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Research Article

PREPARATION AND EVALUATION OF GASTRO RETENTIVE FLOATING TABLETS OF MEBENDAZOLE

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ABSTRACT

The purpose of this research was to prepare a gastro retentive drug delivery system of Mebendazole. Chitosan and hydroxypropyl methyl cellulose of various viscosity were used. Sodium bicarbonate was incorporated as a gas-generating agent. The effects of citric acid and stearic acid on drug release profile and floating properties were investigated. The addition of stearic acid reduces the drug dissolution due to its hydrophobic nature. The specific study was carried out to formulate such a dosage form that can neutralize the acidity locally in the stomach. The granulation was formed by Fluidized bed processor in which top spray technique was adopted for forming the granules.

Keywords: FBP (Fluidized Bed Processor), Mebendazole, Floating System, HPC.

INTRODUCTION

Over the past three decades, the pursuit and exploration of devices designed to be retained in the upper part of the gastrointestinal (GI) tract has advanced consistently in terms of technology and diversity, encompassing a variety of systems and devices such as floating systems, raft systems, expanding systems, swelling systems, bioadhesive systems and low-density systems. Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local action in the upper part of the small intestine, for example treatment of peptic ulcer disease. Furthermore, improved bioavailability is expected for drugs that are absorbed readily upon release in the GI tract. These drugs can be delivered ideally by slow release from the stomach. Many drugs categorised as once-a-day delivery have been demonstrated to have suboptimal absorption due to dependence on the transit time of the dosage form, making traditional extended release development challenging. Therefore, a system designed for longer gastric retention will extend the time within which drug absorption can occur in the small intestine. Gas generating system was adopted to prepare sustain release tablets of Mebendazole by using Chitosan, HPMC, and gas generating agent sodium bicarbonate. Various formulas were formulated to get the desired result. In vitro studies like buoyancy studies and dissolution studies were carried out.

MATERIALS AND METHODS

Mebendazole was obtain as gift sample from Unichem Laboratories Goa. Chitosan was procured as a gift sample from Ajanta Chemicals Paithan. HPMC K4M was obtain as gift sample from Shreya Pharmaceuticals Aurangabad. Rest of the excipient were of the analytical grade purchased commercially.

Method of preparation of tablets

The tablets were prepared by wet granulation method using fluidized bed processor (mini). The tablets were compressed using 10 station rotatry tablet press D tooling. The formula for the preparation of tablets is given below.

Table 1: (Formula 1)

Sr. No	Ingredients	Qty per tab(mg)	Qty per 20 tab(mg)
1	Mebendazole	100	2000
2	HPMC K4M	70	1400
3	Sodium Bicrbonate	50	1000
4	Stearic acid	50	1000
5	Citric acid	10	200

Table 2: (Formula 2)

Sr. No	Ingredients	Qty per tab(mg)	Qty per 20 tab(mg)
1	Mebendazole	100	2000
2	HPMC K4M	90	1800
3	Sodium Bicrbonate	60	1200
4	Stearic acid	50	1000
5	Citric acid	10	200

Table 3: (Formula 3)

Sr. No	Ingredients	Qty per tab(mg)	Qty per 20 tab(mg)
1	Mebendazole	100	2000
2	HPMC K4M	100	2000
3	Sodium Bicrbonate	40	800
4	Stearic acid	50	1000
5	Citric acid	10	200

Table 4: (Formula 4)

Sr. No	Ingredients	Qty per tab(mg)	Qty per 20 tab(mg)
1	Mebendazole	100	2000
2	HPMC K4M	40	800
3	Chitosan	40	800
3	Sodium Bicrbonate	50	1000
4	Stearic acid	50	1000
5	Citric acid	10	200

Table 5: (Formula 5)

Sr. No	Ingredients	Qty per tab(mg)	Qty per 20 tab(mg)
1	Mebendazole	100	2000
2	HPMC K4M	30	600
3	Chitosan	60	1200
3	Sodium Bicrbonate	50	1000
4	Stearic acid	50	1000
5	Citric acid	10	200

Preparation of granules

As seen in the above formula in the first three formula only HPMC K4M was used were as in the last two formula Chitosan was used. The granules were formed using Fluid bed processor. In the first three formula all the ingredients given in the first three formula were dried mixed and granules were prepared by top spray nozzle using simple water. The formed granules were dried in the same equipment.

The granule formed were evaluated for angle of repose, compressibility index and hausner's ratio. In the formula no 4 and formula no 5 all the ingredient were dried mixed except HPMC K4M and loaded in the fluidized chamber. The HPMC K4M was dissolved in ethanol and sprayed over the fluidized material through top spray nozzle. In the same way the granules formed were evaluated for angle of repose, compressibility index and hausner's ratio. The granules formed were compressed using 10 station tablet rotatry press D tolling. The tablets formed were evaluated for hardness test, friability test, weight variation test and floating time was also evaluated.

RESULTS AND DISCUSSION

Table 6: Formula 1

Sr. No	Evaluation parameter	Obs
1	Angle Of Repose(%)	27
2	Compressibility index(%)	14
3	Hausner's ratio	1.2
4	Friability test(%)	0.1
5	Weight Variation test(%)	1
6	Floating time(sec)	255

Table 7: Formula 2

Sr. No	Evaluation parameter	Obs
1	Angle Of Repose(%)	24
2	Compressibility index(%)	13
3	Hausner's ratio	1.2
4	Friability test(%)	0.1
5	Weight Variation test(%)	1
6	Floating time(sec)	210

Table 8: Formula 3

Sr. No	Evaluation parameter	Obs
1	Angle Of Repose(%)	29
2	Compressibility index(%)	10
3	Hausner's ratio	1.3
4	Friability test(%)	0.1
5	Weight Variation test(%)	3
6	Floating time(sec)	290

Table 9: Formula 4

Sr. No	Evaluation parameter	Obs
1	Angle Of Repose(%)	23
2	Compressibility index(%)	15
3	Hausner's ratio	1.1
4	Friability test(%)	0.1
5	Weight Variation test(%)	2.5
6	Floating time(sec)	110

Table 10: Formula 5

Sr. No	Evaluation parameter	Obs
1	Angle Of Repose(%)	25
2	Compressibility index(%)	15
3	Hausner's ratio	1.1
4	Friability test(%)	0.1
5	Weight Variation test(%)	4
6	Floating time(sec)	90

The dissolution for all tablets was carried using USP I paddle apparatus using fluid pH 1.2 as the dissolution medium at 100 rpm. The dissolution was carried out for 12 hours. After every 1 hr 5ml of sample was withdrawn, as such 12 sample withdrawn after each 1 hr and each time the sink condition was maintained adding 5 ml of fresh fluid. The sample withdrawn was analyzed using UV spectrophotometer and maximum absorbance was shown at 254 nm.

Table 11: Dissolution Profile (Drug Release in%)

Time (hr)	Formula 1	Formula 2	Formula 3	Formula 4	Formula 5
1	9	13	15	26	28
2	14	18	21	38	36
3	19	24	29	42	41
4	22	27	33	47	46
5	29	33	39	57	58
6	36	38	48	63	62
7	37	42	56	69	68
8	41	49	64	71	74
9	44	55	68	77	81
10	49	62	75	83	89
11	55	71	81	89	93
12	59	77	84	95	98

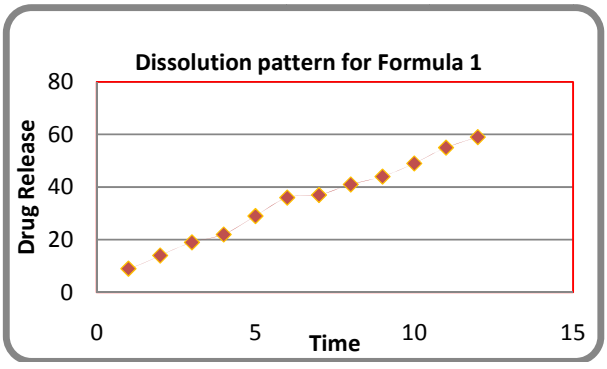

Fig 1: Dissolution Pattern for Formulation 1

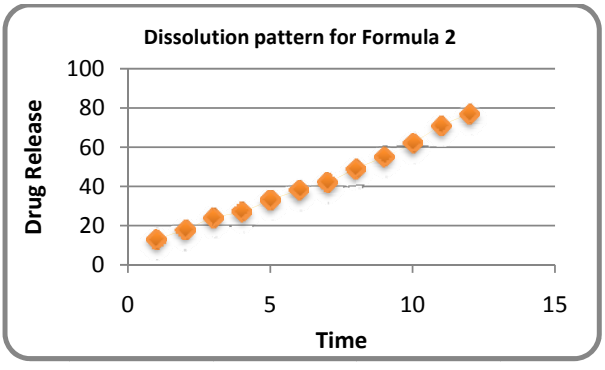

Fig 2: Dissolution Pattern for Formulation 2

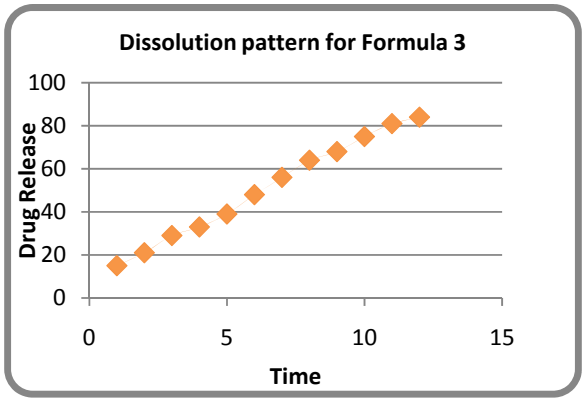

Fig. 3:Dissolution Pattern for Formulation 3

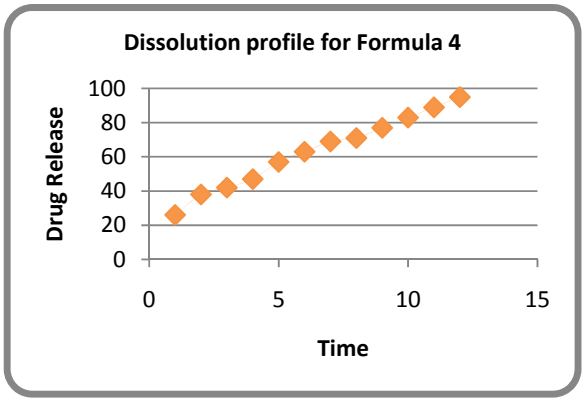

Fig. 4: Dissolution Pattern for Formulation 4

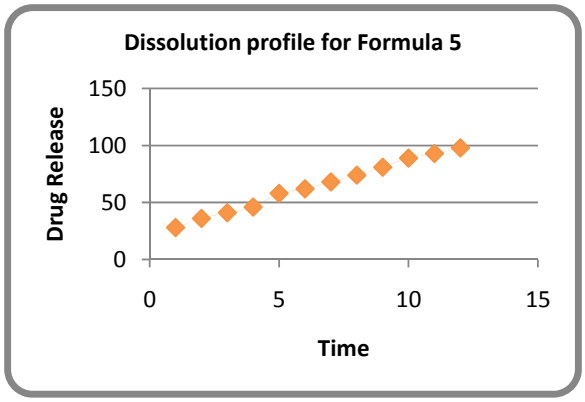

Fig. 5: Dissolution Pattern for Formulation 5

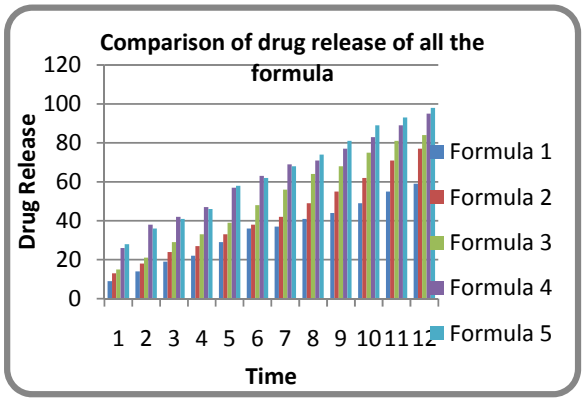

Fig. 6: Drug Release Comparison of all the Formula

CONCLUSION

In all the formulation tablets were successfully compressed wiyhout any major compression problem during operation cycle. The evaluation parameter of the granules showed good result which are tabulated above in the table. From the first three formulation it was came to know that it must be due to the viscosity of the HPMC K4M which must be responsible for slow release of the drug from the tablet. Hence to improve the drug release the quantity of HPMC K4M was reduced and Chitosan was incorporated in the formulation. After the addition of the chitosan the swelling index was increase as well as the drug release and the floating time was improved. It therefore was concluded that successful GRDF was formulated using two polymer i.e. chitosan and HPMC K4M. The granulation performed by fluidized bed processor gave the granules having good flow properties and good compressibility index.

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