Research on: "Formulation, Development and Evaluation of Oro-dispersible film of Sitagliptin Phosphate Monohydrate"

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ABSTRACT

The oral route is considered one of the most convenient routes for the administration of various pharmaceutical dosage forms like tablets, capsules, syrup, suspension and emulsion. Fast Dissolving Drug Delivery systems have developed various fast-disintegrating preparations like mouth dissolving film, and MDT. Oral thin films are new dosage forms that are prepared from hydrophilic polymers which when placed in the mouth, the buccal cavity disintegrates rapidly. Mouth dissolving film is superior as compared to mouth dissolving tablet as the cost of production is low. Geriatric and pediatric patients are facing difficulty in swallowing tablets and capsules, the oral film can bypass it, along with that it has other advantages self-administrable, fast dissolving, and rapid absorption that make it a versatile dosage form. The present study aims to enlighten specifically different polymers along with their concentrations and applications. This study also focuses on the use of, polymers e.g. HPMC E15 HPMC E15, PEG 400, sweeteners e.g. Saccharine, sucralose, different methods which are used for the preparation of oral films and various evaluation parameters of the film. The selected solid dispersions were then utilized for the preparation of film by solvent casting method utilizing HPMC E15 as a film-forming agent and PEG-400 as a plasticizer. Five formulae were prepared and evaluated for their in vitro dissolution characteristics, vitro disintegration time, and physicomechanical properties. The promising film (F3) showed the greatest drug dissolution. (More than 99% within 3 min), satisfactory in vitro disintegration time (20 sec) and physicomechanical properties that are suitable for mouth-dissolving films.

The objective of this study was to design and evaluate Sitagliptin Phosphate Monohydrate mouth dissolving film using solvent casting method for the management of Type-II diabetes mellitus.

KEYWORDS: MDT: - Mouth Dissolving, oral films, pediatric patients, evaluation, Buccal cavity, dosage forms, Tensile strength.

1. INTRODUCTION

Oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates), and most importantly, patient compliance also, solid oral delivery systems do not require sterile conditions and are, therefore, less expensive to manufacture. Several novel technologies for oral delivery have recently become available to address the physicochemical and pharmacokinetic characteristics of drugs, while improving patient compliance. Electrostatic drug deposition and coating, and computer assisted three dimensional printing (3DP) tablet manufacture have also recently become available.

Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms. Thenovel technology of fast dispersing dosage forms is known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar.

By definition, a solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in solution or suspension without the need for the administration of the water, is known as an oral fast-dispersing

dosage form. Difficulty in swallowing (dysphagia) is common among all the age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules. Dysphagia is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy, head and neck thyroid therapy, and other neurological disorders, including cerebral palsy. The most common complaint was tablet size, followed by surface, form and taste. The problem of swallowing tablet was more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water.

1.1 Salient feature of fast dissolving drug delivery system

Ease of administration for patients who are mentally ill disabled and uncooperative.

Require no water.

Overcomes unacceptable taste of the drugs.

Can be designed to leave minimal or no residue in the mouth after administration and also provide a pleasant mouth feel.

Ability to provide advantages of liquid medication in the form of solid preparation.

Cost effective.

1.1.1 Advantages

These rapid-dissolving films offer several advantages,

Due to the presence of a large surface area, films provide rapid disintegrating and dissolution in the oral cavity.
Convenient dosing.

Fast disintegration or dissolution followed by quick effect which is desirable in some cases such as pain.
Oral dissolving films can be administered without water, anywhere, anytime.
Suitability for geriatric and pediatric patients, who experience difficulties in swallowing mentally ill, the developmentally disabled and patients who are un-cooperative, or are on reduced liquid intake plans.
No risk of choking.

Oral dissolving films are flexible and portable in nature so they provide ease in transportation, during consumer handling, storage and enhanced stability.
Beneficial in cases such as motion sickness, acute pain, allergic attack or coughing, where an ultra-rapid onset of action is required.
As compared to liquid formulations, precision in the administered dose is ensured from each strip of the film.

The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first pass hepatic metabolism. This advantage can be exploitedin preparing products with improved oral bioavailability of molecules thatundergo first pass effect.
The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
Improved patient compliance.

Life cycle management.

2. AIM AND OBJECTIVE

The present study aims to formulate and evaluate the Sitagliptin phosphate fast-dissolving oral film by using the solvent casting method.

2.1 OBJECTIVE

The objective of the proposed work is

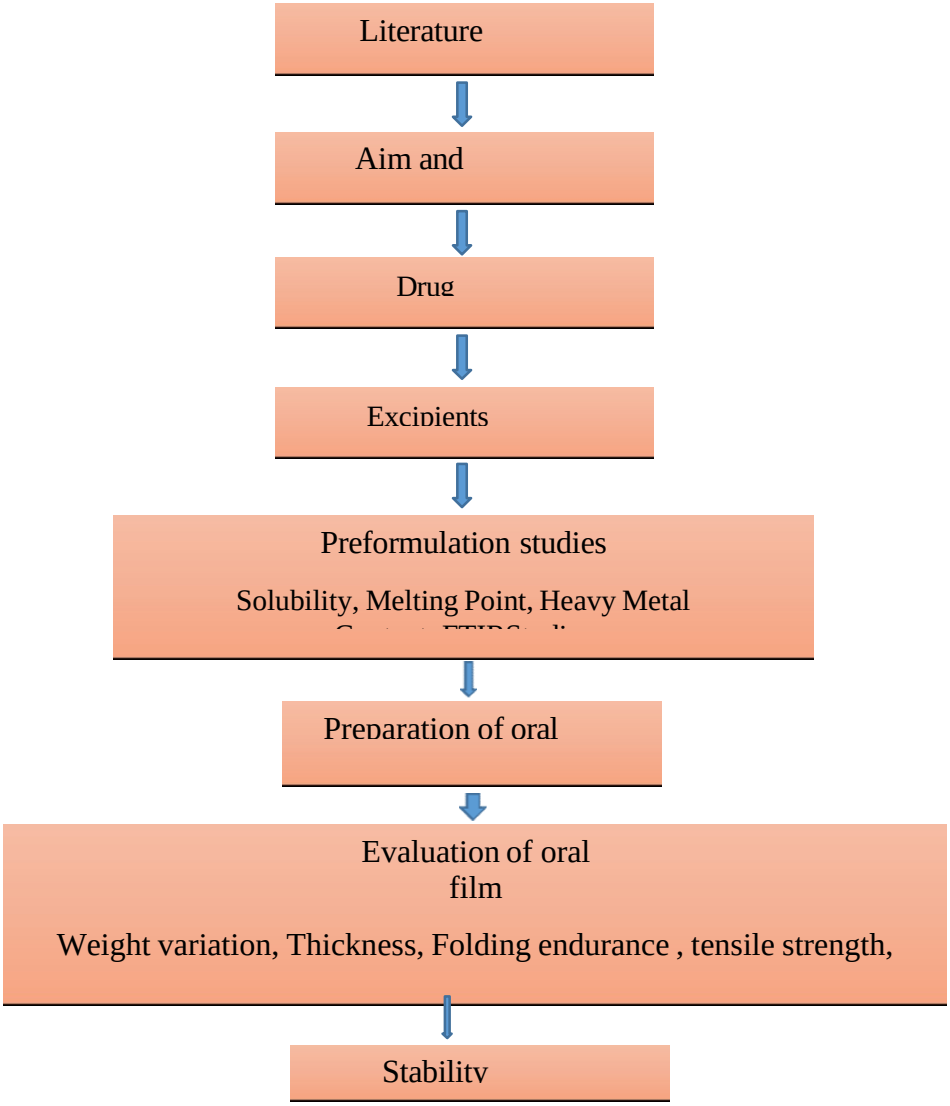
2.1.1 To prepare fast-dissolving oral films of Sitagliptin phosphate by using different concentrations of film-forming polymers and plasticizers.

2.1.2 The formulations are developed and evaluated for pre-compression parameters such as Solubility, Melting point, Heavy metal content, FT-IR studies and post-compression parameters such as Weight variation, Thickness, Folding endurance, Tensile strength, percentage elongation, Drug content, Assay, Disintegration time, dissolution test and SEM analysis.

2.1.3 To improve the patient compliance.

2.1.4 To get the quick onset of action to relieve the symptoms of hyperglycemia.

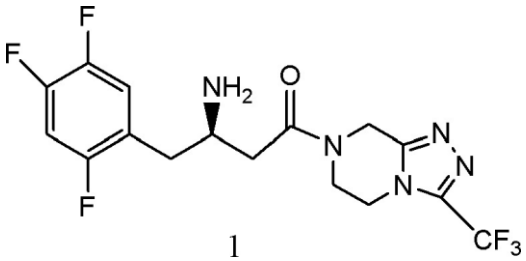
3. PLAN OF WORK



4. DRUG PROFILE

SITAGLIPTIN PHOSPHATE[15, 16]

4.1 STRUCTURE



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(R) -4-oxo-4-[3-(tri fluro methyl)-5,6-dihydro[1,2,4] trizolo [4,3-a] pyrazin-7(8H)-yl-]-1-(2,4,5-triflurophenyl) butane-2-amine.

4.2 CHEMICAL DATA[17]

Formula: C16H15F6N5O
Molecular mass: 407.314 g/mol
Molecular weight: 532.32
Melting point: 205-206°
Physical state: It is a white to off-white, crystalline non-hygroscopic powder.

4.3 MECHANISM OF ACTION[18]

Sitagliptin works to competitively inhibit the enzyme Dipeptidyl peptidase 4 (DPP-4). This enzyme breaks down the incretin GLP-1 and GIP, gastrointestinal hormones released in response to a meal. By preventing GLP-1 and GIP inactivation, they can increase the secretion of insulin and suppress the release of glycogen by the alpha cells of the pancreas. This drives blood glucose levels towards normal. As the blood glucose level approaches normal, the amount of insulin released and glycogen suppressed diminishes, thus tending to prevent an overshoot and subsequent low blood sugar (hypoglycemia).

4.4 PHARMACOKINETICS[19]

4.4.1 Absorption

Sitagliptin is rapidly absorbed, with a 100 mg dose reaching a C_{max} of 950 nm in 1-4 hr ; AVC was 8.52 MC ^{M}. The bioavailability is approximately 87%.

4.4.2 Distribution

Vd is approximately 198L. Plasma protein binding is 38%.

4.4.3 Metabolism

Metabolism by CYP 3A4 and, to a lesser degree, CYP 2C8.

4.4.4 Elimination

Terminal half-life is approximately 12.4 hr and renal clearance is approximately 350 mL/min. Approximately 13 is excreted in the faeces and 87% in the urine via active tubular secretion (79% as unchanged drug). Sitagliptin is a substrate for organic anion transport.

4.5 DRUG INTERACTION

Cyclosporine:
Sitagliptin phosphate plasma concentrations may be increased modestly (approximately 68 %) which is not expected to be clinically important.
Digoxin:
Digoxin plasma concentrations may be increased slightly (approximately 18%); no dosage adjustment is recommended.
Insulin, Sulphonylureas (e.g tolbutamide)
A lower dose of insulin or sulphonylurea may be needed to reduce the risk of hypoglycemia.

4.6 DOSAGE AND ADMINISTRATION[20]

Adults: PO 100 mg once daily.

Renal function impairment
Adults moderate renal impairment (Cr Cl 30 to less than 50 ml/min or approximately serum creatinine levels of more than 1.7 upto 3 mg/dl in men and more than 1.7 upto 2.3 mg/dl in women).
PO 50 mg once daily
Severe renal impairment (Cr Cl less than 30 ml/min or approximate serum creatinine levels of more than 3 mg/dl in men and more than 2.5 mg/dl in women).
PO 25 mg once daily ESRD requiring hemo dialysis or potential dialysis.PO 25 mg once daily Administer without regard to the timing of hemo dialysis.

5. MATERIALS AND METHODS

List of materials

Material	**Manufacturer**
Sitagliptin phosphate monohydrate	Harman Finochem
HPMCE15	Wockhardt
HPMCE50	Wockhardt
PEG400	Wockhardt
Propylene glycol	Wockhardt
Sodium saccharin	Local Vendor

List of Equipment's

Name of Instrument	**Model and Manufacturer**
Digital balance	Mettler ToledoPR203
Hot air oven	Thermo lab
UV Spectrometer	Lab india UV3000
Dissolution test Apparatus	Lab india D58000
Micrometer screw gauge	Mitutoyo,china
Disintegration test apparatus USP	ElectroLab
pH meter	ElectroLab
Stability chamber	Thermo lab Pvt ltd

5.1 PRE-FORMULATION STUDIES[22-25]

Preformulation may be described as the stage of development during which the physicochemical and biopharmaceutical properties of a drug substance are characterized. It is an important part of the drug development process. The information relating to drug development acquired during this phase is used for making critical decisions in subsequent stages of development. A wide variety of information must be generated to develop formulations rationally. Characterization of the drug is a very important step in the pre-formulation phase of product development followed by studying the properties of the excipients on their compatibility.

5.1.1 Solubility[26, 27]

Solubilityis expressedin terms of parts permillion of solvent in which 1g of solid is soluble. Solubility of the powder in different solvents like water, ethanol etc. was determined at 20°c.

5.1.2 Heavy metal content[28,29]

The part of Lead per million parts of powder was examined by comparing sample solution with 10 ppm lead standard solution for 2 gm material.

5.1.3 Melting point[30]

The melting point was carried out by using the capillary tube method.

5.1.4 Compatibility Studies[31-33]

FTIR study was carried out to check the compatibility of the drug with polymers. The infrared spectrum of Sitagliptin Phosphate Monohydrate was determined on a Fourier transform Infra-red spectrophotometer using the KBr dispersion method. The baseline correlation was done using dried potassium bromide. Then the spectrum of a dried mixture of the drug and Potassium bromide was run followed by the drug with various polymers by using an FTIR spectrophotometer. The absorption maximums in the spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum.

FORMULATION DEVELOPMENT OF SITAGLIPTIN PHOSPHATE MONOHYDRATE ORAL FILM[34-36]

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sitagliptin phosphate(g)	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625	0.625
HPMCE15 (g)	1.0	1.25	1.5	-	-	-	1.25	-	1.25
HPMCE50 (g)	-	-	-	1.0	1.25	1.5	-	1.25	1.25
PEG400 (g)	1.5	1.25	1.0	-	-	-	-	1.25	-
Propylene glycol(ml)	-	-	-	1.5	1.25	1.0	1.25	-	-
Citric acid(g)	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Sodium saccharin (g)	0.125	0.125	0.125	0.125	0.125	0.125	0.125	0.125	0.125

Flavor(g)	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Distilled water (ml)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

5.1.5 PROCEDURE[37-40]

The water soluble polymers and plasticizers were dissolved in distilled water. The solution is stirred up for 2 hrs in the magnetic stirrer and kept aside to remove all air bubbles entrapped. Meanwhile, the excipients and drug were dissolved and stirred well for 30 min, after the completion of stirring both the solutions were mixed. Finally, the solution is cast on a suitable petriplate to form a film. The plates were kept in a hot air oven at 60° c for 1 hour. The dried film was gently separated from the glass plate and cut into desired sizes.

Dose calculations Length of glass plate=10cm. Width of glass plate =10 cm. Area of the plate =100 cm^2.

No. of 4cm2 films present whole plate=100/4=25 films. Each film contains 25 mg of the drug.

Films contain 625 mg drug (25×25). Labeled claim 25 mg

5.1.6 Standard Graph of Sitagliptin Phosphate Monohydrate[41-43]

Stock solution was prepared with 50 mg of Sitagliptin phosphate monohydrate in 100 ml of water. From this stock solution 10ml was withdrawn and diluted up to 100ml using water. The calibration curve was prepared by using different concentrations (20 µg/ml- 100µg/ml) by appropriate dilution of stock solution. The absorbance was measured at 267 nm.

5.2 EVALUATION OF ORAL FILM[44]

5.2.1 Thickness[45]

A micrometer screw gauge was used to measure the film thickness. To obtain uniformity of film, thickness is measured at 5 different locations. The thickness of the film should be less than 5 %.

5.2.2 Weight variation[46]

Ten films were randomly selected and their average weight was weighed. Individual films were weighed and compared with the average weight for the deviation.

5.2.3 Folding endurance[47]

To determine folding endurance, a film is cut and rapidly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of folding endurance. Topical folding endurance for film was between100- 150.

5.2.4 Percentage elongation[48]

It was calculated by

Percentage elongation = $\frac{\text{Increase in length of strip} \times 100}{\text{Initial length of strip}}$

5.2.5 Tensile strength[49]

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the formula.

Tensile strength = $\frac{\text{Load at failure} \times 100}{\text{Strip thickness} \times \text{strip width}}$

5.2.6 *In-vitro* disintegration[50,51]

Disintegrating time is defined as the time (sec) at which a film breaks when brought in contact with water or saliva.

Petri dish method

1ml of distilled water was placed in the petri dish and one film was added on the surface of the water and the time was measured until the oral film was dissolved completely.

5.2.7 *In- vitro* dissolution[52]

900 ml of o.1 N HCL was used as a media, at was maintained at 37 +0.5 °c while the basket was set at 100 rpm. A film sample of 4 cm^2 (2×2 cm) was cut and taken into the basket. 5 ml of the sample were taken every 2 minutes and the same amount was replaced with fresh 0.1 N HCL. The withdrawn samples were filtered and analyzed using a UV spectrometer at a wavelength of 267 nm.

5.2.8. Drug content[53]

This test was performed by dissolving a 4 cm^2 area of film in 50 ml of 0.1 N HCL with stirring. This solution was filtered using a whatman filter paper, and the filtrate was diluted to 100 ml with the same buffer in a volumetric flask. This solution was analyzed using UV spectrometer.

5.2.9 Assay

This test was performed by dissolving a 4 cm area of thin film in 50 ml of pH 6.8 phosphate buffer with stirring. This solution was filtered using a Whatman filter paper, and the filtrate was diluted to 100 ml with the same buffer in a volumetric flask. This solution was analyzed using UV spectrophotometer.

5.2.10 Stability studies[54]

The stability studies were carried out according to ICH to assess the drug formulation stability. The optimized F3 formulation was sealed in Aluminum packing laminated with polyethene. Samples were kept at 40 c and 75% RH for 3 months. At the end of the study period, the formulation was observed for change in physical appearance, colour, and drug content and drug release characteristics.

5.2.11 SEM analysis[56]

The morphological study of the oral strip was done by scanning electron microscopy (SEM) at a definite magnification. The study refers to the difference between the upper and lower sides of the films. It also helps in the determination of the distribution of API.

6. PRE-FORMULATION STUDIES

1.1 Solubility

Solubility is expressed in terms of parts per million of solvent in which 1g of solid is soluble. The solubility of the powder in different solvents like water, ethanol etc was determined at 20°c.

6.2 Heavy metal content

The part of Lead per million parts of powder was examined by comparing t h e sample solution with 10 ppm lead standard solution for 2 gm material.

6.3 Melting point

The melting point was carried out by using the capillary tube method.

API characterization - Sitagliptin Phosphate Monohydrate

Sr. No.	Test	Specification	Result
1	Description	White powder	White powder
2	Solubility	Soluble in water	Complies
3	Taste	Bitter	Complies
4	Odor	Odorless	Complies
5	Heavy metals (ppm)	Should not be more than 20 ppm	Less
6	Melting point	Range:205-207°c	206 °c

6.4 CALIBRATION CURVE OF SITAGLIPTIN PHOSPHATE MONOHYDRATE

Stock solution was prepared by 50 mg of Sitagliptin Phosphate Monohydrate in 100 ml of water. From this stock solution 10 ml was withdrawn and diluted up to 100 ml using water. Calibration curve was prepared by using different concentration (20 µg/ml- 100 µg/ml) by appropriate dilution of stock solution. The absorbance was measured at 267 nm. The absorbance of various concentration measured at 267nm is as follows in table 10. Standard curve of Sitagliptin phosphate is shown in figure 11.

Table no 10: Standard graph of Sitagliptin Phosphate Monohydrate

Sr. No.	Concentration (µg/ml)	Absorbance (267nm)
1	20	0.228
2	40	0.436
3	60	0.641
4	80	0.864
5	100	0.998

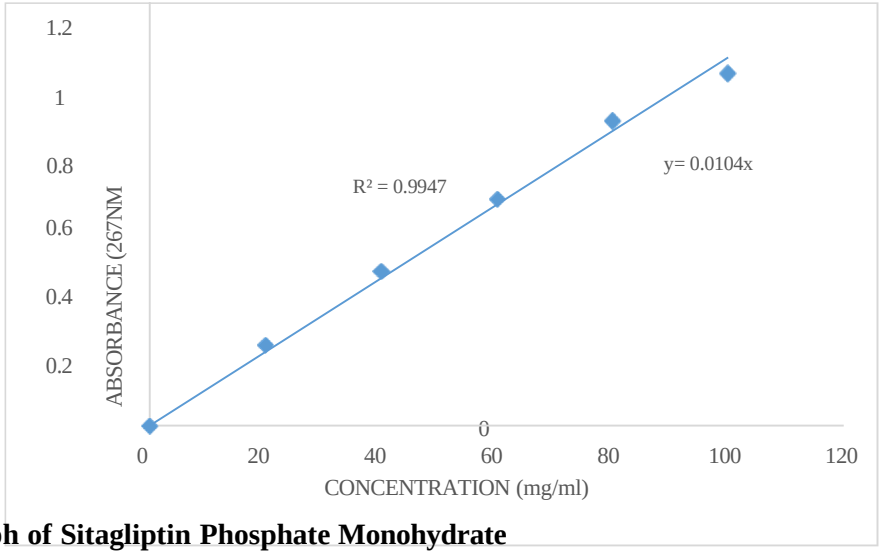
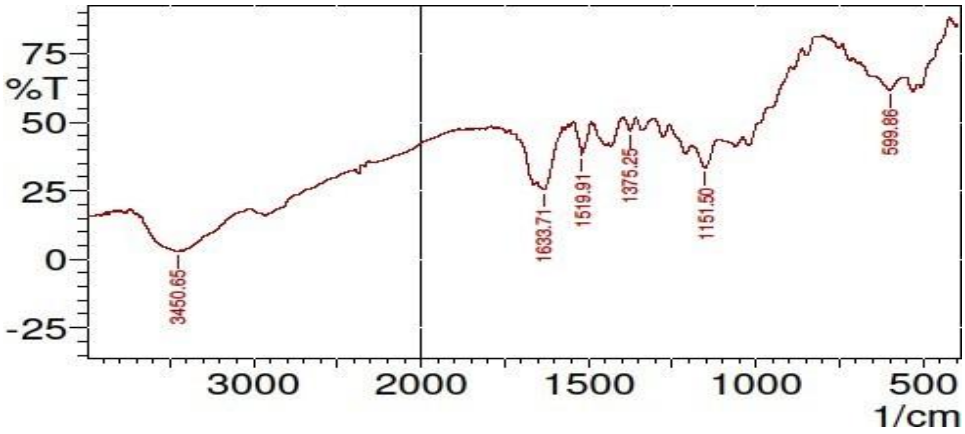


Fig12: Standard graph of Sitagliptin Phosphate Monohydrate

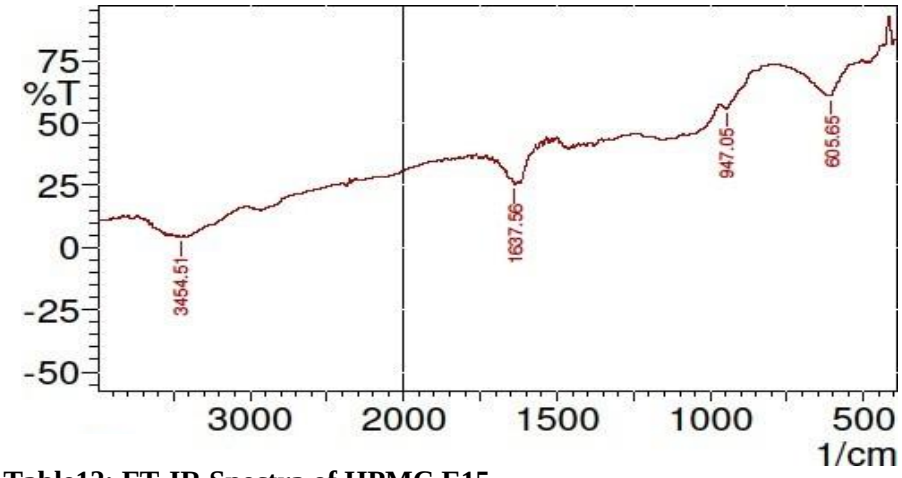
6.5 FT-IR Studies

FTIR study was carried out to check the compatibility of drug with polymers. Infrared spectrum of sitagliptin phosphate was determined on Fourier transform Infra-red spectrophotometer using KBr dispersion method. The baseline correlation was done using dried potassium bromide. Then the spectrum of dried mixture of drug and Potassium bromide was run followed by drug with various polymers by using FTIR spectrophotometer. The absorption maximums in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum.

Result & Discussion

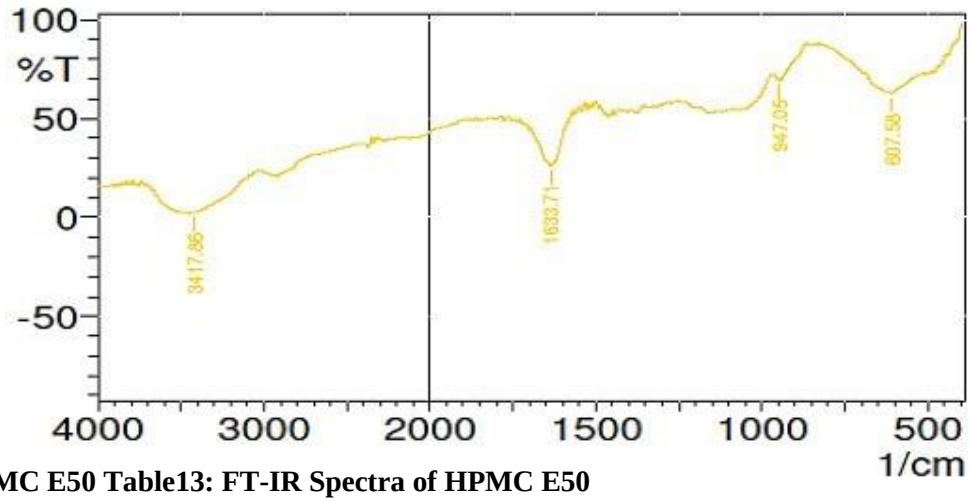


FT-IR Spectra of Sitagliptin phosphate Monohydrate Table11: FT-IR Spectra of Sitagliptin Phosphate Monohydrate



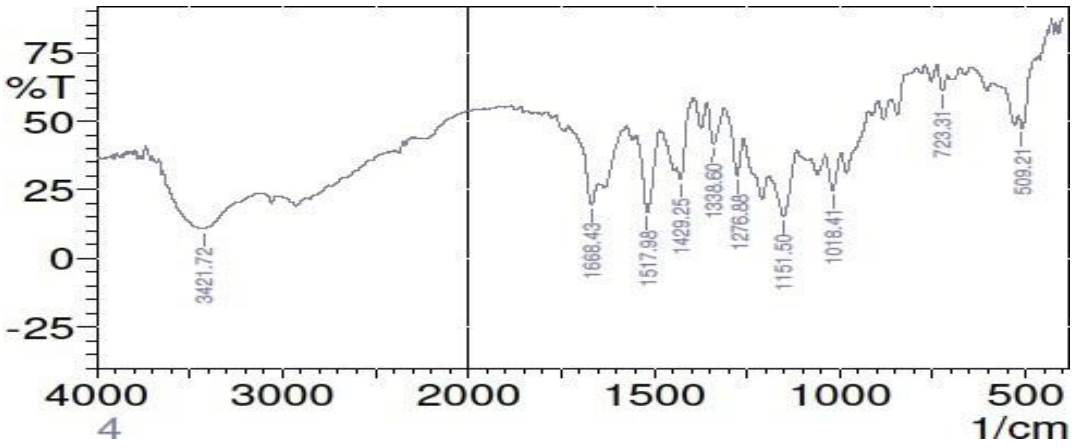
FT-IR Spectra of HPMC E15 Table12: FT-IR Spectra of HPMC E15

Sr. No.	Peak	Intensity	Corr. Intensity	Base(H)	Base(L)	Area	Corr. Area
1	605.65	60.909	1.441	611.43	543.93	11.593	-0.046
2	947.05	55.948	4.051	966.34	860.25	22.036	1.415
3	1637.56	25.336	0.552	1651.07	1635.64	8.863	0.019
4	3454.51	4.455	0.023	3462.22	3452.58	13.003	0.013



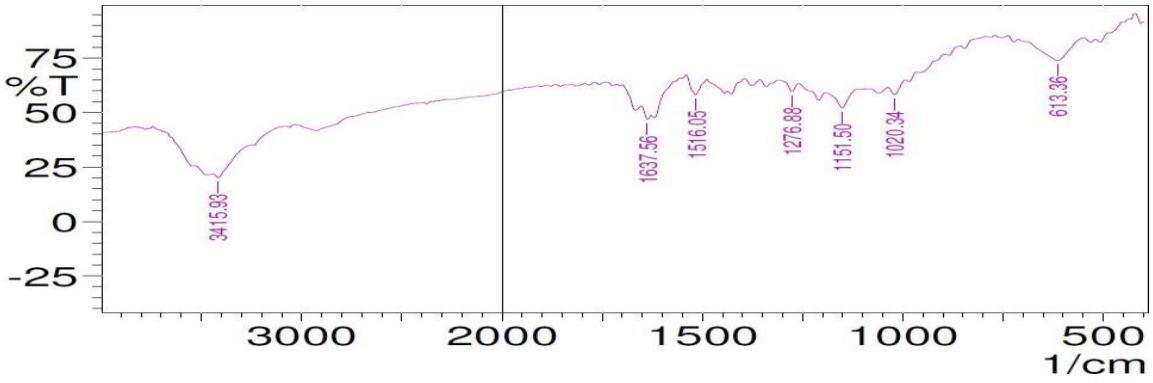
FT-IR Spectra of HPMC E50 Table13: FT-IR Spectra of HPMC E50

Sr. No.	Peak	Intensity	Corr. Intensity	Base (H)	Base(L)	Area	Corr. Area
1	607.58	62.6036	1.6909	617.22	580.57	7.0633	0.1823
2	947.05	69.2787	6.4461	968.27	864.11	11.9589	1.7804
3	1633.71	26.4988	0.5196	1635.64	1627.92	4.3949	0.052
4	3417.86	2.4373	0.4349	3431.36	3394.72	57.4735	1.3563



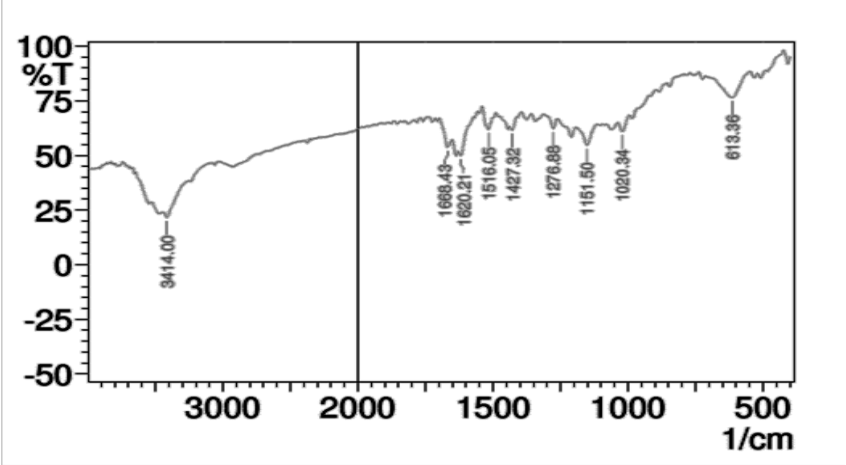
FT-IR Spectra of Sitagliptin Phosphate Monohydrate +HPMCE15 Table14: FT-IR Spectra of Sitagliptin Phosphate Monohydrate + HPMC E15

Sr. No.	Peak	Intensity	Corr. Intensity	Base(H)	Base(L)	Area	Corr. Area
1	509.21	47.35	9.618	518.85	478.35	9.733	1.195
2	723.31	61.02	7.496	738.74	711.73	5.127	0.733
3	1018.41	24.65	13.381	1037.7	997.2	20.677	3.675
4	1151.5	15.266	19.575	1192.01	1114.86	47.294	11.445
5	1276.88	30.095	17.342	1311.59	1259.52	19.707	3.575
6	1338.6	41.608	14.362	1357.89	1311.59	14.661	2.943
7	1429.25	28.691	9.694	1438.9	1392.61	17.337	0.844
8	1517.98	16.845	28.864	1546.91	1487.12	31.57	11.253
9	1668.43	19.401	13.906	1697.36	1649.14	27.051	4.454
10	3421.72	10.728	0.854	3433.29	3143.97	222.048	-7.282



FT-IR Spectra of Sitagliptin Phosphate Monohydrate + HPMCE50 Table15: FT-IR Spectra of Sitagliptin Phosphate Monohydrate + HPMC E50

Sr. No.	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr. Area
1	613.36	73.909	10.211	713.66	549.71	16.616	4.239
2	723.31	58.154	4.755	1037.7	993.34	9.521	0.696
3	1151.5	52.214	7.835	1192.01	1112.93	19.454	1.923
4	1276.88	59.615	4.263	1311.59	1259.52	10.545	0.494
5	1516.05	58.215	8.182	1541.12	1489.05	10.788	1.51
6	1637.56	46.897	3.47	1653	1627.92	7.72	0.349
7	3415.93	20.069	3.568	3442.94	3248.13	109.507	0.838



FT-IR Spectra of Sitagliptin Phosphate Monohydrate + HPMCE15 +HPMCE 50

Sr. No.	Peak	Intensity	Corr. Intensity	Base(H)	Base(L)	Area	Corr. Area
1	613.36	76.445	10.358	680.87	549.71	11.719	3.618
2	1020.34	60.974	5.393	1037.7	995.27	8.238	0.762
3	1151.5	54.71	8.866	1192.01	1114.86	17.204	2.007
4	1276.88	62.386	4.943	1311.59	1261.45	9.048	0.564
5	1427.32	61.595	3.497	1438.9	1411.89	5.287	0.302
6	1516.05	61.92	7.385	1539.2	1500.62	7.169	1.133
7	1620.21	50.03	4.028	1627.92	1571.99	12.983	0.281
8	1668.43	53.824	6.898	1699.29	1651.07	11.082	1.039
9	3414	21.642	4.53	3442.94	3250.05	101.18	1.264

FT-IR Spectra of Sitagliptin Phosphate Monohydrate + HPMCE15 + HPMC E 50

6.6 EVALUATION PARAMETERS

6.6.1 Thickness

A micrometer screw gauge was used to measure the film thickness. In order to obtain uniformity of film, thickness is measured at 5 different locations. The thickness of the film should be less than 5 %. The thickness of fast dissolving films of all formulations given in table 17 and figure 19.

6.6.2 Folding endurance

To determine folding endurance, a film is cut and rapidly folded at the same place till it breaks. The number of times the film could be folded at the same place without breaking gives the value of folding endurance. Topical folding endurance for the film was between100-150. The folding endurance of fast-dissolving films of all formulations is given in Table 17 and Figure 19.

6.6.3 Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the formula.

Tensile strength = $\frac{\text{Load at failure} \times 100}{\text{Strip thickness} \times \text{strip width}}$

The tensile strength of fast-dissolving films of all formulations is given in Table 17 and Figure 19.

6.6.4 Percentage Elongation

It was calculated by

Percentage Elongation = $\frac{\text{Increase in length of strip} \times 100}{\text{The initial length of the strip}}$

The percentage elongation of fast dissolving films of all formulations given in table 17 and figure 19.

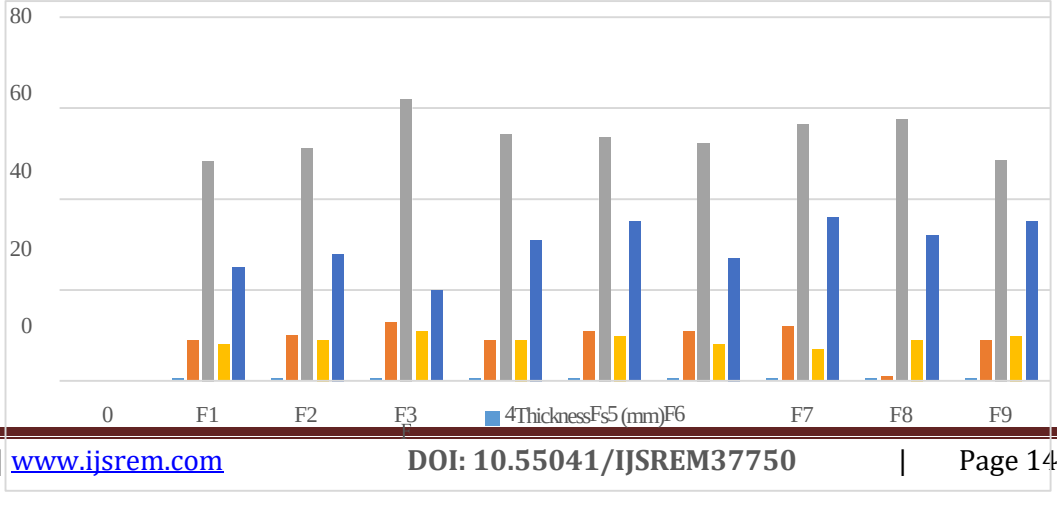
6.6.5 In-vitro disintegration Petri dish method

2 ml of distilled water was placed in the petri dish and one film was added on the surface of water and the time measured until the oral film was dissolved completely.

The in-vitro disintegration time of fast dissolving films of all formulations given in table 17 and figure 19.

Evaluation Parameters

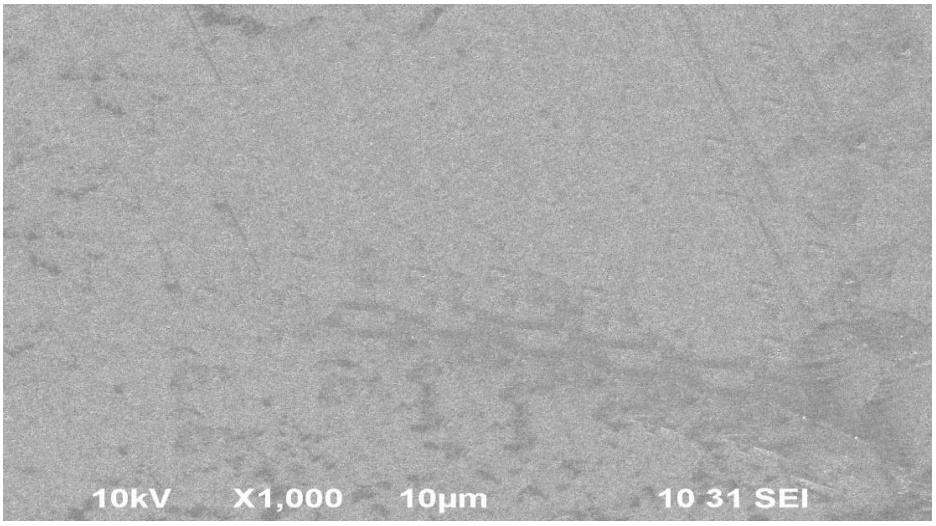
Formulations	Thickness (mm)	Folding endurance	Tensile Strength (g/cm^2)	% elongation	*In-vitro* Disintegration time(sec)
F1	0.58	9	48.41	8	25
F2	0.55	10	51.18	9	28
F3	0.59	13	62.04	11	20
F4	0.51	9	54.25	9	31
F5	0.53	11	53.68	10	35
F6	0.52	11	52.33	8	27
F7	0.55	12	56.45	7	36
F8	0.57	10	57.62	9	32
F9	0.53	9	48.63	10	35



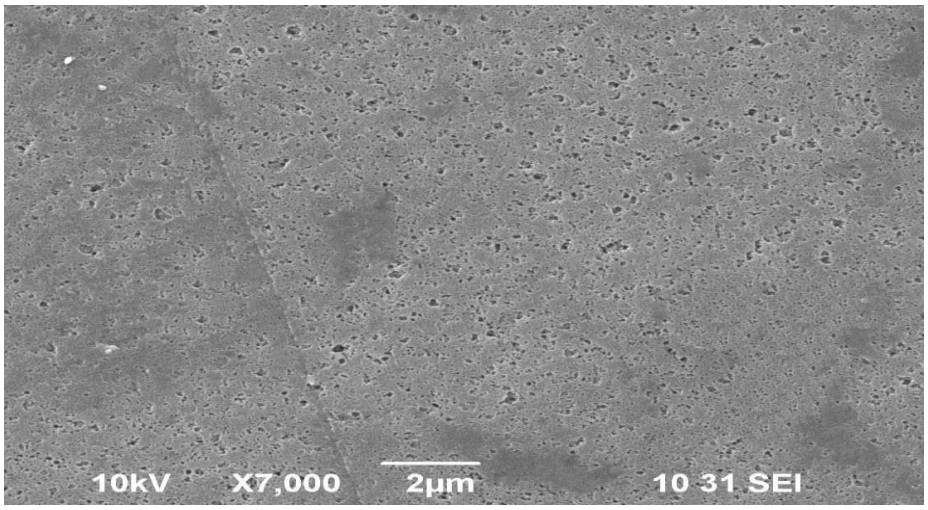
Bar chart of evaluation parameters

2. SEM ANALYSIS

The morphological study of oral strip was done by the scanning electron microscopy (SEM) at a definite magnification. Study refers the difference between upper and lower side of the films. It also helps in determination of the distribution of API.



SEM images 10 µm



SEM images 2 µm

8. DISCUSSION

The present investigation was undertaken to formulate Sitagliptin Phosphate Monohydrate oral films. For the treatment of Diabetes mellitus.

F1-F3 were carried out with HPMC E15 cps, PEG 400, sodium saccharin, citric acid and flavor. The films were clear and transparent. The thickness also uniform. The flexibility also good. The films shown good mechanical properties. According to the assay result the drug was properly loaded in the film.

F4-F6 were carried out with HPMC E50, propylene glycol, sodium saccharin, citric acid and flavor. The films

shows good appearance. The thickness also not uniform. The flexibility of the film was not good. The percentage drug release was found to be.
F7 was formulated with HPMC E15, propylene glycol, sodium saccharin, citric acid and flavor. The appearance of the film was also good but the thickness and disintegration time was more.
F8 was formulated with HPMC E50, PEG 400, sodium saccharin, citric acid and flavor.
F9 was formulated with HPMC E15 & E50 without the addition of plasticizers. The formulated films were more brittleness.
Among all the formulations F3 shown good mechanical properties and less disintegration time of 20 seconds. All the parameters of film were found to be satisfactory. And the dissolution profile was found to be desirable and reproducible.
The morphological study (SEM) of F3 shows more porous. Therefore rapid drug release was achieved for the immediate onset of action.
The stability studies were performed for about 1 month and 3 months. No significant changes were observed in the thickness, tensile strength, in-vitro disintegration and in- vitro drug release.

The film (F3) samples evaluated gave maximum release within 3 minutes indicating the rapid drug release profile which entails in faster onset of action for the medicament. Therefore the oral films have considerable advantage over the conventional dosage forms.

9. SUMMARY AND CONCLUSION

- The primary objective of this work was to develop a mouth dissolving film with Sitagliptin Phosphate Monohydrate, along with basic ingredients like polymers, plasticizers, sweetener, saliva stimulating agent and flavor.
- The films were prepared by solvent casting method.
- HPMC E50 cps, which was not able to impart thickness to the film. HPMC E15 shown good flexibility.
- The plasticizer propylene glycol which was not able to impart flexibility and folding endurance to the film. PEG 400 produced good folding endurance, tensile strength and percent elongation.
- The optimized formulation (F3) was shown good mouth feel, folding endurance, instant drug release as well as good mechanical properties.
- The F3, shown less disintegration time of 20 seconds and 99% drug released within 3 minutes.
- Therefore rapid drug release was achieved for immediate onset of action which is beneficial when compared to conventional tablet dosage form.

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