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Comprehensive Research on the Formulation and Evaluation of Sustained Release Tablets of Nateglinide Using Natural Polymers

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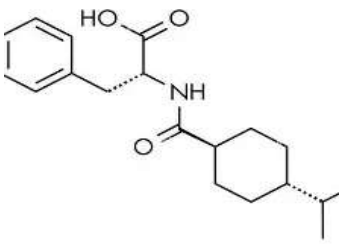
ABSTRACT

The objective of the current research was to formulate and comprehensively evaluate sustained release (SR) tablets of Nateglinide, a short-acting hypoglycemic agent, by employing various natural polymers such as Guar Gum, Xanthan Gum, Ghatti Gum, and Karaya Gum. This research addresses the limitations associated with frequent dosing of Nateglinide by designing a dosage form capable of releasing the drug in a controlled manner over 12 hours. The study involved meticulous preformulation evaluation, optimization of polymer concentration, and post-compression assessments to ensure both the physical stability and prolonged drug release of the developed tablets.

Keywords: Drug, Formulation, Gum, Nateglinide, Pre-formulation, Xanthan

1. INTRODUCTION

Drug delivery systems (DDS) play a pivotal role in modern pharmacotherapy, improving therapeutic efficiency, reducing dosing frequency, and enhancing patient compliance[1,2]. Amongst the different DDS, oral sustained release formulations remain the most preferred due to their ease of use, patient acceptability, and cost-effectiveness. Nateglinide is a meglitinide-class antidiabetic drug with a short half-life (1.5 hours), necessitating multiple daily doses to maintain therapeutic plasma concentration levels. Frequent dosing increases the risk of side effects and non-compliance. Incorporating natural polymers into sustained release tablets offers an advantageous approach by providing controlled drug release, minimizing dose frequency, and maintaining consistent drug plasma levels. This study aims to investigate the role of Guar Gum, Xanthan Gum, Ghatti Gum, and Karaya Gum as release retardants in sustained release formulations of Nateglinide[3,4].



nateglinide

2. MATERIALS AND METHODS

2.1 Study Design

This study employed a systematic formulation approach to develop sustained release (SR) matrix tablets of Nateglinide using various natural polymers. The methodology included a comprehensive sequence of pre-formulation analysis, formulation via direct compression, and post-formulation evaluation including in-vitro dissolution testing and kinetic modeling of drug release profiles[5,6].

2.2 Materials

The following materials were used in this study:

- Active Drug: Nateglinide
- Natural Polymers: Guar Gum, Xanthan Gum, Ghatti Gum, Karaya Gum
- Excipients: Microcrystalline Cellulose, Lactose, Magnesium Stearate, Talc

All materials were procured from certified pharmaceutical suppliers and were used as received without further purification.

2.3 Preformulation Studies

Preformulation studies were carried out to assess the compatibility between Nateglinide and the selected polymers. This involved organoleptic evaluation, solubility analysis, melting point determination, and Fourier Transform Infrared (FTIR) spectroscopy to identify any potential chemical interactions. Powder blend flow properties including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio were evaluated to confirm suitability for direct compression[7].

2.4 Formulation of Sustained Release Tablets[8]

Matrix tablets were prepared using the direct compression technique. Accurately weighed quantities of Nateglinide, selected natural polymer, and excipients were blended and compressed using a rotary tablet compression machine with 9 mm round punches.

2.4.1 Direct Compression Method[9]

The powder blend was prepared by mixing the sieved API, polymers, and excipients uniformly. Magnesium stearate and talc were added in the final blending step to ensure lubrication and flowability. The mixture was then compressed into tablets using appropriate force to ensure uniform hardness and weight.

2.5 Evaluation of Tablets[10]

2.5.1 Pre-Compression Evaluation

Flow properties of the powder blend were assessed by determining the angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio.

2.5.2 Post-Compression Evaluation

The compressed tablets were evaluated for weight variation, hardness (using Monsanto hardness tester), thickness, friability (using Roche friabilator), and drug content using UV spectrophotometry at 210 nm.

2.5.3 In-Vitro Drug Release Study[11]

Dissolution studies were carried out using USP Type II (paddle) apparatus in phosphate buffer (pH 7.4), maintained at 37 ± 0.5°C with a rotation speed of 50 rpm. Samples were withdrawn at specific time intervals and analyzed spectrophotometrically.

2.6 Statistical Analysis

Drug release data were fitted to Zero Order, First Order, Higuchi, and Korsmeyer-Peppas models to determine the release kinetics[12]. The best fit model was selected based on correlation coefficients (R^2 values).

3. RESULTS AND DISCUSSION

3.1 Pre-Compression Evaluation

The pre-compression parameters were evaluated to assess the flow properties of the powder blends intended for direct compression. The results are summarized in Table 1. All formulations exhibited good flow properties as indicated by angle of repose values within the range of 27.9° to 28.4°, Carr's index less than 15%, and Hausner ratio less than 1.25, ensuring suitability for direct compression.

Table 1: The powder blend was evaluated for flow properties before compression, ensuring suitability for direct compression:

Formulation	Angle of Repose (°)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner Ratio
F1	28.4	0.45	0.52	13.46	1.15
F2	27.9	0.44	0.51	13.72	1.16
F3	28.1	0.46	0.53	13.2	1.15

3.2 Post-Compression Evaluation

The tablets were subjected to standard quality control tests post-compression. The physical parameters including weight variation, hardness, friability, thickness, and drug content were within pharmacopeial limits as shown in Table 2.

Table 2: Tablets were tested for uniformity of weight, hardness, thickness, friability, and drug content with results tabulated below:

Formulation	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Weight Variation (mg)	Drug Content (%)
F1	5.2	4.1	0.45	498.2	98.4
F2	5.5	4.2	0.42	501.1	99.2
F3	5.1	4.0	0.47	497.6	98.7

3.3 In-Vitro Dissolution Studies

The in-vitro drug release profiles were assessed using USP Type II dissolution apparatus. Formulation F2 exhibited the most desirable sustained release profile, extending drug release up to 12 hours. The cumulative percentage drug release

versus time is illustrated in Figure 1. In-vitro drug release studies over 12 hours demonstrated Xanthan Gum (F2) provided release.

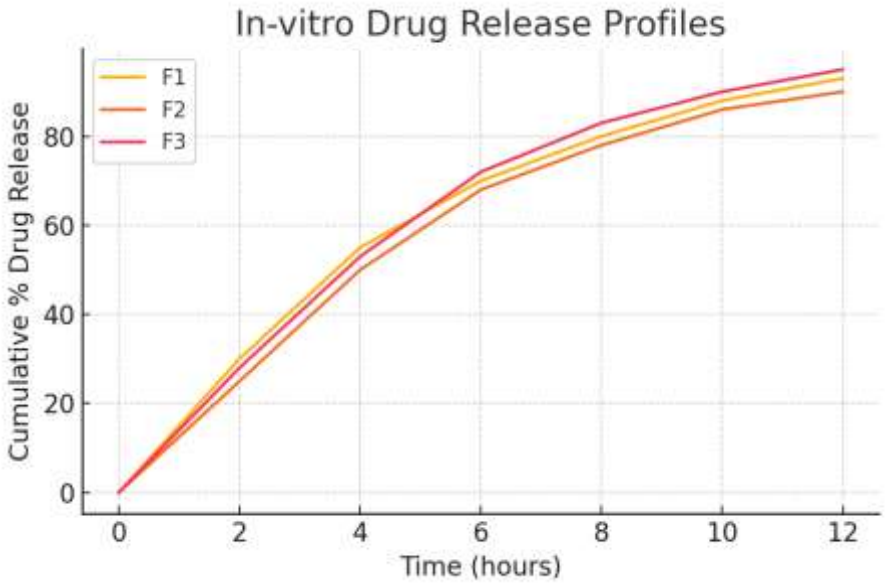


Figure 1: In-vitro drug release profile of formulations F1, F2, and F3.

3.4 Drug Release Kinetics

Drug release kinetics were evaluated using zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. F2 followed zero-order kinetics (R^2=0.983) and non-Fickian diffusion mechanism according to the Peppas model.

3.5 In-vitro Drug Release Study

The dissolution studies were conducted using USP Type II apparatus in 900 mL phosphate buffer (pH 7.4) at 37 ± 0.5°C and 50 rpm. The cumulative drug release was assessed at predetermined intervals. The graphical representation indicates the drug release kinetics for each formulation

4. CONCLUSION

This study demonstrated Xanthan Gum-based sustained release matrix tablets of Nateglinide provide consistent and prolonged drug release up to 12 hours. Among all polymers tested, Xanthan Gum (F2) was most effective, following zero-order release kinetics and non-Fickian diffusion mechanism. This confirms natural polymers' potential in designing cost-effective, biocompatible sustained release oral formulations.

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