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Research Article

FORMULATION AND IN-VITRO EVALUATION OF FLOATING MATRIX TABLETS OF CLARITHROMYCIN

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ABSTRACT

Floating matrix tablets of clarithromycin were developed to prolonged gastric residence time and thereby increase drug availability. The tablets were prepared by wet granulation technique, using polymers such as HPMC-K4M, Corbopol 934P and Sodiumalginat, and other standard exipients. Tablets were evaluated for physical characteristics viz, hardness, percentage friability, floating capacity, weight variation and content uniformity. Further, tablets were evaluated for in-vitro release characteristics for 24hr, by linear regression analysis.

Keywords: : Clarithromycin, Floating matrix tablet, linear regression analysis.

INTRODUCTION

Clarithromycin is stable in gastric medium and has a narrow absorption in gastrointestinal tract, rapid intestinal absorption, highly solute at gastric pH, no effect of food on absorption and it has higher eradication rate in vivo to H.pylori [(I).] Based on this, an attempt was made through this investigation to formulate floating matrix tablets of clarithromycin using different polymers and their combinations. The prepared tablets were evaluated for physical characteristics such as hardness, thickness, percentage friability, floating capacity, weight variation and content uniformity. All the formulations were evaluated for in-vitro release characteristics.

Clarithromycin is a macrolitic antibiotic used to treat pharyngitis, tonsillitis, acute maxillary sinusitis, acute bacterial exacerbation of chronic bronchitis, pneumonia (especially atypical pneumonias associated with Chlamydia pneumonia or TWAR), skin and skin structure infections. In addition, it is sometimes used to treat Legionellosis, Helicobacter pylori, and Lyme disease.

MATERIALS AND METHODS

Materials

Clarithromycin (as a gift sample from Alembic limited, Baddi H.P), HPMC K4M, Carbopopl934P were received as a gift sample from Torrent Research centre (Gandhinagar, India). Sodium alginate, sodium bicarbonate, lactose were obtained commercially from S.D. Fine Chemicals (Mumbai).

METHOD

The floating matrix tablets of clarithromycin were prepared by wet granulation technique.

Formulation of clarithomycin floating matrix tablets:

Clarithromycin was mixed with required quantities of polymers (HPMC K4M or carbopol or S.A), sodium bicarbonate and lactose in mortar for 5 min by using a spatula. Isopropyl alcohol was added drop wise till suitable mass for granulation was obtained. The wet mass was granulated through 40#. The granules were dried at room temperature (35°c) for 1hr,and then blended with talc and magnesium stearete in the weight proportion as mentioned in Table 1 and compressed on 16-station rotatory tablet compressing machine (Rimek, Kadi, India) using a 8-mm standard flat-face die punch set.

Physical characterization

The fabricated tablets were characterized for weight variation, hard-ness, Monsanto hardness tester), thickness using a screw-gauge micro-meter and % friability (Roche-friabilator, Electro lab, Mumbai, India). [II]

Assay of tablets

Twenty tablets from each formulation were weighed and powdered. Powder equivalent to 402 mg of clarithromycin was accurately weighed and transferred to a 100ml volumetric flask and dissolved in a suitable quantity of 0.1N HCL. the prepared solution was diluted up to 100ml with 0.1 N HCL and sonicated for 60 min. five milliliters of the resulting solution was diluted to 100ml0.1 N HCL to get a concentration in the range of 15 µg/ml. a portion of the sample was filtered through 0.45µ membrane filter and analyzed by Shimadzu UV-1700 UV/Vis double-beam spectrometer. [III]

Floating capacity

The in-vitro bouncy was determined by floating lag times as per the method described by Rosa et al. the tablets were placed in a 100 ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time. The experiment was conducted in triplicate.

In-vitro dissolution studies

The release rate of clarithromycin from floating matrix tablet was determined as per British pharmacopoeia (B.P) using dissolution tasting apparatus (paddle method). The dissolution test was performed using 900ml of 0.1N HCL, at 37 ± 0.5 and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 24 hr, and the sample were replaced with fresh dissolution medium. The sample were filtered through 0.45µ membrane filter and diluted to a suitable concentration with 0.1 N HCL. Absorbance of these solutions was measured at 284 nm using a Shimadzu UV-1700 UV/Vis double-beam spectrophotometer.[IV] Duration of time of the tablet constantly float on dissolution medium were noted as total floating time.

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RESULT AND DISCURTION

Weight variation data of the prepared tablets indicated no significant difference in the weight of individual tablet from the average value. Hardness of the prepared tablets was observed to be within the range of 3.5±0.9 to 4.7±0.7 kg/cm².Thickness of all the tablets was found in the range of 2.80±0.42 to 2.92±0.46mm. Friability of all the tablets was found below 1%. The drug content of all the formulation of clarithromycin floating tablets was in the range of 95 to 105% (i.e., a variation of ±5%). This ensured the uniformity of the drug content in the tablets. [V]

Floating capacity of fabricated tablets was determined in 0.1 N HCL. The tablets of all formulations exhibited floating lag time less than 150 seconds. The tablets of carbopol 934P formulation exhibited more floating lag time compared to other formulations. Combination of three polymers shows no significant effect on floating lag time. Partial replacement of corbopol 934P with polyethylene glycol 4000 increases total floating time because of reduces in density.

In-vitro dissolution studies showed that as the concentration of HPMC K4M was increased, drug release rate was decreased (fig.1). The tablets of formulation F1 not showed good dissolution profile and about 40% of drug was released in 1hr, while the tablets of F2 released the drug in controlled manner at minimum level of HPMC content (30% w/w of tablet weight). As the concentration of corbopol 934P was increased drug release rate was decreased (fig.2). Dissolution profiles of formulation F7 and F8 were good because high amount of drug release (30%) at 1 hr. As the concentration was increased drug release rate was decreased [VI-IX](fig.3).

The tablets prepared from combination of three polymers exhibited reduction of dissolution rate as the concentration of carbopol 934P increased (fig.4). As the concentration of PEG 4000 increased in tablet formulation dissolution rate was increased (fig.5). Fabricated tablets showed weight variation, hardness and uniformity of drug content within acceptable limits. A lesser floating lag time and desired total floating duration could be achieved by varying the amount of gas forming agent and using different polymer combinations

Table.1: composition of floating matrix tablets of clarithromycin

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Clarithromycin	402	402	402	402	402	402	402	402	402	402	402	402	402	402	402
HPMC K4M	128	202	258	-	-	-	-	-	-	110	110	110	110	110	110
Carbopol 934P	-	-	-	60	82	124	-	-	-	30	53	68	42	42	42
Sodium alginate	-	-	-	-	-	-	60	82	124	125	125	125	125	125	125
Sodium bicarbonate	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
Lactose	190	114	63	248	239	197	261	239	197	56	33	18	24	17	14
PEG 4000	-	-	-	-	-	-	-	-	-	-	-	-	20	27	30
Magnesium stearet	7	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Talc	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14
Total weight	804														

Table 2: Evaluation of prepared formulation

Batch code	Hardness(kg/cm²)	Friability (%)	Weight(mg)	Content (%)	Floating Lag time(s)	Total floating time(h)
F1	4.3(0.4)	0.07	183(2.5)	99.25	5	>12
F2	4.8(0.5)	0.04	185(2.7)	98.64	11	>12
F3	4.6(0.6)	0.13	178(1.4)	100.17	13	>12
F4	4.5(0.4)	0.08	177(2.3)	99.39	5	4
F5	4.6(0.6)	0.06	179(1.3)	98.53	90	4
F6	4.1(0.1)	0.13	180(1.2)	100.31	120	6
F7	4.3(0.1)	0.08	178(3.2)	99.34	5	2
F8	4.5(0.4)	0.07	184(3.5)	99.13	13	5
F9	4.3(0.4)	0.11	183(2.5)	101.01	18	>12
F10	4.4(0.3)	0.08	181(2.7)	99.46	5	5
F11	4.5(0.6)	0.06	183(2.9)	99.75	10	3
F12	4.3(0.4)	0.13	184(3.1)	101.01	13	3
F13	4.5(0.3)	0.23	182(2.6)	99.34	6	24
F14	4.3(0.6)	0.07	180(3.2)	99.31	8	20
F15	4.7(0.3)	0.21	184(2.4)	101.41	14	18

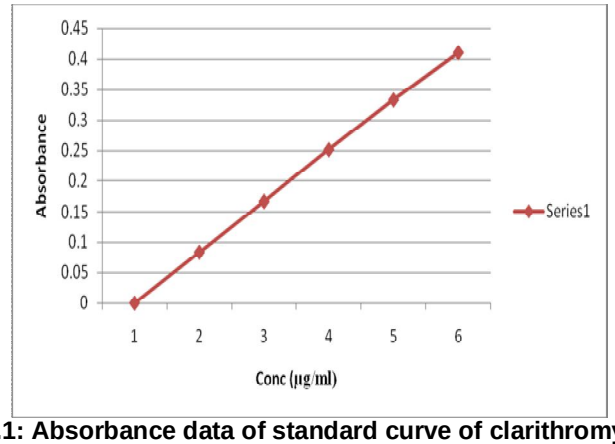


Fig.1: Absorbance data of standard curve of clarithromycin

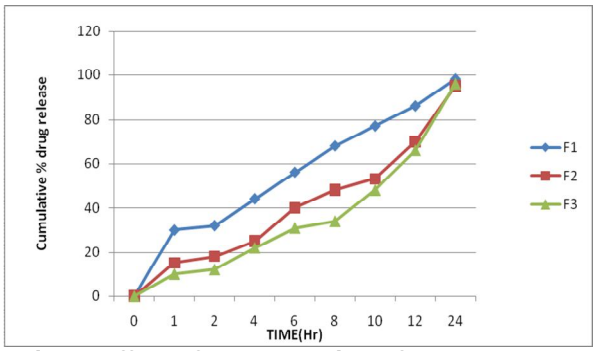


Fig. 2: Effect of concentration of HPMC K4P on drug release profile of F1, F2, andF3

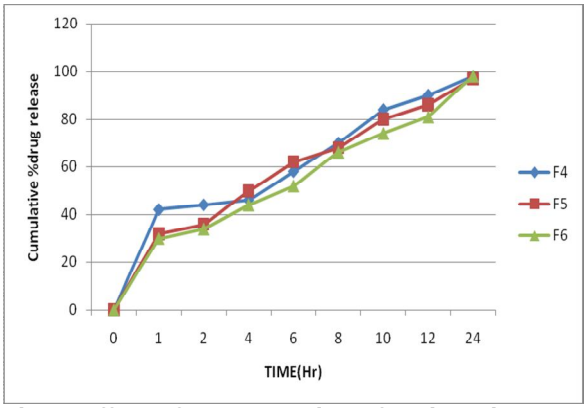


Fig. 3: effect of concentration of carbopol 934 on dug release profile of fornulation F4,F5 and F6

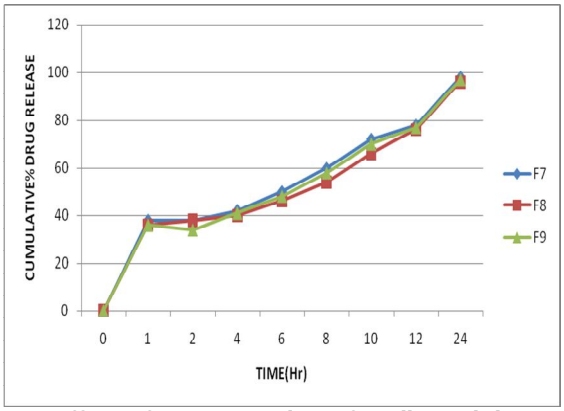


Fig. 4: effect of concentration of sodium alginate on drug release profile of formulation F7,F8 and F9

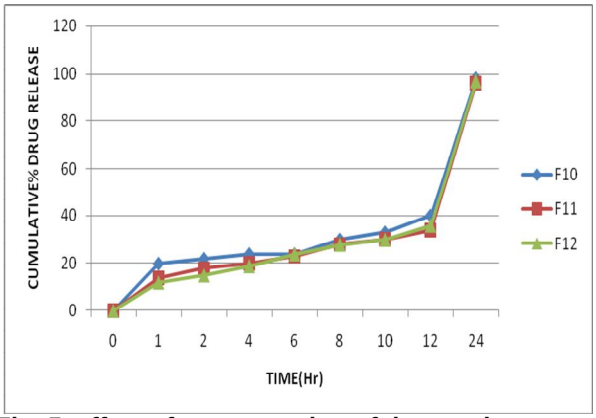


Fig. 5: effect of concentration of three polymers on drug release profile on formulation F10,F11 and F12

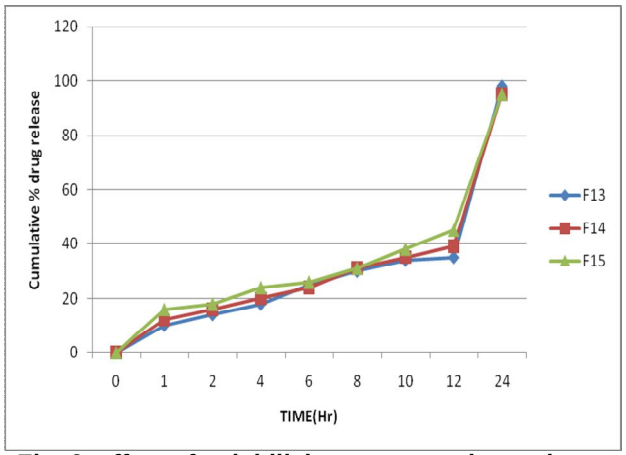
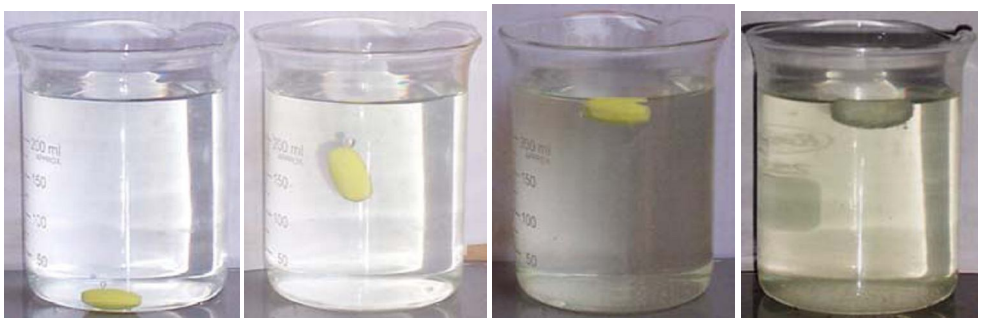


Fig. 6: effect of solubilising agent on drug release profile of formulation F13,F14 and F15



At initial time After 45 sec After 1 min After 8 hr

Fig. 7: in vitro buoyancy of formulation F3

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