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FORMULATION AND EVALUATION OF FLOATING TABLET OF FAMOTIDINE

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Abstract

Drug which have slender absorption window in the gastrointestinal tract (GIT) may have bad absorption. For these drugs, gastroretentive drug shipping structures provide the benefit in prolonging the gastric emptying time. Famotidine belongs to H2-receptor antagonist. It is used extensively for the remedy of remedy of gastro-esophageal reflux disease (GERD) and gastric ulceration duodenal ulcer, pressure ulcer. The low bioavailability (40-45 %) and brief organic half-life (2.5-4.zero hrs) of Famotidine following oral management favours improvement of a sustained launch formulation. The rapid gastrointestinal transit should bring about incomplete drug launch from the drug shipping device above the absorption zone main to bad bioavailability of the drug. The floating tablets have been formulated the use of artificial polymer like HPMC K15M and herbal polymer like chitosan as the discharge retardant polymers, and sodium bicarbonate because the fueloline producing agent to lessen the floating lag time.

The reason of this research turned into to put together floating drug shipping device of famotidine. Famotidine having bad absorption in acidic environment (top GIT). When given orally, it indicates the bioavailability close to 50%. To triumph over those drawbacks, the presentlook at turned into undertaken to research the floating dosage shape of famotidine. Floating pills have been organized the use of Direct Compression. Six formulations have been organized containing gel-forming agent (HPMC K15M) and retardant (Na-CMC) in unique ratio and it turned into found that fueloline producing agent (NaHCO3) reacts with HCL and liberates CO2 which creates pores in pill and elevates swelling and maintains buoyancy. The organized pills have been evaluated for content material uniformity, hardness, friability, buoyancy, swelling index and in-vitro dissolution research. Further decided on formula turned into subjected for brief time period balance research for one and month at temperature of 25°c and 40°c respectively.

1. Introduction

Famotidine is histamine H2-receptor antagonist. It is extensively prescribed in gastric ulcers, duodenal ulcers, Zollinger-Ellision syndrome and gastroesophageal reflux disease. In the control of benign gastric and duodenal ulceration the dose is 40 mg every day through mouth at mattress time, for 4 to 8 weeks.(Basak SC, Rao NK, Manavalan R, Rao RP2004). In gastroesophageal reflux disease the endorsed dose is 20 mg by mouth two times a every day for six to twelve weeks, wherein gastroesophageal reflux disease is related to esophageal ulceration; the endorsed dose is 40 mg two times every day for similar period For symptomatic comfort of heartburn or non-ulcer dyspepsia a dose of 10 mg as much as two times every day is suggested. In the Zollinger-Ellision syndrome the preliminary dose by mouth is 20 mg each 6 hours, increased as necessary, dose upto 80 mg every day were employed1. The low bioavailability (40 – 45%) and brief

organic 1/2 of life (2.5- 4.zero hours) of famotidine following oral administration favours improvement of a sustained launch formulation. (Subramananyam CVS., Setty JT.2002) The gastroretentive drug shipping structures may be retained withinside the belly and help in enhancing the oral sustained shipping of medicine which have an absorption window in a specific area of gastrointestinal tract. These structures assist in constantly freeing the drug earlier than it reaches the absorption window, therefore making sure optimal bioavailability.(Vinod KR, Vasa S, Anbuazagahan S.2008)It has been said that the oral remedy of gastric issues with an h2 receptor antagonist like famotidine or ranitidine utilized in mixtures with antacids promotes nearby shipping of those pills to the receptor of parietal cell wall. Local shipping additionally will increase the stomach wall receptor web website online bioavailability and will increase efficacy of drugs to reduced acid secretion. (Streubel A, Siepmann, Bodmeir J2006).

In the existing research floating pills ofFamotidine have been organized through bubbling approach the use of HPMC K15 M grade. The purpose of the paintings turned into to compare the impact of gel forming polymer methocil on floating homes and launch traits of Famotidine pills. .(Chen YC, Ho H, Lee TY, Sheu MT2013)

Long-term storage increases bioavailability, reduces drug waste, and reduces drug solubility in high pH environments. It is also suitable for local delivery of drugs to the stomach and small intestine. Intestinal storage can help better deliver new products with appropriate treatments and provide better outcomes for patients. Therefore, one of the most effective ways to ensure long-term and predictable drug delivery in the gastrointestinal tract is to use gastrointestinal data to control the residence time in the abdomen, which will provide us with important new therapies.(Prajapati DV, Jani GK, Khutliwala TA, Zala BS.2013)The need for dietary supplements has led to extensive studies and efforts towards the development of drug delivery systems. Over the past three decades, research and exploration of the device in the upper gastrointestinal tract has continued in terms of technology and diversity, including many machines and products such as floating systems, volumizing systems, bioadhesive systems, and high utilization. -density systems. (Khan R.2013)Floating drug delivery systems (FDDS) have a lower density than gastric fluid, thus increasing gastric emptying without affecting gastric emptying in the long term. As the system floats on the stomach contents, the drug is gradually released from the system on demand. Once the drug is released, the remainder of the process is evacuated from the stomach. This leads to an increase in GRT and better control of changes in plasma drug concentrations.(Pawar V.K, Shaswat K, Garg G, Awasthi R.2011)

Experimental:

Materials:-

Famotidine pattern turned into bought from m/s SMS

Pharmaceuticals ltd., Hyderabad., HPMC K100 M(BatchNo : S126012N31) as a present pattern from Dr. Reddy

Laboratories Hyderabad., Sodium Bicarbonate and Ethyl

cellulose turned into bought from S.D. Fine Chemicals

Mumbai. Citric acid, Isopropyl alcohol, Talc and

Magnesium Stearate from Merk India Ltd, Mumbai.

Other chemical compounds used wherein analytical grade.

Materials used in the development of famotidine tablets

Ingredient	**source**
Drug famotidine	SMS pharmaceutical ltd Hydrabad
Ethyl cellulose	Research Fine Lab Mumbai
HPMC K15M	Dr. Reddy laboratories Hydrabad
PVP	EMCURE PHARMA PUNE
Sodium bicarbonate	S.D Fine Chemicals Mumbai
Citric acid anhydrous	Merk India ltd Mmbai
Lactose(DCL)	Merk India ltd Mmbai
Magnesium Stearate	Merk India ltd Mmbai
Talc	Merk India ltd Mmbai

Method

Preparation of famotidine controlled-release matrix tablets Famotidine matrix tablets and other excipients were prepared by direct compression method. Lactose is chosen as a tablet diluent to improve the compressibility and fluidity of the ingredients. Sodium bicarbonate is added as an effervescent agent to aid the buoyancy of the dosage form because carbon dioxide is released when the tablets come into contact with acids. The solvent medium is trapped in the matrix.

SR NO	Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
1)	Drug famotidine	40	40	40	40	40	40	40	40	40
2)	HPMC K15M	200	200	200	175	175	175	150	150	150
3)	Ethyl cellulose	75	50	25	75	50	25	75	50	25
4)	Sodium bicarbonate	30.4	28	28	28	28	28	28	28	28
5)	Citric acid anhydrous	15.2	14	14	14	14	14	14	14	14
6)	PVP	10	10	10	10	10	10	10	10	10
7)	Magnesium Stearate	06	06	06	06	06	06	06	06	06
8)	Talc	1	1	1	1	1	1	1	1	1
9)	Lactose(DCL)	2.4	1	26	1	26	50	26	51	76
10)	Total	380	350	350	350	350	300	300	300	300

Preparation of floating tablets:

Floating tablets have been organized by non-aqueous moist granulation technique said in advance with slight modification. The composition of diverse formulations is given in Table 1. HPMC K15M, Sodium bicarbonate, citric acid, MCC and Lactose cellulose have been jumbled togetherapolybag, and the aggregate turned into handed thru mesh (No.40). Granulation turned into carried out the use of an answer of Ethyl cellulose in enough isopropyl alcohol. The moist mass turned into handed thru mesh No 16. Thereafter, the drug Famotidine turned into brought to the moist granules and combined very well in a plastic bag. The granules have been then dried at 50º C for approximately 2 h with residual moisture content material of 2to 3% w/w.

Steps:-

Mixing of the Drugs and excipients.

Mixing Of Binder Solution With Powder Mix ,

To Form Wet Mass

Coarse Screening Of Wet Mass Using a Suitable

Sieve (6# to 12#)

Drying Of Moist Granules

Screening Of Drug Granules Through a Suitable

Sieve (14# to 20#)

Evaluation of matrices used for preparation of floating tablet of Famotidine:

A. Micromeritics Studies

Matrices of various batches have been evaluated for unique micromeritic properties including angle

of repose, bulk density, tapped density, Carr's compressibility index, Hausner's ratio, etc. earlier than

compression.

Various formulations earlier than compression have been evaluated for their flow properties in phrases of

following parameters.

(i) Angle of repose

Static angle of repose turned into measured in line with the constant funnel and loose status center method

of Banker and Anderson. Blends have been cautiously poured thru the Enar reposograph till the

apex of the conical pile so shaped simply reached the end of the funnel of reposograph. Height oftool turned into constant to four cm.[9] Thus, with r being the radius of the bottom of the granules conical pile and the angle of repose (θ) turned into calculated through the use of the eqn.1

tan θ = h/r, therefore, θ = tan-1 h/r… (1)

(ii) Bulk density/Tapped density

Both bulk density (BD) and tapped density (TD) have been determined. A appropriate quantity of powder Combination from every formulation, formerly gently shaken to interrupt any agglomerates formed, turned into Brought right into a one hundred ml measuring cylinder. After staring at its preliminary quantity, the cylinder in The density tapper tool and density is measured in line with USP technique II (up to1250 Taps). The tapping turned into persisted till no in addition extrade in quantity turned into noted. Volume of Packing after tapping turned into noted. BD and TD have been calculated the use of eqn. 2 and three respectively.

BD = weight of the powder / quantity of the packing… (2)

TD = weight of the powder / tapped quantity of the packing… (3)

(iii) Compressibility index

Compressibility index of the powder turned into decided through Carr's compressibility index[10] as given through equation 4

Carr's index (%) = [(TD – BD) x 100] / TD… (4)

It enables in measuring the pressure required to interrupt the friction among the debris and the hopper.

(iv) Hausner's ratio

It is the ratio of tapped to bulk density [11] and turned into calculated through the use of the eqn. 5

Hauser's ratio = TD/BD ... (5)

B. Evaluation of Floating Matrix Tablets of Famotidine:

The organized tablets of Famotidine have been evaluated for hardness, friability, weight variation, Thickness, diameter, swelling index, floating or buoyancy test, drug content material uniformity and in

Vitro dissolution studies.

(i)Tablet hardness

The resistance of tablet for delivery or breakage, beneath situations of storage, transportation and Handling, earlier than usage, relies upon on its hardness. The crushing power of organized tablets was Decided for ten tablets of every batch the use of Monsanto hardness tester.

(ii) Friability

Friability is the degree of tablet strength. Roche Friabilator turned into used for checking out the friability The use of the subsequent procedure. Twenty tablets have been weighed as it should be and located with in side the plastic Chamber that revolves at 25 rpm for four mins losing the tablets thru a distance of six Inches with every revolution. After one hundred revolutions the tablets have been reweighed and the percentage Loss in tablet weight turned into determined.

% loss = Initial wt. of tablets – Final wt. of tablets/ Initial wt. of tablet x one hundred… (6)

iii) Weight variation

Twenty tablets have been weighed for my part and the common weight turned into determined. Then Percentdeviation from the common weight turned into calculated. According to USP standards, not Extra than the share proven in desk 2 and none deviates through extra than two times that percent [12]

Table 3: Maximum percent difference allowed

Average weight of tablet	Maximum percent difference allowed
130 or less	10
130-324	7.5
More than32. 4	05

(iv) Tablet Thickness/ Diameter

Thickness and diameter of tablets have been critical for uniformity of tablet size. Six tablets have been tested for his or her thickness and diameter the use of vernier calipers and the imply thickness and diameter price turned into calculated

(v) Swelling index

Swelling of tablet includes the absorption of a liquid through tablet matrices ensuing in an increase in weight and quantity of tablet. The volume of swelling may be measured in phrases of % weight benefit by the tablet. For every formulation batch, one tablet turned into weighed and located in a beaker containing 200 mL of 0.1 N Hal. After on every occasion interval, the tablet turned into eliminated from beaker and weighed once more as much as 12 h.[13] The swelling index turned into calculated the use of following equation 7.

Swelling Index % (S.I.) = (Wt-Wo)/Wo*100... (7)

Where, S.I. = Swelling index

Wt. = Weight of tablet at time t Wo = Weight of tablet earlier than setting withinside the beaker

vi) Floating or buoyancy test

The time taken for tablet to emerge at the floor of the medium is referred to as the floating lag time (FLT) or buoyancy lag time (BLT) and period of time the dosage shape continuously stays on the floor of the medium is referred to as the entire floating time (TFT). The buoyancy of the tablets turned into studied in USP kind II dissolution equipment at 37oC±0.5oC in 900 mL of simulated gastric fluid at pH 1.2. The time of period of floatation turned into found visually.[6]

(vii) Content uniformity

For the content material uniformity, ten tablets have been weighed and pulverized to great powder, a amount of powder equal to one hundred mg of Famotidine turned into dissolved in one hundred ml methanol and liquid turned into filtered the use of Whatman clear out paper and diluted as much as 50µg/ml. The Famotidine content material turned into decided through measuring the absorbance at 288 nm the use of UV spectrophotometer, after suitable dilution with methanol.[14]

viii) In-vitro dissolution research

In-vitro dissolution research have been carried out to decide the discharge sample of the drug from the product. Dissolution check for Famotidine floating matrix tablet . turned into done the use of USP Type II dissolution check apparatus. 900 mL 0.1 N HCL turned into used as dissolution media at 37oC±0.5oCtemperature with rotation velocity of paddle at 50 rpm. An aliquot of five mL pattern turned into withdrawn at unique time interval. These samples have been filtered and diluted. Absorbance of the resulting answer turned into measured at 288 nm. Amount of drug launch turned into calculated.[12] Percent drug launch turned into calculated through the use of the eqn. eight as follows

% Drug launch = K × Absorbance … (8)

Where K may be calculated through the use of eqn. nine as follows

K = Std. conc.×vol. of dissolution media×dilution factor×100/std. abs.×dose×1000 …(9)

Kinetic evaluation of drug dissolution data. The dissolution profile of maximum fine formulation turned into suited for 0 order, first order, Higuchi's version and Korsmeyer-Peppas version to ascertainthe kinetic modelling of the drug launch.

The techniques have been followed for determining the maximum suitable version.

Percent drug launched as opposed to time (Zero order kinetic version)[15]

Log percentage drug final as opposed to time. (First-order kinetic model)[16]

Percent drug launched as opposed to rectangular root of time (Higuchi's model)

Log percentage drug launched as opposed to log time (Korsmeyer-Peppas model)[17]

Release Mechanism Analysis

Famotidine drug release data were fitted to the model representing zero order and Higuchi kinetics

to understand its release. Use MS-EXCEL statistical functions to perform regression analysis of the data.

The results are shown in Table 5 and Figure 3 and Figure 4. Diffusion is associated with the concentration-dependent transport of drugs through large amounts of materials present in fluids outside the body. In this study, the in vitro release profile can best be described by the Higuchi equation as the model shows good linearity (R2: 0.991).

Diffusion is the fundamental process of drug release from formulations.

Model	Slope	R^2
0 order	3.701	0.980
Higuchi	14.50	0.991

Conclusion

Controlled release gastroretentive floating matrix tablets of Famotidine can be successfully prepared using various polymers like HPMC K15M and Chitosan. The effervescent based floating drug delivery was a promising approach to achieve in-vitro buoyancy. The addition of gel forming polymer and gas generating agent sodium bicarbonate along using citric acid was essential to achieve in vitro buoyancy. In the present study, an attempt was made to retain the dosage form in stomach for longer period of time. This can be achieved by developing gastroretentive drug delivery system i.e., floating drug delivery system. These tablets mainly prepared by reduction of lag time and may also increase the bioavailability of the drugs by utilizing the drug to full extent avoiding unnecessary frequency of dosing. For the formulation of floating tablets HPMCK15M and Chitosan were used as matrix forming agent. Other excipients used are PVP, talc, sodium bicarbonate and citric acid (gas generating agent), talc and magnesium stearate (lubricating agent). Fourier transform infrared spectroscopy confirmed the absence of any drug/polymer/excipients interactions.

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