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PREPARATION AND EVALUATION OF MEGALOPOROUS MATRIX TABLET OF AMBROXOL HCL

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ABSTRACT

The persistence of this study is the optimization and formulation of Megaloporous network tablet containing Ambroxol HCL to give an underlying prompt impact took after by managed discharge for 36 h from the framework implanted tablets at a consistent rate. These Megaloporous grid tablets were set up with two sorts of granules, insoluble controlling stage framework granule (RMG) which controls the discharge rate of the medication and dissolvable lodging stage lattice granule (HMG) which controls liquid infiltration into the framework and filtering out of medication instantly. The drug release from all manufactured item and reference item took after preferable higuchi model over the zero request and first request dynamic models. The above study indicates hardness and medication discharge was rely on upon the convergence of the sodium starch glycol ate. This study recommends that megaloporous tablets, which could be set up with the straightforward and shoddy route correspondingly to routine tablet to acquire a quick and steady medication discharge which copy bilayer tablets.

KEYWORDS: Megaloporous matrix tablet, RMG, HMG, Ambroxol HCL, Carbopol 934p.

INTRODUCTION

The megaloporus framework has been intended to accomplish zero request drug discharge from a strong per oral measurements structure. This framework depended on the mix of both disintegration and dispersion based discharge. The megaloporous framework can be seen chiefly as single unit gadget containing two structures with basically distinctive infiltration

characteristics. The one structure was called as limiting framework stage and different structures called as lodging grid stage. The megaloporous two stage framework had primarily been intended to accomplish zero request drug discharge from a strong peroral dose structure.1O ral route is the most preferred route for administration of drugs. Tablets are the most popular oral formulation available in the market and preferred by the patients and physician alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered multiple doses and therefore have several disadvantages. 2Sustained release drug delivery aimed at controlling the rate of release as well as maintains desired drug level in the blood that is therapeutically effective and nontoxic for extended period of time, thus achieving better patient compliance and allowing a reduction of both the total dose of drug administered and the incidence of adverse side effects. It provides prolonged but not necessarily uniform release of the drug. The rationale for development of a sustained release formulation of a drug is to enhance its therapeutic benefits, minimizing its side effect while improving the management of the diseased condition.3,4Ambroxol hydrochloride is a metabolite of Bromhexine, belongs to BCS class II drugs used as an expectorant, mucolytic agent to treat acute and chronic diseases. It has short plasma half-life 4 hours require frequent daily dosing (2-3 times). Ambroxol is a metabolite of bromhexine with similar actions and uses. It is chemically described as Trans-4-[(2-amino-3,5-dibromobenzyl)amino]-cyclohexanol. Ambroxol hydrochloride is an expectorant improver and a mucolytic agent used in the treatment of respiratory disorders such as, bronchial asthma, chronic bronchitis characterized by the production of excess or thick mucus .Ambroxol hydrochloride has also been reported to have a cough suppressing effect and anti-inflammatory action. It has been successfully used for decades in the form of its hydrochloride as a secretion releasing expectorant in a variety of respiratory disorders. Its short biological half-life (4 hrs) that calls for frequent daily dosing (3to 4 times) and therapeutic use in chronic respiratory diseases necessitates its formulation in to sustained release dosage forms.[5,6]

MATERIALS AND METHOD

Ambroxol HCL a sample gift from Scott-Edill Pharmacia., HPMC, Central drug house Pvt. Ltd, New Delhi., Carbopol 934 obtained from Loba Chemi Pvt. Ltd, Mumbai., Magnesium Stearate is obtained from Molychem, Mumbai., Sodium Starch Glycolate, Lactose, All materials and solvents used were of analytical grade.

Instruments used

Double Beam UV-VIS Spectrophotometer(UV-1800) Shimadzu Corporation, Japan., FTIR-spectrometer(Alpha), Bruker Optics, Germany., Eight Station Dissolution Apparatus, Labindia Analytical, India., Labindia Analytical, India, Ohaus Instruments, Switzerland., Tablet Friability Test Apparatus, Veego Instruments Corporation, India., Tablet Punching Machine(Multi-punch), Dhiman Udyog, India.

Formulation of Megaloporous Matrix Tablet

Megaloporous matrix tablets were prepared by mixing two type of phase i.e. Restraining phase matrix (RMG) granules which control release rate of drug.Other phase Housing Phase matrix granules (HMG) which control liquid penetration into system.

HMG Preparation

Ambroxol Hydrochloride mixed with corbopol 934 p, lactose, Sodium Starch Glycol ate, for 10 mins then precompressed and then granules were formulated by passing these precompressed matrix tablet through sieve no.22 and then 44 Then granules were dried in petridish.

RMG Preparation

By wet granulation method the Ambroxol Hydrochloride mix with lactose, HPMC by geometric mixing binder solution 10 % w/v prepared by dissolving PVP K 30 in water. Then binder solution mix with above ingredients and dried at 40 º C at semi dried condition, the granules screened through sieve no 22 and 44 & dried in petridish.

Then Mix both RMG & HMG Phase & lubricate with magnesium Stearate and compressed in Tablet Punching machine.

Table 1: Hmg Phase 1.

Sr. No	Formulation Code	Drug (mg)	Carbopol 934 p(mg)	Sodium starch Glycolate (mg)	Lactose (mg)
01	F1	19	30	12.5	50.5
02	F2	19	32.5	12.5	50.5
03	F3	19	35	12.5	50.5
04	F4	19	37.5	12.5	50.5
05	F5	19	40	12.5	50.5
06	F6	19	41.5	12.5	50.5

Table 2: Rmg Phase 2.

Sr. No	Formulation Code	Drug- (mg)	HPMC (mg)	Mg.stearate (mg)	Lactose (mg)	PVP
01	F1	56	37.5	5	50.5	10 %
02	F2	56	32.5	5	50.5	10 %
03	F3	56	35	5	50.5	10 %
04	F4	56	33.5	5	50.5	10 %
05	F5	56	30	5	50.5	10 %
06	F6	56	28.5	5	50.5	10 %

Evaluation of Thickness

The Thickness of tablets was performed on 20 tablets from each of the formulation. Using Vernier caliper was for the study, which permits the accurate measurements and provides information of the variation between the tablets.

Evaluation of Width

The Width of the tablets was performed on 20 tablets from each of the formulation. Using Vernier caliper for the study, this permits the accurate measurements and provides information of the variation between tablets.

Evaluation of Weight Variation Test

Weight variation was carried out to ensure that, each of the tablets contains the proper amount of drug. The test was carried out by weighing the 20 tablets individually from each of the formulation using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average according to I.P limit.

Drug Content Uniformity Test

Tablets were kept in 100 ml volumetric flask containing buffer 7.4 pH for 24 hours. When they get completely dissolved the solution was centrifuged. After centrifuged the supernatant was collected. The absorbance was measured spectrophotometrically at 244 nm. Dilutions were made using phosphate buffer having pH 7.4

Disintegration Time

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 37± 2 ^{0}C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

Dissolution Study

Dissolution study was conducted for all the formulation using USP Type-II apparatus (paddle type). The dissolution test was performed using 900 ml of 7.4 pH phosphate buffer taken as dissolution medium at 50 rpm and 37 ^{0}C± 0.5 ^{0}C. Five milliliters of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. Samples were collected in test tubes after filtration through Watt Mann filter paper. Amount of drug in aliquots was quantified taking the absorbance of sample at 244 nm using Phosphate buffer pH 7.4 (dissolution media) and analyzed by UV-VIS. For comparison, dissolution studies of commercial tablets were also conducted.

In- Vitro Drug Release

The studies of the formulation Batches from F1 to F7 were carried out to know the in-vitro drug release pattern and the procedure was carried out as the procedure discussed earlier. The drug release at different time intervals was determined and calculated to know the release at variable concentration of polymers used. The results obtained were converted in the form of % drug release.

RESULT AND DISCUSSION

FTIR spectrum of Ambroxol Hydrochloride

FTIR spectrum of Ambroxol hydrochloride was performed using wave number ranges. Observed confirmed the presence of Ambroxol Hydrochloride.

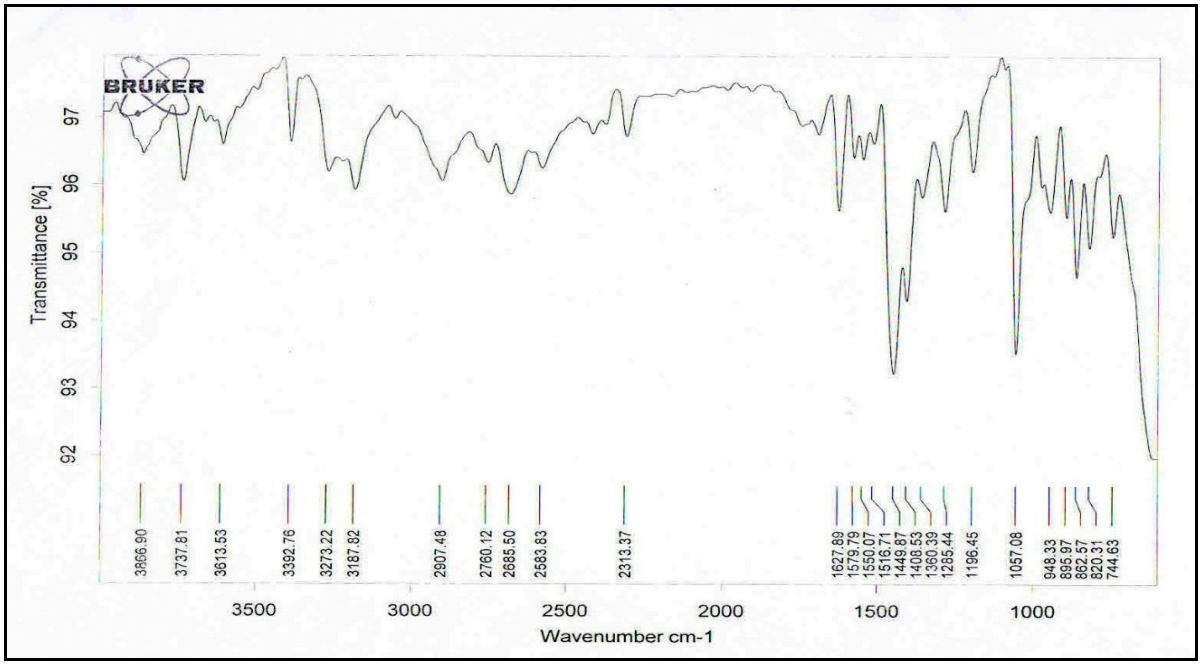

Figure 1: FTIR Spectrum of Ambroxol hydrochloride.

Table No 3: FTIR Spectrum of Ambroxol hydrochloride showing different wave number with Assignment.

Sr.No	IR Absorption Band (cm-1) (Experimental)	IR Absorption Band (cm -1) (Literature)	Functional Groups
1.	3392.7	3400-3345	Intermolecular hydrogen bonded OH, Stretch
2.	3187.2 and 3273.2	3350-3250	Aromatic primary amine, NH stretch
3.	1516.7	1595-1545	C=C stretching, aromatic
4.	744.6	700-600	Bromo compound, C-Br stretch

Table no 4: Evaluation of Width, Thickness and Weight variation test.

Sr. No	Formulation Code	Thickness (mm)	Width (mm)	Weight Variation(mg)
1	F1	4.06±0.40	7.45±0.17	240±0.99
2	F2	3.92±0.26	7.65±0.22	241±1.12
3	F3	4.20±0.25	7.88±0.16	244±1.30
4	F4	3.88±0.20	7.54±0.19	242±0.80
5	F5	4.10±0.22	7.11±0.29	248±0.65
6	F6	4.02±0.32	7.35±0.25	243±0.50

Table no 5: Hardness and Friability.

Sr. No	Formulation Code	Hardness(kg/cm^2)	Friability (%w/w)
1	F1	6.5±0.21	0.84±0.14
2	F2	6.9±0.20	0.56±0.03
3	F3	7.2±0.31	0.1±0.12
4	F4	6.8±0.27	0.76±0.15
5	F5	6.7±0.23	0.68±0.09
6	F6	6.8±0.26	0.88±0.07

Table no 6: Percentage drug content.

Formulation Code	% drug Content
F1	96.12±0.11
F2	97.14±0.42
F3	98.80±0.25
F4	97.32±0.09
F5	98.13±0.35
F6	96.80±0.65

Table no 7: Disintegration time.

Sr. No.	Formulation code	Disintegration time (Hour)
1	F1	1.10
2	F2	1.21
3	F3	1.35
4	F4	1.08
5	F5	1.02
6	F6	1.18

In Vitro Drug Release Study

The graph was plotted between time (hours) and percentage (%) cumulative release and the following graph was obtained.

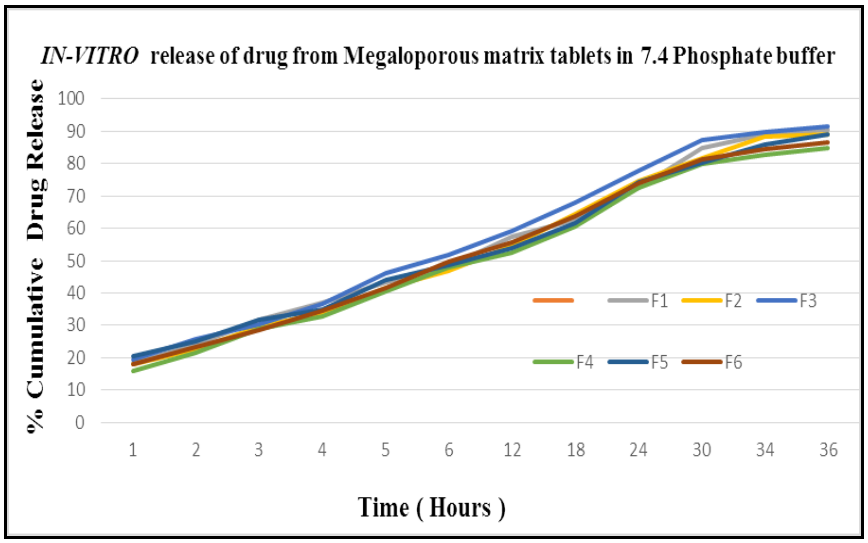

Figure 2: showing *in-vitro* release of drug from Megaloporous matrix tablets.

CONCLUSION

Ambroxol HCL Megaloporous matrix tablets were prepared by mixing two type of phase i.e. One phase is restraining phase matrix (RMG) granules which Sustained release rate of drug and Second phase is Housing Phase matrix granules (HMG) which control liquid penetration into system. To achieve zero order drug release so megaloporous system show better zero order drug release from a solid per oral dosage form as compared to simple matrix tablets. The proposed of Megaloporous inert matrix formulation can be viewed principally as a single-unit device that comprises two structures. On the basis of these studies it can be conclude that Ambroxol Hcl Megaloporous matrix tablets showed better in vitro drug release 90 to 91 Percentage. All tablets showed better result. This study is concluded that Megaloporous matrix tablets approach to be used as orally Sustained release drug delivery system.

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