RESEARCH PAPER

Preformulation and Compatibility Studies of Nateglinide with Selected Natural Polymers

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Abstract:

The present study focused on the preformulation, compatibility evaluation, and preliminary optimization of extended-release matrix tablets of Nateglinide using natural polymers, namely guar gum and xanthan gum. Preformulation studies were carried out to determine the physicochemical characteristics of the drug, including organoleptic properties, melting point, solubility profile, UV spectrophotometric analysis, calibration curve development, HPLC analysis, FTIR spectroscopy, DSC, and XRD studies. The drug exhibited a melting point in the range of 129–130°C and showed maximum absorbance at 216 nm. Calibration curves in methanol and 0.1 N HCl obeyed Beer–Lambert's law with excellent linearity. FTIR, DSC, and XRD analyses confirmed the compatibility of Nateglinide with guar gum and xanthan gum without any significant interaction.

Preliminary optimization trials were conducted to investigate the influence of polymer concentration, polymer type, polymer combination, diluent concentration, and lubricant level on drug release behavior and tablet characteristics. Increased polymer concentration retarded drug release due to enhanced gel formation and matrix integrity. Xanthan gum exhibited stronger release-retarding properties than guar gum, whereas the combination of guar gum and xanthan gum produced a synergistic effect, resulting in controlled and sustained drug release for up to 12 hours.

The optimized formulation demonstrated satisfactory flow properties, compressibility, mechanical strength, and drug release characteristics. Overall, the study confirmed the suitability of natural polymers for the development of extended-release matrix tablets of Nateglinide with improved release control and formulation stability.

Keywords:

Nateglinide, Extended-release matrix tablets, Guar gum, Xanthan gum, Natural polymers.

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Introduction:

Nateglinide is an oral antidiabetic agent belonging to the meglitinide class, widely used in the management of type 2 diabetes mellitus. It stimulates rapid insulin secretion from pancreatic β-cells, thereby controlling postprandial blood glucose levels. However, the conventional dosage form of Nateglinide possesses a relatively short biological half-life and requires frequent administration, which may reduce patient compliance. To overcome these limitations, the development of extended-release matrix tablets offers an effective approach for maintaining prolonged therapeutic drug levels and improving patient adherence. [1]

Natural polymers have gained considerable attention in sustained-release drug delivery systems because of their biocompatibility, biodegradability, non-toxicity, and cost-effectiveness. Among these, guar gum and xanthan gum are widely used hydrophilic polymers capable of forming gel matrices that regulate drug release through swelling and diffusion mechanisms. The combination of these polymers may provide synergistic effects, resulting in improved matrix integrity and controlled drug release behavior. [2]

Preformulation studies play a vital role in dosage form development by providing essential information regarding the physicochemical and compatibility characteristics of the drug and excipients. Parameters such as melting point, solubility, spectral analysis, crystallinity, and thermal behavior help in selecting suitable formulation components and processing methods. Compatibility studies using FTIR, DSC, and XRD further ensure the stability and integrity of the formulation.

Therefore, the present study was undertaken to perform comprehensive preformulation and compatibility studies of Nateglinide with selected natural polymers and to evaluate the influence of formulation variables on the development of extended-release matrix tablets.

Materials and Methods

Materials

Nateglinide was used as the active pharmaceutical ingredient. Guar gum and xanthan gum were selected as natural release-retarding polymers. Microcrystalline cellulose (MCC PH-102) was used as a diluent, while magnesium stearate and talc were employed as lubricant and glidant, respectively. Methanol, 0.1 N hydrochloric acid, phosphate buffer saline (PBS pH 7.4), chloroform, and dichloromethane were used during analytical and solubility studies.

Preformulation Studies

Preformulation investigations entail a detailed examination of the physical and chemical characteristics of the active pharmaceutical ingredient, both independently and in combination with formulation excipients. This initial phase supports the strategic design of dosage forms by integrating biopharmaceutics with key physicochemical factors to achieve an ideal delivery profile.

As a foundational step in formulation, the procured Nateglinide underwent identity verification to confirm its purity and authenticity. Such identification aligns with compendial standards, aiding in the confirmation of material integrity.

- **Organoleptic evaluation:** Approximately 1 g of Nateglinide was spread on a watch glass for qualitative inspection of its visual traits, including texture, hue, distinctive aroma, and flavor profile. [3]
- **Melting point determination**: The melting behavior of Nateglinide was evaluated via the capillary tube technique. A fine sample of the drug was introduced into a sealed-end glass capillary, which was subsequently inserted into a melting point instrument. Observations were noted for the onset of liquefaction and the point of complete fusion. [4]
- **UV spectrophotometric analysis:** To establish the λmax for Nateglinide, 100 mg of the compound was solubilized in methanol and volumetrically adjusted to 100 ml, yielding 1000 µg/ml. A 1 ml portion was further diluted to 10 ml with methanol, resulting in 100 µg/ml. This preparation underwent scanning from 400 to 200 nm on a UV-Visible spectrophotometer, blanked against methanol, to pinpoint the peak absorbance. [5]
- **Calibration curve development**: UV spectrophotometry facilitated the construction of calibration curves for Nateglinide in methanol and 0.1 N HCl environments.

Calibration Curve in Methanol

Stock Solution Preparation:

Precisely 100 mg of Nateglinide was placed in a 100 ml volumetric flask, dissolved, and made up to volume with methanol (1000 µg/ml). Subsequently, 10 ml of this was extended to 100 ml with methanol, producing a 100 µg/ml working stock.

Series Preparation for Calibration:

Volumes of 0.2, 0.4, 0.6, 0.8, 1.0, and 1.2 ml from the stock were pipetted into separate 10 ml volumetric flasks and diluted to volume with methanol, spanning 2–12 µg/ml. Absorbances were measured at 216 nm, using methanol as the reference.

Calibration Curve in 0.1 N HCl

Stock Solution Preparation:

A 100 mg aliquot of Nateglinide was volumetrically dissolved in 0.1 N HCl to 100 ml (1000 µg/ml), followed by a 1:10 dilution to achieve 100 µg/ml.

Series Preparation for Calibration:

Stock aliquots (0.2–1.2 ml) were transferred to 10 ml flasks and adjusted to volume with 0.1 N HCl (2–12 µg/ml range). Absorbance readings were taken at 216 nm against a 0.1 N HCl blank.

HPLC analysis: HPLC analysis quantified Nateglinide in its pure state. The elution system consisted of 0.01 M ammonium acetate buffer (pH 4.0) mixed with methanol (20:80 v/v), delivered at 1.0 mL/min. Column temperature was held at 23 ± 1°C, with photodiode array detection at 216 nm. Injections of 20 µL were made at ambient temperature, with a 10-minute runtime and retention time noted (~8 min). [6]

FTIR spectroscopy: FTIR analysis probed interactions between Nateglinide , Guar gum, Xanthan gum and optimized formulation. Using a Bruker Vertex 70 instrument and KBr pellet technique, samples (drug, polymer, and optimized batch) were blended 1:10 with KBr, compressed into discs, and scanned from 4000–400 cm^{-1}.[7]

DSC: DSC screened for Nateglinide-Polymer interactions. Samples (3–5 mg, powdered) of pure Nateglinide, Xanthan and Guar gum, and optimized formulation were sealed in aluminum pans, heated from 40–200°C at 10°C/min under nitrogen (20 ml/min flow), with an empty pan as reference. [8]

XRD: XRD profiling examined Nateglinide's crystalline state within the formulation. Patterns for Nateglinide, and the optimized formulation were generated on a Bruker D-8 Advance diffractometer (CuKα radiation, 40 kV/40 mA, 5–60° 2θ, 0.03° step, 0.5 s/step). [9]

Solubility profiling: Excess Nateglinide was introduced to 10 ml aliquots of various solvents, with solubility gauged visually. Solvents tested: Distilled water, PBS pH 7.4, 0.1 N HCl, methanol, chloroform, dichloromethane. [10]

Formulation Of Extended-Release Matrix Tablets of Nateglinide

The direct compression method was used to create Nateglinide extended-release matrix tablets because it is easy to use, economical, and appropriate for components that are sensitive to heat and moisture. To guarantee homogeneous particle size distribution and remove agglomerates, precisely weighed amounts of Nateglinide, specific natural polymers (guar gum, xanthan gum, and/or sodium alginate), and diluent (microcrystalline cellulose, MCC PH-102) were each passed through sieve no. 60. To create a uniform powder blend, the sieved ingredients were then put into a dry, clean mortar or an appropriate blender and well blended. The blending process was carried out for approximately 10–15 minutes to ensure uniform distribution of the drug within the polymer matrix. Following this,

magnesium stearate (as a lubricant) and talc (as a glidant) were added to the powder blend. The mixture was further blended gently for 3–5 minutes to avoid over-lubrication, which may adversely affect tablet hardness and drug release.

A rotary tablet compression machine with appropriate punches (usually 8–10 mm flat-faced punches) was then used to compress the finished lubricated blend. To create tablets with sufficient mechanical strength and consistency, compression parameters like hardness and compression force were changed.

Preliminary Optimization Studies

To assess the impact of formulation variables on matrix tablet performance, preliminary optimisation trials were carried out. Guar gum, a natural release-retarding polymer, was used to create matrix tablets of nateglinide at different concentrations of 10%, 20%, and 30% w/w of the total tablet weight while maintaining constant amounts of other excipients. To guarantee that the powder mixture was homogenous, each component was precisely weighed, run through sieve number 60, and blended evenly. A rotating tablet compression machine was then used to compress the lubricated mixture into tablets using a regulated compression force. The produced formulations underwent in-vitro dissolution tests and were assessed for pre-compression and post-compression properties. A thorough investigation was conducted to determine how different concentrations of guar gum affected the drug release profile and matrix integrity. [11]

Determination of the Effect of Polymer Type (Xanthan Gum vs Guar Gum)

Matrix tablets were created employing xanthan gum as a release-retarding polymer at concentrations comparable to those used for guar gum in order to assess the impact of polymer type on drug release behaviour. To guarantee uniformity and repeatability between batches, the formulation process stayed the same. Before compression, all ingredients were completely combined, sieved, and lubricated. Similar compression conditions were used to make the tablets, and their physical characteristics, including hardness, friability, and homogeneity of drug content, were assessed. In-vitro dissolution tests were conducted on the generated batches in order to evaluate the impact of polymer type on matrix formation behaviour and release characteristics.

Determination of the Effect of Polymer Combination (Guar Gum and Xanthan Gum)

Different ratios of guar gum and xanthan gum were used to make matrix tablets containing nateglinide in order to examine the combined influence of natural polymers on drug release behaviour. To investigate the synergistic effects of each polymer on matrix formation and drug release, the total concentration of polymers was kept constant while the fraction of each polymer was varied. To guarantee that the medication was evenly distributed throughout the polymer matrix, each component was precisely weighed, run through sieve number 60, and completely combined. The powder mixture was compressed using a rotary tablet press under ideal circumstances after being lubricated with talc and magnesium stearate. The produced formulations underwent in-vitro dissolution investigations after being assessed for pre-compression and post-compression characteristics. A methodical evaluation of the impact of polymer mixture on swelling behaviour, matrix integrity, and drug release characteristics was conducted.

Determination of the Effect of Diluent (Microcrystalline Cellulose, MCC PH-102)

By altering the quantity of microcrystalline cellulose (MCC PH-102) in the formulation, the impact of diluent concentration on the physical properties and drug release behaviour of matrix tablets was assessed. To investigate the impact of MCC on compressibility and matrix structure, tablets were made by varying the fraction of MCC while keeping medication and polymer levels constant. To create a homogenous mixture, all the ingredients were blended evenly after being sieved through mesh number 60. A rotary compression machine with regulated compression parameters was then used to compress the lubricated mixture into tablets. The prepared batches' mechanical strength, drug content homogeneity, and micromeritic characteristics were assessed. The impact of MCC concentration on drug release behaviour and matrix performance was investigated by in-vitro dissolving tests.

Determination of the Effect of Lubricant (Magnesium Stearate)

Formulations with different amounts of magnesium stearate were made in order to investigate the impact of lubricant concentration on tablet characteristics and drug release profile. The concentration of magnesium stearate was adjusted while keeping all other formulation components constant. Lubricant and glidant were added after the ingredients had been precisely weighed, sieved, and thoroughly blended to guarantee homogeneity. To avoid any negative effects on tablet properties, care was taken to avoid overmixing following lubricant addition. The final blend was compressed into tablets using a rotary tablet press under standardized conditions. The produced tablets' hardness, friability, and consistency of drug content were assessed. To evaluate the impact of lubricant concentration on drug release behaviour and overall tablet performance, additional in-vitro dissolution studies were conducted.

Results and discussion

Preformulation Studies

Preformulation studies were conducted to establish the physicochemical characteristics of Nateglinide and its compatibility with the selected excipients. These evaluations provide essential insights into the drug's identity, purity, and potential interactions with formulation components.

- **Organoleptic Properties**

The organoleptic evaluation of Nateglinide confirmed that it is a white, odorless, crystalline powder with a tasteless profile, consistent with literature reports.

- **Determination of Melting Point**

The melting point of Nateglinide was found to be in the range of 129–130°C, aligning with the reported literature value (128–131°C), confirming its purity and crystalline nature

- **Determination of λmax by UV–Visible Spectroscopy**

The UV–visible absorption spectrum of Nateglinide in methanol exhibited a distinct absorption maximum (λmax) at 216 nm, confirming its purity and suitability for spectrophotometric quantification.

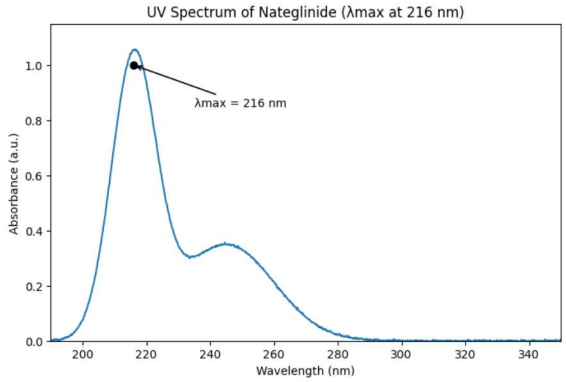

Figure 1: UV–visible absorption spectrum of Nateglinide in methanol (λmax = 216 nm)

- **Calibration Curves in Different Solvents**

Calibration curves of Nateglinide in methanol and 0.1 N HCl were plotted according to Beer–Lambert's law within the concentration range of 2–12 µg/mL. The regression coefficients (R^2) were found to be 0.9991 and 0.9987, respectively, confirming excellent linearity.

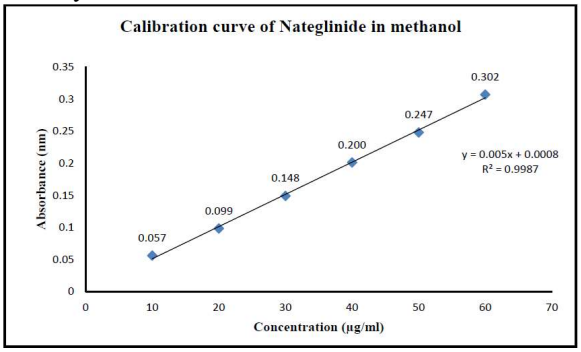

Figure 2: Calibration curve of Nateglinide in methanol

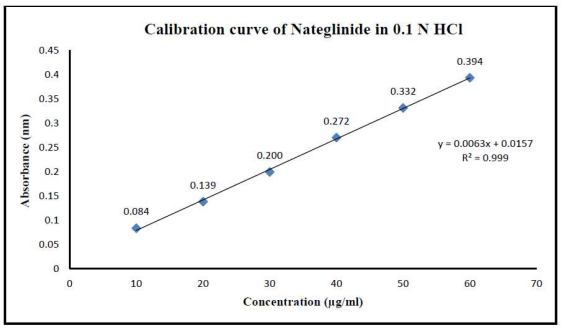

Figure 3: Calibration curve of Nateglinide in 0.1 N HCl

- **High Performance Liquid Chromatography Studies**

The HPLC of Nateglinide was performed and the chromatogram was obtained which showed the retention time of 6.104 min.

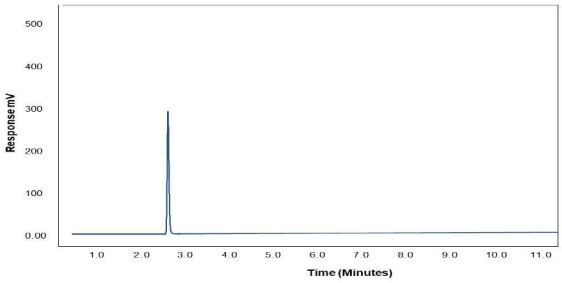

Figure 4: Chromatogram for Nateglinide

- **Fourier Transform Infrared (FTIR) Spectroscopy**

FTIR spectroscopy was performed to investigate the compatibility between Nateglinide and selected natural polymers (guar gum and xanthan gum), as well as the optimized extended-release matrix tablet formulation.

The FTIR spectrum of pure Nateglinide exhibited characteristic peaks corresponding to its functional groups, including N–H stretching (~3230 cm^{-1}), C=O stretching (~1685 cm^{-1}), and C–O stretching (~1245 cm^{-1}). The spectra of guar gum and xanthan gum showed typical polysaccharide peaks, such as broad O–H stretching (~3400 cm^{-1}) and C–O–C stretching (~1020–1100 cm^{-1}). The FTIR spectrum of the optimized formulation showed all major characteristic peaks of Nateglinide without any significant shift, disappearance, or formation of new peaks. This confirms that there was no chemical interaction between the drug and excipients, indicating compatibility and stability of the formulation.

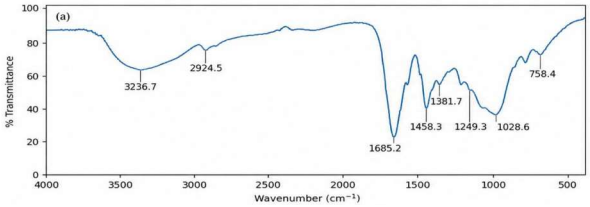

Figure 5 (a) FTIR spectra of Nateglinide

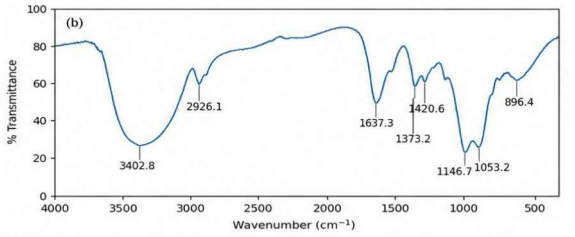

Figure 5 (b) FTIR spectra of Guar Gum

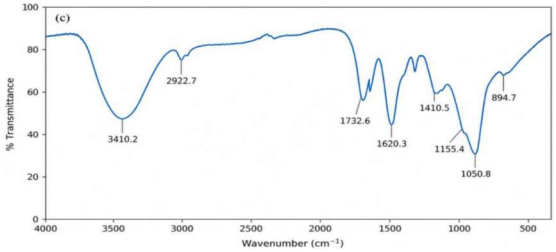

Figure 5 (c) FTIR spectra of Xanthan Gum

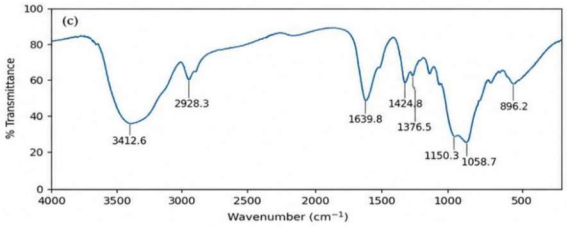

Figure 5 (d) FTIR spectra of optimized Formulation

- **Differential Scanning Calorimetry (DSC)**

The thermal behaviour and compatibility of nateglinide with the chosen natural polymers in the designed extended-release matrix tablet formulation were assessed using differential scanning calorimetry (DSC).

The DSC thermogram of pure Nateglinide (Figure 6 (a)) exhibited a sharp and intense endothermic peak at 129.4°C, corresponding to its melting point. This distinct and narrow peak confirms the crystalline nature and purity of the drug.

In contrast, the DSC thermogram of the optimized extended-release matrix tablet formulation (Figure 6 (b)) showed a slightly broadened peak with reduced intensity at around 127.8°C. The observed shift and broadening of the peak may be attributed to the uniform dispersion of the drug within the hydrophilic polymeric matrix composed of guar gum and xanthan gum, along with a possible reduction in crystallinity of the drug.However, the retention of the characteristic endothermic peak of Nateglinide in the optimized formulation indicates that the drug remains thermally stable and maintains its identity. The absence of any additional peaks or significant peak disappearance suggests that there is no chemical interaction between the drug and excipients. These results confirm the compatibility of Nateglinide with the selected natural polymers and support the suitability of the formulation approach for the development of extended-release matrix tablets.

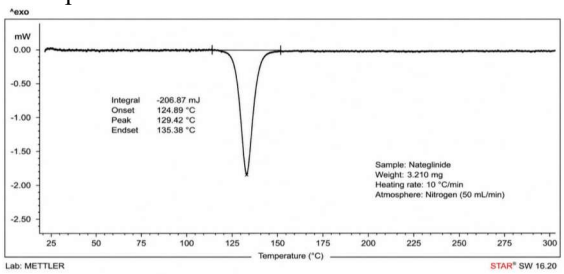

Figure 6 (a): DSC thermograms of pure Nateglinide

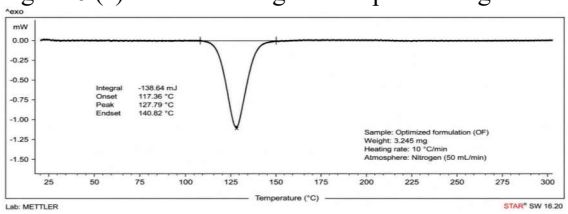

Figure 6 (b): DSC thermograms of optimized formulation

Powder X-Ray Diffraction (XRD)

The physical state and crystallinity of nateglinide in the presence of natural polymers (guar gum and xanthan gum) and in the optimised extended-release matrix tablet formulation were examined using powder X-ray diffraction (XRD) analysis. The XRD pattern of pure Nateglinide (Figure 7 (a)) exhibited sharp, intense, and well-defined diffraction peaks at specific 2θ values, confirming its highly crystalline nature. These distinctive peaks show that the drug's molecules are arranged in an orderly manner.

In contrast, the XRD pattern of guar gum (Figure 7 (b)) showed a broad diffuse halo with the absence of sharp peaks, indicating its amorphous nature. Similarly, xanthan gum (Figure 7 (c)) also exhibited a broad hump, confirming its predominantly amorphous polymeric structure.

The XRD pattern of the optimized extended-release matrix tablet formulation (Figure 7 (d)) demonstrated a significant reduction in the intensity of characteristic drug peaks, along with partial disappearance of some peaks. The pattern appeared more diffused compared to pure Nateglinide, which denotes a change from a crystalline to a semi-crystalline or partially amorphous state. The homogeneous dispersion of the medication within the hydrophilic polymer matrix (guar gum and xanthan gum) during formulation may be the cause of this decrease in crystallinity. The amorphous nature of the

polymers and their interaction with the drug matrix contribute to this transformation.

However, the presence of residual peaks corresponding to Nateglinide confirms that the drug retains its identity and does not undergo any chemical degradation during the formulation process.

Overall, the XRD data show that the produced formulation has less crystallinity, which is good for better dissolving behaviour and regulated drug release. The lack of new peaks supports the acceptability of the chosen natural polymers for the production of extended-release matrix tablets by confirming the drug's compatibility with the excipients.

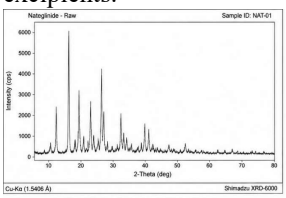

Figure 7 (a): XRD pattern of Nateglinide

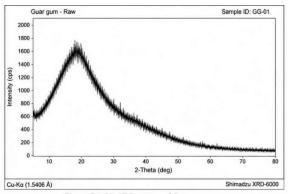

Figure 7 (b): XRD pattern of Guar gum

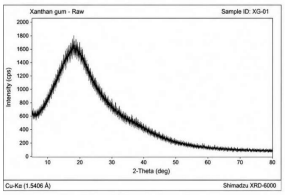

Figure 7 (c): XRD pattern of Xanthan gum

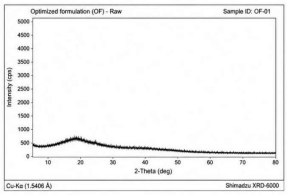

Figure 7 (d): XRD pattern of Optimized formulation

Preliminary studies

Initial research was done to assess how formulation factors affected the effectiveness of nateglinide extended-release matrix tablets. The study focused on polymer concentration, polymer type, polymer combination, diluent level, and lubricant concentration. Below is a discussion of the outcomes.

Effect of Polymer Concentration (Guar Gum)

The effect of guar gum concentration on drug release behavior was studied by preparing formulations containing 10%, 20%, and 30% w/w polymer. Formulations containing 10% guar gum exhibited rapid drug release, with more than 85% drug release within 6 hours, indicating insufficient matrix formation to sustain drug release. As the concentration increased to 20%, the drug release was significantly retarded, showing a more controlled release pattern extending up to 10–12 hours.

At 30% guar gum, the release rate was further reduced, with incomplete drug release observed within the study duration. This may be attributed to the formation of a thick gel layer, which restricts drug diffusion. These results indicate that increasing polymer concentration enhances matrix integrity and slows drug release due to increased viscosity and gel barrier formation.

Table 1: Effect of Guar Gum Concentration on tablet performance

Formulation	Guar Gum (%)	Drug Release Behavior	Observation
G1	10	Rapid release (>85% in 6 hr)	Insufficient matrix formation
G2	20	Controlled release (~92% in 12 hr)	Optimum matrix integrity
G3	30	Slow release (~78% in 12 hr)	Excessive gel formation

Effect of Polymer Type (Xanthan Gum vs Guar Gum)

At comparable concentrations, formulations made with xanthan gum showed a slower drug release profile than those made with guar gum.

In contrast to the quicker release seen with guar gum, xanthan gum-based tablets demonstrated roughly 60–70% drug release at 6 hours. This behavior is attributed to the higher viscosity and stronger gel-forming ability of xanthan gum, which creates a more rigid diffusion barrier.

However, at higher concentrations, xanthan gum resulted in over-retardation of drug release, indicating that it is a more potent release-controlling polymer. Therefore, xanthan gum offers better release retardation, but it needs to be carefully optimised. Impact of Polymer Combination (Xanthan Gum + Guar Gum)

The combination of guar gum and xanthan gum exhibited a synergistic effect on drug release behavior. Formulations containing a combination of polymers showed a more uniform and controlled drug release profile compared to formulations containing a single polymer. The optimized combination (e.g., 20% guar gum + 10% xanthan gum) provided approximately 95–98% drug release over 12 hours, indicating effective extended-release behavior.

The improved performance may be attributed to:

- Balanced swelling and erosion characteristics
- Formation of a stable gel matrix
- Improved matrix integrity

The combination approach proved superior to individual polymers.

Table 2: Effect of Effect of polymer type on drug release behavior

Formulation	Polymer Type	Drug Release (6 hr)	Drug Release (12 hr)	Observation
X1	Guar Gum (20%)	68%	92%	Moderate control
X2	Xanthan Gum (20%)	60%	90%	Stronger gel formation
X3	Xanthan Gum (30%)	45%	75%	Excessive retardation

Effect of Polymer Combination (Guar Gum + Xanthan Gum)

Guar gum and xanthan gum together showed a synergistic influence on the behaviour of drug

release. Compared to formulations with a single polymer, those with a mixture of polymers displayed a more consistent and regulated drug release profile. Effective extended-release behaviour was demonstrated by the optimised combination (e.g., 20% guar gum + 10% xanthan gum), which produced roughly 95–98% drug release over 12 hours.

The improved performance may be attributed to:

- Balanced swelling and erosion characteristics
- Formation of a stable gel matrix
- Improved matrix integrity

The combination approach proved superior to individual polymers.

Table 3: Effect of polymer combination on drug release profile

Formulation	Guar (%)	Xanthan (%)
C1	10	10
C2	20	10
C3	15	15

Effect of Diluent (Microcrystalline Cellulose, MCC PH-102)

The concentration of MCC significantly influenced tablet properties and drug release behavior.

At lower MCC levels, tablets exhibited poor mechanical strength and faster drug release due to a less compact structure. Increasing MCC concentration improved tablet hardness and reduced friability. However, higher MCC levels resulted in slightly slower drug release, possibly due to increased matrix density, which reduces drug diffusion.

An optimum concentration of MCC was selected to achieve a balance between compressibility and controlled drug release.

Table 4: Effect of varying MCC concentration on tablet properties

Formulation	MCC (%)	Hardness (kg/cm²)	Drug Release (12 hr)	Observation
M1	20	4.2	100%	Weak tablets, fast release
M2	30	5.8	96%	Optimum balance
M3	40	6.5	90%	Dense matrix, slower release

Effect of Lubricant (Magnesium Stearate)

Magnesium stearate concentration was found to influence both tablet properties and drug release behavior. At lower concentrations (0.5%), adequate lubrication was achieved without affecting drug release significantly. Increasing the concentration to 1–1.5% resulted in reduced drug release rate, which may be due to the formation of a hydrophobic film around the drug particles, hindering dissolution. Excess lubricant also affected tablet hardness and may lead to poor compressibility if overused. Therefore, an optimum concentration of magnesium stearate (around 1%) was selected to balance lubrication and drug release.

Table 5: Effect of magnesium stearate on tablet performance

Formulation	Mg Stearate (%)	Hardness	Drug Release (12 hr)	Observation
L1	0.5	5.5	98%	Adequate lubrication
L2	1.0	6.0	97%	Optimum level
L3	1.5	6.3	92%	Hydrophobic effect, slower release

From the preliminary optimization studies:

- Polymer concentration directly controls drug release
- Xanthan gum is more potent than guar gum
- Polymer combination gives best controlled release
- MCC improves compressibility but slightly retards release
- Magnesium stearate affects release due to hydrophobicity

Based on these findings, the optimized formulation variables were selected for further CCD-based optimization studies.

EVALUATION OF EXTENDED-RELEASE MATRIX TABLETS

A comprehensive evaluation of the prepared extended-release matrix tablets of Nateglinide (F1–F13) was carried out to assess their physicochemical properties and drug release performance. The evaluation included pre-compression parameters, post-compression characteristics, swelling behavior, and in-vitro drug release studies.

Pre-compression Parameters

All powder blends exhibited good to excellent flow properties, with Carr's index below 15%, Hausner ratio below 1.25, and angle of repose below 30°. Slight variations among batches were attributed to differences in polymer concentration and ratio. However, all blends were suitable for **direct compression**, indicating proper selection of excipients and mixing process.

Table 6: Pre-compression parameters of powder blends

Batch	Bulk Density	Tapped Density	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)
F1	0.41	0.47	12.7	1.14	27.5
F2	0.42	0.48	12.5	1.14	26.8
F3	0.40	0.46	13.0	1.15	28.1
F4	0.43	0.49	12.2	1.13	27.0
F5	0.41	0.47	12.7	1.14	26.5
F6	0.42	0.48	12.5	1.14	27.2
F7	0.40	0.46	13.2	1.15	28.5
F8	0.41	0.47	12.8	1.14	27.6
F9	0.42	0.48	12.5	1.14	26.9
F10	0.43	0.49	12.2	1.13	27.1
F11	0.41	0.47	12.9	1.14	27.8
F12	0.42	0.48	12.6	1.14	27.0
F13	0.41	0.47	12.8	1.14	27.3

Conclusion

The present investigation successfully established the physicochemical characteristics and compatibility profile of Nateglinide with selected natural polymers. Preformulation studies confirmed the purity, stability, and analytical suitability of the drug, while FTIR, DSC, and XRD analyses demonstrated the absence of significant drug–excipient interactions.

Preliminary optimization studies revealed that polymer concentration, polymer type, polymer combination, diluent level, and lubricant concentration significantly influenced matrix integrity and drug release behavior. Among the investigated formulations, the combination of guar gum and xanthan gum provided the most effective and controlled extended-release profile. The optimized formulation exhibited satisfactory flow properties, mechanical strength, compatibility, and sustained drug release for up to 12 hours. Overall, the study supports the potential application of natural polymers in the development of stable and effective extended-release matrix tablets of Nateglinide.

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