IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Preparation And Evaluation Of Oral In-Situ Gel Of Sitagliptin Phosphate.

Komal Bhusare[1]*, Sardar Shelake[2], Nilesh Chougule[3].

Student[1], Ashokrao Mane Institute Of Pharmacy, Ambap-416112

Assistant Professor, Ashokrao Mane Institute Of Pharmacy, Ambap-416112

Professor, Ashokrao Mane Institute Of Pharmacy, Ambap-416112

Abstract: This study focuses on the preparation and evaluation of an oral in-situ gel formulation of Sitagliptin Phosphate, aimed at improving the management of type 2 diabetes mellitus. Sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, enhances glycemic control when used as monotherapy or in combination with other antidiabetic agents. The innovative in-situ gel system is designed for ease of administration and improved patient compliance, forming a gel upon contact with the gastric environment. This formulation leverages the benefits of sustained drug release, reduced dosing frequency, and enhanced bioavailability, addressing the challenges posed by conventional dosage forms. The study employed preformulation assessments, including melting point determination and Fourier transform infrared spectroscopy, to confirm the chemical integrity and compatibility of Sitagliptin with excipients. Viscosity measurements, pH tests, and floating behavior analyses were conducted to evaluate the gel's physical properties. Drug content uniformity and in vitro drug release studies were performed, revealing a controlled release profile suitable for maintaining therapeutic drug levels. The development of this in-situ gel system presents a promising approach to optimizing the therapeutic efficacy of Sitagliptin Phosphate, potentially improving clinical outcomes for patients with type 2 diabetes. The formulation's benefits, such as ease of administration, sustained drug release, and targeted delivery, underscore its potential as an effective oral therapeutic option.

Keywords: In-Situ Gel, Sitagliptin phoshphate, Diabetes mellitus, Evaluation, Dipeptidyl peptidase-4 inhibitor.

1. INTRODUCTION:

1.1. Diabetes mellitus

Diabetes mellitus (DM) is probably one of the oldest diseases known to man. It was first reported in Egyptian manuscript about 3000 years ago. Diabetes mellitus (DM) is the most widespread endocrine disorder prevalent throughout the world affecting 6 % population world over (100 million) with DM. There is either insufficient insulin production, or the inability of the body to use insulin properly, leading to a high blood glucose level. Insulin resistance leads to the vessels of the blood being destroyed and it may destroy the eyes, kidneys, heart and nerves. The term "diabetes" is the Ancient Greek word for "siphon" and "mellitus" is its Latin word meaning "honeyed" or "sweet," which refers to blood being sweet with "honey", in diabetes mellitus [1].

In 1936, the distinction between type 1 and type -2 DM was clearly made [2]. Type I diabetes happens when the immune system attacks insulin-producing ß cells within islets of Langerhans leading to their inflammation or destruction which then brings this type about; while type II usually develops due to presence of insulin resistance all over the body tissues as well as having insufficient amount pancreas secreted hormone called insulin. Type 2 DM was first described as a component of metabolic syndrome in 1988 [3].Type 2 DM (formerly known as non-insulin dependent DM) is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency [4]. Type 2 DM results from interaction between genetic, environmental and behavioral risk factors [5-6].

People living with type 2 DM are more vulnerable to various forms of both short- and long-term complications, which often lead to their premature death. This tendency of increased morbidity and mortality is seen in patients with type 2 DM because of the commonness of this type of DM, its insidious onset and late recognition, especially in resource-poor developing countries like Africa [7].

1.2. In-situ gel:

In the past few years, increasing number of in situ gel forming systems have been investigated and many patents for their use in various biomedical applications including drug delivery have been reported. This interest has been sparked by the advantages shown by in situ forming polymeric delivery systems such as ease of administration and reduced frequency of administration, improved patient compliance and comfort [1]. In situ gel formulations offers an interesting alternative for achieving systemic drug effects of parenteral routes, which can be inconvenient or oral route, which can result in unacceptably low bioavailability and passes the hepatic first-pass metabolism, in particular of proteins and peptides [2]. This novel drug delivery system promotes the importantly ease and convenience of administration, deliverance of accurate dose as well as to prolong residence time of drug in contact with mucosa, that problems generally encountered in semisolid dosage forms. In situ gel formation occurs due to one or combination of different stimuli like pH change, temperature modulation and solvent exchange [3]. Smart polymeric systems represent promising means of delivering the drugs; these polymers undergo sol-gel transition, once administered. From the early 1970's natural and synthetic polymers began to be investigated for controlled release formulations. The advantages of using biodegradable polymers in clinical applications are apparent. Various natural and synthetic polymers are used for formulation and development of in situ forming drug delivery systems [4].

1.2.1. Ideal characteristics of polymers for preparation of in situ gel [14, 15]

- The polymer should be capable of adhering to the mucous membrane.
- It should be well compatible and should not provide any toxic effects.
- Good tolerance and optical clarity is more preferred.
- It should influence the tear behavior.

1.2.2. Advantages of in situ gel system:

- Ease of administration, comfort
- Reduced frequency of administration further improved patient compliance
- Can be administered to unconscious patients. Drug gets released in a sustained and controlled manner
- It show local action and side specificity by acting directly targeted site.
- It show less adverse effects as compared to other pharmacological dosage forms.[1,3]

1.2.3. Disadvantages of in situ gel system [12, 13]

- The sol form of the drug is more susceptible for degradation.
- After placing the drug eating and drinking may become restricted up to few hours.

1.2.4. Pharmaceutical application :[1,2,3]

Oral in situ gel formulations have various pharmaceutical applications, including:

i. **Controlled Drug Delivery:** In situ gels can be designed to release drugs in a controlled manner, prolonging their action and reducing dosing frequency. This is particularly useful for drugs with a narrow therapeutic window or those requiring sustained release profiles.

ii. **Improved Bioavailability:** By increasing the residence time of drugs in the oral cavity, in situ gels can enhance drug absorption and bioavailability. This is beneficial for drugs with poor solubility or those prone to first-pass metabolism.

iii. **Localized Drug Delivery:** In situ gels can target specific sites in the oral cavity, such as the buccal mucosa or periodontal pockets, for localized drug delivery. This is advantageous for treating conditions like oral infections or periodontal diseases.

iv. **Ease of Administration:** In situ gels offer a convenient and patient-friendly mode of administration, especially for pediatric and geriatric populations who may have difficulty swallowing conventional dosage forms like tablets or capsules.

v. **Taste Masking:** In situ gels can be formulated to mask the unpleasant taste of drugs, improving patient acceptance and compliance, particularly for pediatric and geriatric patients.

1.3. Introduction to Sitagliptin phosphate:

The increasing prevalence of diabetes is of concern because of the morbidity and mortality associated with the disease. Complications of uncontrolled type 2 diabetes include cardiovascular disease and microvascular complications, such as peripheral neuropathy, nephropathy, and retinopathy.[3]The societal and economic burdens of type 2 diabetes highlight the importance of tight glycemic control and prevention and management of diabetic complications. In addition to lifestyle modifications, several classes of pharmacologic agents are available that lower blood glucose levels by various mechanisms of action. These include α-glucosidase inhibitors, biguanides (eg, metformin),meglitinides, sulfonylureas, thiazolidinediones, insulin, amylin agonists (eg, pramlintide), and glucagon-like peptide-1 (GLP-1) analogues(eg, exenatide) [4]. In October 2006, the US Food and Drug Administration (FDA) approved sitagliptin phosphate* for use as monotherapy or in combination with metformin or thiazolidinediones to improve glycemic control in patients with type 2 diabetes in conjunction with diet and exercise [5]. Sitagliptin was the first agent worldwide in a new class of medications called dipeptidyl peptidase-4 (DPP-4) inhibitors, providing a new oral therapeutic option. The purpose of this article is to review the pharmacology, pharmacokinetics, pharmacodynamics, clinical efficacy, adverse effects, and cost of therapy of sitagliptin phosphate in adult patients with type 2 diabetes mellitus.

2. Material And Method:

2.1. Material:

Sitagliptin Phosphate was purchased from Swapnaroop pharmaceuticals (Mumbai), Pectin was purchased from Loba Chemie (Mumbai), Sodium Alginate was purchased from Loba Chemie (Mumbai), Calcium carbonate was purchased from Loba chemie (Mumbai).

2.2. Method Of Preparation:

Initially weighed drug and caco3 were added in beaker A containing 5 ml HCl solution and both the drug and caco3 was made to dissolve. Same was done by using sodium alginate and pectin in beaker B with same amount of HCl Further more Contents of beaker A was poured in beaker B and were mixed uniformly making the final solution. This final solution was sonicated on sonicator instrument at a temp of 37°C for uniformity purpose.

Table No. 1. Batches formulated by using various concentration

Std	ID	Run	Build Type	Space Time	Row Status	Factor 1 A: Pectin	Factor 2 B:Sodium Algenate
12	9	1	NA	Center	Normal	4	3
11	9	2	NA	Center	Normal	4	3
8	8	3	NA	Axial	Normal	4	4.41421
4	4	4	NA	Factorial	Normal	6	4
7	7	5	NA	Axial	Normal	4	1.58579
5	5	6	NA	Axial	Normal	1.17157	3
1	1	7	NA	Factorial	Normal	2	2
2	2	8	NA	Factorial	Normal	6	2
9	9	9	NA	Center	Normal	4	3
10	9	10	NA	Center	Normal	4	3
3	3	11	NA	Factorial	Normal	2	4
13	9	12	NA	Center	Normal	4	3
6	6	13	NA	Axial	Normal	6.82843	3

3. Experimental Work:

3.1. Preformulation studies

A preformulation study is an essential step in drug development where the physical and chemical properties of a drug substance are evaluated before formulating it into a dosage form. This helps in understanding its behavior, stability, and compatibility with excipients, aiding in the design of an effective and stable formulation.

3.1.1. Melting Point:

Take a capillary tube and close its one end by heating the end in the flame for 2-3 minutes while continuously rotating it. Take Sitagliptin Phophate fine powder. Dip the open end of the capillary tube in the finely powdered Sitagliptin Phophate. Gently tap the capillary tube on the table to fill the compound in the capillary tube to about a length of 1–2 cm. Attach the capillary to the thermometer with the rubber band and dip the thermometer in Thieles tube containing paraffin oil. Keep continuous watch of the temperature and note the temperature as soon as the substance starts to melt.

3.1.2. Fourier transform infrared spectroscopy (FT-IR):

FTIR spectrum was used as an analytical technique for identification of pure drug sample. The spectra for the sample were recorded using a Bruker Vertex 70 FTIR spectrophotometer by KBr pellet method. The samples were analysed by mixing with potassium bromide (1:10) individually and pressed to form a thin pellet by applying pressure using KBr press. The formed pellets were placed within the sample holder. Spectral scanning was taken in the wavelength region between 4000-400 cm−1. FTIR scans of Sitagliptin Phophate were recorded

3.2. Spectroscopic analysis:

3.2.1. Determination of Lambda max by UV Spectroscopy:

For determining Lambda max of Sitagliptin Phophate, 10 mg of drug was dissolved in Methanol and diluted to 100 ml to form strength of 100 µg/ml with the same solvent. It was then scanned in the range of 400 to 200 nm using Methanol as a blank using UV-Visible spectrophotometer and the maximum wavelength will be determined.

3.2.2. Preparation of calibration curve:

Calibration curve of Sitagliptin Phosphate was prepared with the help of UV spectroscopy. Calibration curve of Sitagliptin Phosphate was prepared in Methanol.

3.3. Calibration curve:

3.3.1. Preparation of stock solution:

Accurately weighed 10 mg of Sitagliptin phophate was transferred in 100 ml volumetric flask. The drug was dissolved and diluted upto the mark with water to give a solution with concentration of 100 µg/ml.

3.3.2. Preparation of working solution:

Appropriate aliquots from stock solution of Sitagliptin Phophate (0.2, 0.4, 0.6, 0.8, 1 and 1.2 ml) were accurately withdrawn in 10 ml volumetric flask and diluted upto the mark with methanol to obtain the final concentration of solution in range of 2-12 µg/ml and scanned at Lambda max. Absorbance of these solutions of Sitagliptin Phophate were recorded at their Lambda max using methanol as blank.

3.4. Evaluation Test

3.4.1. pH Test

A digital pH meter was used to measure the pH of the formulations in triplicate at room temperature.

3.4.2. Viscosity measurement

A Brookfield digital viscometer with spindle number 2 was used to measure the viscosity of the floating in situ gel solution of HCl. The studies were carried out in triplicate and the temperature was maintained at 31.1± 1 ◦C and speed at 60.0 RPM during each measurement.

3.4.3. Density measurement

100 ml of 0.1 N hydrochloric acid was prepared in a 1000 ml measuring cylinder. Take 10 ml HCL solution in situ gel solution (5 ml) was added and volume and weight were recorded. The density (g/ml) of the floating in situ gel of HCl was calculated, and it should be less than the density of the gastric content [19]. The measurement was repeated at least 3 times and reported as mean and standard deviation.

3.4.4. Floating behavior

The floating behavior of floating in situ gel of HCl has carried out by introducing the in situ gel solution (2 ml) into 10 ml of 0.1 N HCl (pH 1.2) at 37 ◦C. The floating lag time and duration of the floating time were then collected. The floating lag time was the time needed for the gels to rise to the surface of the medium and the floating time was the overall amount of time the gels remained floating on the medium surface [24]. The experiment was performed in triplicate. Mean and standard deviation was calculated and reported.

3.4.5. Drug content uniformity

The prepared in situ gel solution was analyzed for drug content using the validated method recommended by USP [28]. Take 2 ml of prepared gel in 10 ml of density bottle and make up the volume by 0.01N HCL. The mixture was then sonicated for 60 min. After that, the mixture was filtered with a filter peper and measured for its absorbance with UV-spectrophotometer at a wavelength of 267 nm. The experiment was carried out three times.

3.4.6. In vitro drug release

The prepared in situ gel solution was analyzed for drug release using a USP dissolution apparatus type II (paddle). 10 ml of the prepared in situ gel solution was injected into the 900 ml of medium (0.1 N HCl). The operating speed was 25 rpm, and the medium solution was stored at 37°C to simulate the conditions of the gastric. Mixture (30 ml) were taken out of the medium and 900 ml of 0.01N HCL to maintain the sink condition after 30, 60, 90, 120, 150, 180, 210, 240, 270 and 300 min. Then withdraw 5 ml sample and add in 5 ml HCL. The HCl concentration in samples was determined as a cumulative percentage release by using a UV-spectrophotometer at a wavelength of 267 nm. The assessment was performed in triplicate. [29,30].

4. Result and discussion

4.1. Preformulation studies

4.1.1. Melting Point:

The pure drug sitagliptin phosphate's reported melting point is 213-216^{0}C while the observed drug's melting point is 210^{0}C. It indicate that the drug in the powder is pure nature and that the powder is sitagliptin phosphate.

Table No.2. Melting point of drug

Drug	Melting Point	Observed melting Point
Sitagliptin	213-216^{0}C	210^{0}C

4.1.2. Fourier Transform Infrared Analysis

Using Fourier transform infrared spectroscopy, the infrared spectra of pure Sitagliptin Phosphate and a physical combination were obtained (Agilent carry 630). This indicates that the drug , along with the excipients, maintained its usual value throughout the formulation. This observation unequivocally shows that the drug and excipients employed in this investigation did not interact.

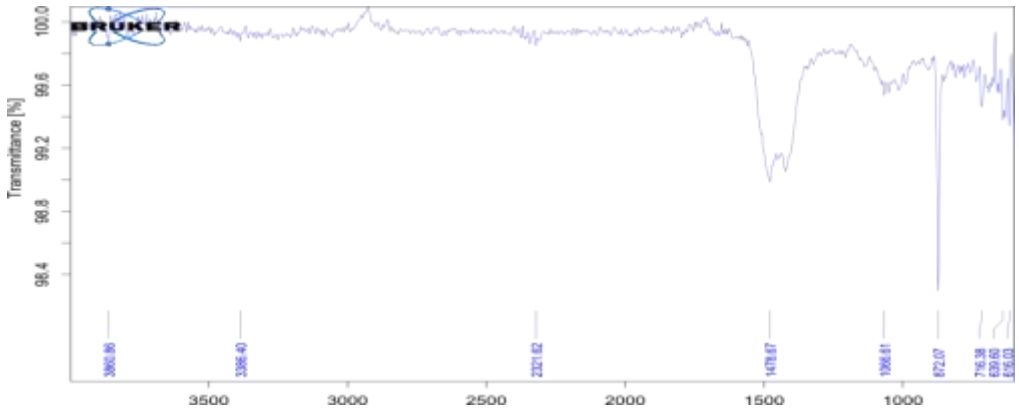

Figure No. 1. FT-IR image of Sitagliptin phosphate

The infrared (IR) spectrum analysis of the pure drug of Sitagliptin Phosphate revealed several key absorption bands indicative of specific functional groups. An absorption band at 1423.99 cm^{-1}, within the range of 1350-1480 cm^{-1}, corresponds to the C-H bending vibrations characteristic of alkanes. Additionally, a prominent absorption peak at 1688.10 cm^{-1}, situated between 1600-1700 cm^{-1}, signifies the presence of a carbonyl group, attributable to the C=O stretching vibrations. The analysis also identified an absorption at 873.91 cm^{-1}, which falls in the range of 880±20 cm^{-1}, indicating the C-H bending vibrations associated with a 1,2,4-trisubstituted benzene ring. Furthermore, a distinct absorption band at 2358.13 cm^{-1}, within the range of 2000-2400 cm^{-1}, corresponds to the N=C=O stretching vibrations, signifying the presence of an isocyanate group. These IR spectral findings provide crucial insights into the functional groups present within the sample, aiding in the structural elucidation of the compound.

Figure No. 2. FT-IR Image of drug with Excipients

The infrared (IR) spectrum analysis of the mixture of pure drug and excipients revealed several notable absorption bands indicative of various functional groups. An absorption band at 1478.67 cm^{-1}, within the range of 1350-1480 cm^{-1}, is characteristic of the C-H bending vibrations found in alkanes. Another significant peak at 1066.61 cm^{-1}, within the range of 1050-1150 cm^{-1}, corresponds to the C-N stretching vibrations typical of amine groups. Additionally, an absorption at 872.07 cm^{-1}, within the range of 880±20 cm^{-1}, indicates the C-H bending vibrations associated with a 1,2,4-trisubstituted benzene ring. Furthermore, an absorption band at 2321.62 cm^{-1}, within the range of 2000-2400 cm^{-1}, corresponds to the N=C=O stretching vibrations, signifying the presence of an isocyanate group. These IR spectral findings provide valuable insights into the structural components of the sample, highlighting the presence of alkane, amine, 1,2,4-trisubstituted benzene, and isocyanate functional groups.

4.2. Calibration curve of Sitagliptin

The Lambda Max of pure Sitagliptin Phosphate was found to be 265 nm. It indicate that given sample of drug is pure in nature and it confirmed that given powder is Sitagliptin Phosphate.

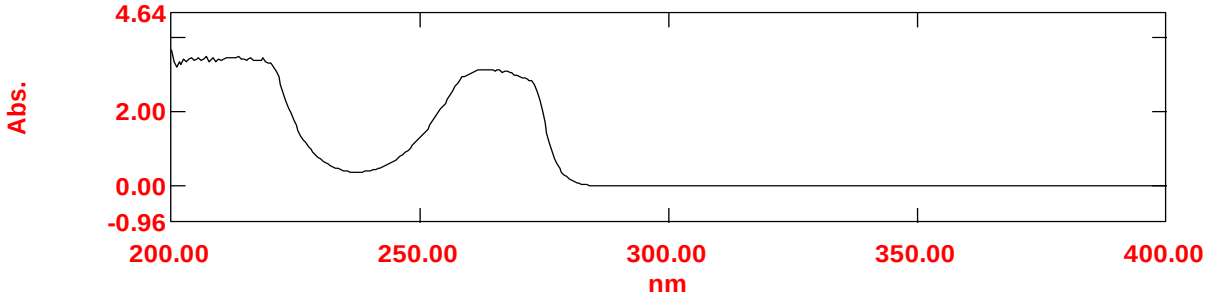

Figure No. 3. UV absorption spectrum of vildagliptin.

4.2.1. Calibration curve:

The graph of Concentration Vs Absorbance for pure Sitagliptin Phosphate was found to be in the concentration range of 0.2-1.0 µg/ml. with the regression coefficient of 0.996.

Tabe No.3. Calibration curve of Sitagliptin

Sr. no.	Concentration	Absorbance
1	0.2	0.134
2	0.4	0.378
3	0.6	0.571
4	0.8	0.797
5	1.0	0.968

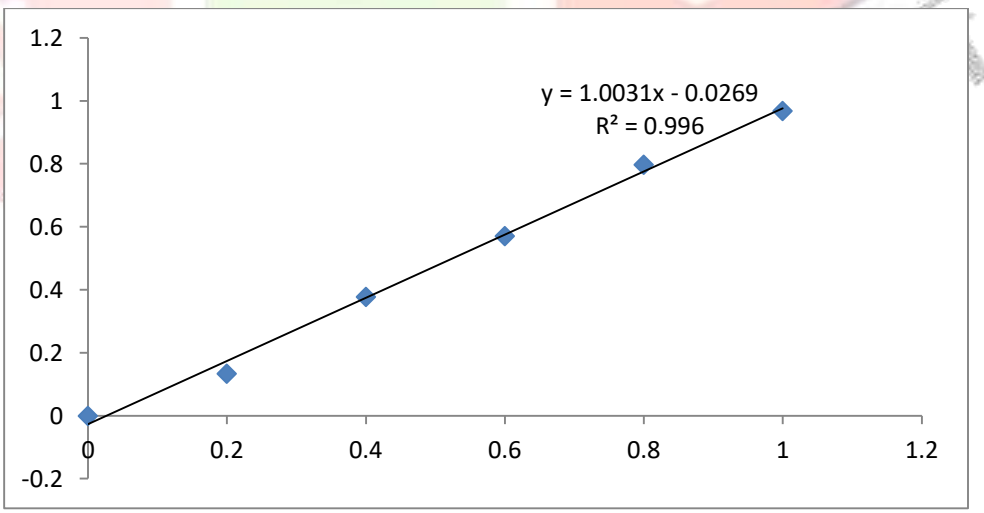

Figure No 4. Calibration curve of sitagliptin phosphate

Table No.4.Various Consstant for Calibration Curve Of Sitagliptin

Parameter	Slope	Intercept	R^2
Value for callibration curve in Methanol	1.003	0.026	0.996

4.3. Evaluation Test

4.3.1.pH Test :

An in-situ gel of sitagliptin phosphate normally has a standard pH of 6.0 to 7.4, which is in the neutral to slightly acidic range. This pH range is ideal for sitagliptin phosphate's bioavailability and efficacy while also maintaining the drug's stability. In situ gel's optimised range of formulation (B1-B9) corresponds to a neutral to slightly acidic pH.

Table No. 5. Table indicating various tests for the formulations B1-B9.

Formulation	pH	Viscosities (cpa.s)	Desnity (g/ml)	Floating time (hr)	Drug content
B1	7.1 ± 0.03	408.9 ± 2.19	**0.87** ± 0.02	19 ± 0.43	87.23 % ± 0.57
B2	6.2 ± 0.07	465.4 ± 1.09	**0.93** ± 0.01	18 ± 0.37	85.42 % ± 0.66
B3	6.8 ± 0.04	597.5 ± 1.76	**0.91** ± 0.05	17 ± 0.52	90.8 % ± 0.47
B4	6.3 ± 0.02	528.4 ± 1.54	**0.89** ± 0.01	18 ± 0.18	88.29 % ± 0.68
B5	6.5 ± 0.05	**357.6** ± 1.13	**0.90** ± 0.02	**21** ±0.44	96.21 % ± 0.59
B6	6.3 ± 0.06	461.8 ± 1.84	**0.84** ± 0.04	20 ± 0.23	93.46 % ± 0.60
B7	6.9 ± 0.03	449.2 ± 0.96	**0.88** ± 0.01	20 ± 0.21	89.83 % ± 0.81
B8	6.7 ± 0.05	574.3 ± 1.93	**0.95** ± 0.03	18 ± 0.37	91.76 % ± 0.53
B9	7.2 ± 0.02	412.1 ± 1.56	**0.94** ± 0.02	17 ± 0.21	94.48 % ± 0.54

4.3.2. Viscosity Measurment :

Viscosity measurement of all the formulations were found to vary according to change in their composition . theresults are reported in table no. 5.

4.3.3.Density Measurment :

In this study, the density of the oral in situ gel in each formulation was ranging from 0.84 to 0.95 g/ml, which was lesser than the density of the gastric contents (1.004–1.010 g/ml). These findings demonstrated that the oral in situ gel exhibited buoyancy characteristics and that the gel was probably kept afloat in the stomach fluid.

4.3.4. Floating Behaviour :

The floating behavior of the in situ oral gel was evaluated in simulated gastric fluid. Based on the obtained results, when all formulations were exposed to the simulated stomach fluid, they immediately began to gel and came to the medium surface within a minute, and remained floated for over 21 h. The floating properties of the formulation mainly depended on CO2 gas which is generated when sodium bicarbonate and calcium carbonate in the formulations reacted with HCl in the stomach. The released CO2 is entrapped inside the oral gel network, creating buoyancy that is required for extended floating.

4.3.5. Drug Content Uniformity:

Drug content of the formulations was determined by UV method. The results are as shown in the table no. 5.

4.3.6. In Vitro Drug Release:

The In-Vitro study was performed by using dissolution test apparatus. From this study it was observed that B5 batch shown a optimum drug release as compared to others.

Table No. 6. In-vitro response of various formulations.

Batch Time (min)	V1 (%)	V2 (%)	V3 (%)	V4 (%)	V5 (%)	V6 (%)	V7 (%)	V8 (%)	V9 (%)
0	0	0	0	0	0	0	0	0	0
30	13.44 ± 1.23	14.82 ± 1.04	11.04 ± 1.41	18.23 ± 2.43	21.65 ± 1.84	19.76 ± 1.28	19.20 ± 1.47	21.26 ± 1.92	14.64 ±2.12
60	22.83 ± 1.45	23.35 ± 0.98	19.90 ± 1.19	27.78 ± 1.59	30.26 ± 2.05	27.12 ± 1.30	25.79 ± 1.86	26.49 ± 1.72	22.31 ±1.23
90	33.89 ±1.97	27.89 ± 2.07	25.58 ±3.61	34.96 ± 1.19	38.43 ± 1.37	33.67 ± 1.87	31.82 ± 1.33	32.64 ± 1.91	31.56± 1.45
120	39.25 ± 1.48	35.41 ± 1.21	33.34 ± 2.84	41.88 ± 1.76	48.87 ± 1.27	41.8± 1.54	37.97 ± 1.29	40.43 ± 1.29	40.34 ± 1.38
150	45.56 ± 2.05	40.23 ± 1.48	45.27 ±1.15	49.67 ± 1.46	59.77 ± 2.83	48.47 ± 1.64	42.28 ± 2.28	46.67 ± 1.25	48.78 ± 1.92
180	51.78 ± 1.55	47.77 ±1.57	57.87 ± 2.25	57.81 ± 1.33	67.49 ± 1.05	63.28 ± 1.71	48.32 ± 1.93	60.55 ± 1.15	56.45 ± 2.34
210	66.59 ± 1.79	54.33 ± 1.07	66.61 ± 1.76	63.59 ± 1.78	79.76 ± 2.12	70.72 ± 0.97	56.36 ± 1.37	69.98 ± 1.89	64.34 ± 1.69
240	73.46 ± 1.40	64.79 ±2.43	74.33 ± 1.81	71.87 ± 2.42	**87.01 ± 1.56**	78.67 ± 1.82	63.58 ± 1.56	74.73 ± 0.89	71.51 ± 1.93

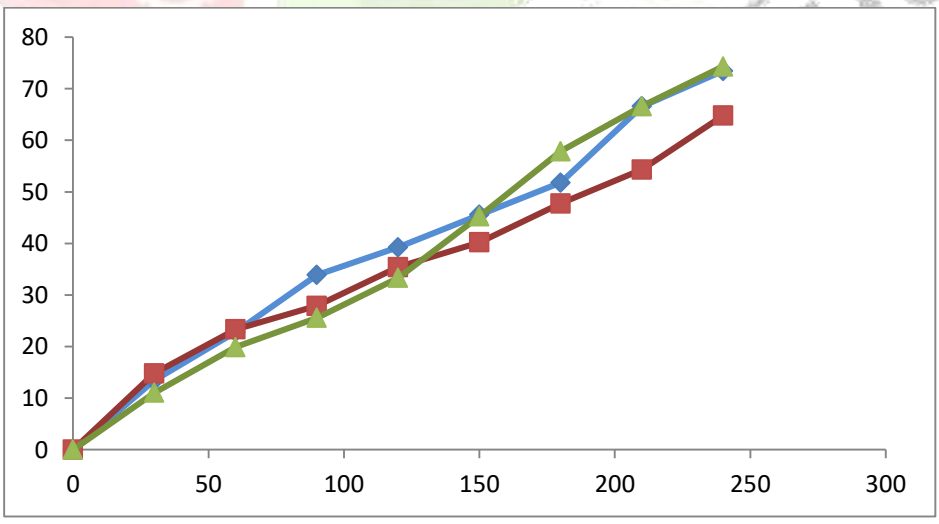

Figure No.5. In-Vitro drug release of B1, B2 and B3

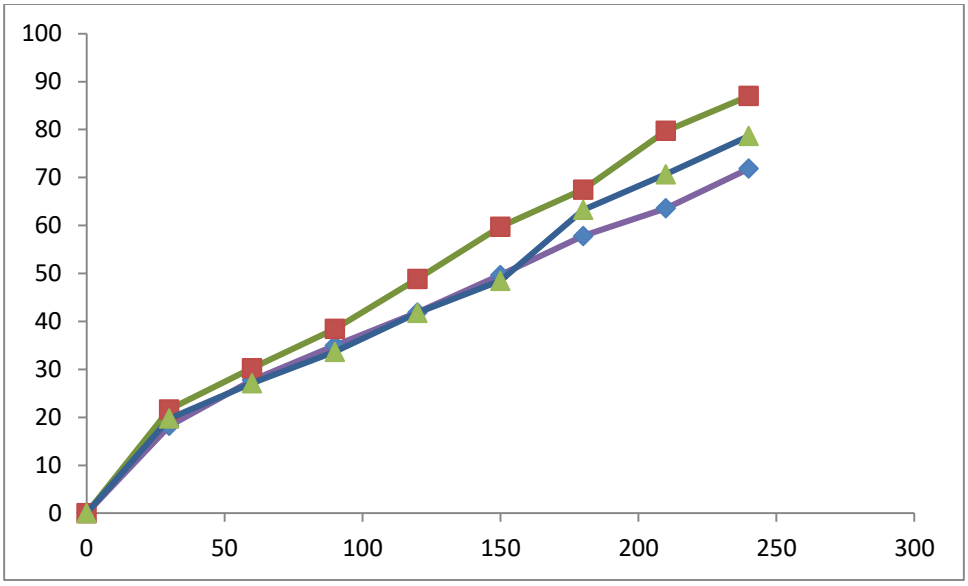

Figure No. 6. In-vitro drug release of B4, B5 and B6.

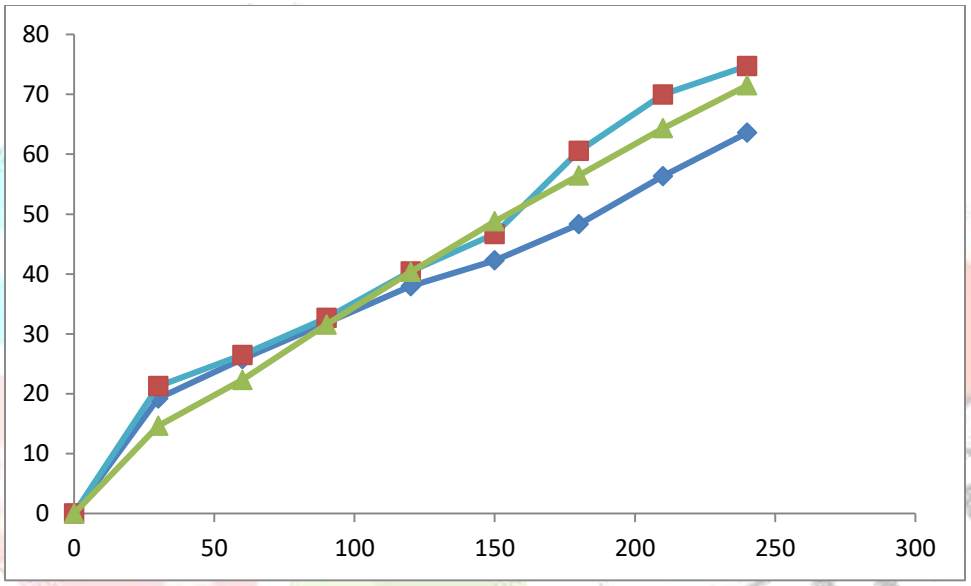

Figure No. 7. In-Vitro drug release of B7, B8 and B9

5. Conclusion:

Diabetes mellitus (DM) is a prevalent and serious endocrine disorder affecting millions globally, characterized by either insufficient insulin production or the body's inability to use insulin properly. This leads to high blood glucose levels, which can damage various organs and systems, causing complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy. Among the two main types of DM, Type 2 is more common and is associated with insulin resistance and relative insulin deficiency. It often leads to increased morbidity and mortality due to its insidious onset and late recognition, especially in resource-poor regions.In managing Type 2 DM, the development of innovative drug delivery systems is crucial. In situ gels present a promising alternative to traditional delivery methods. These systems, which transform from liquid to gel upon administration due to stimuli such as pH changes or temperature modulation, offer several advantages. They provide ease of administration, improved patient compliance, and sustained drug release, making them suitable for systemic drug effects and targeted local delivery, thus minimizing adverse effects.

In formulating sitagliptin as an in situ gel, excipients like pectin, sodium alginate, and calcium carbonate play essential roles. Pectin and sodium alginate help in gel formation, enhancing the drug's bioavailability and stability, while calcium carbonate ensures the gel's buoyancy in gastric fluids.

Experimental evaluations of the in situ gel formulations of sitagliptin phosphate indicate favorable results in terms of pH, viscosity, density, floating behavior, drug content uniformity, and in vitro drug release. These formulations demonstrate potential for enhanced therapeutic efficacy, offering a controlled and sustained drug release profile that could improve patient outcomes in managing Type 2 DM. Overall, the integration of sitagliptin phosphate into in situ gel systems represents a significant advancement in diabetes treatment, providing an effective and patient-friendly therapeutic option.

6. Acknowledgement:

I would like to express my special thanks of gratitude to our principal Sir, Ashokrao Mane Institute of Pharmacy, Ambap. I am really thankful to them to Mr. Sardar S. Shelake Sir for the patience and support in every Methodological aspect of this several other works. Thank you for your honest advices, your help in overcoming so many obstacles, and above all thank you for all your interest. Secondly I would also like to thanks my friends who helped me a lot in finalizing this project within the limited time frame. Last but not the least, my parents are also an important inspiration for me so with due regards, I express my gratitude to them also.

7. Conflict of Interest:

The authors declare that they have no conflicts of interest regarding the publication of this review paper. All authors certify that they have no financial or personal relationships with other people or organizations that could inappropriately influence (bias) their work or this manuscript.

8. References:

[1] Ahmed AM. History of diabetes mellitus. Saudi medical journal. 2002 Apr 1;23(4):373-8.

[2] Diabetes mellitus history- from ancient to modern times. Available at http://science.jrank.org/pages/2044/Diabetes-Mellitus.html. (accessed on 22nd July, 2011)

[3] Patlak M. New weapons to combat an ancient disease: treating diabetes. The FASEB Journal. 2002 Dec;16(14):1853.

[4] Maitra M. , The endocrine system. Robbins and Cotran Pathologic basis of disease. 2005:1155-226.

[5] Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nature reviews endocrinology. 2012 Apr;8(4):228-36.

[6] Genetic basis of type 1 and type2 diabetes, obesity, and their complications. Advances and emerging opportunities in diabetes research: a Strategic Planning report of the DMICC. www2.niddk.nih.gov/NR. (Accessed 22nd December 2011).

[7] Azevedo M, Alla S. Diabetes in sub-saharan Africa: kenya, mali, mozambique, Nigeria, South Africa and zambia. International journal of diabetes in developing countries. 2008 Oct;28(4):101.

[8] Kim J, De Jesus O. Medication routes of administration.

[9] Peppas NA, Langer R. New challenges in biomaterials. Science. 1994 Mar 25;263 (5154): 1715-20.

[10] Zhidong L, Jiawei L, Shufang N, Hui L, Pingtian D, Weisan P. Study of an alginate/HPMC based in situ gelling ophthalmic delivery system for gatifloxacin. Int J Pharm. 2006;315(1):12-7.

[11] SURESH S, BHASKARAN S. Nasal drug delivery: an overview. Indian journal of pharmaceutical sciences. 2005;67(1):19-25.

[12] Kubo W, Konno Y, Miyazaki S, Attwood D. In situ gelling pectin formulations for oral sustained delivery of paracetamol. Drug development and industrial pharmacy. 2004 Jan 1;30(6):593-9.

[13] Jothi M, Harikumar SL, Aggarwal G. In-situ ophthalmic gels for the treatment of eye diseases. International Journal of Pharmaceutical Sciences and Research. 2012 Jul 1;3(7):1891.

[14] Rajas NJ, Kavitha K, Gounder T, Mani T. In-Situ ophthalmic gels a developing trend. Int J Pharm Sci Rev and Res. 2011;7(1).

[15] Khode PD, Dongare PA. In situ gel: A Review of Pharmaceutical and Biological Evaluation and Approaches. Research Journal of Pharmaceutical Dosage Forms and Technology. 2019;11(3):217-26.

[16] Chand Pallavi, Pratibha, Katiyal Preeti. 'Indian Journal of Pharmaceutical and Biological Resarch' (IJPBR) Pharmaceutical Sciences, S.G.R.R.I.T.S., Patel Nagar Dehradun, Uttarakhand, India. 30 Jun 2016, ISSN-2320-9267. Page No.- 11-13.

[17] Nikode S, Dixit G, Upadhya K. In situ gel: application and uses of polymers. World journal of pharmacy and pharmaceutical sciences. 2016;5(7):1638-58.

[18] Ma WD, Xu H, Wang C, Nie SF, Pan WS. Pluronic F127-g-poly (acrylic acid) copolymers as in situ gelling vehicle for ophthalmic drug delivery system. International journal of pharmaceutics. 2008 Feb 28;350(1-2):247-56.

[19] VODITHALA S, KHATRY S, SHASTRI N, SADANANDAM M. International Journal of Current Pharmaceutical Research.

[20] Li, H., et al. (2018). In situ gelling systems based on lyotropic liquid crystals for oral drug delivery. Journal of Controlled Release, 287, 210-222.

[21] Chandel, A., et al. (2017). Oral in situ gel: A review. International Journal of Pharmaceutical Sciences and Research, 8(6), 2228-2236.

[22] HB N, Bakliwal S, Pawar S. In-situ gel: new trends in controlled and sustained drug delivery system. International Journal of PharmTech Research. 2010 Apr;2(2):1398-408.

[23] Kerdsakundee N, Mahattanadul S, Wiwattanapatapee R. Development and evaluation of gastroretentive raft forming systems incorporating curcumin-Eudragit® EPO solid dispersions for gastric ulcer treatment. European Journal of Pharmaceutics and Biopharmaceutics. 2015 Aug 1;94:513-20.

[24] Mahattanadul S. Floating gellan gum-based in situ gels containing curcumin for specific delivery to the stomach. Thai Journal of Pharmaceutical Sciences (TJPS). 2016 May 31;40.

[25] The United States Pharmacopeia : the National Formulary/by Authority of the United States Pharmacopeial Convention ; Prepared by the Council of Experts and its Expert Committees, 39th ed., United States Pharmacopeial Convention, 2016.

[26] Diaz DA, Colgan ST, Langer CS, Bandi NT, Likar MD, Van Alstine L. Dissolution similarity requirements: how similar or dissimilar are the global regulatory expectations?. The AAPS journal. 2016 Jan;18:15-22.

[27] FDA, Dissolution Testing of Immediate Release Solid Oral Dosage Forms, Guidance for Industry, 1997 accessed 3 March 2023), https://www.fda.gov/media/ 70936/download.

[28] Dall T, Nikolov P, Hogan PF. Economic costs of diabetes in the US in 2002. Diabetes care. 2003 Mar 2;26:917-32.

[29] Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, Zinman B. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes care. 2006 Aug 1;29(8):1963-72.

[30] Januvia (sitagliptin) [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2006