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Floating Tablets of Glipizide using *Eurayle Ferox* seeds for the treatment of Diabetis Mellitus

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Review Article

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ABSTRACT

Floating drug delivery systems will be in the stomach for a long time and helps in improving the oral controlled delivery of drugs that have an absorption in the particular region of the GI tract as well as for controlling the release of the drug having site-specific absorption limitation.

Glipizide is an oral hypoglycemic agent, which is used as drug for the treatment of patients with type II Diabetes mellitus. It has bioavailability of 83%. It is mostly absorbed from stomach & hydrolysed in liver. With half-life of 3.4 to 0.7 hours requiring it to be administered in doses of 2.5 to 10 mg per day. Therefore Glipizide is considered a suitable candidate for the design of floating drug delivery system with a view to improve its oral bioavailability.

In the present work, an attempt was made to prepare Non effervescent floating tablet of Glipizide using Eurayle Ferox seed powder and HPMC K15M as polymers by Direct compression method .

All the prepared formulations were evaluated for all the un official tests such as hardness, friability, uniformity of weight, drug content uniformity, drug-polymer interaction, In vitro floating studies, In vitro drug release, swelling index and short term stability studies.

IR spectroscopic studies prove that there was no interaction between drug, polymer and other co-excipients.

Results show that as the amount of Hydroxypropyl methyl cellulose increased, total floating time also increased. This may be accounted to increased gel strength of the matrices. With subsequent hydration and swelling of the polymers a floating mass is produced. Continuous erosion of the surface allows penetration of water to the inner layers, maintaining surface hydration and buoyancy.

The polymer used affected the floating lag time of the formulations.

The In vitro dissolution profiles of all the formulations of Glipizide were controlled over a period of 22 hours. Release of Glipizide from the formulations was found to follow zero order kinetics.

The drug release data showed a good fit to Higuchi model indicating that diffusion is the predominant mechanism controlling the drug release. The value of diffusional exponent 'n' for the Korsmeyer equation suggested that the drug release was by - fickian diffusion mechanism [1-4].

Review Article

Floating systems are low-density systems that have sufficient buoyancy to float over the stomach or gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged

period of time [5-12]. While the system is floating on the gastric contents, the drug is released delayed at the desired rate from the system. After drug release, the contents are emptied from the stomach. This result in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.

Non-effervescent Floating Dosage Forms: Non-effervescent floating dosage forms use a gel forming type hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes thorough mixing of the drug and the gel-forming hydrocolloid. After oral administration, this dosage form swells when comes in contact with gastric fluids and attains a bulk density of < 1 [13-19]. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.

Evaluation of floating drug delivery systems: Various parameters that require to be evaluated in gastroretentive formulations embrace floating period, dissolution profiles, relative density, content uniformity, hardness, and breakableness just in case of solid indefinite quantity forms. within the case of multiparticulate drug delivery systems, differential scanning measuring (DSC), particle size analysis, flow properties, surface morphology, mechanical properties and X-ray diffraction studies are performed [20-24].

1. To collect the relevant literature regarding the drug , dosage form and excipients
2. Collection and processing of eurayle ferox seed powder
3. Physical characterization of eurayle ferox seed powder.
4. Selection of all excipients.
5. Study of the drug and excipients compatibility.
6. Preparation of standard curve
7. To prepare different formulations of sustained release floating matrix tablets of Glipizide.
8. Precompressional studies
9. To evaluate physical properties of tablets like thickness, hardness, friability etc.
10. To evaluate the in-vitro drug release of tablets.
11. Kinetic of drug release model
12. Stability studies.

METHDOLOGY

Processing of Eurayle feroxy seeds [25-29]: Processing of seed continues to be meted out by ancient strategies. Seeds area unit preserved within the morning between 8-11 am so the wet content reaches around thirty one per cent. Water is wet to stay the seeds contemporary and wet content optimum. the opposite steps concerned area unit drying, size grading, pre-heating and tempering, cooking and pop. Seeds area unit currently additional dried to facilitate removal of kernel from the reproductive structure. Seeds area unit undergone completely different size of sieves to differentiate them into 5-7 grades. Uniform heat transfer happens once seeds of same size area unit heated throughout preheating and cooking. hierarchal seeds area unit heated in associate stuff pitcher or forged iron pan with continuous stirring over hearth at 230° - 335° C for about half dozen minutes. Tempering of seeds is followed by storing them in open baskets for 40-50 60 minutes. This loosens the kernel at intervals the reproductive structure and will increase the yield of popped seeds [30-39]. Tempered seeds area unit roast in three hundred metric weight unit tons in associate open pan over hearth at roughly 230° - 335° C. once a crackle sound is detected fifty

seven seeds area unit taken out unbroken on a tough surface and hit with a picket hammer. Seed coat breaks and due to unexpected of pressure, the kernel pops out in a expanded form. Seed coats are then removed manually. The plant tissue of the seed forms the edible half. The popped kernels referred to as Makhana area unit currently polished by rubbing it against baskets fabricated from bamboo splits without delay to avoid absorption of wet. Grading is completed on the premise of size and white. Polished and hierarchal product is finally packed in polythylene lined bags.

In this, the preparation of non effervescent matrix tablets is done in the following manner:

Formulation of Non Effervescent Floating Matrix Tablets [40-48]:

All the Excepients are slected in an oredery manner.

1. Eurayle Ferox seeds are taken for formulating tablets.
2. HPMCK15 which is used as polymer is selected as drug release retardant in the formulation.
3. PVPK30 is taken as a binding agent in formulation of Floating agent.

The floating tablets of Glipizide [49-57] were prepared by mixing glipizide and various proportions of Excepients like E.ferox seeds powder, HPMCK15M and PVPK30. Weighed quantity of drug (dose 10mg) was taken and Eurayle ferox seed powder and HPMCK15 was taken in different ratios, PVPK30 was kept constant (30mg) in all formulations [58-63]. The mixture was directly compressed in a R&D tablet compression machine fitted with flat punches and dies (8 mm diameter). Different formulations are prepared and the tablet weight was adjusted to 420mg and 25 tablets for each batch were prepared. The formula for the different batches is prepered. The hardness for all tablets was kept constant around 4kg/cm² to avoid the impact of hardness on floating behavior of tablets and measured by a Monsanto hardness tester [64-70].

Kinetic of drug release :The cumulative amount of glipizide released from the tablets at different time interval was fitted to various kinetic drug release models like zero order,first order,higuchi,korsmeyer peppas,weibul and hixon's crowel.

Stability studies: The best formulation was selected based on floating behaviour, physical properties and dissolution kinetic models was placed in stability chamber at 30°C RH 75% for 3 months and they are evaluated for hardness, friability, floating behaviour, buoyancy time, drugcontent and dissolution.

RESULTS AND DISCUSSION

In this study, Non effervescent Floating Matrix Tablets of Glipizide were prepared by using Eurayle ferox seed powder, Hydroxy propyl methyl cellulose (HPMC), polymers alone and PVPK30 which is different drug to polymer concentrations used [71-80].

The weighed quantities of drug, polymer and excipients were mixed thoroughly in different ratios and Non effervescent Floating Matrix Tablets were prepared by Direct compression method. The prepared tablets were evaluated for its hardness, friability, uniformity of weight, drug content, swelling index, drug-polymer interaction studies, In vitro floating studies, swelling index studies, in vitro dissolution studies and stability studies [81-86].

Hardness and friability: The hardness of the prepared floating matrix tablets of Glipizide was found to be in the range of 3.2 to 4.5 kg/cm². The friability of all the tablets was found to be less than 1% i.e. in the range of 0.51% to 0.79%.

Uniformity of weight: All the prepared floating tablets were evaluated for weight variation and the results. The percent deviation from the average weight was found to be within the prescribed official limits. Drug content: The low value of standard deviation indicates uniform drug content in the tablets prepared as observed.

Drug polymer interaction studies: The infrared spectra of Glipizide solid admixtures of drug and excipients were recorded between 500-3500 cm^{-1} . IR Spectrum of the pure drug shows the characteristic peaks at 1688. cm^{-1} and 1650 cm^{-1} .

The IR Spectrum of Drug and Ferox seed powder exhibited peaks at 1688. cm^{-1} and 1650. cm^{-1} . The IR Spectrum of Drug and polymer (HPMCK15M) exhibited peaks at 1688. cm^{-1} and 1650. cm^{-1} . In comparison with pure drug, the absorption peak of the spectra for Glipizide showed no shift and no disappearance of characteristic peaks suggesting that there is no interaction between drug and excipients.

In vitro floating studies: In vitro floating studies were performed by placing tablet in a 100 ml beaker containing 0.1N HCl. The floating lag time and floating time was noted visually.

Formulation containing drug and HPMCK15 with Ferox seed powder the floating lag time was found to be in between 1 to 3 seconds and remained under floating condition > 22 hours [87-91]. Swelling index: The swelling index of all the formulations The swelling behavior of all the formulations is due to formation of hydrogel by HPMC and swelling index also increases as the molecular weight and concentration of HPMC increases The swelling index was found to be ranging in between 98.54 to 153% [92-95].

In vitro dissolution studies: In vitro dissolution studies were performed for all the batches of floating tablets of Glipizide using USP II dissolution test apparatus-II at 50rpm, Release of Glipizide from the tablets was studied in 0.1N HCl (900 ml) [96-99].

In the above results, it was observed that as the concentration of the polymers increased, there is a decrease in the drug release rates. An increase in polymer concentration causes increase in viscosity of the gel as well as the gel layer with longer diffusional path. This could cause a decrease in effective diffusion coefficient of the drug and a reduction in drug release rate [100].

Drug release kinetics: The In vitro drug release data was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equations, Higuchi and Korsmeyer models to ascertain the mechanism of drug release. Apart from these four models drug release data were fitted to Hixson Crowells and Weibull models, the results of linear regression analysis of data including regression coefficient are done.

The regression coefficient 'r' value of zero order was observed that the 'r' values of zero order were in the range of 0.944 to 0.996 indicating drug release from all the formulations were found to follow zero order kinetics.

The In vitro dissolution data as log cumulative percent drug release versus log time were fitted to Korsmeyer et al equation, values of the exponent 'n' was found to be in the range of 0.807 to 0.996 indicating that the drug release is by -Fickian diffusion mechanism.

The MDT and Dissolution efficiency was calculated, The release rate was decreased with increase in HPMCK15 proportion This was also observed as increase in HPMC K15 concentration there is increase in the MDT values.

Stability studies: Short term stability study was performed for formulation F₁ at 40±10°C and RH 75% for 3 months. The samples were analyzed for percent drug content, In vitro floating ability and In vitro drug release studies. The results are achieved. No appreciable difference was observed for the above parameters.

CONCLUSION

Non effervescent Floating Drug Delivery Systems provides a simple and practical approach to achieve increased gastric residence time, which leads to increase in drug bioavailability and reduced dosing frequency.

The Non effervescent floating tablets of Glipizide were developed by using Eurayle Ferox seed powder, PVPK₃₀ and HPMC (K₁₅M) as polymers by Direct compression method.

IR spectroscopic studies indicated that the drug is compatible with polymer and co-excipients.

The drug: polymer ratio and ferox seed powder were found to influence the release of drug and floating characteristics from the prepared Non effervescent floating tablets of Glipizide.

The prepared Non effervescent floating tablets of Glipizide showed excellent In vitro floating properties.

The In vitro dissolution profiles of the prepared formulations of Glipizide were found to extend the drug release over a period of 15 hours and the drug release decreased with an increase in Concentration of polymer. The MDT and Dissolution efficiency was calculated, The release rate was decreased with increase in HPMCK₁₅ proportion This was also observed as increase in HPMC K₁₅ concentration there is increase in the MDT values.

Release of Glipizide from most of the floating tablets was found to follow zero order kinetics (0.944 to 0.996) and derived correlation coefficient 'r' (>0.9) indicated good fit of Higuchi model suggesting that diffusion is the predominant mechanism controlling the drug release. When drug release data fitted to Korsmeyer equation, the values of slope 'n' (0.807 to 0.996) indicated that the drug release was by Fickian mechanism.

Among the various formulations studied, formulation containing drug-polymer ratio prepared with HPMC K₁₅M showed promising results releasing ≈ 80.35% of the drug in 15 hours with a floating lag time of 2 sec and floating time of 22 hours has been considered as an ideal formulation and subjected to further short term stability studies.

Optimized was found to be stable at 40°C and RH 75% following a three month stability study. Finally, it may be concluded that this novel drug delivery system i.e Floating Drug Delivery Systems offers a valuable dosage form which delivers the drug at a controlled rate. The Floating tablets provide a better option to achieve increased gastric residence, leading to an increase in drug bioavailability and reduced dosing frequency.

Optimized Formulation has to be evaluated for further pharmacodynamic and pharmacokinetic studies to evaluate clinical safety of these Floating tablets in suitable animal and human models.

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