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FORMULATION AND EVALUATION OF FLOATING TABLET OF RAMIPRIL

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INTRODUCTION

The real challenge in the development of a controlled drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form in the stomach or the upper small intestine until all the drug is completely released in the desired period of time. The residence of a drug delivery system in the upper part of the gastrointestinal tract (GIT) can be accomplished by several drug delivery systems, such as swelling, intragastric floating systems and expandable systems, Bioadhesive systems, high density systems, modified shape systems, delayed gastric emptying systems, and low density super porous systems, FDDS, also called hydrodynamically balanced system. It is an effective technology to prolong the gastric residence time in order to improve the bioavailability of the drug. This technology is suitable for drugs with an absorption window in the stomach or in the upper part of the small intestine, the drugs acting locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid. FDDS have a bulk density lower that gastric fluid and thus remains buoyant in stomach for prolonged period of time without affecting gastric emptying time. The drug is released slowly, while the system is floating on the gastric contents. They are also known as hydro dynamically balanced systems (HBS) as they are able to maintain their low density, Based on mechanisms of floating, two different technologies. Effervescent FDDS Non-effervescent FDDS.

When they reach in stomach CO2 is liberated by the acidity of gastric content and is entrapped in jellified hydro colloid(In case of effervescent systems). When the liberated gas is expelled from the dosage form it creates pores through which water can easily pass and helps in wetting of the polymers. The CO2 generated compounds like calcium carbonate, sodium bicarbonate, citric acid/tartaric acid mixtures can be used.[1] 1.1 Advantages of Floating Drug Delivery System The gastroretensive systems are advantageous for drugs absorbed through the stomach.¬ Examples: Ferrous salts, antacids. Acidic substances like aspirin cause irritation on the stomach wall when come in contact¬ with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs. Administration of prolongs release floating dosage forms, tablet or capsules, will result in¬ dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid would be available for absorption in the small intestine after emptying of the stomach contents. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine. The gastroretensive systems are advantageous for drugs meant for local action in the¬ stomach. Example: antacids. When there is a vigorous intestinal movement and a short transit time as might occur in¬ certain type of diarrhea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.[2] 1.2 Disadvantages of Floating Drug Delivery System Floating system is not feasible for those drugs that have solubility or stability problem in¬ G.I. tract. These systems require a high level of fluid in the stomach for drug delivery to float and¬ work efficiently-coat, water. The drugs that are significantly absorbed through out gastrointestinal tract, which undergo¬ significant first pass metabolism, are only desirable candidate. Some drugs present in the floating system causes irritation to gastric mucosa.[2]

DRUG CHARACTERIZATION AND IDENTIFICATION

Physical Appearance Physical appearance analysis of pure drug was carried out by visual inspection. Result Table 1: Physical appearance of Ramipril. S.No. Physical property Standard Observed 1. Colour White to off white White 2. State Solid Solid Melting Point Melting point was determined by the capillary method using Thels tube. Here Thels tube filled with liquid paraffin and the capillary tube stop at one end and another end used for filling the drug by tapping. The capillary tube attached with thermometer and these assembly dipped in the Thels tube and tube put up on the burner, the rise temperature noted when drug

melt in the capillary tube. Result: The melting point range of Ramipril was found to be melting at 109-1100C. FT-IR Spectroscopy Determination by infrared absorption spectroscopy, the spectrum war compared with that obtained with Ramipril or with reference spectrum of Ramipril. The FT-IR spectra for pure drug was obtained by powder diffuse reflectance on a FT-IR spectrophotometer in the wave number region of 4000-400 cm-1.

RESULT

The characteristic peak was determined by FT-IR spectra, which identified the purity of drug. If characteristics peak of sample are not similar with the reference peak, which shows the impurity of sample. UV Spectrophotometry Analysis of Ramipril Preparation of 6.8 pH phosphate buffer¬ Prepare a 0.2 M solution of potassium dihydrogen phosphate by dissolving 27.218 gm of• substance in 1000 ml of distilled Water. Prepare a 0.2 M solution of sodium hydroxide solution by dissolving 8 gm of substance in• 1000 ml of distilled Water. Take 50 ml of above prepared potassium dihydrogen phosphate solution• & 22.4 ml of above prepared sodium hydroxide solution. Add both the solution & make the volume of the resultant solution 200 ml. Calibrate the solution for using pH meter & adjust the pH 6.8. Standard solution¬ 100 mg ramipril dissolve in 100 ml volumetric with 6.8 phosphate buffer. From these stock solutions(1000 µgml-1), sub stock solution of 100 µgml-1was prepared. For the absorption maxima the 10 µgml-1 concentration ramipril dilution observed in UV.

Estimation of absorption Maxima of drug The identification test of the drug was done by double beam UV/Visible spectrophotometer (Shimadzu 1700) by scanning the drug in the range 200-400 nm. Scanning was done in 6.8 pH phosphate buffer stock solution. Result: ramipril exhibited absorbance maxima (λmax) at 231 nm in 6.8 pH buffer.

PREFORMULATION STUDIES

Solubility Study Solubility may be defined as the spontaneous interaction of two or more substance to form a homogeneous molecular dispersion. The solubility of ramipril was tested in various common solvents. A definite quantity (5 mg) of drug was dissolved in 5 ml of each investigated solvent at room temperature. The solubility was observed only by the visual inspection.

PREPARATION OF CALIBRATION CURVE

Preparation of stock solution¬ Stock solutions of 1000 µgml-1 were prepared by 100 mg ramipril dissolve in 100 ml volumetric with 6.8 phosphate buffer. From these stock solutions, sub stock solution of 100 µgml-1 were prepared and further diluted to get final concentrations of 10 µgml-1 , 20 µgml-1 , 30 µgml-1 , 40 µgml-1 , 50 µgml-1 , 60 µgml-1 prepared standard curve of ramipril. Standard curve preparation¬ These dilution were studied the overlain spectra by using an UV detection system to collect and compare spectral data at absorbance absorption maxima value. These sub stock solutions were further diluted to get the solutions range of 10-60 µgml-1 for Ramipril. Calibration curves were plotted by concentration vs. absorbance Result: Absorption maxima of Ramipril Absorption maxima of drug sample were found 231 nm. www.wjpps.com Vol 8, Issue 5, 2019. 1565 Faarooq et al. World Journal of Pharmacy and Pha.

PRECOMPRESSION EVALUATION

Angle of Repose (θ)• The frictional force in loose powder or granules can be measurement by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. tan θ = h/r θ = tan-1 (h/r) Where, the θ is the angle of repose, h = height, r = radius The granules were allowed to flow through the funnel fixed to stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Bulk Density (G/CM3) and Tapped Density (G/CM3) Both loose bulk density (LBD) and tapped density (TD) were determined. The accurately weighted amount of sample taken in a 25 ml measuring cylinder of Borosil measurement/recorded the volume of packing recorded and LBD and TD calculated by following: LBD (loose bulk density) = Mass of Powder / Bulk Vol. of Packing TBD (tapped bulk density) = Mass of Powder / Tapped Vol. of Packing Compressibility• The Compressibility Index and Hausner Ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index and the Hausner Ratio.

Hausner's ratio (HR) H = Tapped bulk density / loose Bulk density. Carr's index (%)ϖ % Carr Index = (TBD-LBD) ×100/TBD

Result This percent compressibility of powder mix was determined by Carr's compressibility index. Table shows result obtains for percentage compressibility. The percentage compressibility for all the formulations lies within range of 10.96 to 29.04 and formulation F3 and F9 showing good compressibility.

FORMULATION AND POST EVALUATION

Formulation of Effervescent Floating Tablets Method of Effervescent Floating Tablets¬ Effervescent Floating tablets containing Ramipril were prepared by direct compression technique using varying concentrations of different grades of polymer with Sodium bicarbonate and citric acid. All the ingredients were accurately weighed and passed through different mesh sieves accordingly. Then, except Magnesium stearate all other ingredients were blended uniformly in glass mortar. After sufficient mixing of drug as well as other components, Magnesium stearate was added, as post lubricant, and further mixed for additional 2-3 minutes. The tablets were compressed using single station hand operated tablet punching machine. The weights of the tablets were kept constant for all formulation.

Post Compression Evaluation

General Characteristics• General appearance of tablet, its visual identity, size, shape, color of the tablet was evaluated. Thickness• The thickness of 5 tablets was measured by Digital Caliper and average value were shown in results and expressed in mm. Diameter• The diameter of 10 tablets was measured by Digital Caliper and average value were shown in results and expressed in mm. Hardness• The hardness of the tablet was determined using a Monsanto Hardness tester. It is expressed in kilogram (kg). Friability• The Friability of the tablet was determined using Roche Friabilator. It is expressed in percentage (%). 10 tablets were initially weighed (Winitial) and transferred into the friabilator. The friabilator was operated at 25 rpm for 4 min. The tablets were weighed again (Wfinal). The % friability was then calculated by:- % Friability of tablets less than 1 % are considering acceptable.

SUMMERY AND CONCLUSION

A recent advance in novel drug delivery system aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better

patient compliance. One such approach is floating drug delivery system. The present study was an attempt to develop FDDS for Ramipril, for the prevention of complications of cardiovascular disease. The main interest in such a dosage form was to avoid extensive first pass metabolism, degradation in stomach and for prolonged effect or sustained release profile. The effervescent floating tablets of Ramipril were formulated in nine different batches F1 to F9 by using hydrophilic polymers HPMC K100M, HPMC K4M and hydrophobic polymer carbopol 974P along with effervescing agent sodium bicarbonate and citric acid. It was found that carbopol has a negative effect on floating behavior but it was used only for the drug release retardant characteristics. All the formulations were prepared by direct compression method. Addition of citric acid, to achieve buoyancy under the elevated pH of the fed stomach, caused an enhancement in drug release. Polymer swelling is crucial in determining the drug release rate and is also important for flotation. A lesser FLT and a prolonged floating.

duration could be achieved by varying the amount of effervescent and using different polymer combinations. The in vitro drug release profiles obtained for tablets made with combinations of HPMC K4M, HPMC K100M, Carbopol 974P showed lesser FLT (20hrs) with controlled and sustained release of Ramipril. Preformulation studies were carried out. The physical appearance, melting point and FT-IR spectra of drug were found to be concordant with mentioned in BP, which identify the sample. Solubility of ramipril was determined in various aqueous and nonaqueous solvent. Finally it can be concluded that selected drug and polymers fulfill the all parameters which can be required for the optimized effervescent floating drug delivery system. The prepared tablets of all the formulations were evaluated for physical characters like tablet hardness, friability, weight variation buoyancy lag time, total floating time, assay, in-vitro drug release. The main aim was to optimize the formulation for 18 hours in-vitro release and total floating time to more than 20 hours. Ramipril release from the effervescent floating tablets was studied in phosphate buffer pH 6.8. The release profiles of formulation F9 are released 99.8 % of the drug in 18 hours. Finally it can be concluded that effervescent floating tablet containing Ramipril (F9 formulation) gave slow and complete drug release spread over 20 hours.

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