Preparation, Evaluation and Optimization of Antidiabetic in-situ gel of Pioglitazone

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Abstract: **This study investigates the formulation and evaluation of an in-situ gel of pioglitazone, a thiazolidinedione used in the management of type 2 diabetes mellitus. The objective is to develop a sustained release system that enhances pioglitazone's bioavailability and therapeutic efficacy while minimizing adverse effects. The in-situ gel is formulated using a thermosensitive polymer, Pluronic F127, which transitions from liquid at room temperature to gel at body temperature, and a pH-sensitive polymer, Carbopol 940, which enhances gel formation upon contact with physiological pH. This dual polymer system facilitates a controlled release of pioglitazone. The formulation process begins with creating a drug-polymer solution, which is characterized for gelation temperature, viscosity, and mechanical properties through rheological studies. Drug release studies are conducted using simulated body fluids to mimic physiological conditions, and the release kinetics are analyzed to understand the mechanisms of drug diffusion and polymer erosion. In vitro studies demonstrate that the in-situ gel formulation has an appropriate gelation temperature close to body temperature, ensuring easy administration and effective gel formation at the site of action. Viscosity measurements confirm the consistency necessary for the transition from liquid to gel under physiological conditions. The drug release profile shows a sustained release pattern with an initial burst followed by a steady release phase, conforming to the Higuchi model, indicative of diffusion-controlled release. Pharmacokinetic evaluation in diabetic animal models compares the bioavailability of the in-situ gel formulation with conventional oral pioglitazone formulations. Results indicate that the in-situ gel significantly enhances pioglitazone bioavailability, maintaining therapeutic plasma concentrations over an extended period, reducing administration frequency, and potentially minimizing side effects associated with peak plasma levels. In vivo efficacy studies in diabetic animal models demonstrate improved glycemic control with the in-situ gel formulation. The sustained release of pioglitazone results in consistent therapeutic effects, leading to better management of blood glucose levels and enhanced insulin sensitivity over time. Histopathological examinations show no significant tissue irritation or adverse reactions at the administration site, supporting the safety of the in-situ gel.**

Keywords: **Pioglitazone, Diabetes Mellitus, In-situ gel, Carbopol-940, sodium alginate, calcium , novel, delivery, liposomes , transdermal.**

INTRODUCTION

Novel Drug Delivery System:

The development of novel drug delivery systems (NDDS) represents a transformative approach in the field of pharmaceutical sciences, aimed at optimizing drug efficacy, safety, and patient compliance. Traditional drug delivery methods, such as oral and injectable formulations, often encounter limitations like poor bioavailability, rapid degradation, and frequent dosing requirements, which can lead to patient non-compliance. NDDS, including nanoparticles, liposomes, microspheres, hydrogels, and transdermal patches, have emerged to address these challenges by offering targeted, controlled, and sustained drug release. Among these, in-situ gel systems have garnered significant attention for their unique ability to transition from liquid to gel upon administration, triggered by physiological conditions such as temperature, pH, or ionic strength. This transition ensures prolonged retention at the site of action, enhancing the bioavailability and therapeutic efficacy of the drug. In-situ gels are particularly advantageous in providing sustained and localized drug delivery, which can significantly improve patient adherence and clinical outcomes.

Objectives of Novel Drug Delivery Systems:

- Enhanced Bioavailability: Improve the absorption and distribution of drugs to achieve higher concentrations at the target site.
- Targeted Delivery: Deliver drugs specifically to diseased tissues or organs, minimizing systemic exposure and reducing side effects.

- Controlled Release: Release drugs at a predetermined rate to maintain therapeutic levels for extended periods.
- Patient Compliance: Simplify drug administration to improve adherence to treatment regimens, often by reducing the frequency of dosing.

Types of Novel Drug Delivery system:

1. In-situ Gels

2. Liposomes

3. Microspheres

4. Hydrogels

5. Transdermal Patches

6. Nanoparticles

7. Implantable Drug Delivery Systems

8. Microneedle Arrays

In-situ Gel Systems:

The in-situ gelling (Raft forming) system represents a transitional phase between liquid and solid components. Hydrogels, possessing a three-dimensional structure, have the ability to absorb significant amounts of water and biological fluids, leading to swelling. In-situ gels, a subtype of hydrogels, are initially in a solution state but undergo gelation upon exposure to bodily fluids or alterations in pH or temperature. Prior to administration, in-situ formulations exist as sols, transforming into gels upon contact with gastric fluid. These gels can be administered via various routes including oral, ocular, rectal, vaginal, injectable, and intraperitoneal, offering several advantages over traditional drug delivery methods. Among these routes, oral administration is the most widely practiced and preferred. [1]

Novel drug delivery systems, such as gastroretentive formulations including floating systems, mucoadhesive, high-density, and expandable systems, have been developed to enhance drug delivery by providing prolonged gastric residence time. Gastroretentive floating drug delivery systems, characterized by a density lower than gastric fluid, remain buoyant on the gastric fluid surface. Liquid oral medications typically exhibit low bioavailability due to rapid elimination from the stomach. Oral in-situ gels offer a solution to the challenges posed by immediate release and short gastrointestinal residence time of liquid formulations. Initially in a liquid state at room temperature, in-situ gel dosage forms undergo gelation upon contact with gastric contents. This approach prolongs residence time, facilitates sustained release, and proves effective for both systemic delivery and targeted localization at the site of action. [2]

Principle of In-situ Gel:

The principle behind in-situ gel formation entails formulating a stable suspension system using a gelling agent, which includes the dispersed drug and other excipients. Gelation of this sol/suspension system occurs in the gastric environment due to pH changes. The formulation typically utilizes gellan gum or sodium alginate solution containing calcium chloride and sodium citrate. These components complex free calcium ions, releasing them only in the acidic environment of the stomach. Gellan gum or sodium alginate serves as the gelling agent, while the released calcium ions become entrapped within the polymeric chains of gellan gum or sodium alginate, leading to the crosslinking of polymer chains and the formation of a matrix structure. This gelation process involves the formation of double helical junctions, followed by the reaggregation of double helical segments to create a three-dimensional network through complexation with cations and hydrogen bonding with water.

Advantages:

1. Achieves faster floating compared to other floating dosage forms.
2. Enhances patient compliance.
3. Improves therapeutic effectiveness.
4. Simple administration to patients.
5. Prolongs drug contact time at the absorption site (stomach).
6. Facilitates delivery of drugs with limited absorption in the small intestine.
7. Reduces fluctuations in plasma levels.
8. Targets specific stomach conditions such as H. pylori-induced gastric ulcers.[3]

Disadvantages:

1. Variability in gastric emptying rates may affect the consistency of drug release.

2. Potential for dose dumping if gelation occurs too rapidly or inconsistently.
3. Limited applicability to drugs requiring rapid onset of action.
4. Dependency on gastric pH for gelation may pose challenges in patients with altered gastric pH levels.
5. Possible gastrointestinal side effects such as bloating or discomfort due to the gel's presence in the stomach.
6. Increased risk of drug-drug interactions or food interactions due to prolonged gastric residence time.
7. Complex formulation process and potential instability of the gel in storage or transit.[4]

Approaches of In-situ Gel:

1. pH-Sensitive Gels:

These gels undergo gelation or dissolution in response to changes in pH. Polymers such as pectin, methylcellulose, carbopol, and chitosan are often used to create pH-sensitive gelling systems. When exposed to acidic or basic environments, these polymers undergo protonation or deprotonation, leading to changes in their solubility and subsequent gelation or dissolution. Advantages: pH-sensitive gels enable site-specific drug release in response to variations in pH within the body, such as in the gastrointestinal tract. They are valuable for delivering drugs to specific regions of the body with distinct pH environments, enhancing therapeutic efficacy and reducing systemic side effects.

Applications: Commonly utilized in oral drug delivery systems, where the pH gradient along the gastrointestinal tract can be exploited for targeted drug release. They are also employed in colon-targeted drug delivery and vaginal drug delivery systems.[5]

2. Temperature-Sensitive Gels:

These gels undergo phase transition from liquid to gel when exposed to physiological temperatures, typically around body temperature (37°C). Poloxamers (Pluronics) and poloxamines are commonly used thermosensitive polymers in these systems. When the temperature rises, these polymers undergo micellization, leading to gel formation. The reverse transition occurs upon cooling.

Advantages: Temperature-sensitive gels offer controlled drug release based on the local temperature of the administration site, making them suitable for various applications such as injectable formulations and ophthalmic drug delivery.

Applications: Widely used in drug delivery for localized and sustained release, particularly in applications where temperature can be precisely controlled, such as ocular drug delivery and tissue engineering.[6]

Ionic Crosslinking: Gels formed by ionic crosslinking rely on interactions between oppositely charged ions to induce gelation. For instance, alginate gels are formed by the interaction of calcium ions with alginate polymers. When calcium ions are introduced into an alginate solution, they form crosslinks between the negatively charged carboxyl groups of the alginate polymer chains, resulting in gel formation.

Advantages: Ionic crosslinking provides a simple and versatile method for creating hydrogels with tunable properties. These gels offer excellent biocompatibility and are suitable for encapsulating a wide range of drugs, including proteins and peptides.

Applications: Widely used in tissue engineering, wound healing, and drug delivery applications, particularly for injectable formulations and cell encapsulation due to their biocompatibility and mild gelation conditions.[7]

Diabetes Mellitus: Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from defects in insulin secretion, insulin action, or both. Insulin, a hormone produced by the pancreas, plays a crucial role in regulating blood glucose levels by facilitating glucose uptake into cells for energy production or storage. In individuals with diabetes, this regulation is impaired, leading to hyperglycemia (high blood sugar levels) and subsequent complications.There are several types of diabetes mellitus, including:

1. Type 1 Diabetes: This results from the autoimmune destruction of insulin-producing beta cells in the pancreas, leading to an absolute deficiency of insulin. It often manifests in childhood or adolescence and requires lifelong insulin therapy for management.

2. Type 2 Diabetes: This is characterized by insulin resistance, where cells fail to respond effectively to

insulin, combined with inadequate insulin secretion. It is the most common form of diabetes and is often associated with obesity, sedentary lifestyle, and genetic predisposition. Type 2 diabetes mellitus (T2DM) comprises approximately 90% of diabetes cases. In T2DM, there's a reduced response to insulin, termed insulin resistance. Initially, insulin inefficiency prompts increased insulin production to regulate glucose levels. However, with time, insulin production declines, leading to T2DM. While T2DM is typically prevalent in individuals aged over 45, its incidence is rising among children, adolescents, and younger adults due to escalating rates of obesity, sedentary lifestyles, and high-calorie diets.

3. Gestational Diabetes: This occurs during pregnancy when hormonal changes impair insulin action, leading to elevated blood glucose levels. While gestational diabetes typically resolves after childbirth, affected individuals are at increased risk of developing type 2 diabetes later in life.Uncontrolled diabetes can lead to a range of complications affecting various organs and systems in the body, including the eyes (diabetic retinopathy), kidneys (diabetic nephropathy), nerves (diabetic neuropathy), and cardiovascular system (heart disease, stroke). Long-term complications can significantly impact quality of life and increase mortality rates.Management of diabetes involves a combination of lifestyle modifications, pharmacotherapy, and monitoring of blood glucose levels. Treatment aims to achieve and maintain near-normal blood glucose levels to prevent acute complications such as hyperglycemia and hypoglycemia, as well as long-term complications. Pharmacological interventions may include oral antidiabetic drugs, injectable insulin, or other adjunctive therapies.Lifestyle modifications play a crucial role in diabetes management and may include regular physical activity, healthy eating habits, weight management, and smoking cessation. Additionally, regular monitoring of blood glucose levels, glycated hemoglobin (HbA1c), blood pressure, and cholesterol levels is essential for optimizing diabetes control and preventing complications. [8]

MATERIALS AND EQUIPMENTS

1. Materials

Table 1: List of Chemicals:

Sr. No	Chemicals	Manufacturer
1	Calcium gluconate	Pallav
2	Agar-agar	Loba Chemical Pvt. Ltd.
3	Sodium Alginate	Fine Chem Industry
4	Trisodium gluconate	Fine Chem Industry
5	Carbopol 980	Loba Chemical Pvt. Ltd.
6	Pioglitazone	Pallav Chemicals

2. Equipments-

Table 2: List of Instruments:

Sr. No	Instruments	Manufacturer
1	Electronic weighing balance	Wensar
2	Magnetic Stirrer	Remi
3	Sonicator	Labman
4	Dissolution Apparatus	Labindia
5	UV-Visible Spectrophotometer	Shimadzu UV-1900i UV-V is spectrometer
6	pH Meter	Labline

EXPERIMENTAL METHODS

1 preformulation studies -

Solubility

Label beakers for solvents (water, ethanol, methanol) and add 50 mL of each. Add excess pioglitazone to each beaker. Stir at room temperature to reach equilibrium. Filter solutions to remove undissolved pioglitazone. Collect filtrates in clean containers and measure pioglitazone concentration using a UV-Vis spectrophotometer.

Melting point

To melt Pioglitazone, pack a small amount into a capillary tube and fill it with oil. Attach a thermometer to the side arm of the tube, ensuring the bulb is at the same level as the sample. Secure the tube with the sample to the thermometer and heat the sidearm with a Bunsen burner. Gradually heat the tube to the expected melting point of 183°C. Carefully observe the sample as it heats up, recording the temperature at which it begins to melt and when it completely melts. The precise melting point is the temperature at which the sample transitions from solid to liquid.

Calibration by uv spectrophotometer

To prepare pioglitazone standard solutions, use a stock solution of known concentration and dilution with a solvent. Warm up a UV-Vis spectrophotometer and prepare a blank solution using the same solvent. Set the absorbance to zero and transfer aliquots of each solution into separate cuvettes. Measure the absorbance at a wavelength known to correspond to pioglitazone's absorption maximum. Choose the wavelength based on the spectrophotometer's specifications and the compound's absorbance characteristics. Record the absorbance readings for each standard solution. Plot a graph of absorbance versus concentration for the pioglitazone standard solutions using a suitable software tool. Perform linear regression analysis to determine the calibration curve equation ($y = mx + c$), where 'y' is absorbance,'m' is the slope, 'x' is concentration, and 'c' is the y-intercept.

Ir spectroscopy of drug

The KBr Pellet method involves weighing and grinding a small amount of pioglitazone with 100 mg of KBr to create a homogeneous mixture. The mixture is then transferred into a pellet die and compressed using a hydraulic press to form a thin, transparent pellet. The Bruker IR spectrometer is set up, and the software is initialized. A background spectrum is measured with no sample in place, or using a clean KBr pellet. The sample is placed in the sample holder and the pioglitazone is placed directly onto the ATR crystal. Parameters such as resolution, number of scans, and wavenumber range are set. The data acquisition process begins to collect the IR spectrum of the pioglitazone sample.

Formulation of In-situ Gel -

Preparation of Pioglitazone Oral In-situ Gel:Ion-sensitive in-situ gelation method was employed for the preparation of Pioglitazone in-situ gels. In preparation of in-situ gels, sodium alginate was used as a gelling agent, trisodium citrate as a sequestering agent, and the cross-linking agent was Calcium gluconate apart from polymers like .Agar-agar carbopol- 940 were utilized as drug release rate controlling polymer. Different formulations are prepared with various proportions of polymers such as Agar-agar carbopol- 940 several trials were performed varying the concentration of individual polymer to distinguish the ideal concentration needed for preparation. Accurately weighed pioglitazone was solubilized in 10ml of warm de-ionized water with continuous stirring until a uniform solution was obtained. Diverse concentrations of Agar-agar carbopol- 940 were taken, added 70ml of de-ionized water, and gently stirred and heated to 60°C to obtain a uniform solution.

The required quantity of calcium gluconate and sodium citrate were dissolved in 20ml of distilled water Heated to 60oc and added to polymer solution at 60 °C. Then the resultant solution was cooled to 40°C, and added with the drug solution. The chart of formulations is specified in Table

Table No- 3 Formulation of In-situ Gel

Ingrediets	F1	F2	F3	F4	F5	F6	F7	F8	F9
Pioglitazone (mg)	600	600	600	600	600	600	600	600	600
Sodium Alginate (g)	2	2	2	2	2	1.5	2	2	2
Calcium gluconate(g)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Trisodium citrate(g)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Agar-agar (mg)	75	100	125	150	175	50	-	-	-
Carbopol 940 (mg)	-	-	-	-	-	50	75	100	125
Distlled water upto 100 ml	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Evaluation parameter-

1. Physical Appearance:

Color: The color of the gel was observed under natural light and compared to a standard reference.

Odour: Carefully, sniff the prepared gel sample.

2. Gelation Studies

Gelation studies were carried out using 0.1 N HCl. Take 5ml of Formulation and transfer into a beaker containing 100 ml of 0.1 N HCl. In this time required to obtain gel is recorded. In these studies, the gelling capacity (gelling speed and extent of gelation) for all formulations were determined. Gelation characteristics were assessed ranging between + (poor), ++ (good), +++ (very good).

3. PH Measurement:

The pH was measured in each of the Pectin and Sodium Alginate based in situ solutions, using a calibrated digital pH meter at room temperature.

In this test, the pH of a dapagliflozin solution is determined using a digital pH meter. The pH meter is calibrated using buffer solutions of pH 4, 7, and 10. The dapagliflozin solution is prepared, and its pH is measured using the calibrated pH meter. The accuracy of the pH meter is verified by measuring the pH of the buffer solutions. The expected outcome is an accurate pH measurement of the dapagliflozin solution and confirmation of the pH meter accuracy through the buffer solution measurements. The measurements of pH of each data were noted.

4. In vitro drug release study:
The prepared in situ gel solution was analyzed for drug release using a USP dissolution apparatus (Type II) with a paddle stirrer at 50 rpm. This slow speed is necessary to avoid breaking of the gelled formulation. 900 ml of the simulated gastric fluid (0.1N HCl, pH1.2) was used as the dissolution medium and the temperature was maintained at 37±0.5°C. 10 ml of the formulation was introduced into the dissolution vessel without disturbing the dissolution medium resulting in the formation of in situ gel. At each time interval, 5ml of the sample was withdrawn and replenished with fresh medium to maintain sink condition after 30, 60,120,180,240,300,360,420 and 480 min. The samples collected were filtered with a 0.45 µm membrane filter , suitably diluted, and analyzed at 224 nm using UV spectrophotometer.
5. Floating behaviour
The floating ability of the prepared formulations was evaluated in (0.1N HCl, pH 1.2) Solution. The floating time of the prepared formulation took to emerge on the medium surface (floating lag time) was noted .The time the formulation constantly floated on the dissolution medium surface (duration of floating) was also evaluated.
6. Viscosity:
Viscosities of the dapagliflozin insitu gel solution formulations are determined with the help of Brookfield's digital Viscometer (DV-II) +Pro using S21 spindle at 50 rpm and temperature was maintain at 25^0c.The study were carried out in triplicate with fresh samples being used each time and the average reading was taken.
7.Determination of the drug content:
5 ml of the formulation equivalent to 10 mg of the drug was added to 80 ml of 0.1N HCl, pH 1.2, and stirred for 1 hr in a magnetic stirrer. After 1 hr, the solution was filtered and diluted with 0.1 N HCl, pH 1.2. The drug concentration was then determined by ultraviolet (UV) visible spectrophotometer at 224 nm against a suitable blank solution.

RESULT

Pre-formulation Studies:

1. Physical Properties

Table no 4. Organoleptic properties

Criteria	Obesveration
Colour	White to Off white
Odour	Odourless
Nature	Crystalline powder

2 Solubility of Pioglitazo-

Pioglitazone is having low solubility in water, but it is moderately soluble in organic solvents like ethanol, methanol.

Table no 5. Solubility

Solvent	Solubility
Water	Low solubility
Ethanol	Soluble
Methanol	Soluble

3 Melting Point :-

For pioglitazone, the experimentally determined melting point typically falls within a specific range. The melting point of pioglitazone is generally reported to be 184°C.

4. Characterization by UV Spectrophotometer :-

The results of the standard curve for pioglitazone using a UV spectrometer indicate a linear relationship between the concentration of pioglitazone and the absorbance readings at a specific wavelength. The drug had λ max of 272.0 nm.

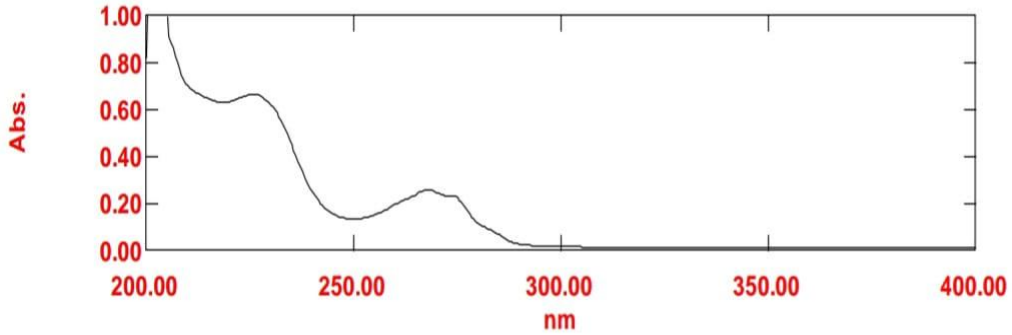

Fig No 1. Absorbance Maxima of Pioglitazone at 224 nm

Table No 6. Calibration of Pioglitazone in Ethanol.

Concentration (μ/ml)	Absorbance
5	0.2228
10	0.3608
15	0.5171
20	0.6908
25	0.8328

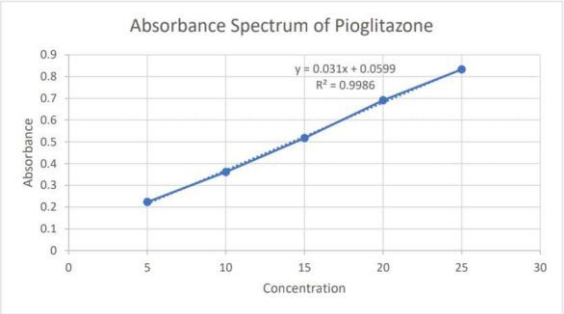

Fig No. 2: Calibration Curve of Pioglitazone

5. Characterization By IR

a) Drug FTIR

The infrared (IR) spectroscopy results of pioglitazone HCL indicate characteristic peaks corresponding to functional groups present in the molecule. Common peaks observed include a broad peak around 3300 cm^-1 corresponding to the N-H stretching vibration, peaks around 1700-1750 cm^-1 indicating the presence of carbonyl groups, and peaks around 1500-1600 cm^-1 corresponding to aromatic C=C stretching vibrations. Additionally, peaks in the fingerprint region (below 1500 cm^-1) provide further structural information. These results confirm the identity and structural features of pioglitazone HCL, aiding in its characterization and analysis.

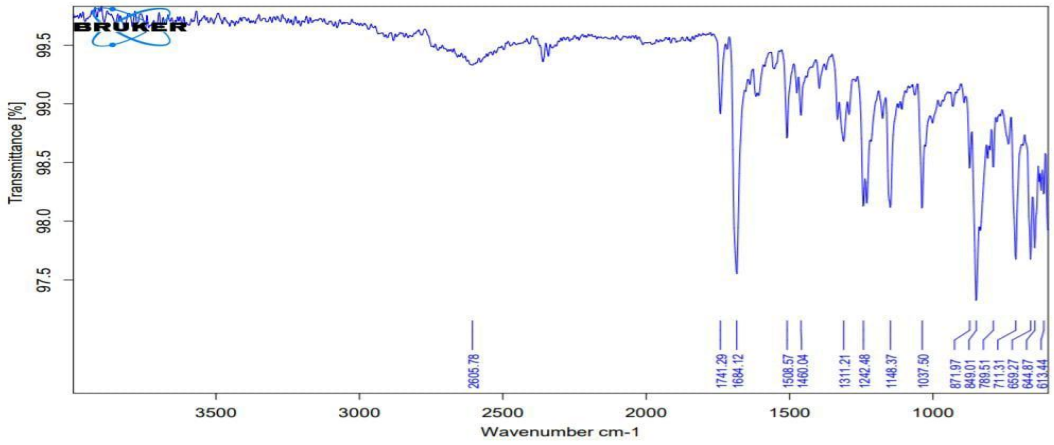

Fig no 3: IR of drug

Table no 7 – Interpretation of data of FTIR

Functional Group	Standard value (cm^{-1})	Observed value (cm^{-1})
N-H	3509-3460	3489
C=O	1745-1680	1721
C-O-C	1250-1150	1210
S-NH	1159-1150	1152

6. Gelling Nature of Polymer :-

The gelling nature of carbapol 940 was evaluated by dissolving each polymer in deionized water and then introducing these solutions into 0.1N HCl. Sodium Alginate exhibited immediate gel formation upon contact with the acid, indicating a rapid and strong gelling capability. While, Carbapol 940 started to gel after approximately 5 minutes, forming a weaker gel compared to Sodium Alginate. These results suggest that Sodium Alginate is a more effective gelling agent in acidic conditions, while carbapol 940 demonstrates moderate gelation properties.

Evaluation parameter: -

1. Physical Appearance & pH:

Table 8: Physical Appearance & pH

Batch	Color	Odour	pH
F1	White	Odourless	7.11
F2	Cream	Odourless	7.29
F3	White	Odourless	6.89
F4	Cream	Odourless	7.24
F5	Cream	Odourless	6.94
F6	Cream	Odourless	7.05
F7	White	Odourless	7.12
F8	Cream	Odourless	7.04
F9	White	Odourless	7.19

2 Gelation Response, Floating Behaviour, Viscosity, Percentage Drug Content:

Table 9: Gelation Response, Floating Behaviour, Viscosity, Percentage Drug Content

Batch	Gelation Response	Floating Lag Time (sec)	Floating Duration (hrs)	% Drug Content	Viscosity (cps)
F1	+ + +	3	>12	92.43	304
F2	+ + +	2	>12	93.84	302
F3	+ + +	3	>18	92.62	307
F4	+ + +	3	>12	94.24	294
F5	+ + +	4	>16	96.07	292
F6	+ + +	2	>24	98.75	310
F7	+ + +	2	>20	92.66	312
F8	+ + +	3	>22	96.53	314
F9	+ + +	3	>23	92.37	312

3. Dissolution Profile:

Table 10: Dissolution Profile of F1-F9

Time (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
0	0	0	0	0	0	0	0	0	0

1	0	0.2	0.5	0.6	0.7	1	0.8	0.6	0.7
2	1.3	1.5	1.8	3.4	6.2	7	6.5	6.3	6.1
3	9.5	9.9	10.3	14.6	18.3	20.4	17	15.5	14.6
4	17.6	18.1	18.9	22.7	26.6	30	24.3	22.8	20.7
5	23.5	24.7	25.5	27.9	34.5	37	33.8	32.5	31.3
6	35.7	36.4	37.3	40.3	43.1	47.7	45.7	44.6	42.3
8	43.6	44.3	45.7	48.2	55.8	59	53.6	52.7	51.4
10	51.4	52.6	53.3	57.6	61.7	66.2	63.8	62.1	60.1
12	57.8	58.4	59.2	63.8	76.3	81	79	77.9	75.6
16	64.9	65.2	67.8	72.4	89.5	96	87.6	85.2	82.3
24	70.5	73.1	78.6	83.3	90.5	98.5	92.3	89.7	88.6

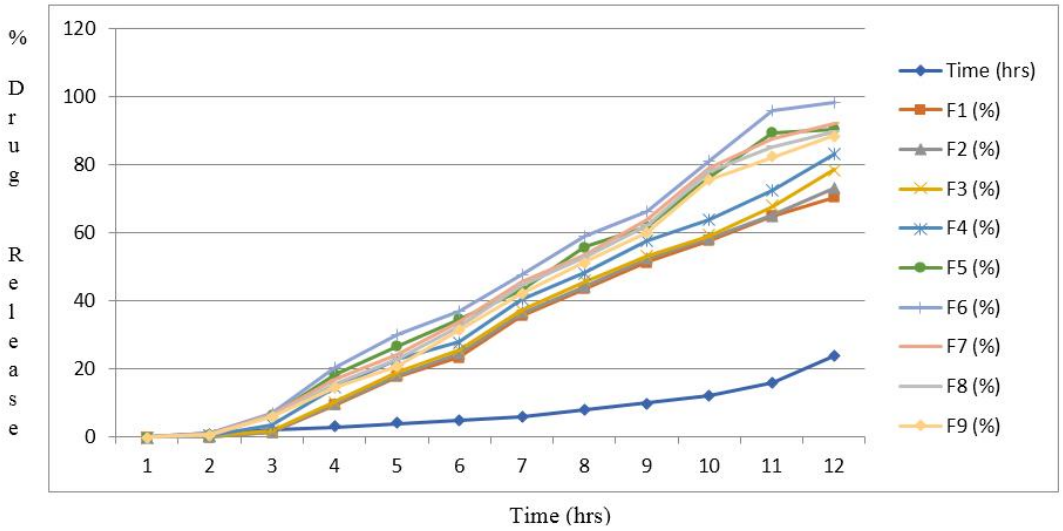

Fig 8: Graph of Dissolution

Fig.9: Formulation of In-situ gel

CONCLUSION

1 The Pioglitazone In-situ gel was prepared using sodium alginate & carbapol 940 as gelling agents, with calcium carbonate enhancing effervescence to emphasize the gel's floating capability.

2 The optimized F6 formulation was developed with sodium alginate at a 1.5g concentration and calcium gluconate at a 0.5g concentration, tri sodium citrate at a 0.5g,agar-agar 50mg .

3 The formulation demonstrated a floating time of greater than 24 hours, with gelation occurring in less than 5 seconds.

4 The viscosity and pH of F6 were found to be 310 cps and 7.05, respectively. The percentage drug content was 98.75%. The drug release profile ranged from 0% to 98.5% over 24 hours, indicating sustained drug release, which justifies the efficacy of the in-situ gel formulation for prolonged therapeutic action.

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