INTERNATIONAL JOURNAL IN PHARMACEUTICAL SCIENCES

Journal Homepage: http://ijpsjournal.com/

OPEN ACCESS™

Research Article

Formulation And In-vitro Evaluation Of Bilayer Tablets Of Sitagliptin Phosphate

Mayur Aware*[1], Sheetal Gondkar[1], Rishikesh Bachhav[2]

[1]*Department of Pharmaceutics, R. G. Sapkal college of Pharmacy, Anjaneri, Nashik-422213*
[2]*Department of Pharmacology, R. G. Sapkal college of Pharmacy, Anjaneri, Nashik-422213*

ARTICLE INFO

Received: 13 Jan. 2023
Revised: 14 Jan. 2023
Accepted: 16 Jan. 2023
Published: 01 Feb. 2023
Keywords:
Sitagliptin Phosphate, bilayered buccal tablets, mucoadhesive polymers
DOI:
10.5281/zenodo.5778984

ABSTRACT

The aim of this work was to plan mucoadhesive bilayered buccal tablets of Sitagliptin Phosphate. Sitagliptin Phosphate is the phosphate salt type of sitagliptin, an orally accessible, serious, beta-amino acid-derived inhibitor of dipeptidyl peptidase 4 (DDP4) with hypoglycemic movement. Sitagliptin might cause an expanded danger in the advancement of pancreatitis. Mucoadhesive polymers like thickener and guar gum alongside methyl crystalline cellulose were utilized for the development of mucoadhesive bilayered tablets. The upgraded plan followed Non-Fickian discharge system. The rate relative bioavailability of Sitagliptin Phosphate from chose bilayered buccal tablets was viewed as 98.7%. Bilayered buccal tablets of Sitagliptin Phosphate was effectively ready and assessed with further developed bioavailability.

INTRODUCTION

Tablets are characterized as a compacted solid dose form containing a medication with or without excipients. As per Indian Pharmacopoeia, drug tablets are strong, level, or biconvex dishes in unit measurement's structure ready by packing a API or a combination of Drug, with or without a diluent. This is the most famous measurement structure, with 70% of all drugs being apportioned as tablets.

Advantages and disadvantages of tablets as dosage forms [1]

Tablets are the most popular dosage form used today and therefore there are several advantages associated with their use. However it is also important to highlight the disadvantages associated with their use.

Advantages

- ❖ Tablets are easy to use and have a stylish dosage form.
- ❖ Different types of tablets are available, offering different drug release rates and clinical duration of action. Tablets can be formulated to provide rapid or controlled drug release, the latter reducing the number of daily doses required (and thus increasing patient compliance).

Tablets can be prescribed to deliver a therapeutic agent to a specific site in the gastrointestinal tract to reduce side effects,

***Corresponding Author**: Mayur Aware
Address: [1] *Department of Pharmaceutics, R. G. Sapkal college of Pharmacy, Anjaneri, Nashik-422213*
Email : awaremayur1998@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- promote absorption at that site and provide local effects (such as ulcerative colitis). I can do it. This may not be easily achieved with other oral dosage forms.
- Tablets can be formulated to contain multiple therapeutic agents (even if there is a physical or chemical incompatibility between each activator). In addition, the release of each therapeutic agent can be effectively controlled by the formulation and design of the tablets.
- All classes of treatments, with the exception of proteins, can be orally administered in the form of tablets.
- It is easier to mask the taste of bitter medicine with tablets than with other dosage forms. Example: Liquid.
- Tablets are generally an inexpensive dosage form.
- Tablets are easy to manufacture to display product identification information. for example. Display the required mark on the surface.
- The chemical, physical and microbiological stability of the tablet dosage form is superior to other dosage forms.

Disadvantages

- Tableting requires a series of unit operations, resulting in higher levels of product loss at each stage of the manufacturing process.
- Absorption of therapeutic agents from tablets depends on physiological factors. for example. Gastric emptying rate.
- The compressive properties of certain therapeutic agents are low and can cause problems in subsequent formulation and manufacture in the form of tablets.
- Administration of tablets to specific groups. for example. Children and the elderly can have problems due to dysphagia. These problems can be overcome by using the effervescent tablet dosage form.

Bilayer tablets[2,3]

Bilayer tablets are prepared with a drug layer for immediate release, the second layer is designed to release the drug later, either as a second dose or in sustained release form. Double-layer tablets are also for sustained release tablets, where the combination of the two drugs, the continuous release of two separate incompatible substances, and one layer is the immediate release as the initial dose and the second layer is the maintenance dose. It is suitable.

Applications

1. Used in combination therapy.
2. Used to administer loading and sustained doses of the same or different drugs.
3. It is used for floating double layers, one layer being the floating layer and the other layer being the drug release layer.
4. Used to administer two different drugs with different release profiles.

Advantages

1. Double-layer tablets are suitable for preventing direct contact of the two drugs, so the two maximize the effectiveness of the combination of the two drugs.
2. Improves patient compliance and improves the effectiveness of medication.
3. Compared to traditional delivery systems, it requires less daily dose, which improves patient convenience.
4. A two-layer lock can be designed to change the release because one layer can be left extended and the other layer can be retained as an immediate release.
5. The combination of low dose solids is a very useful tool for treatment.

Disadvantages

1. Adds complexity and bilayer rotatary presses are expensive.
2. Insufficient hardness, layer separation, reduced yield.
3. Inaccurate individual layer weight control.
4. Cross-contamination between the layers.

The main purpose of this study is sustained release of drug administration to ensure safety and improve drug efficacy and patient compliance. When the drug is administered in conventional dosage form, it should be administered several

times daily to produce the desired therapeutic effect. It happens because of the frequent fluctuations in the dose of plasma levels of the drug. If the drug coverage does not match the biological half-life, large peaks and valleys can occur depending on the drug concentration on the blood curve. Significant fluctuations resulting from conventional drug administration are likely to produce periods of ineffectiveness when drug concentrations fall below minimum therapeutic levels.

METHODOLOGY[4,5,6]

PREFORMULATION STUDIES

CHARACTERIZATION OF DRUG

Colour and Appearance: The sample was observed visually.

Melting Point: Melting point of drug was determined by Melting point test apparatus.

pH Determination: A 2% saturated solution of Sitagliptin Phosphate was prepared in distilled water and pH was measured by digital pH meter.

Solubility: Solubility study was carried out as per the I.P. 2007. In this maximum amount of solvent required to dissolve the solute was determined.

UV Spectral Analysis of Sitagliptin Phosphate

Determination of absorption maximum in 0.1N HCl

The absorption maximum of the standard solution was scanned between 200-40 nm regions on Shimadzu-1700 Pharmaspec UV-VISIBLE spectrophotometer. The absorption maximum obtained with the substance being examined corresponds in position and relative intensity to those in the reference spectrum represented.

Preparation of Standard Curve of Sitagliptin Phosphate in 0.1N HCl[7]

Preparation of 0.1N HCl: 0.1N HCl was prepared by diluting 8.5 ml of hydrochloric acid in 1000 ml of distilled water.

Procedure Accurately weighed 100mg of Sitagliptin Phosphate was dissolved in little quantity of 0.1NHydrochloric acid and volume was adjusted to 100ml with the same to prepare a standard solution having concentration of 1000µg/ml. From this above solution 1ml was pipette out and transferred to a 10 ml volumetric flask and the volume was adjusted with 0.1N Hydrochloric acid to a concentration of 100µg/ml. From this stock solution, aliquots of 0.2, 0.4, 0.6, 0.8 and 1.0 ml was pipette out and transferred to 10ml volumetric flasks and final volume was made with 0.1N Hydrochloric acid for giving concentrations ranged from 2.0 to 10 µg/ml. The absorbance of these solutions was measured in UV-Visible spectrometer at 227nm using 0.1NHydrochloric acid as blank.

Assay of Sitagliptin Phosphate

Accurately weighed 25 mg of Sitagliptin Phosphate was dissolved in little quantity of 0.1N HCl and volume was adjusted to 25 ml with the same to prepare standard solution and the volume was adjusted with 0.1N HCl to get a concentration of 1000µg/ml. From this stock solution, 0.1ml was pipette out and transferred to 10 ml volumetric flask and final volume was adjusted with 0.1N HCl. Absorbance values of these solutions were measured against blank at 227 nm using UV-Visible spectrophotometer. The percentage purity of drug was calculated by using calibration graph method.

Infrared Spectrum

The infrared spectrum of Sitagliptin Phosphate was recorded by using FTIR (Perkin elmer-Pharmaspec-1) instrument. A small quantity of sample was mixed with equal quantity of potassium bromide and placed in sample cell to record its IR spectra.

DRUG - POLYMERS COMPATABILITY STUDIES

Research on drug polymers is very important in the design of formulations. In the formulation, it is essential to assess the possible interactions between the active ingredient and the polymer. The choice of polymer is drug, drug administration, compatibility with the same drug, and final product.

Fourier Transform Infrared Spectroscopy (FTIR)

Sitagliptin phosphate powder was mixed with several polymers in a 1: 1 ratio. Next, the sample

was scanned with FTIR (Perkin ElmerPharmaspec-1) in a wavenumber range of 4000 to 400 cm-1.

Differential Scanning Calorimetry (DSC) Study

Sitagliptin phosphate powder is mixed with several polymers in a 1: 1 ratio. Drug-polymer mixtures are mixed to maximize a similar effect of hiding the interaction. The mixture should be tested under nitrogen to eliminate the oxidative and pyrolytic effects at the standard heating rate of DSC (2, 5, or 100 ° C / min). Pure drug thermograms are used as references in temperature ranges that include thermal changes due to drug and polymer mixing. The occurrence or disappearance of one or more peaks in a macromolecular thermogram is considered an indicator of interaction.

PREPARATION AND EVALUATION OF POWDER BLENDS

PREPARATION OF POWDER BLENDS

All materials were weighed and individually threaded through # 40 mesh. The drug and polymer were first mixed in a mortar, then the remaining ingredients were added and mixed for 20 minutes. Finally, the mixture is fed through a # 20 mesh and used to evaluate flow characteristics.

EVALUATION OF MICROMERITIC PROPERTIES OF POWDERS

- **Angle of Repose**

The angle of repose was determined by the funnel method. Accurately weighed granules (10 g) were placed in a funnel. The height of the funnel was adjusted so that the tip of the funnel only touched the top of the grain pile. The granules were able to flow freely through the funnel on a clean surface. The diameter of the grain cone was measured and the rest angle was calculated using the following formula:

$$\tan \theta = h/r$$

Where h is the height of granules cone and r is the radius of the granules cone.

- **Bulk Density and Tapped Bulk Density**

Accurately weighed granules (10 g) of each formula were gently shaken to grind the formed agglomerates and placed in a graduated cylinder. The volume occupied by the granules giving the bulk volume was measured. The graduated cylinder was tapped until no further volume change was observed, resulting in the struck volume. Both the bulk density (BD) and thread bulk density (TBD) of the granules were determined using the following formula.

BD = Weight of the granules/Volume of the granules T

BD = Weight of the granules/Tapped volume of the granules

- **Carr's Compressibility Index**

The compressibility index of the granules was determined using following Carr's compressibility index formula.

Carr's Compressibility Index (%) = [(TBD-LBD)/ TBD] x100

Relationship between % compressibility and flowability is shown in the Table 5

- **Hausner's ratio**

Hausner's ratio is the ratio between tapped density and bulk density. Hausner's ratio less than 1.25 indicates good flow properties while Hausner's ratio greater than 1.25 shows poor flow of granules.

FORMULATION OF BILAYER TABLETS

Formulation development of Sitagliptin Phosphate IR layer

Table 1: Formulation development of Sitagliptin Phosphate IR layer

Sr. No	Ingredients	Formula (mg)
1.	Sitagliptin Phosphate	50
2.	Crosspovidone	5
3.	Methyl crystalline cellulose	20
4.	Mannitol	20
5	Magnesium Stearate	3
6	Talc	2

Formulation development of Sitagliptin Phosphate SR layer

Table 2: Formulation development of Sitagliptin Phosphate SR layer

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sitagliptin Phosphate	200	200	200	200	200	200	200	200	200
Xanthan Gum	50	-	-	100	-	-	25	25	-
Guar gum	-	50	-	-	100	-	25	-	25
Sodium alginate	-	-	50	-	-	100	-	25	25
Starch	40	40	40	40	40	40	40	40	40
Talc	3	3	3	3	3	3	3	3	3
Mannitol	94	94	94	44	44	44	94	94	94
Magnesium stearate	5	5	5	5	5	5	5	5	5
PVP (2%)	8	8	8	8	8	8	8	8	8

FORMULATION AND CHARACTERIZATION OF BILAYER TABLETS

Sitagliptin phosphate double layer tablets were prepared by the direct compression method. Drugs and polymers in the IR and SR layers were sifted through # 60 before use in the formulation.

Formulation of the IR Layer

The IR components were accurately weighed and added to the mixer in ascending order. The powder mixture was mixed for 20 minutes. To obtain a uniform distribution of the drug in the formulation and use it for pre-formulation research.

Formulation of the SR Layer

The SR component was accurately weighed and added to the blender in ascending order. The powder mixture was mixed for 20 minutes. To obtain a uniform distribution of the drug in the formulation and use it for pre-formulation research.

Compression of Bilayer Tablet

In this study, double-layer locks were manually prepared using a single-station punching machine. An accurately weighed amount of SR powder mixture was manually introduced into the matrix cavity. The SR layer is compressed with a light compressive force. The accurately weighed IR powder mixture was then manually fed into the SR layer matrix and compressed with an 8 mm flat punch (Rimek mini press-1 Karnavati Engineering Ltd, Gujarat).

Dose Calculation

For sustained drug release up to 24 hr, the immediate dose of drug was calculated from total dose of Sitagliptin Phosphate extended release tablet.

$$Dt = Dose\ (1 + 0.693 \times t/t1/2)$$

Where, Dt = Total dose, Dose = Immediate release dose, t = Total time period for which sustained release is required, t1/2 = Half-life of drug

EVALUATION OF BILAYER TABLETS

Physico-Chemical Properties of Tablets

Appearance

The tablets were visually observed for any capping, chipping and lamination.

Size and thickness

Tablet size and thickness may vary without changing weight due to differences in granulation density, pressure applied to the tablet, and tablet

compressor speed. The thickness of the tablets was determined using calipers. Three tablets of each type of formulation were used and the average value was calculated.

Hardness

Tablet hardness has certain requirements to withstand mechanical impact during handling, manufacturing, packaging and transportation. The hardness of the tablets was measured using a hardness tester (Monsanto tester). The tablet was held along an elongated shaft between the tester's two jaws. At this point, the reading is considered to be zero kg / cm2. Next, a constant force was applied by turning the knob until the tablet broke. The value at this point is recorded in kg / cm2.

Friability

Friability is a measure of tablet strength. In this test, several tablets are exposed to the combined effect of impact scrubbing using a plastic chamber that rotates at a speed of 25 rpm for 4 minutes and drops the tablets at a distance of 6 inches per rotation. A pre-weighed tablet sample was placed in Roche's refrigerator and rotated 100 times. The tablets were then dusted and weighed again. The brittleness percentage (% F) was calculated as,

% Friability = (Initial weight - Final weight / Initial weight) x 100.

Weight Variation

The weight variability test is performed by taking 20 tablets at random and weighing them individually. Divide the composite weight by 20 to get the average weight of the tablets. Up to two individual body weights deviate from the average body weight expressed in% of tolerance and cannot deviate more than twice that percentage.

Drug content

We took 20 tablets of each formulation and measured the amount of drug present in each tablet. Powder equal to 25 mg was taken, added to 25 ml 0.1N HCl and subsequently stirred for 10 minutes. It was filtered through a 0.45 µ membrane filter, diluted to a concentration of 10 µg / ml, and the absorbance of the resulting solution was UV measured at 227 nm using 0.1 NHCl.

In vitro dissolution of tablets

The rate of release of sitagliptin phosphate from bilayer tablets was determined using a USP Type I solution tester (basket method; Veego Scientific VDA-8DR, Mumbai, India). A sample of solution (5 ml) was removed from the lysing device and the sample was replaced with a new solution medium. The sample was filtered through a 0.45 µ membrane filter and diluted in the appropriate medium to the appropriate concentration. The absorbance of these solutions was measured at 227 nm using a UV-VISIBLE Shimadzu-1700 Pharmaspec spectrophotometer. For each formulation, the experiment was performed in triplicate.

STABILITY STUDIES

The purpose of the stability test is to provide evidence of how the quality of a drug or drug changes over time under the influence of various environmental factors such as temperature, humidity, and light that provide storage conditions. That is. Recommended reassessment period and validity period. In general, it takes time to observe the rate at which a product deteriorates at normal room temperature. To avoid this unwanted delay, the principles of accelerated stability research have been accepted. The International Council for Harmonization of Harmonization (ICH) guidelines, entitled "Stability Testing of New Drugs and Products," describe the stability testing requirements for medical registration applications in the European Union, Japan, and the United States.

RESULTS AND DISCUSSION

CHARACTERIZATION OF DRUG

Colour and Appearance

The drug (Sitagliptin Phosphate) colour is “White to almost white powder” as same as the reported reference.

Melting Point

The Melting point of Sitagliptin Phosphate was found to be 122.9^{0}C. The reported melting point of Sitagliptin Phosphate is 120-124^{0}C. Hence, observed values are complies with USP.

Solubility study: Freely soluble in water, sparingly soluble in methanol, practically insoluble in methylene chloride.

SPECTROSCOPIC STUDIES

UV Spectroscopy: Determination of λmax and Preparation of Calibration Curve of Sitagliptin Phosphate by using 0.1NHCL

UV absorption spectrum of Sitagliptin Phosphate in 0.1N HCl shows λmax at 227nm. Absorbance obtained for various concentrations of Sitagliptin Phosphate in 0.1N HCl are given in Table 1. The graph of absorbance versus concentration for Sitagliptin Phosphate was found to be linear in the concentration range of 2-10 µg /ml.

The drug obeys Beer- Lambert's law in the range of 2-10 µg /ml.

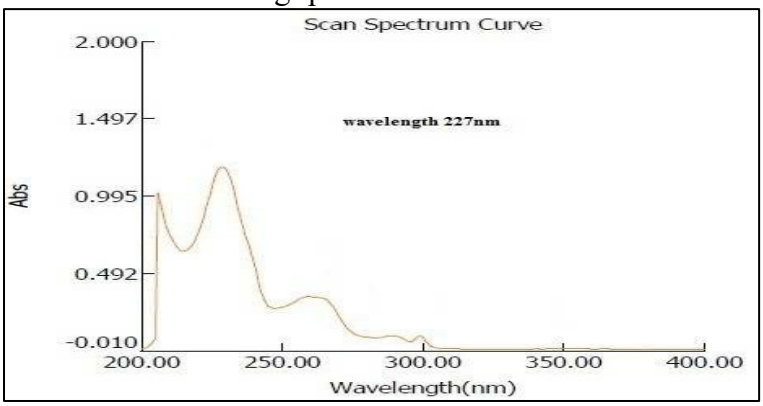

Fig 1: Absorption maximum of Sitagliptin Phosphate in 0.1N HCl

Table 3: Concentration and Absorbance data for Calibration Curve of Sitagliptin Phosphate in 0.1 N HCl

S. No.	Concentrations (µg/ml)	Absorbance at 227nm.
1	0	0
2	2	0.135
3	4	0.251
4	6	0.367
5	8	0.480
6	10	0.594

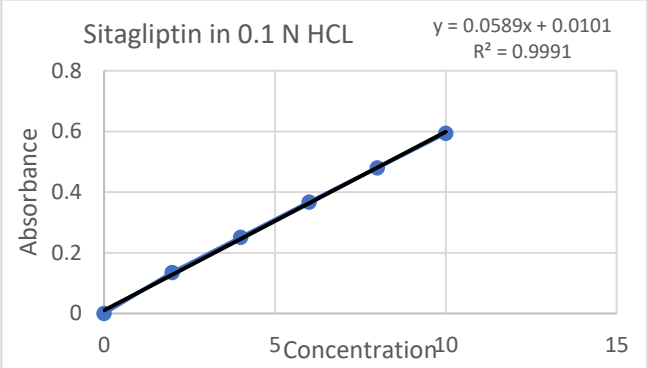

Fig 2: Calibration Curve of Sitagliptin in 0.1 N HCL

Fourier Transform Infra-Red Spectroscopy (FTIR)

The IR spectrum of Sitagliptin Phosphate is shown in figure 3. The interpretation of IR frequencies are shown in table 4.

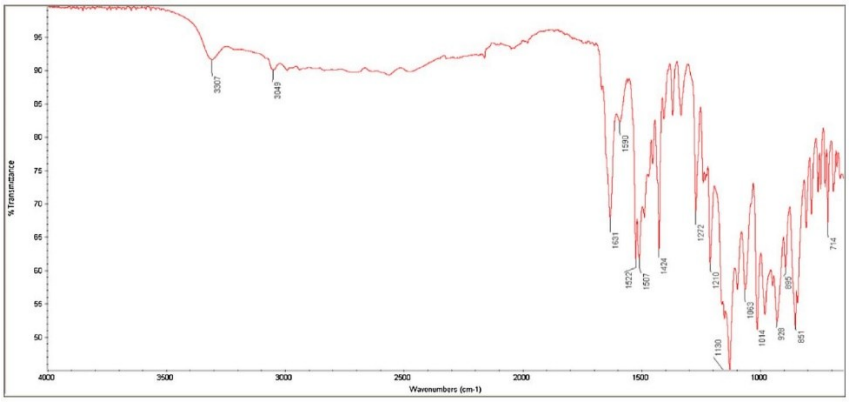

Fig 3: FTIR spectra of Sitagliptin Phosphate pure drug

Interpretation of FTIR Spectrum

Table shows the peaks observed at different wave numbers and the functional group associated with these peaks. The major peaks are identical to functional group of Sitagliptin Phosphate. Hence, the sample was confirmed as Sitagliptin Phosphate.

Table 4: Characteristic frequencies in IR Spectrum of Sitagliptin Phosphate.

Functional groups	Wavenumber (cm^{-1})
N-H stretching	3307
Aromatic C -H stretching	3049
C-O stretching	1631
N-H bending	1580

DRUG - POLYMERS COMPATIBILITY STUDIES:

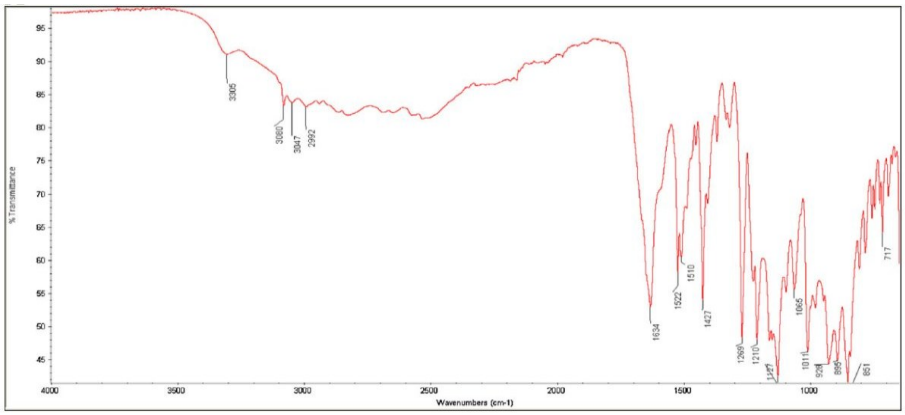

Fig 4: FTIR spectroscopy of Physical mixture

Table 5: Characteristic frequencies in IR Spectrum of Physical Mixture

Functional groups	Presence of Wavenumber (cm^{-1})
N-H stretching	Yes
Aromatic C -H stretching	Yes
C-O stretching	Yes
N-H bending	Yes

Table 6: Preformulation parameters of Sitagliptin Phosphate SR granules

Formulation	Bulk density (gm/ml)	Tapped Density (gm/ml)	Angle of repose (θ) (^{0})	Carr's index(%)	Hausner's ratio
F1	0.43±0.007	0.59±0.006	21.45±1.7	17.34±1.7	1.634±1.2
F2	0.41±0.004	0.62±0.009	27.52±0.4	19.54±0.8	1.382±0.7
F3	0.38±0.009	0.53±0.007	34.62±1.5	23.65±1.1	1.442±1.0
F4	0.53±0.005	0.59±0.004	31.43±0.5	21.45±0.9	1.238±1.3
F5	0.45±0.007	0.54±0.005	24.65±1.3	20.61±1.8	1.327±1.3
F6	0.47±0.005	0.58±0.004	27.95±1.4	25.49±1.3	1.643±0.9
F7	0.52±0.008	0.61±0.006	24.27±1.6	19.62±0.9	1.225±0.7
F8	0.49±0.006	0.54±0.003	31.48±0.9	17.50±1.2	1.505±1.2
F9	0.36±0.009	0.58±0.007	26.65±1.0	22.48±1.7	1.605±0.4

Table 7: Preformulation parameters of Sumatriptane Succinate IR layer.

Preformulation parameters	Formulation
Bulk density (gm/ml)	0.42±0.008
Tapped density (gm/ml)	0.54±0.005
Angle of repose $(\theta)^0$	24.11±1.4
Carr's index (%)	22.42±1.8
Hausner's ratio	1.7±1.2

Angle of repose

Angle of repose ranged from 21.45±1.7 to 34.62±1.5. The flow properties of granules in all formulations exhibit good flow.

Bulk density and Tapped bulk density

The values of BD and TBD were found to be in the range from 0.36±0.009 to 0.53±0.005 gm/cc and 0.53±0.005 to 0.62±0.009 gm/ml respectively. So, it shows that all formulations having good flow properties and packability.

Carr's Compressibility Index

The Carr's Compressibility Index were in the range from 17.34±1.7 to 25.49±1.3%. This indicates good flow properties of granules.

Hausner's ratio

The Hausner's ratios were found in the range from 1.225±0.7 to 1.643±0.9. So it indicates good flow properties.

EVALUATION OF TABLETS

Evaluation of Physico-chemical properties of tablet

Table 8: Physico-Chemical Properties of Tablets.

Formulation	Wt. variation (%)	Friability* (%)	Hardness **(kg/cm^2)	Thickness ** (mm)	Assay*(%)
F1	0.6012	0.25±0.15	5.5±0.7	6.9±0.9	99.49±0.17
F2	0.5988	0.34±0.19	6.0±0.9	6.8±0.2	100.16±0.16
F3	0.6006	0.26±0.17	6.5±0.2	7.0±0.6	99.88±0.25
F4	0.6018	0.12±0.12	9.3±0.7	7.1±0.4	100.5±0.17
F5	0.6005	0.19±0.15	8.6±0.4	6.9±0.2	98.36±0.25
F6	0.5996	0.32±0.13	6.7±0.8	6.8±0.8	98.98±0.16
F7	0.6005	0.28±0.19	6.8±1.2	7.0±0.5	99.60±0.25
F8	0.6008	0.26±0.12	8.4±1.8	6.9±0.6	99.09±0.25
F9	0.6001	0.15±0.16	9.4±0.9	7.2±0.2	100.72±0.19

Appearance

The tablets were observed visually and did not show any defects such as capping, chipping and lamination after punching.

Thickness

The thickness of formulations ranged from 6.8±0.2 mm to 7.2±0.2mm.

Weight Variation

The percentage deviation from average tablet weight for all the formulations ranged from 499±1.2 to 501±1.5mg. The results are within the specified limits. Hence all formulations complied with the test for weight variation as per IP.

Hardness

It was found that the values are ranged from 5.5±0.7 to 9.4±0.9 kg/cm2 . Hardness values were satisfactory and indicated good mechanical strength of tablets.

Friability

The results are ranged from 0.12±0.12 to 0.34±0.19%. So, the percentage loss of Friability of all the formulations was found to be less than 1%.

Drug content

Drug content was found to be uniform among different batches of tablets and ranged from 98.4±0.5 to 100.7±0.9%.

These results showed that the all formulations having percentage drug content within the specified limits as per USP.

IN-VITRO DISSOLUTION STUDIES

In-vitro dissolution profile Dissolution profile (% drug release) of formulations F1-F9

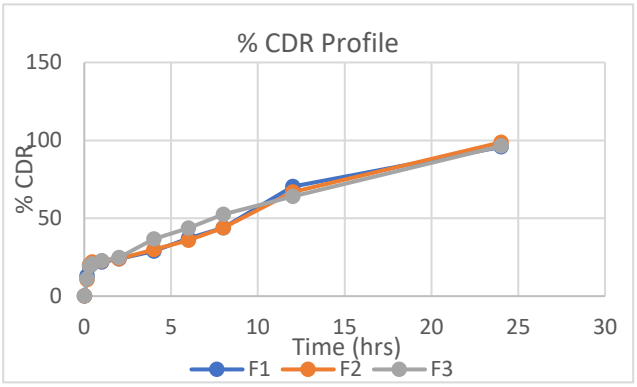

Fig 5 : Cummulative percentage drug release profile of F1, F2, F3

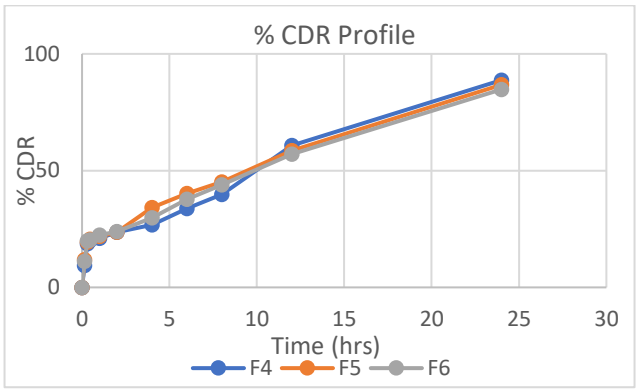

Fig 6: Cumulative percentage drug release profile of F4, F5, F6

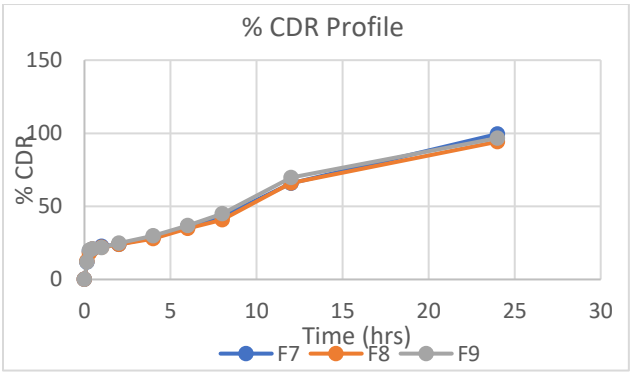

Fig 7: Cumulative percentage drug release profile of F7, F8, F9

The formulations F1, F2 and F3 showed drug release 95.70, 98.68.96.34-24 hours, whereas F4, F5 and F6 showed drug release 88.76, 86.76, 84.79- Showing 24 hours, these have a high capacity for delay and therefore polymer content. Decreased with the following three formulations, F7 showed 99.47 drug release up to 24 hours, and F8 and F9 showed 94.21, 96.69% drug release up to 24 hours. Therefore, the drug released from formulation F7 shows a good delay and is considered to be the best formulation.

Kinetics of In-vitro Drug Release

Diffusion of drugs through most types of polymer systems is often best explained by Fick diffusion (diffusion index, n = 0.5), but processes other than diffusion are important. There is also relaxation of the polymer chains that affect the drug release mechanism. This process is described as anomalous or non-fick spread (n = 0.5-1.0). The release of the initially dry glassy hydrophilic polymer that swells and becomes rubbery when added to water indicates anomalous diffusion due to the rearrangement of the polymer chains. The thermodynamic state of the polymer and the concentration of the penetrant are responsible for the various types of diffusion. The third type of spread is Case II spread (n = 1), which is a special case of non-fick spread. The data were adapted to various kinetic models to obtain the kinetic parameters of the decomposition profile.

Table 9: Different Kinetic models for Formulations F1-F9

Code	Zero order		First order		Higuchi		Korsemayer's-Peppas		Best fit model
	R^2	K_0 (mg/h^{-1})	R^2	K1 (h^{-1})	R^2	K ($mg\ h^{-1/2}$)	R^2	n	
F1	0.9676	0.0166	0.9684	0.0002	0.9742	0.0694	0.9885	0.4032	Peppas
F2	0.9738	0.0164	0.9746	0.0002	0.9778	0.0686	0.9911	0.3970	Peppas
F3	0.9335	0.0162	0.9344	0.0002	0.9745	0.0678	0.9913	0.3775	Peppas
F4	0.9277	0.0136	0.9285	0.0001	0.9681	0.0567	0.9834	0.3596	Peppas
F5	0.9604	0.0137	0.9612	0.0001	0.9719	0.0569	0.9738	0.3475	Peppas
F6	0.9703	0.0138	0.9711	0.0001	0.9722	0.0573	0.9711	0.3482	Matrix
F7	0.9726	0.0169	0.9736	0.0002	0.9602	0.0718	0.9893	0.4051	Peppas
F8	0.9481	0.0293	0.9485	0.0003	0.9911	0.0861	0.9889	0.4462	Matrix
F9	0.8343	0.0296	0.8347	0.0003	0.9882	0.0870	0.9855	0.4476	Matrix

The data obtained from the in vitro decomposition studies were adjusted to the zero-order, first-order, Higuchi, and korsmeyers-peppas equations. To confirm the exact mechanism of drug release, the korsmeyer-peppas equation places two seemingly independent drug transport mechanisms, Fickian diffusion and Case II transport, to account for drug release from swelling polymers. increase.

STABILITY STUDIES

From the results it was found that formulation F7 is the best formulation amongst the 9 formulations. Thus formulation F7 was selected for stability studies.

Stability studies at the end of First month (30 days)

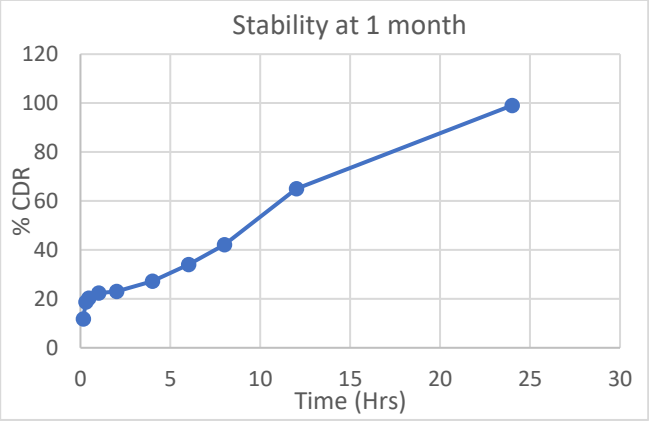

Fig 8: *In-vitro* dissolution profile of formulation F7 at the end of 1 month of stability

Stability studies at the end of Second month (60 days):

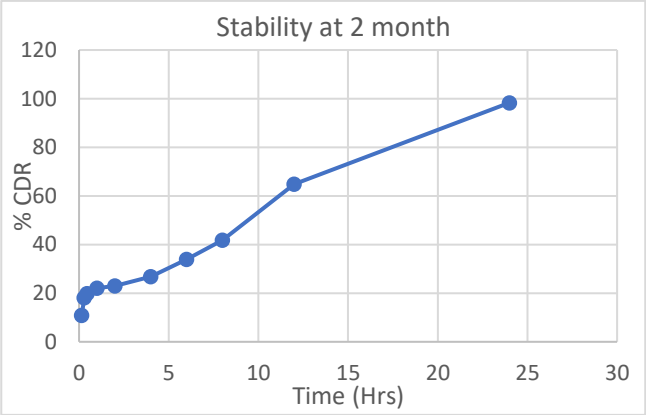

Fig 9: *In-vitro* dissolution profile of formulation F7 at the end of 2 months of stability

Stability studies at the end of Third month (90 days):

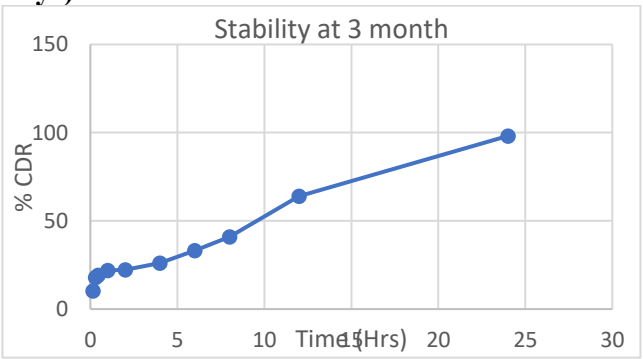

Fig 10: *In-vitro* dissolution profile of formulation F7 at the end of 3 months of stability

At the end of the 3-month stability study, no statistically significant differences were observed in the optimized formulation hardness, percentage of drug content, and percentage of cumulative drug release. Therefore, it can be concluded that the

pharmaceutical product F7 is stable for short-term storage conditions.

SUMMARY

In this study, we developed a two-layer drug delivery system for sitagliptin phosphate tablets and evaluated it in vitro. For the treatment of migraine, citagliptin phosphate bilayer tablets were prepared using polymers such as guar gum, xanthan gum, sodium alginate. Degradation studies of F72 layer tablets containing guar gum and xanthan gum concluded that it was the best of the other formulations and showed the most desirable drug release. An optimized prescription will be considered. The optimized F7 formulation has been subjected to stability testing, and the formulation is stable in short-term stability testing. Pre-formulation studies were performed on the powder mixture and evaluated to determine flow properties according to angle of repose, apparent density, wire density, car index, and Hausner ratio. The data obtained from these studies showed that the powder mixture had good flow properties. Tablets are prepared with different proportions of polymers by direct compression and wet granulation techniques. The formulated tablets were evaluated for physical properties such as thickness, hardness, brittleness, weight variation, and drug content. All physical parameters of the prepared tablets meet the IP specifications. Evaluation studies of all formulations showed drug content, weight variation and brittleness according to the criteria given by IP.

The hardness of all formulations was within limits. In vitro lysis studies carefully show that of the nine formulations, the F7 formulation was found to be the best with good drug release delay. The values of the regression correlation coefficient were concluded by kinetic modelling of the solution profiles of the drugs in all formulations. The formula F7 with an R2 value is between 0.5 and 1.0. Therefore, it can be concluded that the F7 preparation follows the release of the drug pepper. From the stability data, we can conclude that there were no significant changes in any of the parameters. Therefore, the F7 preparation is considered to be a very stable preparation. General studies suggest that xanthan gum and guar gum polymers exhibit satisfactory properties. Of the nine formulations, formulation F7 showed the optimal drug release profile. Therefore, it can be concluded that the F7 preparation is useful for the release of bimolecular membrane drugs.

REFERENCES

1. Anonymous. Indian Pharmacopoeia. Published by the Controller of Publication, Govt. of India, Ministry of Health and Family Welfare, New Delhi, I and II, 2007, 179-183, 662-663.
2. Anonymous. United State Pharmacopoeia. The United States Pharmacopoeial convention Inc, Rockville, MD, USA, 2007; 1988-1989.
3. Anonymous. http://www.wikipedia.com/Sitagliptin Phosphate.
4. Aulton M. Pharmaceutics: The Science of Dosage Form Design, International Student Edition, Newyork, 2007, 168-179, 304-321, 347-668.
5. Banker G and Rhodes C. Drug and Pharmaceutical Sciences, Modern Pharmaceutics, 3rd edition, 72: 333-394.
6. Bhalala chirag, Chauhan Sachin, Balaraman R, Seth A. K., Shah Chainesh, Dhamat Khushal and Hitesh Gevariya. Formulation and evaluation of sustained release bilayer tablets of Metformin HCl and Pioglitazone HCl, World Journal of Pharmaceutical research, 2012; 1(2): 242 257.
7. Bentley's. Text book of Pharmaceutics, 8th edition, pg.no.140.
8. Bogner RH. Bioavailability and Bioequivalence of extended release oral dosage forms, US pharmacist, 1997; 22: 3-12.
9. Brahmankar D.M. and Jaiswal S.B. Biopharmaceutics and pharmacokinetics: A Tretise, 1 st edition, Vallabh prakashan, New delhi, 2006; 335-337.
10. Chien YW. Novel drug delivery system, Informa healthcare, 2nd edition revised and expanded, 2010; 50: 139-140.

11. Chinam Niranjan Patra, Arethi Bharani Kumar, Hemant Kumar Pandit, Satya Prakash Singh and Meduri Vimala devi. Design and evaluation of sustained release bilayer tablets of propranolol hydrochloride, Acta Pharm, 2007; 479–489.
12. Sharmin Rahman, Md. Abdullah Al Masum, Florida Sharmin, S. M. Ashraful Islam andMd. Selim Reza. Formulation and Evaluation of Bi-layered Sustained Release Matrix Tablets of Tramadol Hydrochloride, *Journal of Applied Pharmaceutical Science*, 2(6), 129-134, 2012.
13. Shidhaye SS, Saindane NS, Sutar S and Kadam V. Mucoadhesive bilayered patches for administration of sumatriptan succinate, AAPS Pharma Sci Tech, 9(3), 909-916, 2008.
14. Sinko P. J. Martin's physical pharmacy and pharmaceutical sciences, 5th edition, Lippincott Williams & Wilkins, New York, 523-558, 2008.
15. S. Jayaprakash, S. Mohamed Halith, K.Kulathuran Pillai, Priya Balasubramaniyam, P. U. Mohamed Firthouse and M. Boopathi. Formulation and evaluation of bilayer tablets ofamlodipine besilate and metprolol succinate S. Der Pharmacia Lettre, 3 (4), 143-154, 2011.
16. Sonara GS, Jain DK and More DM. Preparation and *in vitro* evaluation of bilayer and floating bioadhesive tablets of rosiglitazone maleate, *Asian J. Pharma. Sci*, 2(4), 161-169. 2007.
17. Stephen D. Silberstein. Trends in Pharmacological Sciences, 27(8), 410-415, 2006.
18. Sweetman SC (Eds), Martindale. The complete drug reference, 33rd edition, Great Britain, Pharmaceutical press, 456-458, 2002.
19. Turner S, Federici C, Hite M and Fassihi R. Formulation development and human in vitro- in vivo correlation for a novel, monolithic controlled release matrix system of high load and highly water-soluble drug niacin, Drug Development and Industrial Pharmacy, 30, 797-807, 2004.
20. Vogeleer J. Bilayer tablets – why special technology required, The courtoy R292F tablet press, designed for quality bilayer tablets, 1(1), 1-6, 2002.
21. Yellanki SK, Bigala R, Jawad ali syed, Deb SK and Goranti S. Design and in vitro evaluation of mucoadhesive minitablets for nasal drug delivery of sumatriptan succuinate, Asian J Pharma Clin Res, 3(3), 218-220, 2010.
22. Yie WC. Novel drug delivery systems, 2edition, Madison Avenue (NY), Marcel Dekker,Inc, 1992.
23. https://go.drugbank.com/salts/DBSALT002821
24. https://pubchem.ncbi.nlm.nih.gov/compound/Sitagliptin-phosphate
25. http://www.chemspider.com/Chemical-Structure.26466580.html

HOW TO CITE: Mayur aware, Sheetal gondkar, Rishikesh bachhav, Formulation and In-vitro Evaluation Of Bilayer Tablets Of Sitagliptin Phosphate, Int. J. in Pharm. Sci., 2023, Vol 1, Issue 2, 49-61