International Journal of Pharmaceutical Applications ISSN 0976-2639.
Vol 3, Issue 1, 2012, pp 289-292 http://www.bipublication.com

FORMULATION AND EVALUATION OF SUSTAINED RELEASE FLOATING TABLETS OF CIPROFLOXACIN WITH HEPATO-PROTECTANT.

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ABSTRACT:
The study was taken up with a view to increase the elimination half-life of the antibiotics which would provide consistent and prolonged plasma drug concentrations in the body. In the present research work formulation and evaluation of sustained release floating matrix tablets of Ciprofloxacin has been done. Sodium bicarbonate is used in the formulations as a source of Carbondioxide. Ciprofloxacin has been selected as the drug of choice owing to the fact that it is having a bioavailability of only 60%. It is stable at the gastric pH (acidic 1.2) and is having an elimination half-life of 7 hours. It is soluble in acidic medium and thus a floating tablet of the drug would increase the extent of Absorption.
The matrix type of system is prepared with the help of swell-able polymer hydroxypropylmethylcellulose k15M. It is formulated in such a way that when in contact with the acidic gastric contents, CO_2 is liberated and gets entrapped in swollen hydrocolloid, which provides buoyancy to the dosage forms. More over DL-methionine has been added as a hepato- protective agent that makes the formulation a unique one.
The resulting formulation has been evaluated for all the necessary parameters like Weight variation , Thickness, Hardness, Friability, Drug content uniformity, Floating lag time, Floating duration time. Besides the above tests other parameters, dissolution studies and in-vitro drug release also has been conducted successfully. Thus the above formulation has been proven to be much more superior to the existing tablet forms.
Key words: floating matrix tablets, bioavailability, Ciprofloxacin, hepatoprotective.

INTRODUCTION:

The hydrodynamic balanced system (HBS) also called Floating drug delivery system (FDDS) is an oral dosage form (capsule or tablet) designed to prolong the residence time of the dosage form within the GIT [1-3]. It is a formulation of a drug with gel forming hydrocolloids meant to remain buoyant in the stomach contents [4]. Drug dissolution and release from the dosage form retained in the stomach fluids occur at the pH of the stomach under fairly controlled conditions [5-7].

Ciprofloxacin:

Ciprofloxacin is a first generation fluoroquinolone broad spectrum antibiotic having a Molecular weight of 331.4 g/mole. It is a faintly yellowish to light yellow crystalline substance. The antibiotic is known to have a bioavailability of about 60% and is mostly excreted out by renal route. It has a half life of 4hours. Ciprofloxacin is a broad-spectrum antibiotic active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting DNA gyrase, a type II topoisomerase, and

topoisomerase IV,[40] enzymes necessary to separate bacterial DNA, thereby inhibiting cell division.

HPMC:

Hydroxy propyl methylcellulose is mixed alkyl hydroxyl alkyl cellulosic ether and may be regarded as the propylene glycol ether of methylcellulose. It is an odorless, tasteless, white or creamy white fibrous granular powder. It soluble in cold water, forming a viscous colloidal solution which makes the formulation to float and imparts necessary matrix charecterstics required for the formulation(8) it is insoluble in alcohol, ether and chloroform. It has a gel point at 50^0C to 90^0C.

Sodium bicarbonate:

Sodium Hydrogen Carbonate, Baking soda. As odorless, white crystalline powder with a saline taste. The crystalline structure is monoclinic prisms, Soluble in water, practically insoluble in ethanol and ether. In the effervescent formulations it is used as a gas generating agent. It liberates Co_2 in an acidic gastric content which provide buoyancy to the dosage form [9,10]. Its concentration in the effervescent formulations may vary from 25-40%

Dl-Methionine:

DL Methionine is an essential amino acid. It must be supplied to the body through protein intake, and is necessary for the body to produce SAMe. It also aids in the body's detoxification process. The benefits of DL Methionine made use of protecting liver from hepatotoxicity of drugs and antibiotics.

MATERIALS AND METHODS:

The formulation of effervescent tablets was done by the following materials. Ciprofloxacin,(A generous gift from Euro Labs, Hyderabad), DL-methionine (hepato-protectve), Avicel, sodium-bi-carbonate,(Merck, Specialities Pvt Ltd, Mumbai), magnesium staearate, (S.D. Fine Chemicals, Mumbai), aerosil , (S.D. Fine Chemicals, Mumbai**,** HPMC K15M. Signet Chemical Corporation, Mumbai).

Four formulations F1, F2, F3, and F4 were prepared which had varying concentrations of the polymer HPMC K15M and Avicel. Accurately weighed quantities of polymer, Avicel were taken in a mortar and mixed geometrically. To this mixture required quantity of Ciprofloxacin and DL-methionine was added and mixed slightly with pestle. This mixture was passed through 40# and later collected in a plastic bag and blended for 5 min. To this required amount of sodium bi carbonate was added and again mixed for 5 min. Later required quantity of magnesium stearate and aerosil were added and the final blend was again passed through 40#. Thus obtained blend was mixed thoroughly for 10 min and compressed into tablets with 6mm Round Punches and corresponding dies at a hardness of $6kg/cm^2$ on a rotary tablet punching machine (11)

Composition of ciprofloxacin floating tablets.

Ingredients	F 1	F 2	F 3	F 4
Ciprofloxacin Dl-methionine	100 25	100 25	100 25	100 25
Avicel	80	68	58	48
HPMC K15M	30	40	50	60
NaHCO3	10	10	10	10
Mg.Stearate	2	3	3	3
Aerosil	3	4	4	4
TOTAL WEIGHT	250	250	250	250

RESULTS:

All Formulations were evaluated for Compressibility index, Angle of repose and Hausner ratio. The results indicated the pre-compressed blend gas good flow

FLOW PROPERTIES OF THE FINAL POWDER BLEND

Formulation code	Compressibility index	Angle of repose	Hausner ratio
F 1	12.3	28.7°	1.15
F 2	15.9	29.3°	1.19
F 3	12.8	27.6°	1.13
F 4	15.7	28.1°	1.17

All Formulations were tested for physical parameter like hardness, thickness, weight variation, friability and drug content. All estimated parameters were found to be within the limits [11].

FORMULATION CODE	HARDNESS (kg/cm^2)	THICKNESS (mm)	WEIGHT VARIATION (mg)	FRIABILITY (%)	DRUG CONTENT (%)
F 1	4.0	3.384±0.05	249.46±3.121	0.78	97.23
F 2	4.5	3.276±0.06	257±1.665	0.82	99.12
F 3	4.0	3.186±0.03	255±2.109	0.80	98.32
F4	5.5	3.186±0.04	253±4.170	0.8	99.54

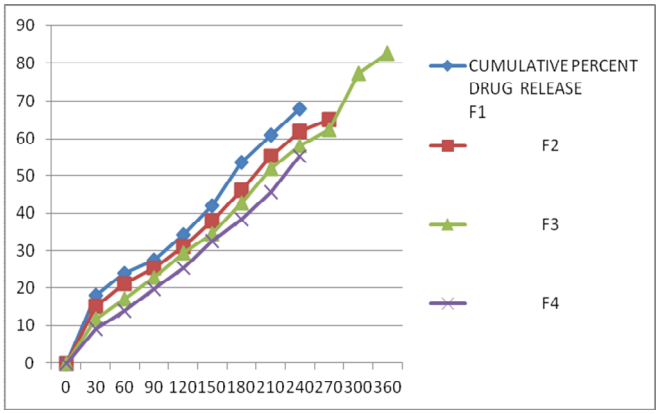
The resulting floating tablets were also assessed for their floating lag time and total floating time [8, 12].

S.NO	FORMULATION CODE	FLOATING LAG TIME	TOTAL FLOATING TIME
1	F 1	20 SEC	2 hr 43 min
2	F 2	14.44 SEC	3 hr 55 min
3	F 3	11 SEC	5hr 20 min
4	F 4	32.91 SEC	6 hr 57 min

IN-VITRO DRUG RELEASE OF FLOATING TABLETS

Cumulative percent drug release of ciprofloxacin floating tablets with HPMC k15m polymer

TIME (min)	CUMULATIVE PERCENT DRUG RELEASE	CUMULATIVE PERCENT DRUG RELEASE	CUMULATIVE PERCENT DRUG RELEASE	CUMULATIVE PERCENT DRUG RELEASE
	F1	F2	F3	F4
0	0	0	0	0
30	18	15	11.7	9.2
60	24	21.2	17	14
90	27.5	25.5	22.7	19.7
120	34.3	31.2	29.6	25.3
150	42	38	34.5	32.7
180	53.6	46	42.6	38.4
210	61	55.3	51.9	45.5
240	68	62	58.2	55.3
270	70	65	62.5	58
300	72	68	64	60.1
360	75	70	66.2	62



Discussion:

The above work has been planned and aimed for the increase of the bioavailability of the ciprofloxacin. Thus it is observed from the invitro

studies that the incorporation of the antibiotic into the floating dosage form has released the drug to varying extents depending upon the concentration of the polymer used. Instant release dosage form of ciprofloxacin is known to release the complete drug with in 40 minutes where as the floating dosage forms have released the drug in several hours depending upon the concentration of various ingredients. Also the antibiotic ciprofloxacin has been extensively metabolized by hepatic first pass and .incorporation of the DL-methionine in all the four formulations has proven to be a hepato protective agent. It did not show any incompatibility with other ingredients of the formulation. Also the results for evaluation for various parameters show that the formulations are within the comparable limits of conventional dosage forms.

CONCLUSION

Sustained release floating tablets of Ciprofloxacin were successfully prepared with hydrophilic polymers like HPMC K15M.

From the Preformulation studies for drug excipients compatibility, it was observed that no physical incompatibility existed between the drug and excipients.

The formulated batches were evaluated for physical parameters, floating properties and dissolution profiles. The physical properties like weight variation and friability of all formulations complied with the pharmacopoeial specifications. The drug content of all tablets was in the range of 98 – 102%. Thus a superior formulation of the antibiotic has been formulated with all the necessary parameters of dosage forms.

References

1. Hwang S. J., H. Park and K. Park, "Gastric Retentive Drug-Delivery Systems", *Crit. Rev. Ther. Drug Carrier Syst.* 1998; 15: 243–284.
2. Deshpande, C.T. Rhodes, N.H. Shah," controlled release drug delivery system for prolonged gastric residence: an overview," *Drug Dev.Ind. Pharm.* 1996; 22: 531-539.
3. Seth and J. Tossounian, The hydrodynamically balanced system HBSTM: A novel drug deliverysystem for oral use, *Drug Dev.Ind. Pharm.* 1984; 10: 313–339.
4. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. *Pharm Res*. 1997;14:815-819
5. Whitehead, J. T. Fell and J H Collett, "Development of a Gastroretentive Dosage Form", *Eur. J. Pharma. Sci*, 1996; 4:182.
6. Erni W, Held K. The hydrodynamically balanced system: a novel principle of controlled drug release. *Eur Neurol*. 1987; 27: 215-275.
7. Floating Drug Delivery Systems: A ReviewArora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating Drug Delivery Systems: A Review. *AAPS PharmSciTech*. 2005; 06(03):
8. Timmermans and A. J. Moes, "Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: new data for reconsidering the controversy", *J. Pharm. Sci.*, 1994; 83: 8–24.
9. Timmermans and A. J. Moes, "How well do floating dosage forms float?", *Int. J.Pharm.*,1990; 62: 207–216.
10. Bolton S, Desai S, inventors. Floating sustained release therapeutic compositions. US patent 4 814 179. March 21, 1989.
11. Condtrolled Drug Delivery – Concepts and Advances by S.P.Vyas and Roop K.Khar