INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
ISSN: 2231-6078
12(2): April.-June.: (2022), 24-29

Research Article

Formulation,Characterization and Evaluation of Floating Microcapsule of Saxagliptin

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Abstract

Floating Microcapsules loaded with Saxagliptin were prepared using solvent diffusion-evaporation method using HPMC and EC in different ratio like 1:1, 1:1.5, 1:2 w/w. Drug and polymer in proportion of drug and polymers were dissolved in 1:2 mixture of solvent system of ethanol and dichloromethane. This clear solution was poured slowly in a thin stream into the aqueous solution of 1% polyvinyl alcohol. The In vitro drug release data of the optimized formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, in order to determine the mechanism of drug release. When the regression coefficient values were compared, it was observed that an 'r' value of Microcapsule was maximum zero order i.e 0.923 hence indicating drug releases from formulations was found to follow zero order for floating Microcapsules.

Keywords: Microcapsules, Saxagliptin, Zeta potential.

Introduction :

Microcapsules have focal points like proficient retention and upgraded bioavailability of the medications because of a high surface to volume proportion, a substantially more cozy contact with the bodily fluid layer and particular focusing of medications to the ingestion site.

Microsponges incorporate micro particles and microcapsules (Having a centre of medication) of 1-1000m in distance across and comprising either totally of a floating polymer or having an external covering of it, individually.

A portion of the uses of Microcapsules are depicted in detail as following: -

1. Controlled and supported discharge measurement shapes.
2. Microcapsule can be utilized to plan enteric-covered measurement shapes, with the goal that the medicament will be specifically caught up in the digestive system instead of the stomach.
3. It has been utilized to shield drugs from natural dangers, for example, mugginess, light, oxygen or warmth. Microcapsule does not yet give an ideal boundary to materials, which debase within the sight of oxygen, dampness or warmth; however an extraordinary level of insurance against these components can be given.
4. The partitions of incongruent substances, for instance, pharmaceutical eutectics have been accomplished by exemplification. This is where coordinate contact of materials realizes fluid development.
5. The security improvement of contradictory ibuprofen chlorpheniramine maleate blend is proficient by microencapsulating them two preceding,blending.
6. Microcapsule can be utilized to diminish the instability. A typified unstable substance can be put away for longer circumstances without considerable dissipation.
7. Microcapsule has additionally been utilized to diminish potential peril of treatment of dangerous or harmful substances. The harmfulness happened because of treatment of fumigants, herbicides bug sprays and pesticides have been beneficially diminished after microencapsulation.[1-5]

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Materials and Methods[6-13]

Preformulation

Preformulation study is the first step in the rational development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties a drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable & bioavailable dosage forms which can be mass produced. Obviously, the type of information needed depend on the dosage form to be developed. Preformulation studies include studies of:

1. The physiochemical properties of drug and an assessment of their relevance to the final formulation.
2. The chemical and physical stability of drug.
3. Chemical /physical compatibility of the active with potential excipients. These studies give clues as to how to achieve the desired performance of the finished products.

Even after developing a formulation and method of manufacture on these principles, it is still necessary to confirm stability and bioavailability, but there is a smaller probability that the formulation will fail. If two or three formulations are developed in parallel, there is even greater probability that one will be significantly minimize the risks of failure and increase the likelihood of producing a high quality.

Some specific benefits of conducting preformulation studies

1. **Minimizing development cost:** By optimizing the formulation before commencing bioavailability and bioequivalence studies, fewer such studies need be conducted.
2. **Avoiding failures during long-term stability:** Failure after say 2 or 3 years of long-term stability testing can set back a program significantly. Sound predictions as to the chemical and physiochemical stability of the active, and compatibility with excipients, other actives and the container, can minimize the failures.

Characterization of drug: Physiochemical Properties of Saxagliptin

Physical evaluation

It refers to the evaluation by sensory characters, appearance, of the drug, etc.

Solubility:

Solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, Chloroform) Shake vigorously and kept for some time. Note the solubility of the drug in various solvents (at room temperature).

Melting point:

It is one of the parameters to judge the purity of drugs. In case of pure chemicals, melting points are very sharp and constant. Since the drugs contain the mixed chemicals, they are described with certain range of melting point.

Procedure for determine melting point:

A small quantity of powder was placed into a fusion tube. That tube was placed in the melting point determining apparatus (Chemline CL-725) containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted.

A) Determination of pH:

Procedure:

About 100mg of the Powder was taken and dissolved in 10ml of distilled water with sonication and filtered. The pH of the filtrate was checked with standard glass electrode.

Identification Test FTIR Spectroscopy

Infra- red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. The region from 0.8 µ to 2.5 µ is called Near Infra-red and that from 15 µ to 200 µ is called Far infra-red region.

Preparation of Floating Microcapsule of Saxagliptin

Floating Microcapsules loaded with Saxagliptin were prepared using solvent diffusion-evaporation method using HPMC and EC in different ratio like 1:1, 1:1.5, 1:2 w/w. Drug and polymer in proportion of drug and polymers were dissolved in 1:2 mixture of solvent system of ethanol and dichloromethane. This clear solution was poured slowly in a thin stream into the aqueous solution of 1% polyvinyl alcohol. The emulsion was continuously stirred for 3 h at a speed of 500 rpm at 27±2°C. The floating Microcapsules were collected by decantation, while the non- floating Microcapsules were discarded. The Microcapsules were dried overnight at 40±2°C and stored in desicator.

Evaluation of Floating Microcapsules.

Percentage Yield

The prepared Microcapsules with a size range of 1µm to 1000µm were collected and weighed from different formulations. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the Microcapsules.

$$\text{Percentage Yield} = \frac{\text{Actual weight of product}}{\text{Total weight of Drug and polymer}} \times 100$$

Drug Entrapment

The various formulations of the Floating Microcapsules were subjected for drug content. 10 mg of Floating Microcapsules from all batches were accurately weighed and crushed. The powder of Microcapsules were dissolved in 10 ml 0.1 N HCl and centrifuge at 1000 rpm. This supernatant solution is than filtered through whatmann filter paper No. 44. After filtration, from this solution 0.1 ml was taken out and diluted up to 10 ml with 0.1 N HCl. The percentage drug entrapment was calculated using calibration curve method.

$$\text{Entrapment Efficiency \%} = \frac{\text{Actual content}}{\text{Theoritical Drug Content}} \times 100$$

Floating behavior:

Ten milligrams of the floating Microcapsules were placed in 0.1 N HCl (100 mL). The time between introduction of dosage form and its buoyancy on 0.1 N Hcl, and the time during which the dosage form remains buoyant were measured. The time taken for the dosage form to emerge on surface of medium is called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and total duration of time during which the dosage form remains buoyant is called Total Floating Time (TFT).

Percentage buoyancy =

$$\frac{\text{Microparticles remained floating}}{\text{Total Mass of Floating microparticles}} \times 100$$

Measurement of mean particle size

The mean size of the Microcapsules was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer(Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the Microcapsules suspended in 5 ml of distilled water was used for the measurement.

Determination of zeta potential

The zeta potential of the drug-loaded Microcapsules was measured on a zeta sizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell.

In-vitro Release Studies

The drug release rate from Floating Microcapsules was carried out using the USP type II (Electro Lab.) dissolution paddle assembly. A weighed amount of Floating Microcapsules equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCI (pH=1.2) maintained at 37 ± 0.5°C and stirred at 50 rpm. One ml sample was withdrawn at predetermined intervals and filtered and equal volume of dissolution medium was replaced in the vessel after each withdrawal to maintain sink condition. The collected samples analyzed spectrophotometrically at 277nm to determine the concentration of drug present in the dissolution medium

Result and Discussion

Evaluation of Saxagliptin Microcapsules
(A)Percentage Yield

Percentage yield of different formulation was determined by weighing the Microcapsules after drying. The percentage yield of different formulation was in range of 76.65±0.32–85.45±0.56%. The maximum Percentage Yield was found in formulation F3, 85.45±0.56 as compare to all formulation.

Drug Entrapment

The drug entrapment efficacies of different formulations were in range of 63.23±0.65- 76.56±0.65% w/w.

The maximum Percentage Yield, Drug Entrapment, Percentage Buoyancy and floating lag time was found to be formulation F3 in floating Microcapsule. The optimized formulation of both batches subjected to further studies.

Particle size analysis

The mean size of the Microcapsules was determined by photo correlation spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the Microcapsules suspended in 5 ml of distilled water was used for the measurement. The results of measurement of mean particle size of optimized formulation F3 of floating Microcapsule was found to be 128.4nm.

Zeta Potential

The zeta potential of the drug-loaded Microcapsules was measured on a zeta sizer (Malvern Instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water at 25°C in triplicate.

Results of zeta potential of optimized formulation F4 of floating Microcapsule was found -35.69 mV**.**

In vitro drug release study of Saxagliptin loaded Microcapsule Comparative release study of all formulation F1-F6

The In vitro drug release data of the optimized formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, in order to determine the mechanism of drug release. When the regression coefficient values were compared, it was observed that an 'r' value of Microcapsule was maximum zero order i.e 0.923 hence indicating drug releases from formulations was found to follow zero order for floating Microcapsule.

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Table 1: Solubility of Saxagliptin

Solvent used	Saxagliptin
Distilled Water	Sparingly Soluble
0.1 N Hydrochloric acid	Soluble
Ethanol	Freely Soluble
Methanol	Freely Soluble
Ethyl acetate	Slightly Soluble
0.1 N NaOH	Sparingly Soluble

Table 2: Melting point of Saxagliptin

S. No.	Melting Point of Saxagliptin	Average Melting Point of Saxagliptin
1.	103-106°C	103-106°C
2.	103-107°C	
3.	103-106°C	

Table 3 : pH of the Saxagliptin

S. No.	pH of the solution	Average pH of the solution
1.	6.68	6.683±0.057
2.	6.69	
3.	6.68	

Table 4: Loss of drying of drug sample

S. No.	Initial weight	Final weight after 15 minutes	% loss of drying	Avg. % loss of drying
1.	1gm	0.998 gm	0.2%	0.366±0.152
2.	1gm	0.995 gm	0.5%	
3.	1gm	0.996 gm	0.4%	

Table 5: Formulations of the floating Microcapsules prepared

Sr. No	Formulation Code	Saxaglipti n (mg)	HPMC (mg)	EC (mg)
1.	**F1**	50	50	50
2.	**F2**	50	50	75
3.	**F3**	50	50	100
4.	**F4**	50	100	50
5.	**F5**	50	100	75
6.	**F6**	50	100	100

Table 7: Drug Entrapment for Different formulations

S. No.	Conc. (µg/ml)	Absorbance
1	5	0.139±0.002
2	10	0.275±0.003
3	15	0.395±0.001
4	20	0.524±0.002
5	25	0.645±0.001

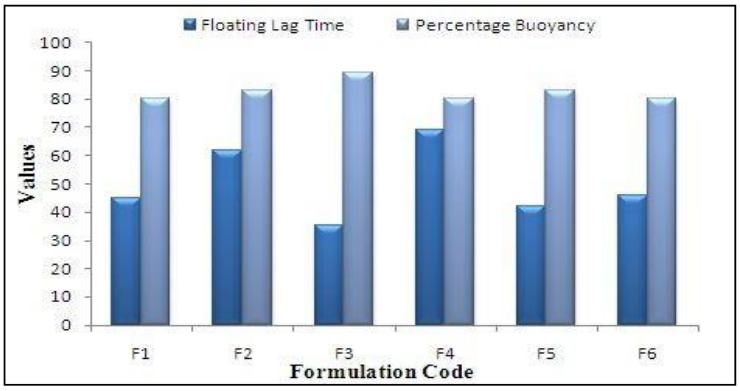
Table 6: **Percentage Yield for Different Formulation**

Formulation	Percentage Yield
F1	82.32±0.51
F2	79.89±0.32
F3	85.45±0.56
F4	82.10±0.41
F5	78.21±0.62
F6	76.65±0.32

Table 8: Percentage Buoyancy and floating lag time of floating Microcapsule

Formulation	Floating Lag Time	Percentage Buoyancy
F1	45±3	80.23±0.45
F2	62±1	82.85±0.65
F3	35±2	89.45±0.21
F4	69±5	79.95±0.32
F5	42±3	83.14±0.47
F6	46±4	80.14±0.74

Figure 1: Floating Lag Time and Percentage Buoyancy for Different Formulatiion



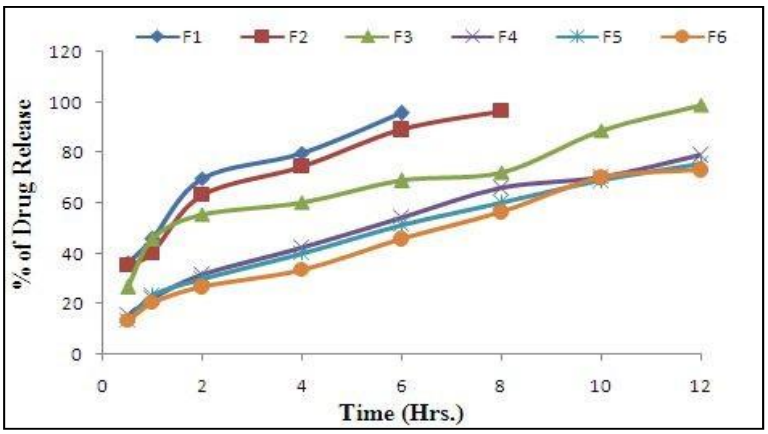


Figure 2: Graph of release study of formulation F1-F6

Table 9 : Release Study data of formulation F1-F6

Time	% of Drug Release					
(hr)	F1	F2	F3	F4	F5	F6
0.5	36.45	35.45	26.65	15.65	13.24	13.25
1	45.65	40.25	45.65	22.12	23.56	20.23
2	69.89	63.12	55.32	31.48	29.89	26.65
4	79.98	74.65	60.36	42.23	40.12	33.65
6	95.65	88.98	68.89	54.45	51.15	45.65
8	-	96.32	72.32	65.85	60.12	56.45
10	-	-	88.95	70.23	68.89	69.98
12	-	-	98.89	78.89	75.45	73.12