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Research Article

Formulation and Evaluation of Gastroretentive Dosage form of Ciprofloxacin Hydrochloride.

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ABSTRACT

The present study aims at developing a Gastroretentive swellable and floating matrix tablet formulation of ciprofloxacin hydrochloride for the effective treatment of infections caused by susceptible organisms. Ciprofloxacin hydrochloride is a fluoroquinoline antibiotic drug. Ciprofloxacin HCl is more stable in acidic medium and it has a narrow absorption window which is sited at stomach and proximal portions of the small intestine, so it fulfils the required criteria for selection of drug for Gastroretentive dosage form. Ciprofloxacin HCl Gastroretentive tablets were formulated by using wet granulation method and starch, poly vinyl pyrrolidone as binders, HPMC as suspending and stabilizing agent (polymer), croscarmellose sodium, Sodium Starch Glycolate, Crospovidone as disintegrates, sodium bicarbonate as alkalizing agent, Magnesium stearate as Lubricant and starch as diluent. The tablets were evaluated for Post compression Parameters. All the parameters were within the Pharmacopoeial limits and the In-vitro dissolution studies showed that the drug release was fast in Formulations F_2, F_6 and F_{10} containing Sodium Starch Glycolate as Super disintegrant when compared to all other Formulations.

Keywords: Ciprofloxacin HCl, Wet Granulation, Disintegrants, Gastroretentive dosage form.

INTRODUCTION

Drug is an active chemical entity used for diagnosis, prevention and treatment of disease; they also modify physiological state of the body. The oral route of drug administration is the most important method of administrating drugs for systemic effects. Oral route of drug administration has wide acceptance up to 50 to 60% of total dosage forms. Solid dosage forms are popular and most preferred route due to its advantages. Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They offer safe and convenient ways of active pharmaceutical ingredients (API) administration with excellent physiochemical stability in comparison to some other dosage forms, and provide accurate dosing. The control of gastrointestinal transit of orally administered dosage forms using Gastroretentive drug delivery systems (GRDDS) can improve the bioavailability of drugs that exhibit site-specific absorption. Prolonged gastric retention can be achieved by using floating, swelling, bio-adhesive or high-density systems.

A controlled drug delivery system with prolonged residence time in the stomach is of particular interest for drugs which are locally active in the stomach (misoprostol, antacids antibiotics against H. pylori). GRDDS is useful for drugs which have an absorption window in stomach or in the upper small intestine (eg.L-dopa, P-aminobenzoic acid, furosemide), drugs which are unstable in the intestine or colonic environment (eg.captopril),

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Table .No 1: Formulation Batches of Ciprofloxacin HCl Gastroretentive Tablets

Formula Code	API (mg)	HPMC K100LV (mg)	HPMC K15M (mg)	HPMC K100M (mg)	CPD (mg)	SSG (mg)	CCS (mg)	Starch (mg)	SBC (mg)
F1	580	116	-	-	232	-	-	-	116
F2	580	116	-	-	-	232	-	-	116
F3	580	116	-	-	-	-	232	-	116
F4	580	116	-	-	-	-	-	232	116
F5	580		116	-	232	-	-	-	116
F6	580		116	-	-	232	-	-	116
F7	580		116	-	-	-	232	-	116
F8	580		116	-	-	-	-	232	116
F9	580		-	116	232	-	-	-	116
F10	580		-	116	-	232	-	-	116
F11	580		-	116	-	-	232	-	116
F12	580		-	116	-	-	-	232	116

Table.2: Evaluation of Post compression Parameters

Formulation	Wt. Variation	Hardness Kg/cm^2	Friability %	Content Uniformity
F-1	1.044±1.21	9.0	0.34	93±2.3
F-2	1.043±0.49	9.0	0.45	94±1.2
F-3	1.065±0.88	9.0	0.25	98.2±1.5
F-4	1.093±1.42	9.0	0.28	94.8±2.5
F-5	1.099±1.14	9.0	0.26	99±3.5
F-6	1.032±1.21	9.0	0.35	98.4±2.8
F-7	1.022±1.11	9.0	0.23	96±2
F-8	1.032±1.00	9.0	0.23	101±1.8
F-9	1.031±1.55	9.0	0.25	96±2
F-10	1.042±1.88	9.0	0.27	98±1.9
F-11	1.045±1.99	9.0	0.52	99±1
F-12	1.043±1.89	9.0	0.25	97±2.2

All the values are expressed as mean±SD, n=3.

exhibit low solubility at high pH values (diazepam, verapamil) and drugs which alter normal flora of the colon (antibiotics). Various techniques used in the preparation of control release tablets are Tablet molding technique, Direct compression technique, Wet granulation technique, Mass extrusion technique. In the present investigation, Wet Granulation Method was taken as it was a robust process which helps in reducing elasticity problems and imparts flowability to a formulation. The Binders used were poly vinyl pyrrolidone and Starch. The commonly used Superdisintegrants are Croscarmellose sodium, Sodium Starch glycolate and

Table.3: Summary for Floating Studies

Formulation	Lag time(sec)	Total floating time(hrs)
F-1	120	>12
F-2	360	>12
F-3	210	>12
F-4	90	3
F-5	150	>12
F-6	580	>12
F-7	200	>12
F-8	120	4
F-9	150	>12
F-10	260	>12
F-11	80	>12
F-12	17	4

Table.4: In-vitro Dissolution studies

Formulation	1hr	2hr	4hr	6hr	8hr	10hr	12hr	14hr	18hr	20hr	24hr
F-1	15.1	24.9	34	45	50	65.5	70.1	74	82	91	97
F-2	13	20.1	32	43	62	69	72	80	89	94	99
F-3	19	26	37	48	65	63	77	84	90	95	99.8
F-4	30	43	49	55	64	79	84	92	96	98.2	99.98
F-5	10.1	19	23.2	29.3	33	39.5	48	54	62	69	75
F-6	12.2	22	29.3	35	42	53.5	59	63	69	73	79.6
F-7	17	24	32	39	43	50	55.5	64	72	79	82
F-8	25.6	34	39	44.7	54	62	67	75	79.8	80.5	92
F-9	13.2	21	30.5	42	49	64.3	69	73	79	85	92
F-10	15	19.9	25	30.1	39	45	52	64	75.5	80.9	89
F-11	17	20.1	29	34	45.4	53	64.6	75	79.5	80.2	93
F-12	25.6	41.2	47	54	62	75	79	82	89	92	95.6

Crospovidone. The use of various Binders and Super disintegrants effects the Disintegration time and Dissolution studies.

The bacterial action of ciprofloxacin results from inhibition of enzymes topoisomerase-II and topoisomerase-IV, which are required for bacterial DNA replication, transcription repair and recombination and used in urinary tract infection, lower respiratory tract infection, acute sinusitis, complicated intra abdominal infections. The objective of the present investigation was to prepare ciprofloxacin HCl Gastroretentive tablets by wet granulation method using croscarmellose Sodium, Sodium Starch Glycolate, Crospovidone, Starch, Poly vinyl pyrrolidone, HPMC, Magnesium Stearate as excipients in the formulation.

Table.5: Summary for Swelling Property

Formulation	0 min	5 min	30 min	60 min	120 min	240 min	420 min	600 min
F-1	0	29.5	35	50	62	74.9	82	89
F-2	0	40	60	81	93	95	99	100
F-3	0	21	32	56	65	70	75	80.5
F-4	0	11	23	29	32	45	52	65
F-5	0	28	32	53	62.5	73	80	85
F-6	0	38	63	82	90	92	98	99
F-7	0	19	32	55	64	69	74	79
F-8	0	10	22	25	33	47	54	70
F-9	0	32	36	50	63	70	84	89
F-10	0	39	55	65	75	85	89	95
F-11	0	19	30	47	58	64	72	82
F-12	0	10.5	22	28	34	45	56	68

MATERIALS AND METHODS

Materials: Ciprofloxacin HCl was obtained as a gift sample from AUROBINDO pharma ltd. and all other excipients and chemicals used were of analytical grade.

Methods: The method used in the formulation of ciprofloxacin HCl Gastroretentive tablets was wet granulation method. All the batch formulations are formulated by wet granulation method. Accurately weigh specified quantity of raw materials such as ciprofloxacin, Poly vinyl pyrrolidone, Super disintegrants, HPMC, Magnesium stearate in a weighing balance. Floating matrix tablets containing Ciprofloxacin HCl were prepared by wet granulation technique using varying concentrations of different grades of polymers with sodium bicarbonate. API, Polymer, swelling agent and sodium bicarbonate were weighed and passed through sieve # 40 mixed homogeneously in a polybag for about 5-10 min. and was taken in a glass mortar.

Evaluation Post compression Parameters: The formulated tablets were evaluated for the following parameters such as weight variation, hardness, friability, %swelling and Invitro dissolution studies and the results has been tabulated in table.

RESULTS AND DISCUSSION

Drug excipients compatibility studies: Physical compatibility studies were assured by FT-IR studies. The crude drug sample and the complete formula of the final formulation were chosen for the study. The FT-IR spectra's of the above samples were studied after a period of 30 days from preparation of the mixtures, to facilitate prompt detection of incompatibility. Based on the spectral data it has been observed that there are no shift of any major peaks in appearance or disappearance of the peak.

Evaluation of post compression Parameters: The Post compression Parameters such as Weight variation, Hardness, Friability, content uniformity was evaluated and the results were tabulated in Table.2.

Floating Test: The time between introduction of dosage form and its buoyancy in 0.1N HCl medium and Floating Lag Time, Total Floating Time were measured and tabulated in table-3.

In-vitro Dissolution Studies: The In-vitro dissolution studies were conducted by using USP Type 2 Apparatus, 900 ml of pH 0.1N HCl was used as Dissolution Medium. Speed was maintained at 50 rpm and temperature maintained at 37˚C ± 0.5^0c. The samples were withdrawn up to 24hr and measured by UV Spectrophotometer at 276 nm and the results were tabulated in Table.4.

Percentage Swelling: The swelling behaviour of dosage form can be done in dissolution apparatus-II by using 900ml of distilled water as medium rotated at 50rpm at 37^0c and measured its dimensional changes, weight gain or water uptake at regular intervals and the results were tabulated in Table.5.

CONCLUSION

In the present work, Formulations of Ciprofloxacin Gastroretentive tablets were prepared by wet granulation Method. Twelve formulations were formulated and evaluated for both Post compression Parameters such as Weight variation, Hardness, Friability, content uniformity, In-vitro Dissolution studies and floating property, swelling property were evaluated and the results were tabulated. Formulation F2, F6 and F10 containing sodium starch Glycolate as super disintegrant shows good swelling nature but the maximum swelling was obtained at latter hours comparative to that of formulations containing CP and better Dissolution than other Formulations. Hence, Formulations F2, F6 and F10 show the best formulation among the twelve formulations containing different Binders and Super disintegtants.

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