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FORMULATION AND INVITRO EVALUATION OF LAMIVUDINE FLOATING TABLETS

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AIM AND OBJECTIVE

Lamivudine comes under class II drugs according to BCS classification. It is poorly water soluble drug. It has maximum solubility in pH 1.2 and therefore it will be beneficial to retain the drug in stomach for longer period of time for better absorption. It has been reported that conventional release of Lamivudine in stomach causes stomach pain as a side effect.

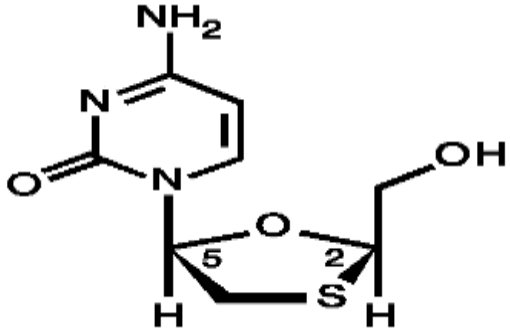
Hence it was found necessary to develop a gastric retentive dosage form containing lamivudine in order to increase the gastric residence time to enhance its absorption and their by its oral bio availability. Also the slow release of the drug in stomach may avoid the stomach pain associated with immediate release of the drug.

The aim of our present study was to design, develop and optimize the floating tablets containing lamivudine in order to increase its gastric retention time for enhancing absorption in stomach as well as to produce a controlled release of the drug for a longer time using polymers such as Carbopol, HPMC and Eudragit S100.

DRUG PROFILE

Lamivudine
Chemical IUPAC name: (2R, cis) – 4 – amino – 1-(2 – hydroxy methy -1,3-oxathiolan –5 – yl) – (1H)-pyrimidin – 2 – one.

Empirical Formula: C8H11N3O3



Mechanism of Action
Lamivudine was originally developed as an antiretroviral drug. The drug is metabolised intracellularly to active triphosphate moiety by both infected and uninfected cells.

Lamivudine triphosphote act as a substrate for HBV polymerase. The formation of further viral DNA is blocked by incorporation of lamivudine triphosphate into the viral chain and be subsequent chain termination. Lamivudine triphosphate does not interfere with normal cellular DNA metabolism.

METHODOLOGY

Determination of λmax
Absorption spectra of Lamivudine

a) Stock solution of 1mg/ml of Lamivudine was prepared by dissolving 100mg of a drug in small quantity of HCl at (pH1.2) and sonicated for few minutes and diluted with HCl at pH(1.2).
b) The stock solution was serially diluted to get solutions in the range of 2-10µg/ml and λmax of the solution was found out from 200-400nm.
c) The λ max of the solution was found to be 280nm.

Determination of standard curve

a) Stock solution of 1mg/ml of Lamivudine was prepared by dissolving 100mg of drug in small quantity of HCl at pH (1.2) and sonicated for few minutes and diluted with 100ml of HCl at pH (1.2).
b) The stock solution was serially diluted to get solution in the range of 2-10µg/ml and λmax of the solution was found out.
c) The absorbance of the different diluted solutions was measured in a UV spectrophotometer at 280nm of the drug.

d) A calibration curve was plotted by taking concentration of the solution in µg on X-axis and absorbance on Y-axis and correlation co-efficient "r" was calculated.

Swelling index

Swelling index is the volume in millilitres occupied by 1gram of drug including any adhering mucilage after it has swollen in a aqueous liquid for 4 hour. The swelling index of polymer was carried out by using BP55 method. In a 25ml ground –glass stoppered cylinder graduated over a height of 125 mm in 0.5 ml divisions. About 25 ml of water was added and shaken vigorously every 15 min for 1 hour and then allowed to stand for 4 hours. The volume occupied by the disintegrating agent including adhering mucilage was measured. The swelling index was calculated from the mean of three determinations.

EVALUATION OF POWDER BLEND

Preformulation study is the characterization of the physiochemical parameters of the drug substance by the application of biopharmaceutical principles with the goal of designing an optimum drug delivery system. The characterization of drug and the drug – excipient compatibility information decides most of the subsequent events and approaches in development of the formulation**.** Preformulation study involves the physiochemical characterization of the drug, solubility determination of the drug, determination of the drugexcipient compatibility, development of the analytical methods and the stability studies.

The prepared powder blend were subjected to evaluation as per the methods suggested in the Indian Pharmacopoeia like Angle of repose, Bulk density, Tap density, Compressibility index, Hausner's ratio. The swelling studies were performed by the method suggested in the British Pharmacopoeia

RESULTS AND DISCUSSION

Calibration curve of lamivudine

Concentratio.n (µg/ml) Absorbance

0. 0
1. 0.0791
2. 0.1353
4. 0.2656
6. 0.3884
8. 0.4961
10. 0.6153

Compression of Tablet

The tablet was prepared by direct compression technique. The target weight of the prepared tablet was 370mg . The designed hardness is between 2-3kg/cm2. All the tablets were found to be uniform in size and shape and no processing problems were encountered during compression process.

Evaluation of post compression parameters

The thickness of the prepared tablets was found to be between 4.25mm to 4.95mm and friability was between 0.35% to 0.76%. The drug content in all the prepared tablets was found to be satisfactory within the acceptable limits with the values of 90.80 to 97.88%. All the physical parameters values were found to be within the pharmacopoeial limits.

Compatibility studies

IR spectra matching approach was used for detection of any possible chemical interaction between drug and polymer. A physical mixture (1:1) of drug and polymer was prepared and mixed with the suitable quantity of potassium bromide. About 100mg of mixture was compressed to form a transparent pellet using a hydraulic press at 6tons pressure .It was scanned from 4000 to 400 cm-1 in FTIR spectrometer. The IR spectrum of the physical mixture was compared with those of pure and polymers and matching was done to detect any appearance or disappearance of peaks. The IR spectrums of the sample and of the Lamivudine working/reference standard in the range of 4000 cm-1 to 400 cm-1 were taken by preparing dispersion in dry potassium bromide under the same operational conditions mentioned above. The spectrum is then superimposed.

SUMMARY

The present study was aimed at preparing floating tablet containing Lamivudine for sustained release of drug and study the effect of swellable polymer , release retardant polymer on rate of release and floating lag time. Lamivudine is more soluble in acidic pH and hence it will be beneficial to increase its gastric residence time in order to improve its oral absorption as well as by controlling the release rate, the side effects associated with burst release of the drug can be eliminated.

Formulation

In this study, Carbopol and HPMC were chosen as the swellable polymer and Eudragit S100 was chosen as release retardant polymer. A total of 9 formulations were made with Carbopol and Eudragit S100 combination at three different proportions. Another set of 9 formualtions were made using HPMC and Eudragit S100 combination. Carbopol and HPMC were used in the range of 60, 90 and 120mg, whereas Eudragit S100 was used at the level of 0, 30 and 60mg.

Preformulation Studies

Preformulation studies of the prepared powder blend of all the 18 formulations were performed. Parameters like angle of repose, bulk density, tapped density, compressibility index, hausner's ratio and swelling studies for the polymers were studied. The results obtained from the above studies showed that the prepared blend was having satisfactory fluidity and compressibility and hence can be processed into tablets by direct compression method. The swelling studies also proved that the chosen polymers have sufficient swelling

capacity in order to use them in floating drug delivery systems.

CONCLUSION

Gastro retentive dosage forms are gaining more importance in the field of drug delivery research especially for those drugs whose absorption and oral bioavailability can be improved when it is delivered in acidic conditions. In this study we have successfully developed oral floating tablets of Lamivudine with the use of polymers like carbopol, HPMC, and eudragitS100. The formulations showed excellent floating characteristics with good matrix integrity and sustained release of the drug spread over 12 hrs. Since the gastric residence time of the drug can be substantially increased by these types of sustained release formulations, it can be expected that drug will have complete absorption and improved bioavailability and also a reduction in the frequency of drug administration because of the sustained release effect. This may also decrease the stomach pain associated with repeated administration of conventional Lamivudine tablets. From this research work we have concluded that oral floating systems can be developed successfully using a combination of carbopol/HPMC and Eudragit S100 .Further studies using animal model will throw more light on the effectiveness of the formulation *in vivo.*

REFERENCES

1. Heller Jin Crit. Rev. Ther. Drug carrier system, 1993; 10: 253.
2. Joseph R. Robinson and Vincent H.L Lea in Controlled Drug delivery, 2nd edition, 373.
3. Robinson JR, Lee V.H.L: Controlled drug delivery; 2nd edition. Marcel Dekker, Inc. Ny, 1987; 373-421.
4. R. Garg. G. D. Gupta., Progress in controlled gastro retentive system, Tropical *Journal of Pharma. Rese*, September 2008; 7(3): 1055-1066.
5. Wilson CG, Washington N. The stomach: its role in oral drug delivery. In: Rubinstein MH, ed. Physiological Pharmacetical: Biological Barriers to Drug Absorption. Chichester, UK: Ellis Horwood, 1989; 47-70.
6. L. Whitehead, J. T. Fell and J H Collett, "Development of a Gastroretentive Dosage Form", *Eur. J. Pharma. Sci.*, 1996; 4(1): 182.
7. Shweta Arora, Floating Drug Delivery Systems: A Review. *AAPS PharmSciTech*, 2005; 6(3): 372-287.
8. Amit Kumar Nayak, Gastroretentive drug delivery systems: a review, 2010; 3(1). http://www.ajpcr.com/2010Vol3Issue1/250.pdf.
9. Amnon Hoffman, Pharmacokinetic and pharmacodynamic aspects of gastroretentive dosage forms, Int J Pharm, 2004: 277: 141-153.
10. J.M.Patil, Trends in floating drug delivery system, *Journal of sci. And Res..*, 2006; 65: 11-21.
11. Timmermans J, Andre JM. Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: new data for reconsidering the controversy. *J Pharm Sci*, 1994; 83: 1824.
12. Li S, Lin S, Daggy BP, Mirchandani HL, Chien TW. Effect of formulation variables on the floating properties of gastric floating drug delivery system. *Drug Dev Ind Pharm.*, 2002; 28: 783-793.