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FORMULATION AND EVALUATION OF METRONIDAZOLE SUSTAINED RELEASE FLOATING TABLETS

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Abstract: Writing this essay on the floating drug delivery system (FDDS) had as its main goal organizing the latest research on the fundamental role that flotation plays in gaining gastric retention. The buoyancy mechanism served as the foundation for the various techniques utilized in the creation of FDDS, including the construction of both effervescent and noneffervescent floating tablets. Metformin HCl was created in an oral sustained-release floating tablet format.Metronidazole's continuous release floating pills may be a more sensible and effective way to provide superior therapeutic effects over time. In the current study, metronidazole floating tablets were effectively made employing a variety of concentrations through the use of sustained release polymers such as Xanthan gum, carbopol 934, and hydroxyl propyl methyl cellulose K100 in the dry granulation process.After analysis, it was determined that the post time, weight variation, friability, and other factors were within the official bounds.

Comparing Carbopol 934 to the other medications, this one has a slower rate of dissolution. Based on the dissolution behavior analysis of all the formulations, F9 exhibits the best results, followed by F7 and F8. The best results are shown by this trio of formulations: that is the medication release just 57.2% at the ten –hour mark. As a result, the investigation found that Carbopol 934 exhibits.

Keywords: Floating drug delivery system, .Metronidazole, Xanthan gum, Carbopol 934,Hydroxylpropyl methyl cellulose K100.

I. INTRODUCTION

Oral Drug Delivery systems:

The term "Drug Delivery" covers a very extensive range of techniques used to deliver therapeutic agents into the human body. Drugs are administered with a us ain of curing patient ailments. Drugs are never administered in their pure form but arn converted in a suitable formulation so that its onset and intensity of action as well as total duration of action can be checked. Among the various routes of drug delivery oral route is most widely used route of drug delivery. But conventional dosage form offers few limitation which could be resolved by modifying the existing dosage form.

Advantages of Oral Drugs Delivery System:
Simple and convenient to use
Drugs readily available by prescription
Oral route less objectionable than parenteral

Disadvantages of Oral Drug Delivery System:
Patient compliance
Dosages are largely empirical
Erratic absorption makes response unpredictable

Limitations of conventional oral dosage forms:
Poor patient compliance, chances of dose missing.
See-saw fluctuations.
Multiple drug therapy enhances the risk of toxicity as well as overall cost of treatment.

Approaches to overcome these limitations:
Development of new, better and safer drugs with long life and large therapeutic indices.
Effective and safer use of existing drugs through concepts and techniques of controlled and targeted drug delivery systems.
Anatomy and physiology.
Pharmacodynamics and pharmacokinetics profile of drugs.
Physiochemical characteristics of drugs and delivery mode under study.

The oral controlled release formulations have been developed for those therapeutic agents that are easily absorbed from the G.I.T, having a shorter half-life, eliminated quickly from the blood circulation, narrow absorption window as these will release the drugs slowly into the GI.T
Controlled release dosage forms provide continuous release of drugs at the specific site for a predetermined time at a predetermined rate.

Sustained Release Dosage:
Sustained release dosage form is defined as well characterized and reproducible dosage form, which is designed to control drug release profile at a specified rate to achieve desired drugs concentration either in blood plasma or at target site.This system will provide actual therapeutic control that would temporal (time related), spatial (site related) or both.

Advantages of sustained drug delivery systems:
Reduce see-saw fluctuations
Total amount of dose decreases
Improved patient compliance
Increased safety of drugs
More uniform drug effects
Reduce Gl side effects

Disadvantages of sustained drug delivery systems:
Chances of dose dumping
Dose retrieval is difficult
High cost of formulation
Need for additional patient education
Reduce potential for accurate dose adjustment
The physician has less flexibility in adjusting dosage regimen, as it is fixed by dosage from design

Sustained release floating tablets:

Floating systems are more popular in comparison with other GRDDS because they don't have any adverse effect on the motility of GIT. Floating drug delivery system have lower density compare to Gastric fluid which enables them to float over the surface of gastric fluid. Drug release form the system take place slowly at the rate required which result in reduced fluctuation in the plasma concentration along with increased GIT. Hydrophilic polymers are most use excipients such as natural or synthetic or semi-synthetic. Carbopol 974 NF, HPMC K4M are semi-synthetic polymers. Xanthan gum, Chitosan, Locust gum, Gaur gum, Pectin, Starch, etc are the natural polymers. Sodium bicarbonate use as gas former in the formulation to float the tablets in gastric fluid.This tablets will achieve the high concentration of antibacterial agent in the gastric mucosa.

II. MATERIALS AND METHODOLOGY

Table 2.1: List of chemicals used

S.No	Name of the materials	Functions
1	Metronidazole	Antibiotic
2	Microcrystalline cellulose	Diluent
3	Hydroxypropyl methyl cellulose	Thickening agent
4	Carbopol	Thickening agent
5	Xanthan gum	Thickening agent
6	Sodium bicarbonate	Antacid
7	Starch	Binder
8	Talc	Glidant
9	Magnesium stearate	Lubricant

Table 2.2: Composition of different formulations (batch F1 to F9)

S.No	Name of the ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1	Metronidazole	200	200	200	200	200	200	200	200	200
2	Microcrystalline cellulose	90	65	40	90	65	40	90	65	40
3	Hydroxypropyl methyl cellulose	100	125	150	-	-	-	-	-	-
4	Carbopol	-	-	-	100	125	150	-	-	-
5	Xanthan gum	-	-	-	-	-	-	100	125	150
6	Sodium bicarbonate	20	20	20	20	20	20	20	20	20
7	Starch	80	80		80		80		80	
8	Talc	5	5	5	5	5	5	5	5	5
9	Magnesium stearate	5	5	5	5	5	5	5	5	5
Total Net (mg)		**500**	**500**	**500**	**500**	**500**	**500**	**500**	**500**	**500**

Dry Granulation Procedure:

- Weight all the ingredients.
- Take the mortar and pestle and add the MCC, Sustained release polymer and Metronidazole.
- Add the Starch powder and Sodium bicarbonate powder.
- Mix all the ingredients.
- Dry screening.
- Mixing with other ingredients: A dry lubricant and glidant is added to the granules either by dusting over the spread-out granules or by blending with the granules.
- Tableting: Last step in which the tablets is fed into the die cavity and the compressed.

III. RESULTS

Calibration of Metronidazole

Table 3.1: Calibration of Metronidazole

Concentration (µg/ml)	Absorbance at 277nm
0	0
10	0.211
20	0.433
30	0.597
40	0.791
50	0.988

Standard plot of Metronidazole

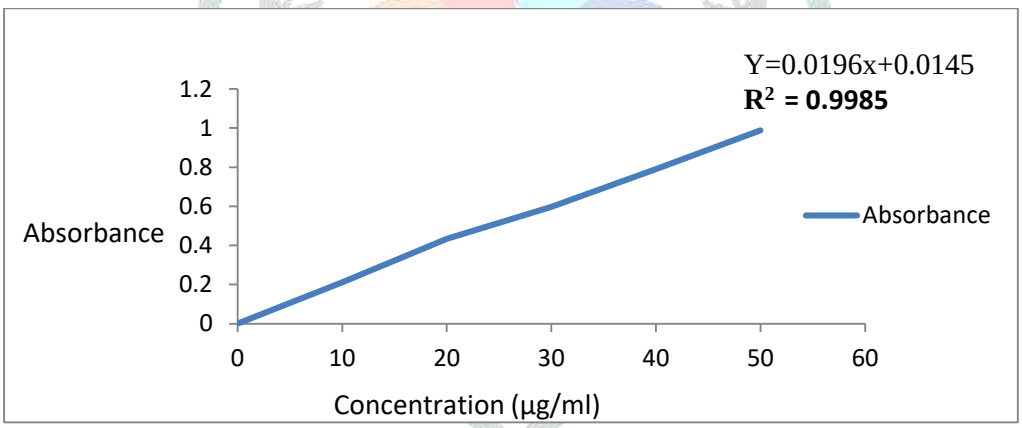

Fig 3.1: Standard calibration curve for Metronidazole

Precompression studies

Table 3.2: Evaluation parameter values of all formulations

Formulations	Hardness (Kg/cm^2)	Weight Variation	Friability	Floating Time (hrs)
F1	2.5	±7	15	10
F2	3.2	±5	18	10
F3	3.8	±6	23	10
F4	3	±8	16	10
F5	4.2	±6	13	10
F6	3.4	±5	24	10
F7	4.2	±4	1	10
F8	3.5	±7	0	10
F9	5.5	±3	0	10

Table 3.3: Dissolution release values of all formulations

Time (hrs)	% Drug release in 900ml 0.1N HCl (pH buffers 1.2) 100 rpm, 37±0.5^{0}C,								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
10 min	19.23	21.67	18.25	15.62	13.26	5.67	3.61	1.603	**1.809**
1hr	28.26	35.13	29.14	28.13	23.66	8.66	10.2	4.26	**2.713**
2hr	32.64	41.26	39.26	30.63	36.24	13.26	26.1	8.43	**10.40**
3hr	49.78	47.61	46.14	34.28	42.19	27.81	28.4	12.30	**18.99**
4hr	57.47	58.26	52.26	42.16	53.7	38.6	30.2	18.63	**25.32**
5hr	61.29	67.84	59.26	55.6	62.38	46.5	33.8	24.23	**36.63**
6hr	71.46	73.16	66.12	60.89	71.6	59.6	34.3	25.2	**42.73**
7hr	79.24	76.29	76.79	62.62	75.36	65.2	35.7	26.1	**47.93**
8hr	83.62	80.16	81.46	70.31	80.26	73.3	36.9	28.2	**50.65**
9hr	89.34	82.36	85.76	72.66	83.64	80.6	40.4	30.1	**55.62**
10hr	93.64	87.64	88.69	75.2	87.36	82.3	42.3	30.6	**57.2**

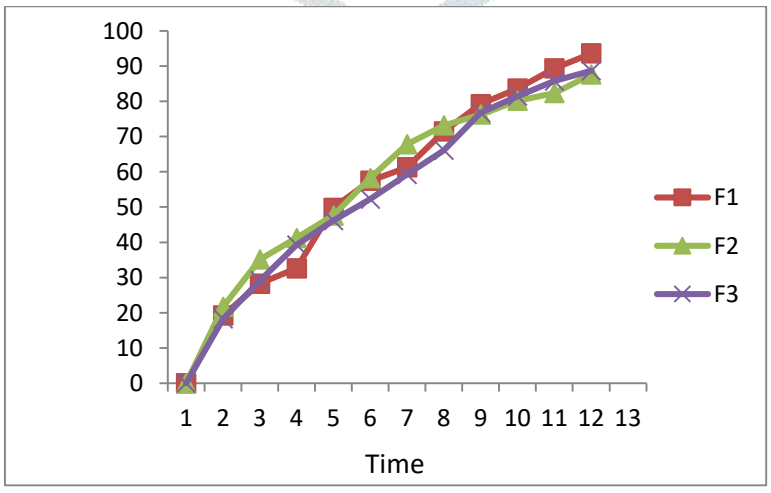

Fig 3.2: Dissolution profile of sustained release floating tablet by HPMC K100

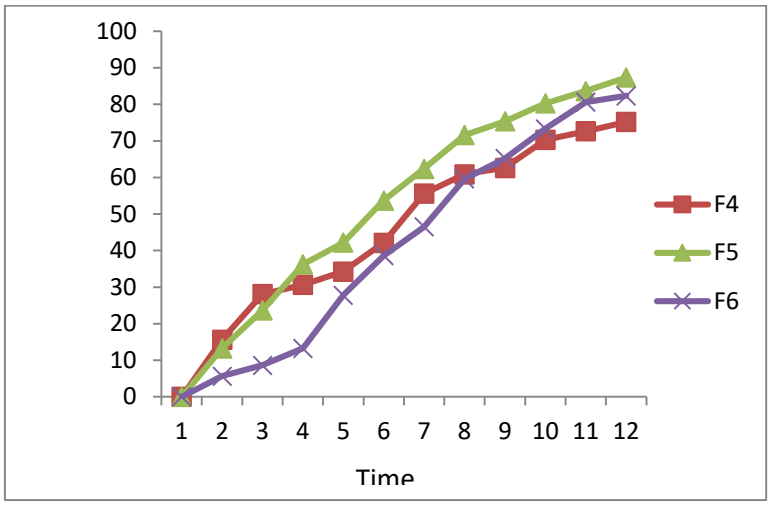

Fig 3.3: Dissolution profile of sustained release floating tablet by Xanthan gum

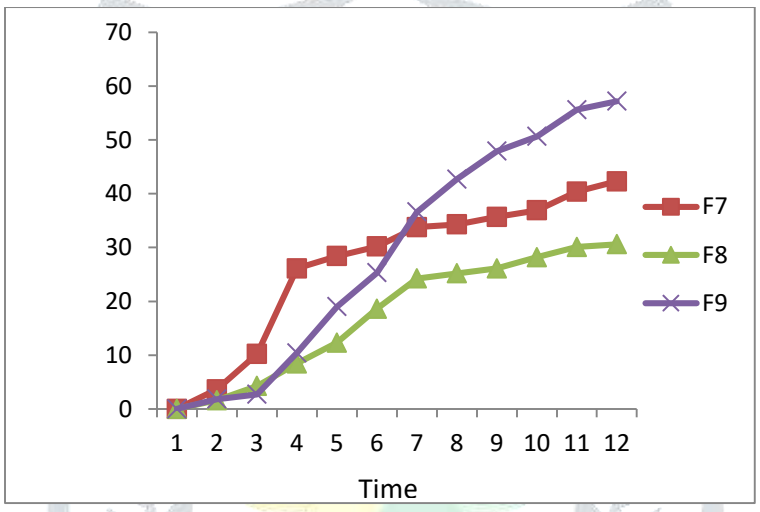

Fig 3.4: Dissolution profile of sustained release floating tablet by Carbopol 934

IV.CONCLUSION

The tablets of various formulation were subjected to various evolution test such as weight variation, friability, hardness and drug release by dissolution studies according to the procedure specified in the I.P. The results of the test were tabulated and found to be within the pharmacopoeial limits. This studies indicated that all the prepared formulation were good.

The release of drug form sustained release floating tablets were preparation by 3 polymers like Carbopol 934, HPMC K100, Xanthan gum acts as sustained release polymers. The carbopol 934 formulation shows best release compared with remaining polymers.

Carbopol 934>Hydroxypropyl Methyl Cellulose K100> Xanthan gum.

By using Carbopol 934 preparation we prepared F7, F8 and F9 formulation. Out of these three formulation F9 is showed best result.

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