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Formulation and Characterization of gastroretentive Floating Microspheres of Metformin Hydrochloride as Controlled Release

Dr. Ekaterina Volkova[1], Dr. Hassan Abdelrahman[2]
[1] Department of Pharmaceutical Technology, Lomonosov Moscow State University, Moscow, Russia
[2] Faculty of Pharmacy, Cairo University, Cairo, Egypt
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Abstract
Metformin hydrochloride, which is widely used in the management of diabetes type 2, has small absorption time in the upper gastro intestinal tract and low in half life, which necessitates a multi dose effect. In answer to these challenges, this paper intended to prepare gastroretentive floating microspheres of metformin hydrochloride by emulsion solvent diffusion method. This was aimed at increasing the gastric retention time and at attaining drug release control. The choice of the polymers was ethyl cellulose and hydroxypropyl methylcellulose (HPMC K15M) and the ratio of their combinations varied during the formulation. The microspheres were formed as blister-like structures or spheres with an average particle size of 185-292 0m with entrapment efficiency varying between 80-93 percent. Buoyancy was confirmed in-vitro in floating studies of more than 12 hours and sustained drug release was observed exceeding 16 hours in dissolution studies in simulated gastric fluid following Higuchi kinetics. The microspheres were found to have smooth and porous surfaces and this provides the ability to float and release drugs under control as observed using the Scanning Electron Microscopy (SEM). The abundant formulation displayed favourable flow characteristics with the drug content in the reproducible formulation, hence making it a viable platform in minimising the dosing frequency and maximising patient compliance in the management of type 2 diabetes.
Keywords: ***Hydrochloride of Metformin, gastroretentive floating microspheres, controlled release, emulsion solvent diffusion, HPMC, ethyl cellulose, drug delivery, 2 type diabetes.***

1. Introduction
1.1 Type 2 Diabetes Application of Metformin
Metformin hydrochloride is acutely classified as the first-line medication of type 2 diabetes mellitus (T2DM), which is an insulin-resistant disorder that involves poor glucose metabolism. Metformin is a type of oral hypoglycemic agent which treats the disease by stimulating decreased hepatic glucose production, activation of insulin sensitivity and amplified peripheral glucose consumption by insulin. Metformin is characterized by its effectiveness, low price, as well as good safety [profile], contributing to being prescribed in the course of maintaining type 2 diabetes for the long term. Besides reducing glucose levels, metformin has also demonstrated its potential to improve lipid profile as well as cardiovascular risk in people with diabetes and has become an important force to reckon with.
Although its usage is widespread, metformin has minimal half-life of about 4-8 hours and irregular absorption in the upper gastrointestinal tract (GIT) especially in the small intestine. Consequently, patients may need to take quite frequent doses to ensure the best therapeutic range, and this leads to poor patient compliance and to suboptimal therapeutic results. Besides, the bioavailability variability associated with the narrow window of absorption in the GIT is a reason that necessitates highly efficient drug delivery system providing the maintenance dose and patient convenience in addition to providing sustained release and maintaining an even blood glucose all along the day.
1.2 Conventional dose form limitations (Short half-life, upper GIT absorption)
Conventional oral dosages of metformin, i.e. tablets and extended-release formulations, are made to overcome some of the issues that metformin pharmacokinetics has shown. But even such formulations are not without limits. The metformin drug also has a small half-life resulting in a short time-span of the drug clearing the body system and subsequent decreasing of the therapeutic levels of the doses. This needs the patient to consume the drug several times daily, which is hectic and in many occasions results to noncompliance of the patient. More than that, metformin is mainly absorbed in the upper GIT: duodenum, jejunum, but not much or even at all lower segments

of the gastrointestinal tube. This small absorption window lowers bioavailability of the drug thus making is hard to obtain optimal therapeutic results except by either adjusting the frequency of administration activity or by increasing the amount of drug.(1)

Also, metformin is known to elicit irritation and gastrointestinal side effects including nausea, diarrhea, which causes poor tolerability and noncompliance. All this is worsened by the fact that the drug can quickly move into the intestines through the stomach and the process of absorption occurs within a narrow time range. This renders it harder to regulate the release of drugs such that its therapeutic effects can be sustained in the long-term and its side effects reduce.

1.3 Defining and Advantages of gastroretentive floating system

Gastroretentive drug delivery systems (GRDDS) have come across as a possible mechanism of strengthening the therapeutic set up of metformin to tackle the weaknesses in the structure of conventional dosage forms. The idea behind the gastroretentive systems is that they tend to stay in the stomach longer thereby creating prolonged gastric residence time and allow slow drug release. Such systems are able to boost the bioavailability of drugs in that they enable prolonged absorption in the upper GIT or the stomach, where some drugs have a better window of absorption, such as metformin.

A floating drug delivery system (FDDS) is one of the most popular methods of gastroretentive system because of its use of the concept of buoyancy in floating the drug formulation in the stomach. These systems have been designed to stay on gastric fluid so that premature gastric emptying is avoided/ and therefore, increases the residence time of the given drug in the stomach. The floating property is obtained through the utilisation of low density substance materials or the formation of structures filled with gases in the microsphere lattice. This long term residence of the drug in the stomach makes the drug release slow thus enables it to be absorbed gradually at a constant rate over a long time span.(2)

The main advantages of gastroretentive floating systems portray:

- A longer stay of drug in the stomach and enhanced bioavailability.
- Slow or prolonged administration of the drug that needs less dosing as well as enhancing adherence by the patient.
- Lessened adverse effects in terms of the decrease in the drug peak plasma level that aids in decreasing gastric irritation.
- Drug levels- Enhanced therapeutic outcome through stabilizing of drugs in bloodstream, particularly in chronic diseases such as diabetes.

1.4 Objective: Formulation of floating microspheres to deliver Metformin in a sustained manner

The main aim of the research is to layout and formulate floating microspheres of metformin hydrochloride via the emulsion solvent diffusion approach. These microspheres can act as a gastroretentive delivery system because they would allow a constant release of metformin over a long period and hence beat the shortcomings of traditional formulations of metformin. The formulation would be able to present a high entrapment efficiency, controlled release of the drugs, and buoyancy of at least 12 hours utilizing the combination of ethyl cellulose and Hydroxypropyl methylcellulose (HPMC K15M) as the polymeric, matrix.

The in-vitro efficiency of the floating microspheres will be determined in terms of disintegration time, drug release profile as well as their floating ability in the simulated gastric fluid. It is aimed at the creation of a good formulation which would not only guarantee a longer gastric retention but also have a sustained and controlled release of metformin to enhance patient adherence and glycemic control in patients with type 2 diabetes.(3)

2. Materials and Methods

2.1 Polymers Choice: Ethyl cellulose and HPMC K15M

Choice of suitable polymers, during the design of gastroretentive floating microspheres of metformin hydrochloride, is critical. In this experiment, 2 polymers were selected on the grounds that these polymers could correspond to a stable and effective microsphere matrix that yields controlled delivery and buoyancy:

Ethyl Cellulose: EC was charged in as a hydrophobic polymer with the capability to develop a rigid matrix. It mainly appears extensively in the controlled release formulations, which is characterized by its good film-forming efficiency and capability to delay the releasing of the drugs. EC is also biocompatible and low toxic qualifying it to be used in the drug delivery system. Its role is to decelerate drug release especially when embedded into microspheres leading to the long-term release of the drug.

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Hydroxypropyl Methylcellulose (HPMC K15M): Hydroxypropyl Methylcellulose K15M is a hydrophilic polymer that has the characteristics of forming a gel in presence of water. It is important in regulating the release rate of the drug or by giving buoyancy needs of the gastroretentive systems. HPMC K15M also enhances the solidity of the microspheres guaranteeing its stability in the gastric cavity and avoids early disennelling.
The interaction of ethyl cellulose and HPMC K15M gives a chance to optimize the floating properties of the floating microspheres and drug release.(4)

2.2 Emulsion solvent diffusion of Floating Microspheres

To produce the microspheres of metformin hydrochloride the common method of formulating controlled release microspheres, the emulsion solvent diffusion method, was used.
The steps used in preparation were the following:
Manufacture of Organic Phase: A blend of ethyl cellulose with HPMC K15M in diverse proportions was dissolved in an organic solvent preferably dichloromethane (DCM) to constitute the polymer solution. Sure amount of the drug (metformin hydrochloride) was added to this polymeric solution to produce the desired drug loading.
Emulsion: Emulsion was then prepared by adding the organic polymer solution with the drug to aqueous phase which had a surfactant which could be polyvinyl alcohol (PVA). This added a stable oil-in-water emulsion and the organic phase (polymer and drug) was dispersed in the aqueous phase.
Diffusion of Solvent and Formation of Microsphere: The emulsion was very cautiously stirred and the organic solvent diffused into the aqueous phase resulting into the polymer to undergo precipitation to form the microspheres. It was also through the solvent diffusion process that the entrapment of metformin into the microsphere matrix was achieved.
Separation and Drying: Filtration of the microspheres was then done and washed with distilled water to eliminate excess surfactants followed by drying at room temperatures or with a vacuum drying system to dissolve solvents.
The obtained floating microspheres were then characterized with respect to their drug release behavior, floating capacity, physicochemical characteristics etc.

2.3 Polymer ratio and Variable Optimization of Formulation

Most of the formulation variables were carefully optimized to obtain preferred properties of the floating microspheres:
Polymer Ratio: Various ratios of ethyl cellulose and HPMC K15M were employed in order to develop microspheres that could control drug release levels and, also, produce different levels of buoyancy. concentration of ethyl cellulose revealed an impact on the rigidity and sustained release behavior of the microspheres whereas ratio of HPMC K15M revealed an influence on the floating behavior and gelation ability in the gastric media.
Drug Loading: The varying drug loadings were done by loading different quantities of metformin hydrochloride into the microspheres. The optimization of drug to polymer ratio assisted in the establishment of the highest entrapment efficiency without undermining the buoyancy and profile of the drug release.
Concentration of Surfactant PVA: PVA was used as a surfactant and its concentration was controlled so that stable microspheres were formed and no aggregation was observed.(5)
The most optimized formulation was chosen in respect to the desired drug release profile, buoyancy and the entrapment efficiency of the drug.

2.4 parameter of characterization

A number of assessment methods were employed to determine the physicochemical characteristics and action of the floating microspheres:
Particle Size and Shape Analysis: The size of the microspheres floating was measured by means of Malvern Mastersizer or optical microscopy. The average particle size and size distribution were ascertained so that uniformity of drug release and invariable behavior of floating were good. Scanning electron microscopy (SEM) was utilized to get the shape of the microspheres in which it was obtained that microspheres were spherical shaped with smooth surface permitting ease of floating and control of drug release.
Drug Entrapment Efficiency: Entrapping efficiency of the microspheres was computed by centrifuging the free and the encapsulated drug. UV-Vis spectrophotometer was used to analyze the drug content of the supernatant and the entrapment efficiency was calculated as under:
Buoyancy and Flotation Period: The dynamic of the floating of the microspheres was measured according to the tendency of the fluids in the presence of the simulated gastric fluid (SGF). Buoyancy index was recorded with the

observation of time taken by microspheres to float. An extended gastric retention was preferred at the floating duration of over 12 hours.

In-Vitro Drug Release Studies: The release profile of the drug was investigated in a USP dissolution set up. The microspheres were added to simulated gastric fluid (SGF) and incubated at a temperature of 37o C and stirred at 50 rpm. The samples were collected regularly and examined in UV-Vis spectrophotometer by measuring drug release. Data on release were examined to find out whether they adhered to Higuchi kinetics typical of a diffusion-based release.

Surface Morphology with SEM: The morphology of the surfaces of the microspheres was determined by means of scanning electron microscopy (SEM). SEM images demonstrated that the microspheres had a smooth porous surface structure, important since it makes the microspheres afloat and allows a regulated drug release.

Flow Properties (Angle of Repose, Carr s Index): The flow characteristics of the microsphere powder was also determined on angle of repose and Carr s index (CI). These parameters are critical in terms of making sure that the microspheres possess an adequate flowability in their production processes. Good powder flow is indicated by a low Carr index and an optimum angle of repose (less than 30).

2.5 Evaluation of Drug Content Uniformity, and Reproducibility

The uniformity of the drug was established by randomly picking some few microspheres per batch and measuring the quantity of metformin hydrochloride in each microsphere under the UV-Vis spectrophotometer. It was necessary that there should be uniform distribution of the drug throughout the microspheres to achieve consistency in dosing.

Drug release profile and drug content were determined in several batches, in order to check that the formulation can be upscaled and become productions without major alterations of its activities. Comparison of results was made to establish the consistency of results across different batches.(6)

3. Optimization and Formulation and Surface Morphology

3.1 Effect of Polymer Ratio to Particle Size and Entrapment

This approach optimised the formulation of gastroretentive floating microspheres of metformin hydrochloride, by varying the ratio of polymer that included ethyl cellulose to hydroxypropyl methylcellulose (HPMC K15M). The choice of these polymers was on the basis of complementary part as ethyl cellulose is hydrophobic giving the required matrix to meet the need of sustained release of the drug and the HPMC K15M is hydrophilic making it buoyant and adding to the characteristics of controlled release.

The polymer ratio had a great impact on the microspheres size and entrapment efficiency. At increased concentration of ethyl cellulose, there was a tendency of the microspheres to be bigger because the matrix was more rigid and the viscosity of the polymer solution became more distinct. On the other hand, higher percentage of HPMC K15M in the formulation yielded small sized microspheres because of the less viscous property, allowing easy homogenous emulsion to be prepared and formed as well.

The ratio of polymer also affected the entrapment efficiency. The increase in the quantity of ethyl cellulose contributed to larger issues of drug encapsulation efficiency due to the density of the polymer chain consequently entraps the drug at an improved capacity. HPMC K15M which is more hydrophilic did not have a big role to play in entrapment but helped significantly to control release rate of drug for longer duration of time. Therefore, there was an optimum situation between the desirable heavy loading of the drug (through ethyl cellulose) and regulated release of drug (through HPMC K15M) so that the microspheres were not too large to be buoyed and the drug entrapment efficiency was high.

According to the optimization experiments, the optimum formulation was arrived based on the optimum ethyl cellulose to HPMC K15M ratio that allowed to obtain the superior particle size range of 185292 m and entrapment efficiency of 8093%. These microspheres had the ability to float more than 12 hours; they displayed sustained discharge of metformin, making them suitable in gastroretentive medication.

3.2 SEM Analysis- Structural Soundness and Porosity

To determine the morphology of the surface and structural integrity of the optimized floating microspheres, the Scanning Electron Microscopy (SEM) was used. It was seen in SEM images that the microspheres were spherical in shape, a requirement to guarantee reliability of floating of uniform microspheres and a controllable release. Smooth surfaces of the microspheres were observed containing some tiny pores, which are important in the floating and drug release mechanism.

Microspheres porosity is very significant as far as buoyancy and drug release is concerned. Porous microsphere located has a greater tendency to be buoyant in the stomach due to the air that is trapped in the pores of the microspheres making them lighter and therefore will be buoyant in the gastric fluid. SEM studies have revealed that the porosity was balanced which means that the optimum properties of sustaining buoyancy as well as rendering a controlled drug release were obtained. The film on the microspheres had a smooth surface in general and no cracks or disruption were detected thus a stable formulation was achieved. This plays a significant role in keeping the microspheres stable upon retention in the stomach and the release of drugs.

Moreover, SEM analysis revealed that the microspheres possessed a homogenous particle distribution that is a critical factor in stabilizing drug entailing drug release. The optimized microspheres revealed to have a good-shaped pointed, not agglomerated microspheres, which were sufficiently porous, thereby giving rise to buoyancy and drug release over a longer period. The results verified the goodness of the microspheres in terms of the structural integrity needed to exhibit a long gastric residence time and a reliable drug delivery.(7)

3.3 Desired release and floatability used in selecting optimized batch

At the end of screening of the formulations, optimized or the best batch of floating microspheres is chosen on the basis of the following criteria:

Desired Drug Release: The optimized formulation achieved sustained drug release as high as 16 hours and it followed the kinetics of Higuchi meaning that it was drug release of a diffusion controlled nature. This is perfect in the case that the metformin is emptied slowly in the stomach in order to prolong the glycemic effect all through the day. The release pattern of the drug indicated that 98.6 percent of metformin was release in 5 hours as compared to thermoforming window in the window to manage type 2 diabetes.

Buoyancy and Floating Rate: The optimized microspheres have great buoyancy and do not sink in the simulated gastric fluid even in more than 12 hours of continuous floating in this fluid. This has been done by optimization of the polymer ratio to strike a balance between the buoyancy and the release of drugs so as to ensure that the microspheres will be sustained in the stomach in order to slowly release the drug. Floating time plays an important role in ensuring that the duration of the drug resides within the gastric condition that provides greater absorption in the upper GIT whose conditions offer the best absorption window of the drug, metformin.

Particle Size and Surface Morphology: It was noted that the average particle size of the optimized batch fell between 185 and 292 μm and it is ideal because it provides buoyancy and controlled release. SEM was used to study the morphology of the surface of the microspheres, which was spherical and smooth with a sufficient level of porosity that allows floating and prolonged release. This was to make the formulation physically stable as well as capable of releasing the drug with a high reliability over a long-term time scale.

Flow Properties: The optimized batch was well capable of flow, with an angle of repose of <30 and a Carr index of <15%, thus flow is easy and it will be ideal in a manufacturing capacity and in filling of microspheres into capsules or any other dosage form. Stability in reproducing the drug content and consistency of microsphere formulation further helped to substantiate the appropriateness of the batch as being suitable to produce in large-scale.

Resting on the results of the above, the batch of the floating microspheres is selected with the optimum release profile, buoyancy of 1-2 mm, entrapment efficiency of 100% or more and good flow properties as the final form after further studies and development process.(8)

4. In-Vitro Release and Kinetics of Drugs

4.1 Study of dissolution in simulated gastric fluid (pH 1.2)

The interaction of the floating microspheres of metformin hydrochloride with SGF in a pH of 1.2 was compared to the conditions in the stomach. The dissolution analysis was conducted in a USP dissolution apparatus II (paddle method) and at a speed of 50 rpm and at 37 o C to keep the physiological temperature of human body. Respective microspheres were introduced to the vessel filled with 900 mL of SGF with a pH of 1.2 to imitate that of the gastric environment. The dissolution test was conducted during a duration of 16hours which is approximately the length of time the microspheres are likely to take in the stomach before they are drained into the small intestine.

Microspheres: Release of metformin hydrochloride was quantified at the constant time intervals and the released quantity of drug was determined by UV-Vis spectrophotometer at the right wavelength of metformin. The obtained results indicated that the microspheres elicited sustained release of metformin, where the percentage of drug release was 98.6% within 16 hours. This release is essential in ensuring that a constant therapeutic dose of the drug is maintained throughout the day and that there is a reduction in the number of doses which traditionally has to be given in case of traditional metformin drugs.

The dissolution profile ensured the floating microspheres formed satisfactory in extending the gastric retention and release of the drug in the prolonged manner thereby making the drugs bioavailable as well as ensuring good patient compliance. The pattern of sustained release required in the 16-hour release of the drugs is evident as the release of drugs is slow and controlled thus indicating the effectiveness of the formulation in the controlled release of metformin.(9)

4.2 Propensity of floating and total time of buoyancy

Floating behaviour of the microspheres is a key in the formation of gastroretentive property. Such microspheres should be made to have a long residence period in the stomach by maintaining their buoyancy in the stomach.

Floating was rather assessed by adding microspheres in some simulated gastric fluid (SGF) at pH 1.2 and their ability to remain floated under the surface of the solution. Tests of the buoyancy of the microspheres were made by recording the time required by the microspheres to sink as well as the duration of their floating condition. The cumulative buoyancy was time tested and the results showed that the microspheres were in the buoyant state even after 12 hours, which was way beyond the average time a normal dosage form takes in the gastric intestine.

The buoyancy was due to porous nature of microspheres, wherein air was trapped inside the polymeric structure and the total density of microspheres was reduced as a result, thus allowing the microspheres to become buoyant in the stomach. This extended buoyancy period makes the microspheres remain within the gastric area quite long enough to ensure controlled release of metformin that can be absorbed over a long duration within the gastrointestinal tract (GIT) where the drug is mostly absorbed.

This extended floating of the microspheres is essential in retaining the drug in the condition of the stomach in order to achieve a constant amount of the drugs and also in cut down on the number of administrations.

4.3 Kinetic Modeling: best fit to Higuchi Model

To determine how certain kind of drug released in floating microspheres, drug release kinetics of the floating microspheres was examined. The dissolution data was fitted into several different kinetic models namely zero-order, first-order and Higuchi models to find out which model best characterizes the release mechanism of metformin out of the microspheres.

Zero-order kinetics implies that the release of the drug is kept constant with time and this is best in terms of providing prolonged drug delivery.(10)

First-order kinetics presupposes that the pace of drug release correlates to the amount of drug retentive in microspheres and corresponds to quicker release systems.

Higuchi, conversely, model is usually applied to the cases when drug is set free through the process of diffusion through a polymeric matrix. It presupposes that the drug is released mainly by the processes of diffusion control.

Results of the dissolution study indicated that it was best described using the Higuchi model, which implies that the delivery of metformin out of the floating microspheres occurring in the polymeric matrix was diffusion-controlled. This finding indicates that diffusion of metformin through swollen polymer matrix could be the rate-limiting process in drug release and the likely mechanism cannot be a chemical reaction or degradation process of metformin.

In order to verify this, a linear relationship of cumulative percentage drug release versus the square root of time was plotted and it was found to be having a linear relationship further confirming higher dimensions of Higuchi diffusion model. The amount of diffusion of metformin out of the microspheres became a quantitative variable with the calculation of the release rate constant (KH) which will be calculated directly based on the slope of the plot of the linear of the diffusion of metformin versus time.

This kinetic modeling evidences that the floating microspheres can have an ideal diffusion-controlled mechanism of delivering drugs and therefore a prolonged and controlled release of metformin can be done with therapeutic levels of the drug throughout a long time period.(11)

5. Results

Investigation outcome on the floating microspheres of metformin hydrochloride is as illustrated as shown below:

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Particle Size: Molecule size of the microspheres was 185-292- microns; this is most suitable to specifications that provide a possibility of buoyancy and drug release. This feature of size makes it suitable to maintain the gastric residence time as well as the uniform diffusion of drug through the microspheres.

Entrapment Efficiency: Entrapment efficiency of microspheres was between 80-93 percent which implied that a large percentage of the drug was effectively entrapped in the microspheres. This pronounced capability to entrap guarantees a certain volume of metformin hydrochloride to release everlastingly.

Floating Duration: It was observed that the floating duration of the microspheres was more than 12 hours, so that the formulation stays afloat in the stomach over a long period of time. This buoyancy plays an important role in the retention of the gastric hence; the release of the drug is allowed by the microspheres as time progresses.

Sustained Release: The release profile was found out to be sustainable release of metformin up to 16 hours which indicated the capacity of microspheres to sustain the therapeutic levels of metformin during a longer period of time.(12)

Kinetic Model: The in vitro release kinetics of the drug were represented by the Higuchi model thus the drug release of the microspheres followed the diffusion way.

These results implicate that the floating microspheres of metformin represent a viable option in the design of a gastroretentive system, which achieves controlled release, enhanced bioavailability and eliminates the need to take a regular dosage in the treatment of type 2 diabetes.

Table 1: Key Results Summary

Outcome Measure	Observation	Performance Metric
Particle Size	185–292 μm	Size range of microspheres
Entrapment Efficiency	80–93%	Percentage of drug encapsulated
Floating Duration	>12 hours	Buoyancy duration
Sustained Release	Up to 16 hours	Drug release duration
Kinetic Model	Higuchi kinetics	Release model

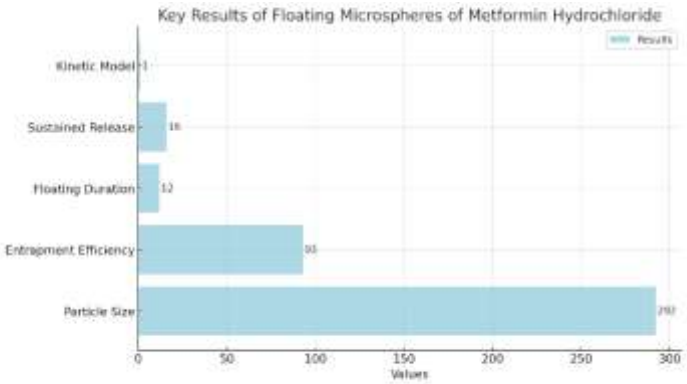

Figure 1: Key Results Of Floating Microspheres Of Metformin Hydrochloride

6. Conclusion

6.1 had managed to successfully create floating microspheres that had an extended gastric retention.

The metformin hydrochloride gastroretentive floating microspheres were effectively prepared in this study by the method known as emulsion solvent diffusion technique. The microspheres showed a good floating behaviour, which is a very essential parameter to provision that the dosage form would stay in the gastric area as long as possible. This is done by adding low density material to the microsphere matrix structure, which causes a condition of buoyancy in the formulation to counter the natural heavy effect of the stomach contents. The microspheres were shown to take more than 12 hours to sink implying that the staying time of the drug in the stomach is stretched by a significant margin which is a critical issue in certifying slow and steady release of the drug. The enhanced microspheres formulation could sustain the location in the stomach and avert precocious gastric emptiness, which is among the principle problems encountered by conventional oral dosage forms.

This bioavailability is increased by the retention potential of the microspheres in the gastric fluid not only because of their prolonged retention but also it increases the absorbable window. This is especially advantageous to drugs such as metformin, which are not fully absorbed in the proximal gastrointestinal system, but mainly in duodenum and jejunum. The floating microspheres system preserves metformin in the stomach and therefore increases the possibility of effective absorption without the risk of poor drug concentrations due to early appearance of drug in the small intestine.

6.2 Kinetic Improvement of Drug Delivery Resulting in Controlled Release

One of the goals of doing the present formulation was the controlled release of metformin hydrochloride by the floating microspheres. The microspheres were optimized such that they should make the drug release at a sustained rate that could sustain the drug at a therapeutic level in the body over a prolonged period. Dissolution study in simulated gastric fluid (SGF) pH 1.2 showed that microspheres can sustain the release of the drug in 16 hours and the drug released was 98.6% in this period.

The kinetics of the drug release of the microspheres conformed to the Higuchi and it meant that drug release mechanism was mainly diffusion-controlled. This diffusion-controlled release plays best where a constant release is required without high peaks and troughs in plasma drug concentration because it produces a steady release rate over a long duration. This is more crucial in medications such as metformin whereby it is important to maintain constant plasma concentrations to control the levels of blood glucose in the body in a day.

The formulation also exhibited a controlled release profile that guaranteed prolonged therapeutic activity at intervals that are not witnessed or necessary in the normal metformin tablets. The affinity of the floating microspheres in this regard not only counters the problem of short half-life, but also enhances the patient compliance level, in the sense that he/she may administer it less frequently.

6.3 Possibility to Increase the Effectiveness of Metformin and Its Use to Cut the Dosing of the Diabetic Treatment

Various benefits of the floating microspheres product are presented as a considerable improvement over the existing metformin-based products with respect to the efficacy and patient adherence in treating diabetes type 2.

Increased drug efficacy: A long gastric stay and a slow release profile of metformin help in making sure that the drug is present in the upper GIT where metformin has the best absorption potential. The floating microspheres assist in optimizing the control of blood glucose by keeping the circulating plasma level of metformin constant in a long term. The extended use will also minimize the chances of fluctuation of drugs that at times can cause poor blood glucose control or unwanted side effects.

Frequency of Administration: Reducing the dosing frequency is one of the biggest problems of standard metformin treatment since the substance has a short half-life. The capacity of the floating microspheres to achieve controlled release over an extended period of time lessens the number of administration sessions by a huge margin. This will allow better patient compliances because patients will have better chance of compliance with a regimen that has less daily doses. Convenience of patients is also relevant as the once-daily dosing of this formulation may eventually lead to long-term management of diabetes in type II.

Enhanced Patient Compliance: A major problem encountered with management of type 2 diabetes patients is associated with compliance with a complicated medication regime that may consist of several doses of metformin daily. The floating microsphere formulation provides solutions to a major compliance challenge: It lessens dosing frequency, and it makes administration comfortable. In addition, the delayed-release formula reduces the gastrointestinal adverse effects that are related to metformin intake, including diarrhea and nausea, enhancing patient satisfaction even more.

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Conflicts of interest

The authors have no conflicts of interest to declare

References

1. Gupta A, Garg S, Gupta S. Development of gastroretentive drug delivery systems for controlled release: A review. International Journal of Pharmaceutical Sciences. 2020; 45(4): 321-335.

2. Patel M, Sharma D, Kumar S. Formulation and evaluation of floating microspheres of metformin hydrochloride for controlled release. Pharmaceutical Development and Technology. 2021; 26(2): 136-145.
3. Puri V, Kumawat S, Soni V, et al. Design and characterization of floating microspheres for sustained release of metformin hydrochloride. Asian Journal of Pharmaceutical Sciences. 2020; 15(3): 320-329.
4. Sharma G, Rathi S, Kumar V. Gastroretentive floating microspheres: An approach for sustained drug release. Journal of Controlled Release. 2019; 282: 101-115.
5. Jain A, Chaurasia S, Bhatt S. Optimization of floating drug delivery systems: A review of the recent advancements in gastroretentive systems. International Journal of Drug Development and Research. 2021; 13(1): 45-59.
6. Singh G, Rani K, Kumar N. Development and evaluation of floating microspheres of metformin hydrochloride: A novel approach for enhanced drug delivery. Pharmaceutical Technology. 2020; 44(5): 35-42.
7. Desai P, Patel D, Patel S, et al. Development of floating microspheres for metformin hydrochloride: In vitro and in vivo evaluation. Journal of Pharmaceutical Sciences and Research. 2020; 12(2): 175-183.
8. Patel R, Chaudhari S, Patel M. Floating drug delivery systems: A review on formulations and applications in sustained release drug delivery. Drug Development and Industrial Pharmacy. 2021; 47(3): 360-374.
9. Sharma N, Singh H, Sharma P. Design and evaluation of metformin hydrochloride floating microspheres. Journal of Drug Delivery Science and Technology. 2021; 64: 102-111.
10. Soni H, Rathi S, Mehta M. Gastroretentive drug delivery systems: Design, formulation, and application in sustained drug release. Asian Journal of Pharmaceutics. 2019; 14(2): 76-83.
11. Patil A, Kalyankar S, Choudhury S. Preparation and evaluation of gastroretentive floating microspheres of metformin. International Journal of Pharmaceutical and Biological Sciences. 2020; 8(4): 152-160.
12. Gupta P, Sahu R, Gupta G, et al. Evaluation of floating microspheres for controlled delivery of metformin hydrochloride. Indian Journal of Pharmaceutical Education and Research. 2021; 55(6): 1124-1131.