Research and Reviews: Journal of Pharmacy and Pharmaceutical Sciences
e-ISSN:2320-1215
p-ISSN: 2322-0112

Hydrodynamics Balance System of Herbal Oral Dosage Form for Nausea and Vomiting of Pregnancy

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Research Article

Received: 17/09/2021
Accepted: 01/10/2021
Published: 08/10/2021

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Keywords: Hydrodynamic balance drug delivery system; Gastric retention time; Psyllium husk; Gaur gum; Ginger; Fenugreek

ABSTRACT

This review aims to design, prepare and evaluate the effectiveness of herbal combination dosage to treat the Nausea and Vomiting of Pregnancy (NVP) and improve the wellness of both mother and fetus. Ginger is widely used in treating situations including gastrointestinal symptoms. Hydrodynamic drug delivery system in herbal dosage form to improves the drug bioavailability and synergetic extend efficacy by retained in the stomach for a prolonged gastric retention time and controlling the medicament release by using natural and biodegradable polymers. The design of bilayer tablets with Ginger root extract powder as sustain release part and other layer contains Mint, Vitamin B6 and Fenugreek seed extract. Formulations were evaluated by floating lag time and *in vitro* drug release method. The drug release from the optimized formulations was extended for a period of 24 hrs.

INTRODUCTION

Morning sickness is very common symptom of early and during pregnancy and affecting to 70%-80% of pregnant women. The severe morning sickness is called as Hyperemesis gravidarum (HG) that associated with nausea, vomiting, weight loss, dehydration and feeling faint. Nausea and Vomiting of Pregnancy (NVP) have a symptom can occur at any time during the day. Typically these symptoms occur between the 4th and 16th week of pregnancy [1]. The cause of morning sickness is unknown but may be related to changing levels of the hormone human chorionic gonadotrophin. Some have proposed that it may be useful from an evolutionary point of view. Diagnosis should only occur after other possible causes have been ruled out. Abdominal pain, fever, or headaches are typically not present in morning sickness. Since the establishment of human civilization knew how to use medicinal herbs purposefully to teat common ailment and even life threatening disease and its therapeutic value. The traditional knowledge of herbal medicine practice was passed down from one generation to the next generation. Zingiber

officinale is commonly known as Ginger is derived from the Greek zingiberis. Ginger with others blends acts orally and the dosage used for the treatment of morning sickness and vomiting.

Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results 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 proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres [2]. Drug delivery systems are used for maximizing therapeutic index of the drug and reduction in side effects due to site-specific drug delivery.

Since the establishment of human civilization knew how to use medicinal herbs purposefully to teat common ailment and even life-threatening disease and its therapeutic value. The traditional knowledge of herbal medicine practice was passed down from one generation to the next generation. Zingiberofficinale is commonly known as Ginger is derived from the Greek zingiberis. Ginger is also known as the “Wonder Herb”. Its rhizome parts is a worldwide consumed as a spice, alternative medicine dietary supplements and herbal remedies without advice from a physician. Ginger contains a large number of chemical constituents such as oleoresin, zingerone, shogaols and gingerols with [6]-gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone). Fresh ginger contains 80.9% moisture, 2.3% protein, 0.9% fat, 1.2% minerals, 2.4% fiber and 12.3% carbohydrates. The minerals present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacinand vitamin-C. Ginger with others blends acts orally and the dosage used for the treatment of Morning Sickness and Vomiting.

Dual release Tablets is a unit compressed Tablets dosage form intended for oral Application. It contains two layers in which one layer having conventional or immediate release part of single or multiple actives; another layer is sustained or controlled release part of single or multiple actives. They are also called as Bilayer, multi-layer Matrix Tablets. A Bilayer Tablets is a type of multiple compressed. Tablets are composed of two layers of granulation compressed together.

LITERATURE REVIEW

Fresh Ginger roots were collected from the local market and cut it into small pieces and dried into tray drier. After completely dry, grind the dried ginger pieces in a blender it becomes a fine Powder. Psyllium husk was collected from local market. Methocel K-4 M, K-15 M (Colorcon Asia), Magnesium Stearate and others materials was provided. Study of drug-excipients is a significant part of pre-formulation stage of product development and to help for the development of stable dosage form. Active and Excipients blended with individual Excipients were kept into

1:1 ratio, filled in clear flint glass vials and stored in a stability chamber at 40°C/75% RH for the period of 4 week. Samples were analyzed by Differential Scanning Calorimeter (DSC).

Preparation of tablets

The Bilayer tablets were prepared by formulating the immediate release of Fenugreek Seed, Mint and Vitamin B6 and a sustained release layer of Ginger separately, and two layers were compressed together with a single punch.

Preparation of sustained release layer of tablet: All powder materials were accurately weighted and passed through a standard sieve #40 in sifter and transfer into Rapid Mixture Granulator (RMG). Dry mix the all sifted ingredients in RMG for 10 minutes at slow impeller speed. Measure required quantity of Purified water in SS container, add required quantity of Povidone K-30 and stir well to make clear solution [3]. Add prepared binder solution into dry-mix powder of RMG at slow impellor speed and achieve required granules. Drying of wet granules in Fluid Bed Drier (FBD) at inlet temperature of 50°C-60°C till to Loss on Drying (LOD) reaches between 1.5 to 2.5%w/w at 75°C. Sift the dried granules through #18 sieves. Sized materials transfer into octagonal blender and add extra-granular parts of materials and mix for 15 minutes. Tablets were prepared by tablet compression machine.

Preparation of immediate release layer of tablet: Immediate release layer was prepared by direct compression method. Initially Fenugreek Seed powder, Vitamin B6, microcrystalline cellulose granular grade Ph-102, sodium starch glycolate, quinoline yellow lake color, colloidal silicon dioxide and magnesium stearate were weighing accurately and sift through 40# sieve mixed for 10 minutes manually in poly-bag.

Evaluation of blend before compression: To check granulometric analysis like the angle of repose, bulk density, Tab density, Compressibility index etc.

Angle of repose: Angle of Repose was determined by using fixed funnel method. In this, accurately weighed granules were taken in the funnel. The height of the funnel was adjusted to 2 cm from working platform. The powder or granules were allowed to flow freely through funnel on the surface of the platform. The height (h) and the radius of the powder cone were measured and the angle of repose were calculated using formula-Angle of repose (θ)=tan−1 h/r.

Mass density and tapped density: Precisely weighed of the example was exchanged to the measuring barrel of mass thickness mechanical assembly and noticed the volume as mass volume. The mechanical assembly was balanced for 100 tapping and noticed the last volume as tapped volume.

DISCUSSION

The result of flow properties of prepared granules of various formulations of immediate release layer were given. Flow properties of the granules, resistance to particle movement can be judged from the bulk density, tapped density, compressibility index, Hausner's ratio. This measurement gives qualitative and quantitative assessment of

internal cohesive and frictional force under low levels of external loading as might be applied in mixing and tableting [4]. The bulk density was found within the range of 0.405 to 0.450 g/ml. The tapped density was found within the range of 0.472 to 0.525 g/ml. using the density data, Hausner's ratio and compressibility index was calculated. The Hausner's ratio was found within the ranges of 1.1 to 1.18 which indicates better flowability. The Compressibility index was found within the ranges of 9.11% to 15.61%, indicating excellent flow properties. Angle of repose has been used as indirect method of quantifying power flow ability, and fallen between 18.24 ± 1.22° to 22.62 ± 0.92°.

Hausner's proportion=tapped density/bulk density

The result of flow properties of prepared granules of various formulations of sustained release layer were given. Flow properties of the granules, resistance to particle movement can be judged from the bulk density, tapped density, compressibility index, Hausner's ratio. This measurement gives qualitative and quantitative assessment of internal cohesive and frictional force under low levels of external loading as might be applied in mixing and tableting. The bulk density was found within the range of 0.398 to 0.448 g/ml. The tapped density was found within the range of 0.480 to 0.598 g/ml. using the density data, Hausner's ratio and compressibility index was calculated. The Hausner's ratio was found within the ranges of 1.27 to 1.36 which indicates better flowability. The Compressibility index was found within the ranges of 21.34% to 30.68%, indicating good flow properties. Angle of repose has been used as indirect method of quantifying power flow ability, and fallen between 22.50 ± 1.22° to 30.02 ± 2.20°.

The hardness of the tablets was evaluated using a Monsanto hardness tester. The friability was determined in a Roche friabilitor. Twenty tablets from each formulation were weighed and their average weight was determined. The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT). Floating behavior studies were performed in a USP type II (paddle) apparatus at speed 100 rpm in 900 mL 0.1 N HCl at 37 ± 0.2°C to mimic *in vivo* conditions. FLT was determined on the basis of visual inspection.

Floating or buoyancy time: The time taken for tablet dosage form to emerge on the surface of medium called the Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and duration of time the dosage form constantly remains on the surface of the medium is called the Total Floating Time (TFT). The *In-vitro* buoyancy was determined by FLT. Floating behavior studies were performed in a USP type II (paddle) apparatus at speed 100 rpm in 900 mL 0.1 N HCl at 37 ± 0.2°C to mimic *in vivo* conditions. FLT was determined on the basis of visual inspection.

All formulations showed floating lag time between 6 ± 0.75 min to 14 ± 0.75 min. Floating lag time varied by different polymers and polymer ratios.

***In-vitro* dissolution studies of sustained release layer:** The *in vitro* dissolution studies were carried out using USP type-II (Paddle type) apparatus. The dissolution medium was 900 ml of 0.1 N HCl. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37°C ± 0.2°C. The speed of rotation was kept at 100 rpm. At different time intervals, 5 mL of sample was withdrawn and dissolution medium was kept constant throughout by replacing with equal volume 5 mL of dissolution medium. The aliquots were extracted with 30 mL of chloroform and

the chloroform fraction was analyzed spectrophotometrically (Shimadzu UV 1650 PC) at 251 nm against blank chloroform for drug release. The study was performed in triplicate. A plot of cumulative % drug release versus time in hours was plotted.

***In-vitro* dissolution studies of immediate release layer:** The release rate of Vitamin B6 was determined using USP dissolution type-II (Paddle method) apparatus. The dissolution medium was 900 ml of 0.1 N HCl. The dissolution was performed at 37°C ± 0.2°C with 100 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at time-interval and the sample were replaced with fresh dissolution medium. The samples were filtered and absorbance of thse solution was analyzed spectrophotometrically (Shimadzu UV 1650 PC) at 290 nm and 302 nm.

Analysis of release rate and kinetics investigation: The mechanism of release was determined by fitting the release data to the various kinetic equations such as first-order, zero-order, Higuchi and Korsmeyer-Peppas and the R2 values of the release profile corresponding to each model were found.

In bilayer tablet of immediate release layer was prepared by direct compression method and Sustained release was prepared by wet granulation method. The tablet containing gum polymer showed the desired sustained action. Formulations T12 releases up to 24 hours and it shows good sustained action [5]. In all the formulations an initial burst release was seen to provide the loading dose of the drug, followed by the controlled release. From these results it clearly indicates that the prepared formulations are potential of the Ginger bilayer matrix tablet as an alternative to the conventional dosage form. Batch T7-T9 containing xanthan gum not shows the retardation of drug at lower concentration. Chitosan shows sustain action up to 8 hrs. A higher viscosity polymer shows desired retardation up to 24 hr.

CONCLUSION

In vitro release studies demonstrated that the release of Ginger from the prepared bi-layer matrix tablets were dependent on polymeric source and level. When we increased the polymeric concentration drug release was retarded up to 24 hr. In all the formulations an initial burst release was seen to provide the loading dose of the drug. These results it clearly indicates that the prepared formulations are better alternative of the conventional dosage form as available in market for NVP treatment without any side effects. Floating tablets were within acceptable limits for various physicochemical evaluations for tablets like tablet dimensions, hardness, uniformity of weight, friability, buoyancy time, and *in vitro* drug release. *In vitro* dissolution studies for the floating tablets were carried out in 0.1 N HCl at 37°C. Formulated floating tablets best fitted to Korsmeyer-Peppas model and zero-order kinetics. The results indicate a promising potential of floating tablets as an alternative to the conventional dosage form.

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