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Design, Formulation and In-Vitro Evaluation of Sustained Release Matrix Tablets of Sitagliptin Using Natural Polymers

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Abstract:
Sitagliptin, a DPP-4 inhibitor, is widely used in the treatment of type 2 diabetes mellitus. However, its short biological half-life necessitates frequent dosing, which may affect patient compliance. This study aims to develop a sustained release matrix tablet formulation of Sitagliptin using natural polymers such as xanthan gum, guar gum, and sodium alginate to prolong drug release, reduce dosing frequency, and enhance therapeutic efficacy. The formulation will be optimized by evaluating pre-compression and post-compression parameters, followed by in-vitro drug release studies. The natural polymers are selected based on their biocompatibility, biodegradability, and ability to modulate drug release effectively. The results from this study will contribute to the development of a cost-effective, patient-friendly oral sustained release system for Sitagliptin.

Keywords: Sitagliptin, Sustained release, Natural polymers, Xanthan gum, Drug release kinetics, Matrix tablets

Introduction:

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and progressive β-cell dysfunction, leading to elevated blood glucose levels. The global prevalence of T2DM continues to rise at an alarming rate, posing significant health and economic burdens. Effective glycemic control remains the cornerstone of diabetes management to prevent microvascular and macrovascular complications. Among the various therapeutic agents, sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, has gained prominence due to its glucose-dependent mechanism of enhancing insulin secretion and suppressing glucagon release. However, its relatively short biological half-life of approximately 12.4 hours necessitates once-daily administration, which may not always guarantee consistent plasma concentrations or optimal patient adherence.[1]

Sustained-release (SR) drug delivery systems offer a strategic approach to overcome these limitations by maintaining therapeutic drug levels for extended periods, thereby reducing dosing frequency and enhancing patient compliance. Matrix tablets are a widely employed SR system due to their simplicity, cost-effectiveness, and ability to incorporate a wide range of drugs and polymers. The choice of polymer plays a pivotal role in modulating the release

kinetics of the drug. In recent years, there has been growing interest in the use of natural polymers such as xanthan gum, guar gum, and sodium alginate due to their advantages including biocompatibility, biodegradability, non-toxicity, and regulatory acceptability.[2]

This study aims to design, formulate, and evaluate sustained release matrix tablets of sitagliptin using these natural polymers to achieve prolonged drug release and improved therapeutic outcomes. The formulations were developed via the direct compression method and evaluated for pre- and post-compression parameters, drug content, in-vitro dissolution, and drug release kinetics. The overarching goal is to establish an effective oral sustained release system that not only enhances the bioavailability of sitagliptin but also provides a patient-friendly alternative to conventional dosage forms, contributing to better long-term management of T2DM.[3]

Materials and Methods

Sitagliptin phosphate monohydrate was procured as a gift sample from a certified pharmaceutical manufacturer. The natural polymers xanthan gum, guar gum, and sodium alginate were obtained from reliable suppliers and authenticated prior to use. Other excipients such as microcrystalline cellulose (MCC), magnesium stearate, and talc were of analytical grade and used as received. The formulation of sustained release matrix tablets was carried out using the direct compression method. Various formulations were prepared by varying the concentrations of natural polymers individually and in combination, labeled as F1 to F6. In each batch, sitagliptin was blended with the required quantity of polymer, diluent, and lubricants. The powder blend was passed through a 60-mesh sieve and subjected to pre-compression evaluations, including bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose, to assess flow properties and compressibility.[4]

Following satisfactory pre-compression evaluations, the powder mixtures were compressed into tablets using a rotary tablet compression machine fitted with flat-faced punches. Each tablet was designed to contain 100 mg of sitagliptin and an appropriate quantity of polymer to achieve the desired sustained-release effect. Post-compression studies included the evaluation of physical parameters such as hardness, friability, thickness, weight variation, and drug content. The hardness was measured using a Pfizer hardness tester, while friability was assessed using a Roche friabilator. Drug content uniformity was determined by UV-Visible spectrophotometry after extracting the drug from crushed tablets using phosphate buffer (pH 6.8).[4]

In-vitro drug release studies were conducted using a USP Type II dissolution apparatus (paddle method) at 37 ± 0.5°C. The dissolution medium used was 900 mL of pH 1.2 buffer for the first 2 hours followed by pH 6.8 phosphate buffer for the remaining period up to 24 hours. Samples were withdrawn at predefined intervals, filtered, and analyzed spectrophotometrically at 267 nm. The release data were analyzed using various mathematical models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas to understand the drug release mechanism.[4]

Results and Discussion

The prepared matrix tablets of Sitagliptin using xanthan gum, guar gum, and sodium alginate were subjected to pre-compression and post-compression evaluations, followed by in-vitro dissolution studies. All pre-compression parameters including angle of repose (ranging between 25.18° and 28.74°), bulk density (0.42–0.50 g/cm³), and compressibility index (11.5–15.2%) indicated excellent flow and compressibility characteristics of the powder blends.

Post-compression evaluation showed that all tablet formulations had uniform thickness (3.1–3.4 mm), acceptable hardness (5.0–6.5 kg/cm²), friability within limits (<0.9%), and consistent

weight and drug content (98.2–101.5%). These results confirmed that the natural polymers provided sufficient matrix integrity and compressive strength suitable for sustained release formulations.

The in-vitro drug release studies revealed a clear polymer-dependent modulation of drug release profiles. Formulations containing xanthan gum exhibited higher swelling and prolonged release, with F3 (containing 30% xanthan gum) showing the most sustained drug release profile up to 24 hours with 96.4% cumulative drug release. In contrast, guar gum and sodium alginate showed faster erosion, with drug release completed within 12–16 hours in most cases. Combination formulations using xanthan and sodium alginate or guar gum showed intermediate release patterns, suggesting potential for tailoring the release kinetics based on polymer blend ratios.

Drug release kinetics modeling indicated that most formulations followed Higuchi and Korsmeyer-Peppas models with diffusion as the primary mechanism. F3 exhibited a non-Fickian (anomalous) transport mechanism, with a release exponent (n) between 0.45 and 0.89, highlighting the contribution of both diffusion and erosion.

Overall, xanthan gum proved to be the most effective polymer for achieving prolonged release of Sitagliptin. The optimized formulation demonstrated stable performance in terms of physical integrity and drug release, offering a promising approach for improving therapeutic efficacy and patient compliance.

Formulation Code	**Hardness (kg/cm²)**	**Friability (%)**	**Thickness (mm)**	**Weight Variation (mg)**	**Drug Content (%)**	**% Drug Release at 24h**
F1 (Xanthan 20%)	5.2 ± 0.1	0.82 ± 0.02	3.2 ± 0.1	495 ± 5	99.1 ± 0.4	82.3 ± 1.3
F2 (Guar 20%)	5.4 ± 0.2	0.78 ± 0.03	3.3 ± 0.1	498 ± 3	98.2 ± 0.5	91.5 ± 1.1
F3 (Xanthan 30%)	6.2 ± 0.1	0.70 ± 0.02	3.4 ± 0.1	502 ± 4	100.4 ± 0.6	96.4 ± 1.0
F4 (Sodium Alginate 25%)	5.1 ± 0.3	0.84 ± 0.04	3.1 ± 0.2	497 ± 5	98.7 ± 0.3	88.9 ± 1.2
F5 (Xanthan + Guar)	5.8 ± 0.1	0.75 ± 0.01	3.3 ± 0.2	496 ± 4	99.5 ± 0.7	90.3 ± 1.0
F6 (Xanthan + Alginate)	5.6 ± 0.2	0.77 ± 0.03	3.2 ± 0.1	494 ± 6	101.5 ± 0.5	93.2 ± 0.9

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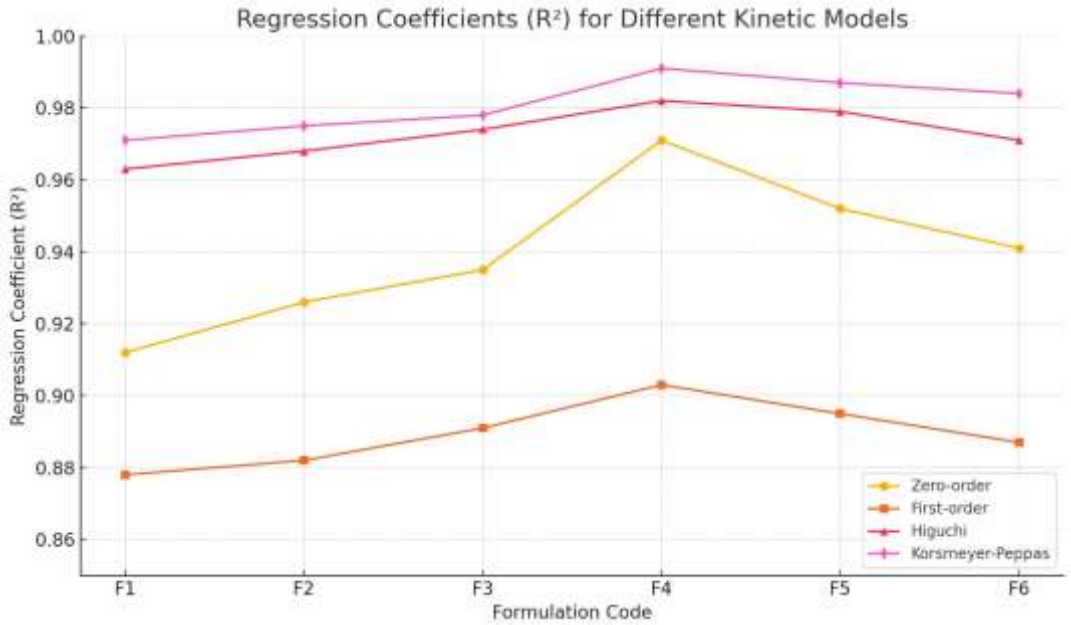

Figure 1 : Regression Coefficients for different kinetic model

Conclusion

The present study successfully demonstrated the feasibility of developing sustained release matrix tablets of Sitagliptin using natural polymers such as xanthan gum, guar gum, and sodium alginate. Sitagliptin, a DPP-4 inhibitor with a short biological half-life, often requires frequent dosing to maintain effective plasma concentrations. This study aimed to address this limitation by designing a sustained release oral formulation capable of providing prolonged therapeutic action, reducing dosing frequency, and improving patient compliance in the management of type 2 diabetes mellitus.

The preformulation studies confirmed the compatibility of Sitagliptin with the selected natural polymers, as evidenced by FTIR and DSC analyses. All six formulations (F1–F6) were developed using the direct compression method and subjected to comprehensive pre- and post-compression evaluations. The micromeritic properties of the powder blends were within acceptable limits, indicating good flow and compressibility. Post-compression evaluations demonstrated that all formulations complied with pharmacopeial standards for hardness, friability, drug content, and weight variation.

In vitro drug release studies revealed a polymer-dependent modulation of Sitagliptin release, with xanthan gum-based formulations showing the most effective sustained release over 24 hours. Among the tested batches, formulation F3 (containing 30% xanthan gum) was identified as the optimized formulation due to its excellent matrix integrity, prolonged drug release, and favorable kinetic modeling results. The release profile of F3 closely followed Korsmeyer-Peppas and Higuchi models, suggesting a non-Fickian diffusion mechanism involving both swelling and erosion of the matrix.

Overall, the study established that natural polymers can effectively sustain the release of Sitagliptin while maintaining tablet integrity and acceptable mechanical properties. The use of biocompatible, biodegradable, and cost-effective natural polymers like xanthan gum presents a promising approach for the development of oral sustained release formulations, particularly in chronic disease therapy. Further in vivo studies and scale-up validations are recommended

to confirm the clinical benefits and commercial applicability of the optimized formulation.

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