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DEVELOPMENT OF FAST DISSOLVING SUBLINGUAL WAFERS OF SITAGLIPTIN BY FILM FORMER

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ABSTRACT

Sitagliptin, A DPP-4 inhibitor, is commonly used in the treatment of diabetes mellitus. But, due to its late onset and adverse effect on kidney, its hyperglycemic activity is drastically changed. Hence, the present investigation was concluded with an attempt to design fast dissolving oral films of Sitagliptin phosphate using various polymers and plasticizers. The present research aimed to formulate fast dissolving oral films using various polymers and plasticizers using the solvent casting method. Preformulation studies were conducted to check the compatibility between the drug and the excipients. Nine batches were prepared and were put through various evaluations parameters like % elongation, thickness, weight variation, *in-vitro* drug dissolution, strength, drug content, assay, and SEM analysis. Based on the results, F3 was found to be an optimized batch. A comparative *in-vitro* drug dissolution study was conducted between the marketed product and the film. Stability studies of optimized batch F3 were conducted and found to have no physicochemical changes and no significant changes in the drug release study. The study concluded that oral fast dissolving film of sitagliptin phosphate improved the onset time of the drug and reduces the adverse effects compared to the traditional oral dosage form and can facilitate the reduction in symptoms of hyperglycemia.

KEYWORDS: Fast-dissolving film, Diabetes mellitus, Sitagliptin, plasticizers, *in-vitro* drug

dissolution study, & Tensile strength.

I INTRODUCTION

One of the greatest feats of human history is the development of new technologies in every field we can imagine. We have upgraded from being primitive beings to now being advanced enough to explore space. But with all these advancements, we have faced a lot of challenges through time. One of the hardest challenges we are facing nowadays is related to health. Stress, infectious diseases, mental problems, and many more. Advancements in the medical field helped us a lot in tackling these problems but they remain and causes a lot of damage to our daily life. One of the most common disorders we face is diabetes. It can be heredity or acquired due to lifestyle problems and it's one of the hardest challenges that this world is facing. The most common type of diabetes that occurs is Diabetes Mellitus.

Diabetes mellitus (DM) is a metabolic disorder occurring from a defect in insulin secretion, insulin action, or both. Insulin deficiency leading to chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism. It is one of the most common metabolic disorders with over 200 million diabetic individuals in the world.

Several pathogenic processes are involved in the development of diabetes; these range from autoimmune destruction of the cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. Deficient action of insulin on target tissues and hyperglycemia are the basis of the abnormalities in carbohydrate, fat, and protein metabolism, causing diabetes 'characteristic clinical features, micro and-macro vascular complications, and Increased risk of cardiovascular disease.

Diabetes mellitus, according to the new classification system (American Diabetes Association 2004) is classified into four types.

- Type 1
- Type 2
- Gestational diabetes
- Other specific Types

TYPE 1 DIABETES MELLITUS (INSULIN-DEPENDENT DIABETES MELLITUS)

Type 1 diabetes mellitus (T1D) is identified by β-cell destruction caused by an autoimmune process, usually leading to absolute insulin deficiency This type of diabetes, which accounts

for only 5–10% of all diabetes, is juvenile-onset diabetes; results from cellular-mediated autoimmune destruction of the β-cells of the pancreas by CD4 and CD8 T cells and macrophages infiltrating the islets.

In this case, insulin therapy is required for survival, to prevent the development of ketoacidosis, coma, and death.

OTHER TYPES

These include a variety of specific types of diabetes that are found, including o Genetic defects of ß-cell function

- o Genetic defects in insulin secretion
- o Diseases of the exocrine pancreas
- o Endocrinopathies
- o Drug-induced or chemical induced
- o Infections (congenital rubella, cytomegalovirus, and others)
- o Uncommon forms of immune-mediated diabetes
- o Other genetic syndromes sometimes associated with
- o Diabetes Gestational diabetes

TYPE 2 DIABETES MELLITUS (NON-INSULIN-DEPENDENT DIABETES MELLITUS)

Type 2 Diabetes Mellitus (T2D) is a complex heterogeneous group of metabolic condition characterized by elevated levels of serum glucose; according to WHO, it is defined as resulting from a defect in both insulin secretion and insulin sensitivity. β-cell dysfunction includes abnormalities in pulsatility and kinetics of insulin secretion, quantitative and qualitative abnormalities of insulin, β-cell loss, and its progression.

Type 2 Diabetes is a huge toll on human suffering and the economy. The total number of people with diabetes is estimated to rise from 171million in 2000 to 366 million in 2030, with India, China, and the USA is the top 3 countries estimated to have the highest numbers of people with diabetes.

GESTATIONAL DIABETES

Gestational Diabetes (GD) Mellitus refers to the onset or initial recognition of glucose intolerance during pregnancy, usually in the second or third trimester. It occurs in about4% of

all pregnancies. Patients with GD have a 30% to 50%chance of developing DM, usually Type 2 DM.

OTHER TYPES

These include a variety of specific types of diabetes that are found, including Each type of diabetes includes a variety of causes ranging from genetic factors to lifestyle issues. Type 1 is generally caused due to the immune destruction of the beta cells of the pancreas, which, eventually leads to diminishing the secretion of insulin. It can present at any age but is mostly shown during adolescence and childhood. Other factors include genetic and environmental triggers like infections. On the other hand, Type 2 diabetes is more of an acquired type, generally caused due to insulin resistance in the liver and the skeletal muscles and increase glucose levels. This also causes the over-production of free fatty acids and relative deficiency of insulin. Other factors that contribute to this type include age, obesity, lack of physical activities, increase in consumption of sugary foods, racial/ethnic background, and other conditions associated with insulin resistance like polycystic ovary syndrome.

Symptoms of diabetes include Polyuria, Polydipsia, Polyphagia, blurred vision, genital itching, slow wound healing, and weight loss.

Drug therapy includes series of categories:

- Sulfonylureas: Tolbutamide, Chlorpropamide, Gliclazide, Glipizide, and
- Glibenclamide.
- Bigunides: Metformin, Phenformine,
- Meglitinide analogues: Repaglinide, Nateglinide,
- α Glucosidase inhibitors: Acarbose, Miglitol, and many others

One of the most commonly used categories used for the treatment of diabetes is DPP-4 inhibitors. In this, one of the most commonly used drugs is Sitagliptin. Chemically, Sitagliptin is (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. It comes under the category of DPP-4 Inhibitors and is used regularly for the treatment of hyperglycemia. Sitagliptin works by competitively inhibiting 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, there can increase the secretion of insulin and suppress the release of glucagon by the alpha cells of the pancreas. This drives blood glucose levels

towards normal. Its half-life is around 12.5 Hrs. One of the major side effects this drug shows is renal impairment. With the delayed onset of the drug, the present research is the perfect scenario to work on the development of a better dosage form to reduce adverse effects and quick onset and providing a better treatment regime for Hyperglycemia.

Historically, oral administration is the most popular route due to ease of ingestion, pain avoidance, versatility (to accommodate various types of drug candidates), and foremost, patient compliance also, solid oral delivery systems do not require sterile conditions, hence 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.

One of the most important developments in the pharmaceutical industry is the introduction of a fast-dissolving drug delivery system. It was first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who face difficulties in swallowing traditional oral solid dosage forms. These novel technologies of fast dispersing dosage forms are known as fast dissolve, rapid dissolve, rapid melt, and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar.

It shows significant advantages over conventional dosage forms like tablets, capsules, syrups, etc These can improve acceptance and compliance in patients with dysphasia. Similarly, from the market point of view, the introduction of FDDS will assist life cycle management of drugs especially if the drug is patent protected.

Some of the salient features include:

1. Ease of administration for mentally challenged and uncooperative patients.
2. Require no water.
3. Taste masking of the drugs.
4. Provides pleasant mouthful and can be designed to leave no traces after administration.
5. Can provide features of a liquid dosage form in the form of solid dosage form
6. Cost-effective.

With features like this, our present sample for the research proves to be a perfect candidate for

the preparation of the fast-dissolving film to provide quick onset and less toxicity and provide an effective treatment for hyperglycemia.

FAST DISSOLVING FILMS

Oral films are novel technologies in the production of oral disintegrating dosage forms. They are thin elegant films of edible water-soluble polymers of various sizes and shapes like square, rectangle, or disc. The stripes may be flexible or brittle, opaque, or transparent. They are formulated to provide rapid disintegration on the tongue without the need for water. Fast disintegrating films (FDF s) have a large specific surface area for disintegration. The films eliminate the danger/fear of choking, are easy to handle and administer, require a simple and conventional packing that is easy to produce thus overcoming the short fails of oral fast disintegrating tablets. A major drawback of these dosage forms is low drug loading capacity and limited taste-masking options.

The fast disintegrating film is a thin film of 1-10 mm thickness, with an area of 1-20 cm2 of any geometry. Drugs can be introduced up to a single dose of about 15 mg. The immediate dissolution in the saliva is due to a special matrix made from water-soluble polymers it has usually low tack for ease of handling and application. However, on wetting the wet tack and much adhesiveness properties of the system are designed to adhere the film at the site of application. The flexibility and strength of films are selected to smoothen the manufacturing process and processes like rewinding, die-cutting, and packing.

The fast disintegrating film is placed on the patient tongue is mucosal tissue, which gets instantly wetted by saliva. The film hydrates quickly and adheres to the site of application. It then rapidly disintegrates and dissolves to release drugs for oral mucosal absorption, or for gastric absorption on swallowing.

Table 1: A comparison between oral dissolving films and oral disintegrating tablets.

Oral dissolving films	Oral disintegrating tablets
It is a film	It is a tablet
Greater dissolution due to large surface area	Lesser dissolution due to less surface area
Better durable than oral disintegrating tablets	Less durable as compared with oral films
More patient compliance	Less patient compliance than films

Now, the present research aims to formulate and evaluate fast dissolving films of Sitagliptin using various concentrations of film-forming agents and plasticizers, using the solvent casting

method. Through our research, we will be able to improve patient compliance with the drug and also to provide a quick onset to reduce the symptoms of hyperglycemia.

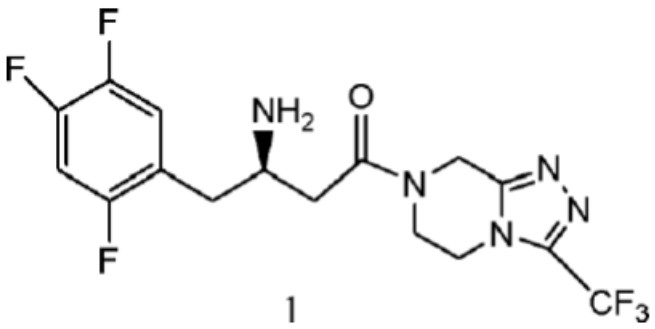

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Fig 1: Structure of Sitagliptin

II MATERIALS AND METHODS

➢ **MATERIALS:** Sitagliptin phosphate was obtained as a gift sample from Dr. reddy's laboratory, Hyderabad, HPMC E15 from Accent microcell industries, Ahemdabad, PEG 400 from BASF, Mumbai, Propylene glycol from Spectrum Chemicals, Gulbarga, and Sodium Saccharin from Aptuit Laurus Ltd, Hyderabad. All chemicals used obtained were of either AR/LR grade or the best possible pharma-grade supplied by the manufacturer.

➢ **METHODOLOGY**

- **Pre-formulation studies:** An exhaustive pre-formulation study was performed to pervade the physicochemical properties of the drug molecule which further helps in establishing a robust dosage form. The pre-formulation study was done with the following parameters:

o **Solubility:** Expressed as parts per million of solvent in which 1g of solid is soluble. For our research, solubility was determined in various solvents like water, ethanol, etc at 20°C

o **Heavy metal content:** 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

o **Melting point:** The melting point was carried out using the capillary tube method

o **Compatibility studies:** FTIR study was performed to check the compatibility of the drug with polymers. The infrared spectrum of sitagliptin phosphate was determined on an FTIR spectrophotometer using the KBr dispersion method. The baseline correlation was done using dried potassium bromide. Then the spectrum of a dried mixture of drug and Pottasium bromide was run followed by drug with various polymers by using 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:** 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 entrapped bubbles. Meanwhile, the excipients and drug were dissolved and stirred well for 30 min, and after the completion of stirring both the solutions were mixed. Finally, the solution was cast on a suitable Petri plate 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 the desired sizes.

Table 2: Formulation trials of Sitagliptin fast dissolving film.

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
HPMC E15 (g)	1.0	1.25	1.5	-	-	-	1.25	-	1.25
HPMC E50 (g)	-	-	-	1.0	1.25	1.5	-	1.25	1.25
PEG 400 (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

- **Evaluation parameters**

o **Thickness:** It was measured using a micrometer screw gauge. For uniformity, the thickness was measured at five different places. The thickness should be less than 5%.

o **Weight variation:** For weight variation, five films were randomly selected, weighed individually, and compared with the average weight for the deviation.

o **Folding endurance:** To determine the endurance, a film was cut and folded multiple times at the same place till it broke off. The number of times it could be folded gives the endurance of the film. It should be between 100-150

o **Percentage elongation:** It is calculated using the formula

$$\%\ elongation = \frac{increase\ in\ lengthof\ strip\ X\ 100}{intial\ length\ of\ the\ strip}$$

o **Tensile strength:** It is calculated using the formula

$$Tensile\ strength \frac{load\ at\ failure\ X\ 100}{strip\ thickness\ X\ strip\ width}$$

- **In-vitro disintegration:** Disintegrating time is defined as the time (sec) at which a film breaks when brought in contact with water or saliva.

Petri dish method: 2 ml of distilled water was placed in the petri dish and one the film was added to the surface of the water and the time was calculated until the oral film was dissolved completely.

- **In-vitro dissolution:** 900 ml of o.1 N HCL was used as a medium. It was maintained at 37 +0.5 °c while the basket was set at 100 rpm. A film sample of 4 cm2 (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.
- **Drug content:** This test was conducted 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 a UV spectrometer
- **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 a UV spectrophotometer.
- **Stability studies:** The stability studies were conducted according to ICH to assess the drug formulation stability. Optimized F3 formulation was sealed in Aluminium packing laminated with polyethylene. 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, color, drug content, and drug release characteristics
- **SEM Analysis:** The morphological study of the oral strip was performed using 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.

➢ RESULTS AND DISCUSSION

- **Pre-formulation studies**

These studies were performed to pervade the physicochemical properties of the drug to assess the best dosage form.

Table 3: Results of Pre-formulation studies of Sitagliptin phosphate.

S.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

o **FTIR spectroscopy:** This was performed to check the compatibility studies between the drug and the excipients.

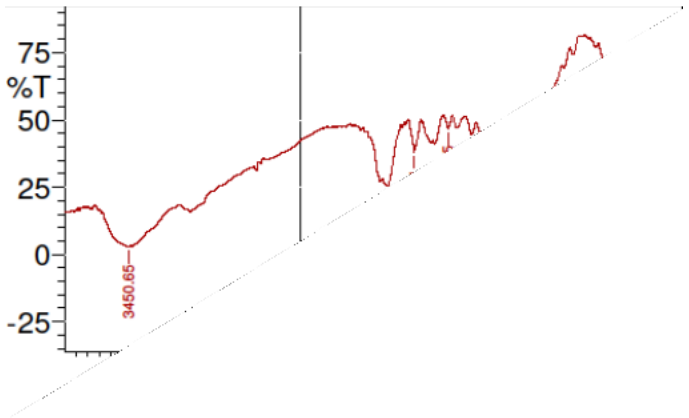

Fig 1: FTIR spectrogram of Sitagliptin.

Table 4: IR spectra of Sitagliptin.

No.	Peak	Intensity	Corr. Intensity	Base (H)	Base (L)	Area	Corr
1	599.86	61.564	5.035	644.22	561.29		
2	1151.5	33.276	9.285	1190.08			
3	1375.25	46.849	4.9				
4	1519.91	38.144					
5	1633.71						
6							

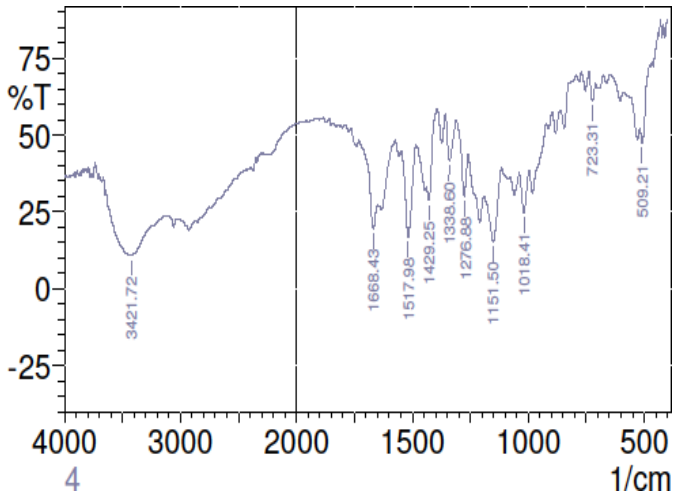

Fig 2: IR spectra of Sitagliptin phosphate+ HPMC 15.

Table 5: IR spectra of Sitagliptin phosphate+ HPMC 15.

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

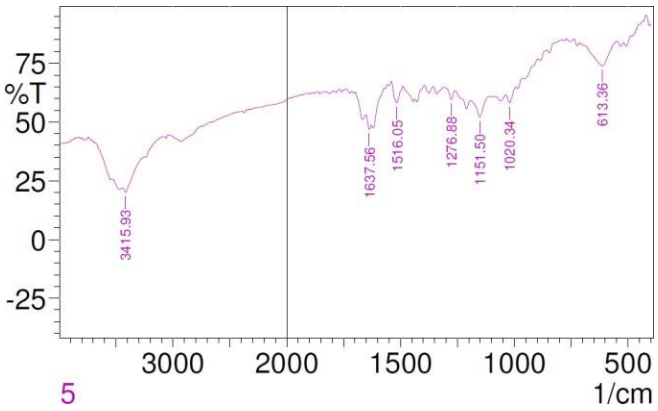

Fig 3: IR spectra of sitagliptin phosphate+ HPMC 50.

Table 6: IR spectra of sitagliptin phosphate+ HPMC 50.

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

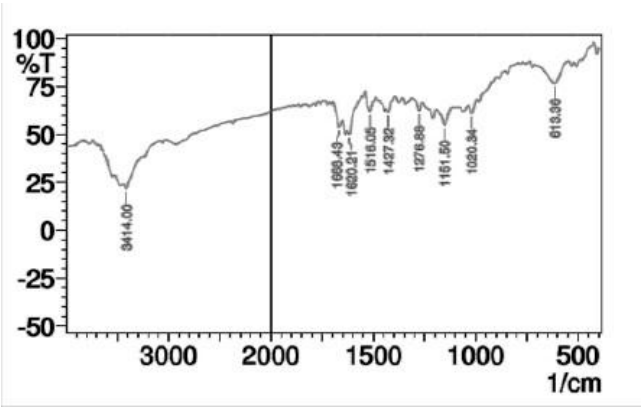

Fig 4: IR spectra of sitagliptin phosphate+HPMC 15+HPMC 50.

Table 7: IR spectra of sitagliptin phosphate+HPMC 15+HPMC 50.

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

- **Evaluation parameters**

o **Thickness, % elongation, folding endurance, tensile endurance, and *in-vitro* disintegration**

Table 8: Results of evaluation parameters of different formulations of sitagliptin phosphate fast dissolving films.

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	1.0	57.62	9	32
F9	0.53	9	48.63	10	35

o **Weight variation**

Table 9: Weight variation of Sitagliptin phosphate film.

Formulations	Weight variation (mg)
F1	69
F2	68
F3	68.2
F4	69.4
F5	70.2
F6	69.4
F7	68.3
F8	70.6
F9	69.2

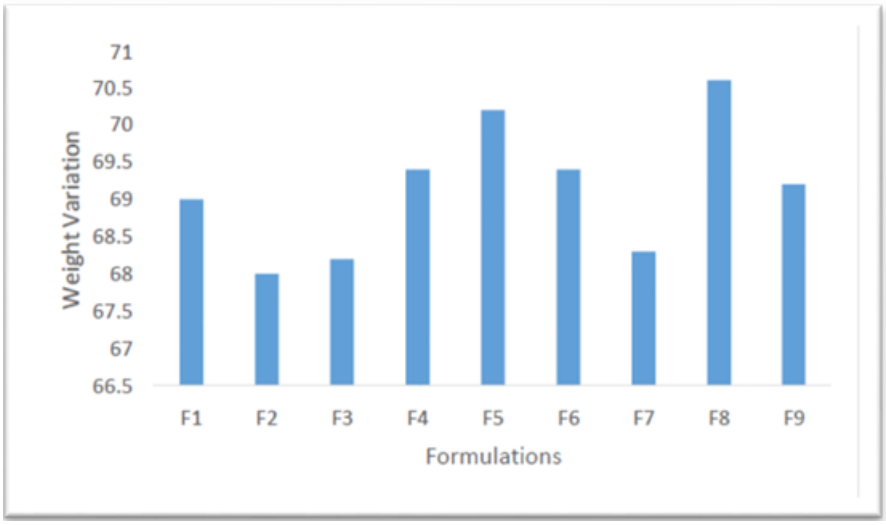

Fig 5: Bar graph showing weight variation.

- **Drug content and assay:** This was performed to check the overall content of the film and to check the uniformity of the dosage form.

Table 10: Results of drug content and assay of sitagliptin phosphate.

Formulations	Drug content (mg)	Assay (%)
F1	24.86	97.25
F2	23.25	98.14
F3	25.01	99.87
F4	22.91	98.34
F5	24.55	98.45
F6	23.88	97.22
F7	24.78	98.33
F8	24.63	97.87
F9	23.52	98.12

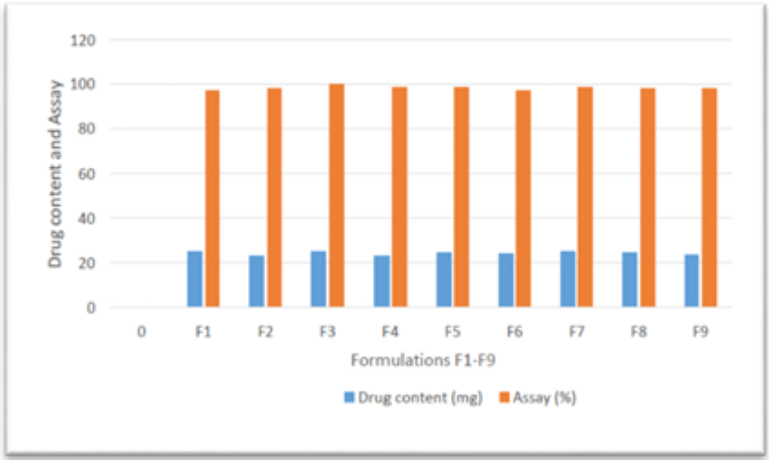

Fig 6: Bar graph for drug content and assay.

- ***In-vitro* dissolution**: This was performed for both the formulated dosage forms as well as marketed formulation. Out of the 9 prepared formulations, F3 shows the optimum results. A cumulative percentage of drug release was observed. A comparative study between F3 and the marketed product was also observed.

Table 11: *In-vitro* drug dissolution of F1-F9.

Percentage drug released									
Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	19	21	17	23	23	21	21	17	20
1.0	32	36	37	42	41	38	38	34	36
1.5	52	58	43	58	54	57	55	58	61
2.0	71	68	78	73	72	69	69	71	70
2.5	84	86	82	81	79	84	82	82	81
3.0	93	97	99	95	94	92	97	97	96

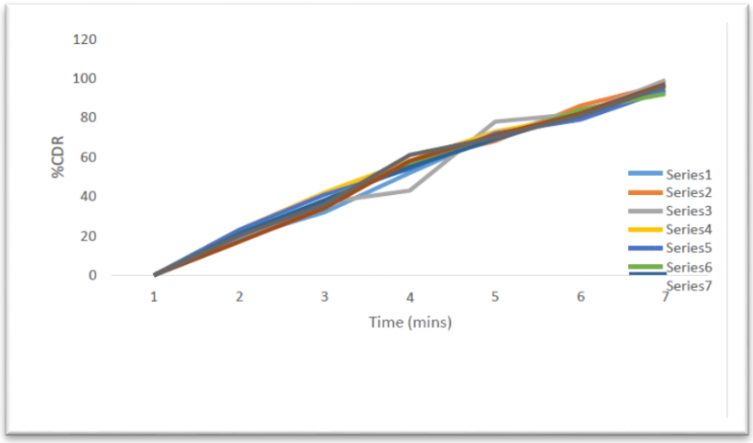

Fig 7: Graphical representation of drug dissolution (F1-F9).

Table 12: *In-vitro* drug dissolution of optimized batch(F3)

Time (mins)	Absorbance (267 nm)	Concentration µg/ml	Amount release mg/ml	Cumulative amount release	Cumulative percentage release
0.5	0.050	4.807	17.30	17.3	17
1.0	0.086	8.260	37.21	37.2	37
1.5	0.100	9.611	43.26	43.3	43
2.0	0.181	17.40	78.31	78.3	78
2.5	0.220	21.15	82.21	82.2	82
3.0	0.228	23.36	98.63	98.6	99

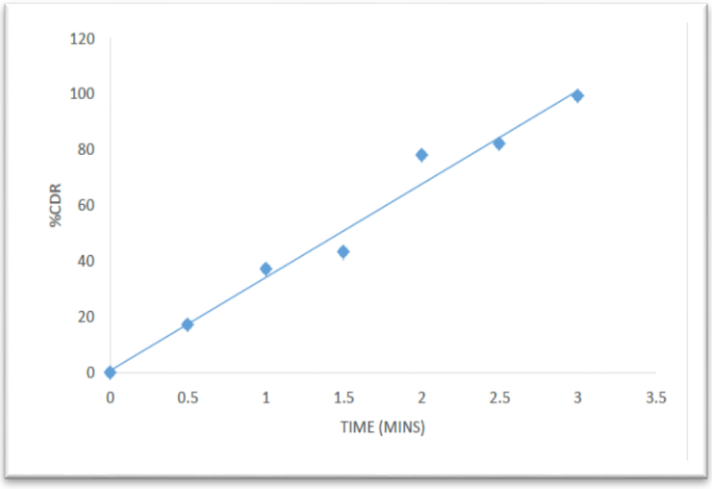

Fig 8: Graphical representation of drug dissolution of the optimized batch(F3)

***Table* 13: *In-vitro* drug dissolution profile for the marketed product.**

Time (mins)	Absorbance (267 nm)	Concentration µg/ml	Amount release mg/ml	Cumulative amount release	Cumulative percentage release
10	0.038	3.65	16.44	16.4	16
20	0.079	7.59	34.2	34.2	34
30	0.110	10.58	47.6	48.0	48
40	0.147	14.13	63.61	64.0	64
50	0.178	17.16	77.02	77.0	77
60	0.218	20.46	94.33	94.3	94

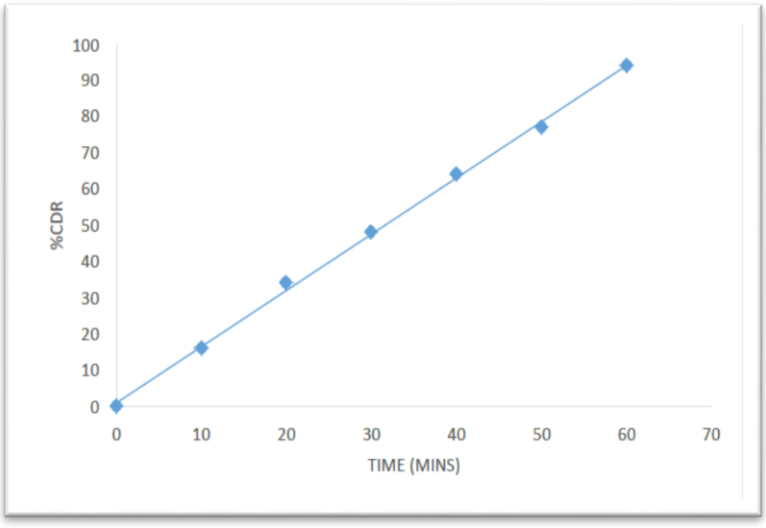

Fig 9: *In-vitro* drug dissolution of marketed product.

Table 14: Comparative *in-vitro* drug dissolution of optimized formulation and marketed formulation.

Time (mins)	Absorbance (267 nm)	Concentration µg/ml	Amount release mg/ml	Cumulative amount release	Cumulative percentage release	Cumulative percentage release of formulation 3
10	0.038	3.65	16.44	16.4	16	17
20	0.079	7.59	34.2	34.2	34	37
30	0.110	10.58	47.6	48.0	48	43
40	0.147	14.13	63.61	64.0	64	78
50	0.178	17.16	77.02	77.0	77	82
60	0.218	20.46	94.33	94.3	94	99

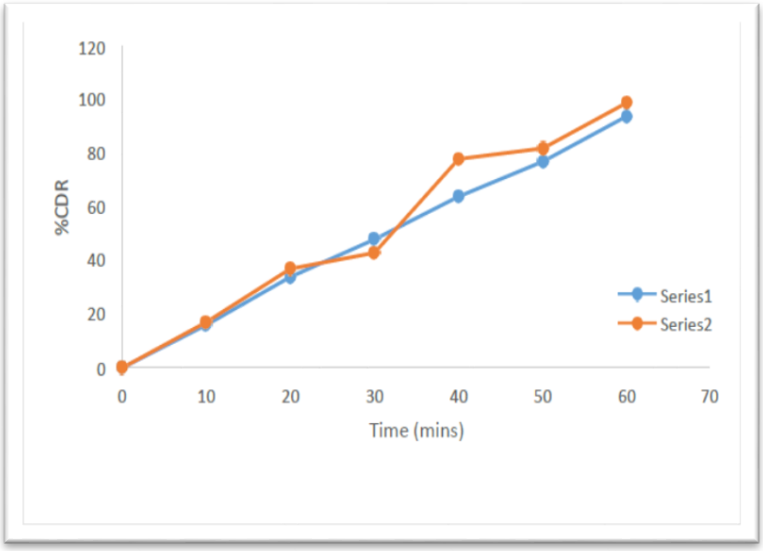

Fig 10: Comparative drug dissolution of optimized batch and marketed formulation.

- **Stability studies:** The stability studies were conducted according to the ICH guidelines. Optimized formulation F3 was studied for stability studies. At the end of the study period, the formulation was observed for change in color, physical appearance, drug content, and drug release. Based on the stability data, both physical and chemical stability are satisfactory. Photostability studies show that formulation is non-light sensitive.

Table 15: Stability studies for the optimized batch of Sitagliptin phosphate fast dissolving film[Condition (40°C/75%RH)]

Parameters	Initial	1 month	3 month
Thickness (mm)	0.59	0.59	
Folding endurance	13		
Tensile strength (gm/cm^2)			
in-vitro disintegration tim			
in-vitro dis			

- **SEM Analysis:** The morphological study of the oral strip was conducted using scanning electron microscopy (SEM) at a definite magnification. The study provides a descriptive study of the distribution of API in the formulation and also helps in understanding the upper and lower side of the film.

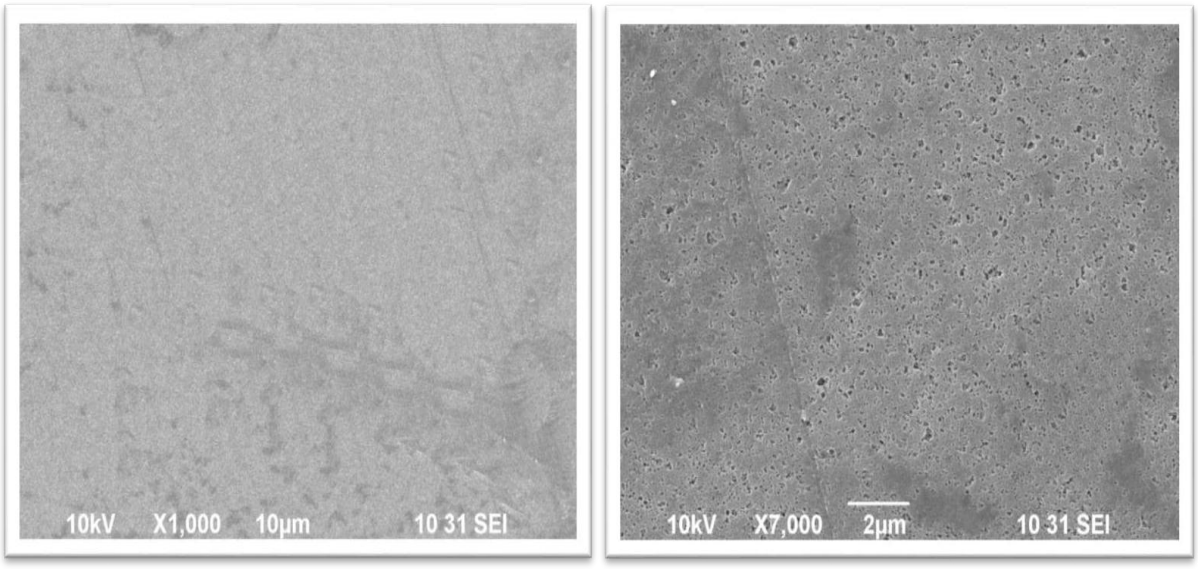

Fig 11 & 12: SEM images of the upper and lower side of the film respectively.

III CONCLUSION

Over the past century, advancements in the pharmaceutical industry have skyrocketed. With various dosage forms available right now in the market, the oral dosage form will still be the most preferred form of dosage form due to ease and other benefits. Diabetes Mellitus, one of the persisting disorders is still one of the most complicated ailments to treat. Now, with the

advancements in quick-acting, fast dissolving oral dosage forms, we can move a step forward to reduce the symptoms and will help a lot to design a dose regime in the treatment of hyperglycemia. Sitagliptin, one of the DPP-4 inhibitors, is one of the commonly used drugs, due to its adverse action on kidney and late-onset, was the perfect sample for our research. We prepared the fast- dissolving films of sitagliptin phosphate using various polymers and plasticizers. We used the solvent casting method for the formulation of our films. In total 9 batches were prepared. These batches were passed through various quality control tests. We checked the compatibility of the API with the excipients as well. Out of these 9 batches, the F3 batch was found to be the most optimized batch. We compared it to the marketed formulation. With the obtained results, we can conclude that fast dissolving films tremendously improved the onset of the drug compared to the marketed product and hence, helps in reducing the symptoms of hyperglycemia.

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