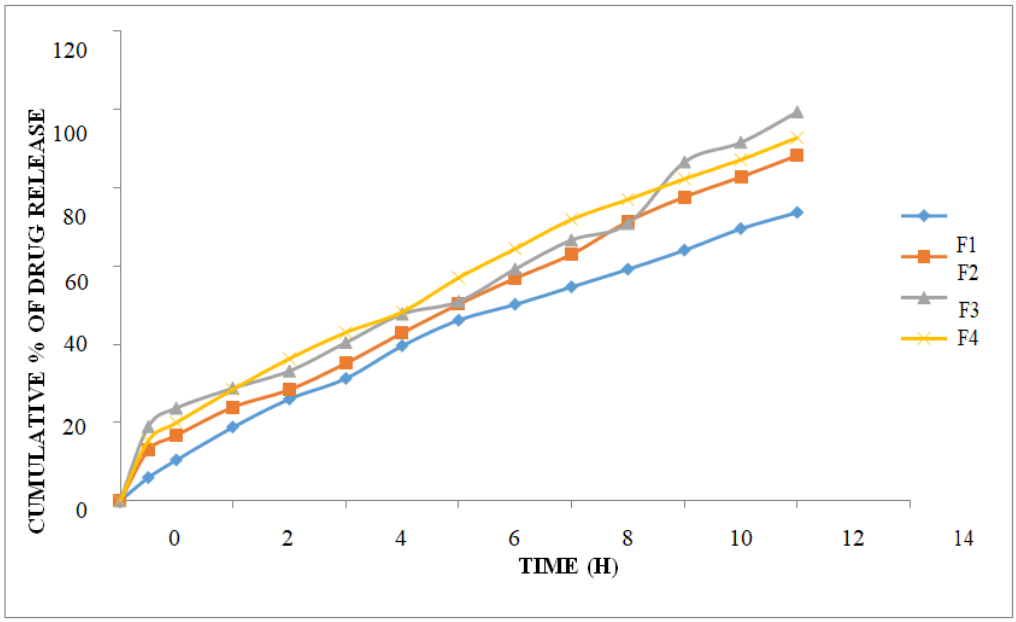

Fig 4: Dissolution data of Flurbiprofen Floating tablets containing Gum Copal

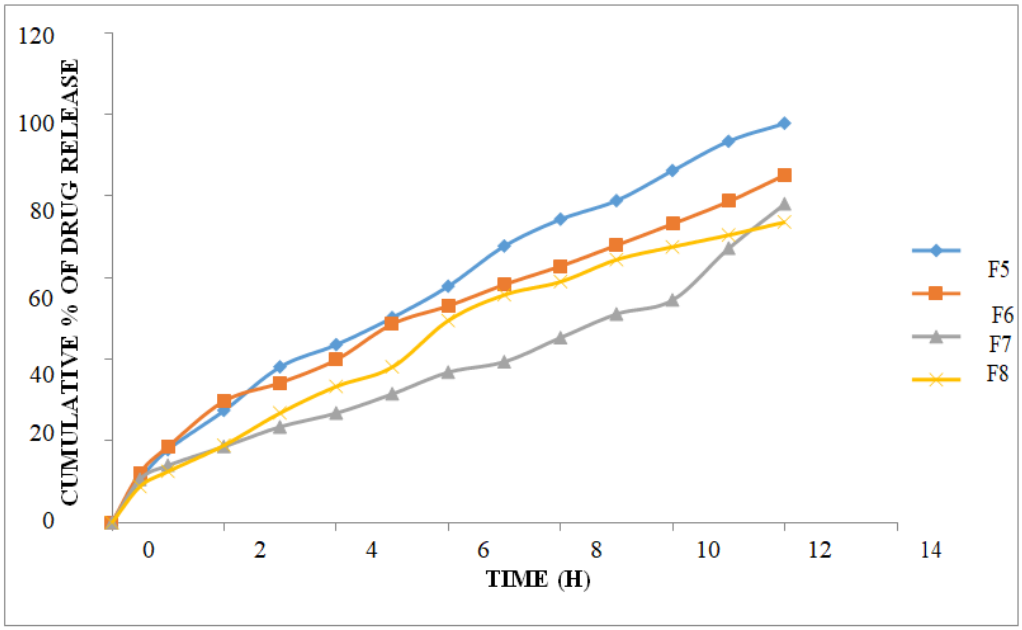

Fig 5: Dissolution data of Flurbiprofen Floating tablets containing Gum Damar

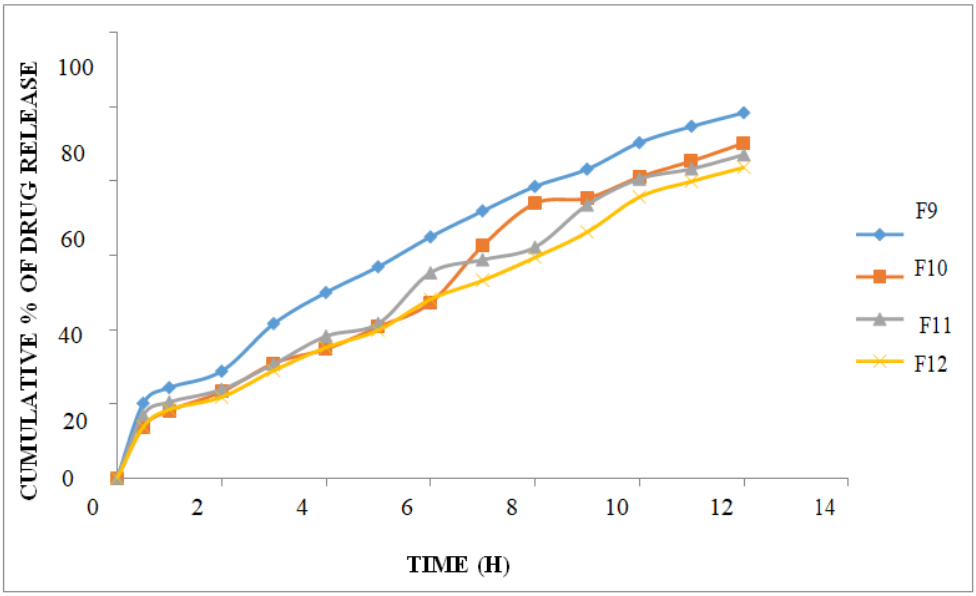

Fig 6: Dissolution data of Flurbiprofen Floating tablets containing Psyllium Husk

From the dissolution data it was evident that the formulations prepared with Gum Copal as polymer were retarded the drug release more than 12 hours.

Whereas the formulations prepared with Gum Damar retarded the drug release up to 12 hours in the concentration 40 mg. In higher concentrations the polymer was unable to retard the drug release.

.

From the dissolution data, it was revealed that formulations prepared with Psyllium Husk retard the drug release up to 12 hrs.

Hence from the above dissolution data it was concluded that F9 formulation was considered as optimised formulation because good drug release (98.31%) in 12 hours

Application of Release Rate Kinetics to Dissolution Data for optimised formulation

Table 5: Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE /t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3- Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
20.1	0.5	0.707	1.303	-0.301	1.903	40.200	0.0498	-0.697	79.9	4.642	4.307	0.335
24.32	1	1.000	1.386	0.000	1.879	24.320	0.0411	-0.614	75.68	4.642	4.230	0.412
28.76	2	1.414	1.459	0.301	1.853	14.380	0.0348	-0.541	71.24	4.642	4.145	0.496
41.53	3	1.732	1.618	0.477	1.767	13.843	0.0241	-0.382	58.47	4.642	3.881	0.760
49.92	4	2.000	1.698	0.602	1.700	12.480	0.0200	-0.302	50.08	4.642	3.686	0.956
56.86	5	2.236	1.755	0.699	1.635	11.372	0.0176	-0.245	43.14	4.642	3.507	1.134
64.9	6	2.449	1.812	0.778	1.545	10.817	0.0154	-0.188	35.1	4.642	3.274	1.367
71.86	7	2.646	1.856	0.845	1.449	10.266	0.0139	-0.144	28.14	4.642	3.042	1.600
78.45	8	2.828	1.895	0.903	1.333	9.806	0.0127	-0.105	21.55	4.642	2.783	1.859

83.12	9	3.000	1.920	0.954	1.227	9.236	0.0120	-0.080	16.88	4.642	2.565	2.076
90.25	10	3.162	1.955	1.000	0.989	9.025	0.0111	-0.045	9.75	4.642	2.136	2.505
94.62	11	3.317	1.976	1.041	0.731	8.602	0.0106	-0.024	5.38	4.642	1.752	2.889
98.31	12	3.464	1.993	1.079	0.228	8.193	0.0102	-0.007	1.69	4.642	1.191	3.450

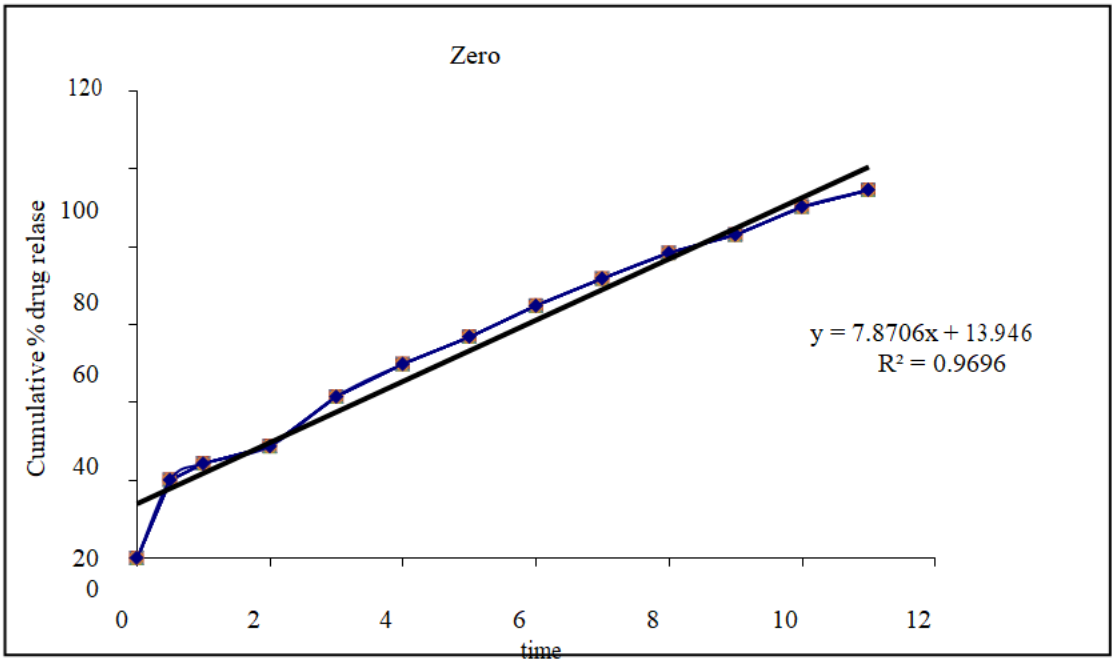

Fig 7: Zero order release kinetics

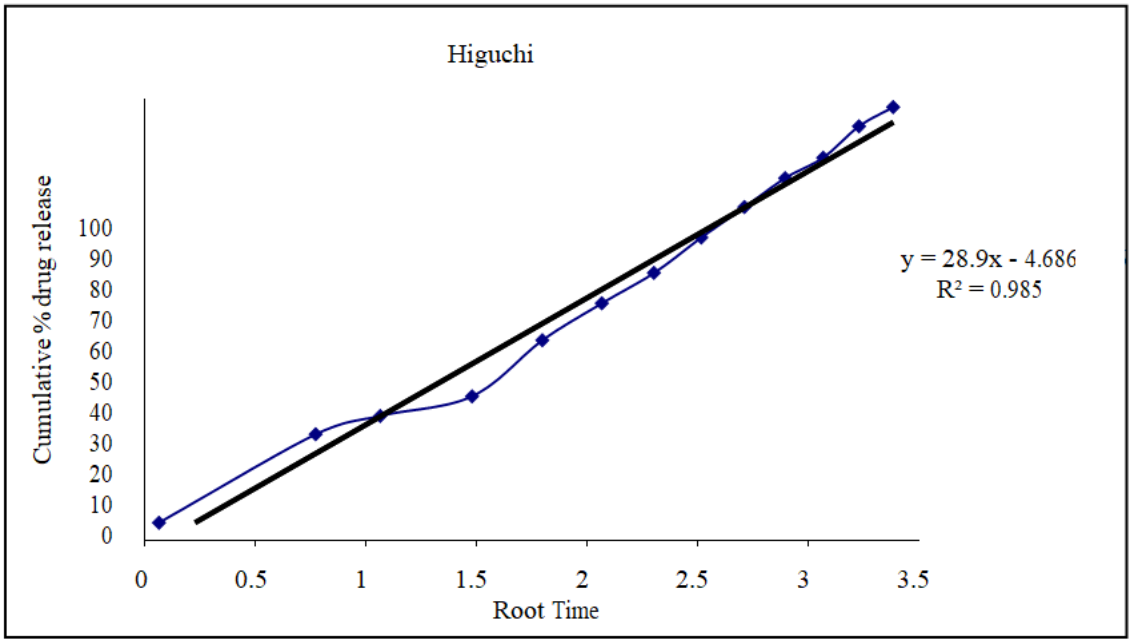

Fig 8: Higuchi release kinetics

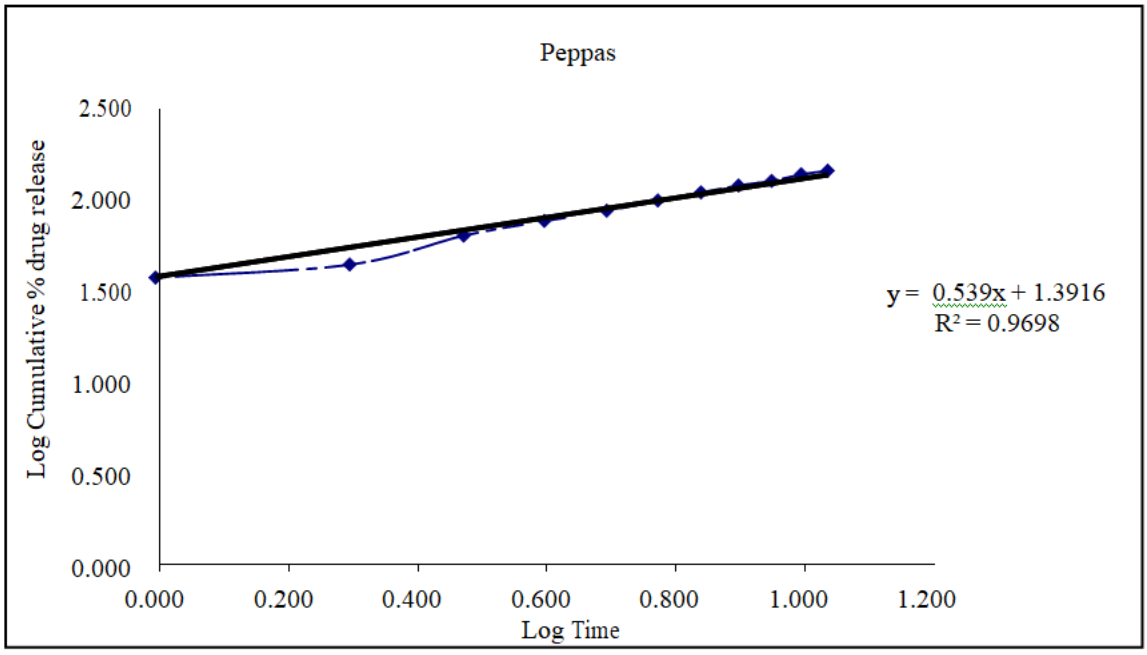

Fig 9: Kors mayer peppas release kinetics

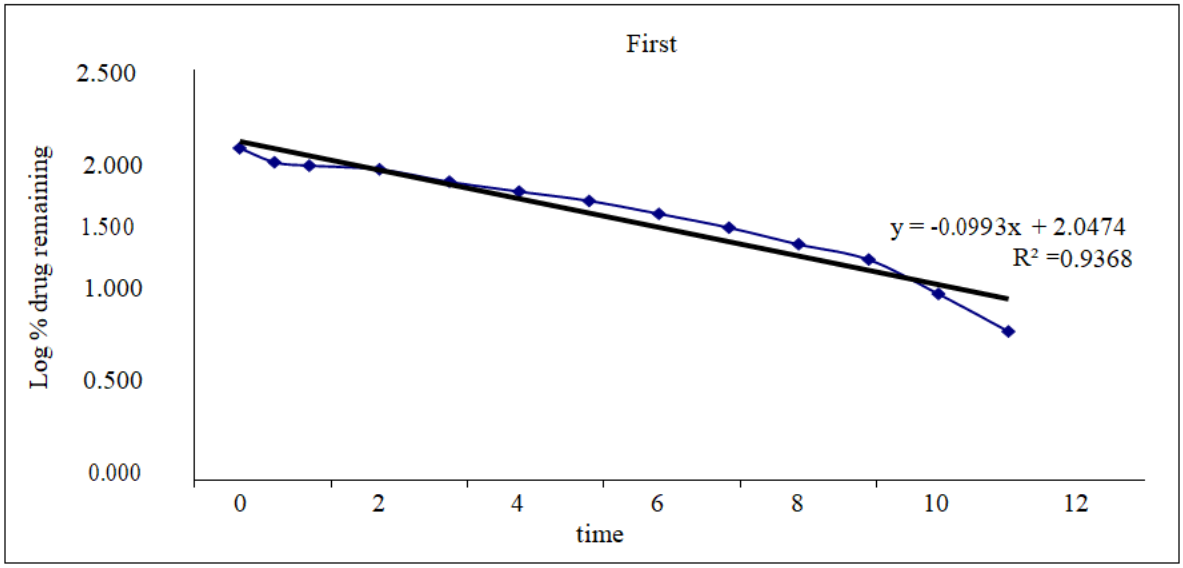

Fig 10: First order release kinetics

Optimised formulation F9 was kept for release kinetic studies. From the above graphs it was evident that the formulation F9 was followed Higuchi release kinetics mechanism.

Drug – Excipient compatibility studies
Fourier Transform-Infrared Spectroscopy

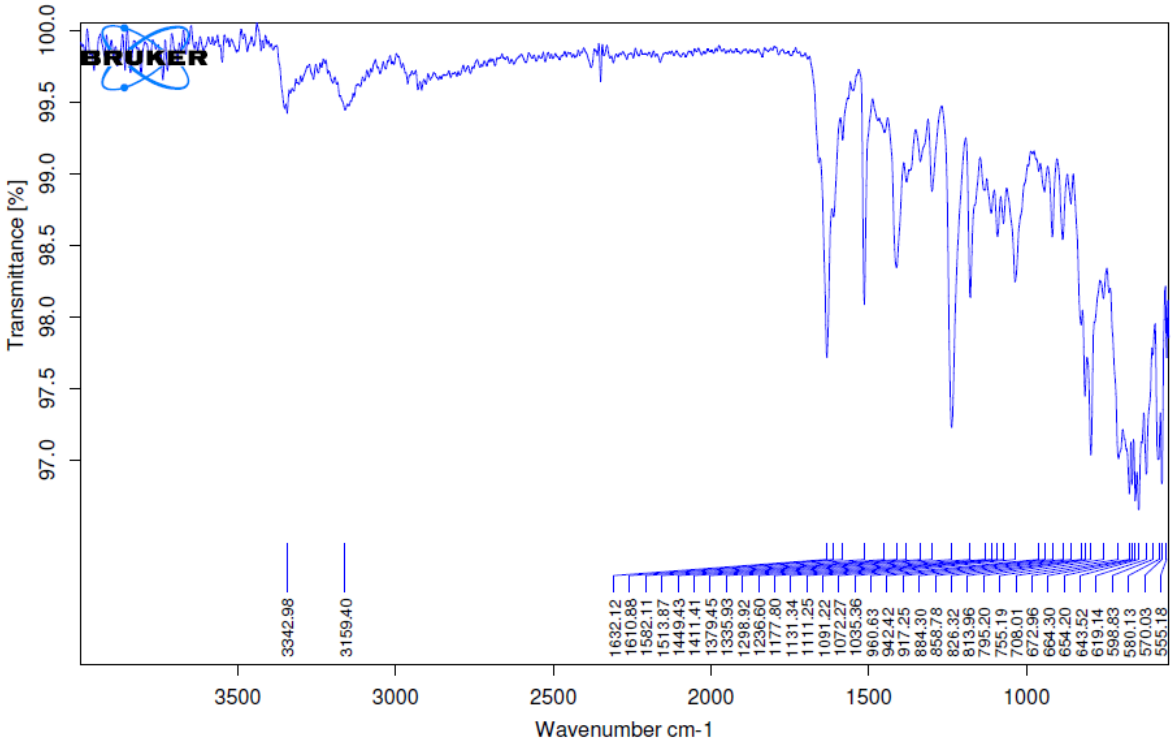

Fig 11: FTIR Spectrum of pure drug

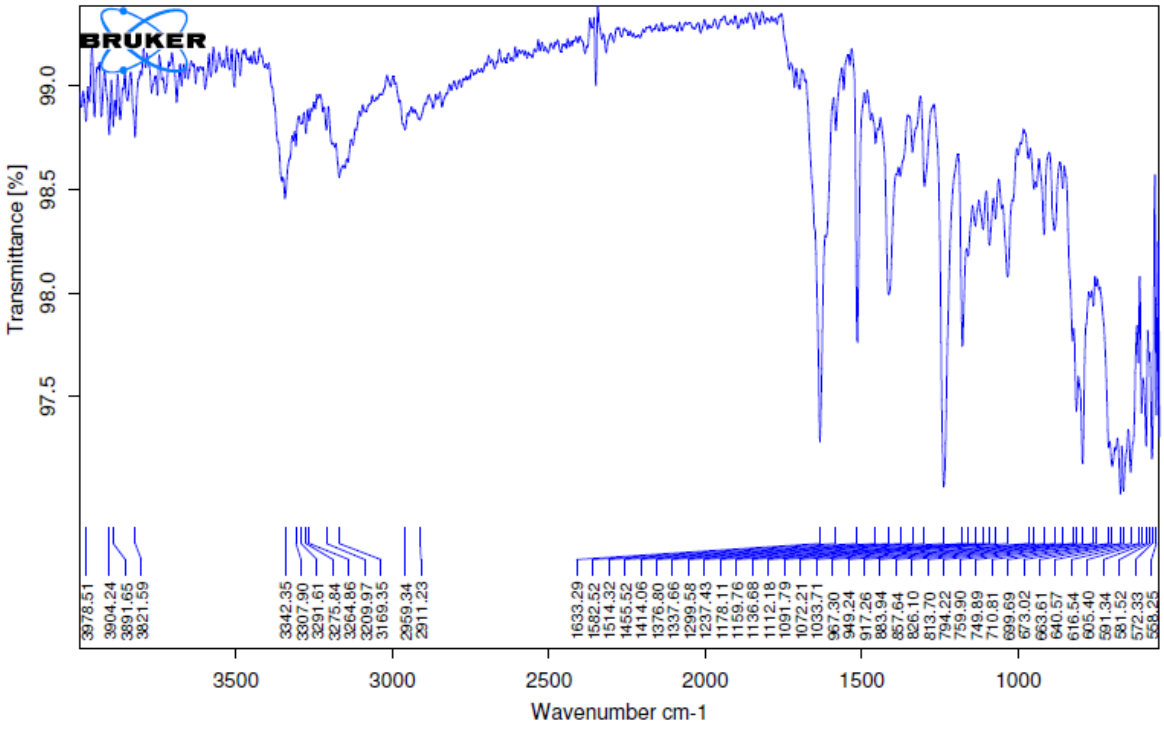

Fig 12: FTIR Spectrum of optimised formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions. Flurbiprofen is also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

CONCLUSION

The research was undertaken with the aim to formulate and evaluate the floating tablets of Flurbiprofen using Gum Copal, Gum Damar, and Psyllium Husk as polymers. From results obtained, it was concluded that the formulation of floating release tablet of Flurbiprofen containing polymers (Gum Copal, Gum Damar, Psyllium Husk) was taken as ideal or optimized formulation for 12 hours release as it fulfills all the requirement of Floating release dosage form. All the formulations were able to floating 8 to 11hrs with controlling the release rate throught out the time. F9 formulation was considered as optimized with 98.31 % release of drug content. From the above graphs it was evident that the formulation F9 was followed Higuchi release kinetics mechanism.

REFERENCES

1. Lachman L, Liberman ha. The theory and practice of industrial pharmacy. p. 293-302.
2. Joseph R. Robinson, Vincent H. L. Lee. Controlled drug delivery: fundamentals and applications. 2nd ed. New york: Marcel dekker; 1978. p. 24-36. https://www.worldcat.org/title/controlled-drug-delivery-fundamentals-and-applications/oclc/858014856
3. D. M. Brahmankar, Sunil B. Jaiswal. Biopharmaceutics and pharmacokinetics : a treatise. 1st ed. Vallabh prakashan. NewDelhi; 1995.p. 64-70.https://www.worldcat.org/title/biopharmaceutics-and-pharmacokinetics-a-treatise/oclc/775010126
4. Yie W Chein, Novel drug delivery systems. 2nd ed. New york: Marcel dekker; 1992. p. 4-56. https://www.worldcat.org/title/novel-drug-delivery-systems/oclc/855678872
5. Ansel. Pharmaceutical dosage form and drug delivery system. lipincott. 7th ed. p. 553.
6. Gennaro r.a. Remington,the science and practice of pharmacy. 20th ed. New york: lippincott williams:. 2000:1045.
7. Banker gs, rhodes ct. modern pharmaceutics. 3rd ed. new york: Marcel dekker; 1996. p. 678-721.
8. Swathi chilukala, Gastro retentive Drug Delivery of Cyclobenzaprine Hydrochloride, J. Gastroenterology Pancreatology and Hepatobilary Disorders. 2018; 2(1). https://doi.org/10.31579/2641-5194/006
9. V. Iannuccelli, G. Coppi, M.T. Bernabei, R. Cameroni.Air compartment multiple-unit system for prolonged gastric residence. Part I. Formulation study. International Journal of Pharmaceutics.1998; 174(1–2):47-5. ISSN 0378-5173, https://doi.org/10.1016/S0378-5173(98)00229-4.
10. Garg R, Gupta GD. Progress in controlled gastroretentivedelivery systems. Trop .J Pharm Res 2008; 7(3): 1055-66. https://www.ajol.info/index.php/tjpr/article/view/14691/2771