OriginalArticle

Development and Characterization of Natural Polymer Based Nifedipine Sustained Release Matrix Tablet

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Abstract

In this study, Xanthan gum (xg), tamarind gum (TG), and fenugreek gum were used to create a sustained release matrix tablet of nifedipine (NFD). With different ratios of drug and polymer, sustained release tablets were created using the direct compression method. When creating the formulation for sustained release, drug and polymer ratios were optimized. A drug release formulation that was optimized for time was discovered. Three different rate-controlling materials combined with a triple mixture of two additional rate-controlling materials were used to modulate the release rates. For the dissolution rate study, 0.1N HCl pH 1.2 was used for two hours, followed by 12 hours in phosphate buffer pH 6.8. We observed and took note of the effects of three different polymer concentrations as well as polymer blend concentration. Using the Higuchi expression, the data on dissolution was examined. Sustained release matrix tablets that contained a polymer blend of Xanthan gum, Tamarind gum, and Fenugreek gum were found to successfully sustain the release of medication for up to 12 hours. Formulation F3 contained 25% fenugreek mucilage and 20% xanthan gum, respectively, out of all the prepared formulations. By way of diffusion, erosion, and release, the drug's release rate conforms to Higuchi kinetics. In comparison to other batch products that had been prepared, the profile of formulation F3 was appropriate and strong.

Key words: Sustained release; Xanthan gum; Tamarind seed gum; Fenugreek seed gum.

INTRODUCTION

The dosage formulations for sustained-release (SR) drugs can produce the best therapeutic effects, maintain efficacy over a longer period of time, and reduce toxicity. For oral sustained-release dosage forms administered via the gastrointestinal (GI) route, oral hydrophilic matrix tablets are among the most popular delivery methods. It provides precise drug release modulation due to hydration of the constituent polymer(s), flexibility to obtain the preferred drug release profiles, economic effectiveness, and patient satisfaction, and provided a constant, prolonged, and uniform therapeutic effect in blood levels of the drug as opposed to conventional systems.The naturally occurring sources of polysaccharides, include cellulose ethers, xanthan gum, tamarind seed gum, fenugreek seed gum, scleroglucan, locust bean gum, and guar gum, among others [1].People of all ages are suffering from a variety of psychological disorders in the current climate due to the changing way of life and demanding daily tasks. The demand for psychotropic drugs is therefore increasing. Many novel drugs in this situation always try to take market share from established products. In terms of safety, reducing side effects, etc., it provides some extra benefits [2]. The BCS-II class drug nifedipine is not very soluble. For the treatment of hypertension, it is an L-type calcium channel blocker. With a bioavailability between 84% and 86% and a half-life of six hours, it is a good substance. A twice- or three-times-daily administration is therefore required. As a result, due to improved patient compliance and clinical safety, it is a suitable candidate for the formulation of sustained-release formulation [3].Tamarind seed gum, xanthan gum, and fenugreek mucilage are all recognized as potential hydrophilic polymers in previous research. The pharmaceutical excipients listed here are all secure and non-toxic. In order to create formulations for sustained release, these hydrophilic natural polymers can be used with both water-soluble and poorly soluble drugs.The goal of the current research was to create sustained release matrix tablets of nifedipine that could be taken once daily. To do this, different combinations of tamarind seed gum, fenugreek mucilage, and xanthan gum were used, along with other excipients such as lactose, MCC, magnesium stearate, and talc [4].

MATERIAL AND METHOD

Materials

The Haridwar-based Akums Drugs & Pharmaceuticals Ltd. gave us nifedipine as a gift. Akshar Chem Pvt Ltd, an Indian company, provided the tamarind seed gum, fenugreek seed gum, and xanthan gum. Himedia Chemicals provided Talc,

Microcrystalline cellulose, and Magnesium stearate. Analytical-grade substances were used for the remainder of the chemicals and reagents.

Method

Drug excipient compatibility studies

We used the FTIR and DSC methods to investigate drug excipient compatibility studies [5, 6].

Formulation of tablets

The direct compression technique was used to create the tablets. Xanthan gum, tamarind seed gum, and fenugreek mucilage are present in varying concentrations in the formulations, which also contain various percentages of drugs and polymers (Table 1). Every powder was run through a sieve with a mesh size of 100. Uniform mixing was done when mixing the lactose and polymer. The mixture of the drug and lactose and polymer was blended for 20 minutes after the addition of the drug. Next, the mixture was put through sieve number 12. Talc and magnesium stearate were blended with the final mass. A 12 mm die punch (KBr Press) was used to compress the lubricated mass into tablets. To achieve tablet hardness between 6 and 7 kg/cm2, compression pressure was altered while each formula was being tabletized. A 500 mg tablets total weight was maintained [7].

Evaluations of powder blend

By measuring the angle of repose, Carr's index, Hausner's ratio, and other variables, the flow property of a powder blend was assessed. Table 2 displayed the findings [8].

Evaluation of sustained release matrix tablets formulation

The following parameters-weight variation, hardness, thickness, friability, and drug contentwere used to assess the prepared sustained release matrix tablets in accordance with official procedures [9]. Table 3 displayed the findings.

In vitro dissolution study

Using a six station USP XXVII type II (paddle) apparatus at 37 °C 0.5 °C and 50 rpm, an in vitro drug release study for the prepared matrix tablets was carried out for a period of 12 hours. The dissolution medium was phosphate buffer solution, pH (PBS) from the beginning of the study until the end. Three copies of each study on dissolution were performed. At regular intervals, a 10 ml aliquot of the sample was taken, filtered, and then diluted ten times with the dissolution medium before being measured spectrophotometrically at 248 nm. Both the formulation and the drug's cumulative% drug release were computed. Figure 5 exhibits the outcomes.

Dissimilarity and similarity factor

To track differences in drug release, the test product's dissimilarity factor (f1) was calculated in comparison to the reference product [10]. It determines the percentage (%) difference in the two curves at each time point and measures the relative error between the two curves.

$f1 = 100*\Sigma (Rt – Tt)/ \Sigma Rt$

Where Rt and Tt are, respectively, the reference and test products' mean% dissolution.

The mean squared difference in the percent of dissolved solids between the test and reference products, along with the logarithmic reciprocal square root of one, is known as the similarity factor (f2). A comparison between the test sample and the reference release profile was made using this calculation.

$f2 = 50 \times \log10 \{100/[1 + 1/n \times \Sigma(Rt – Tt)2]0.5\}$

The curve was fitted using PCP Disso software, where n = number of sampling points.

Stability studies

The manufactured Nifedipine sustained release tablet, containing 100 mg of medication, was kept in bottles and stored at 25 °C-60% RH and 40 °C- 75% RH. Tablets were examined for physical parameters such as thickness, hardness, brittleness, percentage of drug content, and drug release profile three months after being manufactured [11].

RESULTS AND DISCUSSION

Drug excipient compatibility study

The FTIR spectra of the medication nifedipine (NFD) revealed distinctive peaks at 3858.75 cm-1 (hydroxyl group secondary of NFD), and 3670.03 cm-1. The glucan backbone gum, including tamarind seed gum (TG) and Xanthum gum (XG), is represented at (glucan backbone of TG), 3359.77cm-1 (aromatic CH NFD), 3120.28 cm-1. Figures 1 and 2 show the combined NFD-mix (FTIR data) of nifedipine drug and polymers. There is no doubt that the drug moiety's functionalities, including peak intensities, have not changed. This implies that the excipients are suitable for use in the formulation and that the excipients and the drug are compatible.To find out whether a drug and gum interaction might be possible, more DSC was done. Thermograms did not show any evidence of drug-excipient interaction.With a heating rate of 100 °C/min from 30 to 350 °C in a nitrogen atmosphere (30 ml/min), a DSC was used to obtain the DSC curve of the pure drug nifedipine. In order to determine the temperature necessary to melt both physical mixtures and pure substances, thermograms were obtained and analyzed. The compatibility of drugs and excipients is ensured by the DSC results. Propranolol HCl and nifedipine drug with excipients are both shown in the DSC thermogram (Figures 3 and 4,

respectively, and DSC spectra of PRP, 5.34-5.36).The results of FTIR and DSC revealed that there was no chemical interaction between the drugs and excipients, and all of the characteristic peaks of the drugs were observed.

Evaluations of powder blend

By measuring the Carr's index, angle of repose, and Hausner's ratio-all necessary to produce solid dosage forms with a tolerable weight variation-the flow ability of the powder blend was assessed. [12] The results of the evaluation of the powder blend parameters for all sustained release matrix tablets showed that the bulk density and tapped density for all formulations were in the ranges of 0.46 0.01 to 0.51 0.01 and 0.40 0.01 to 0.45 0.01 respectively, and that the percent compressibility for all formulations was in the range of 15.91 0.3 to 12.37 0.4. The Hausner's ratio for all powder blends was found to be in the range of 1.

Evaluation of compressed tablets

The hardness value of the sustained release matrix tablets formulation was within the range of 6.0 0.02 to 6.2 0.03 kg/cm2, and another indicator of tablet strength is friability, which increases as fenugreek mucilage concentration increases. In the current study, we evaluated the compressed of sustained release matrix tablets using the following evaluations parameters: thickness, hardness, weight variation, friability, and drug content [13].

In vitro drug release study

The effect of polymer level on the release of the drug from matrix tablets was studied for tablets containing 15%, 20%, and 25% of the polymer. The release rate of the medication is influenced by the quantity of xanthan gum and fenugreek mucilage used. Given the polymer's extremely low viscosity, this might be caused by erosion of the material. Consequently, it can be concluded that the drug release is delayed to a greater extent the higher the percentage of polymer. The in-vitro dissolution study release data from various formulations was fitted to the mathematical models. First order, the matrix system Higuchi equation, and the Korsmeyer-Peppas model were among the kinetic models. The data from model fitting, for all nine formulations under consideration, are shown in the graph above. Overall curve fitting revealed either the Higuchi equation or the Korsmeyer-Peppas model was used to predict the drug release from the sustained release matrix tablets.The dissolution data from batches F1 to F9 were fitted using the models Korsmeyer-Peppas, Higuchi, First Order, Hixson Crowell, and Zero Order. [14] To determine which model best would describe how drugs are released from tablets, the coefficient of regression (R2) value was used as a criterion. Table 4 contains the R2 scores for various models.The results for formulation F3 with R2 value of 0.9784 confirmed that the formulation followed Higuchi matrix model indicating that Nifedipine release from controlled drug delivery system were by both diffusion and erosion mechanism. The mean diffusion exponent values (n) obtained from Korsmeyer equation ranged from 0.5831 to 0.6612 indicating that all these formulations presented a dissolution behavior controlled by Non Fick's Diffusion (When n tends towards 0.5).Data were fitted into Korsmeyer-Peppas equation to verify the diffusion mechanism. For a matrix tablet, a "n" value of less than 0.5 indicates Fick's diffusion and a "n" value of between 0.5 and 1 indicates Non-Fick's diffusion.

Stability study

The optimized Nifedipine sustained release tablet did not exhibit any changes in the physical parameters or the drug content, according to the findings of accelerated stability studies performed in accordance with ICH guidelines. Furthermore, tests on the optimized formulation stored under accelerated test conditions show that the drug release profile has not changed statistically from the in vitro studies that were conducted on it.

Table 1 Formulation table according to 3^2 factorial designs

Formulation code / Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nifedipine	80	80	80	80	80	80	80	80	80
Xanthan Gum	125	75	100	125	75	100	125	75	100
Tamarind Gum	60	75	100	60	75	100	60	75	100
Fenugreek Mucilage	75	100	125	75	100	125	75	100	125
MCC	75	80	45	70	80	34	82	85	64
Lactose	75	80	40	80	80	51	68	75	41
Mg. Stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5

Table: 2 Evaluation of powder blend

Formulations	Angle of Repose ± SD (degrees)	Bulk Density ± SD(gm/ml)	Tapped Density± SD(gm/ml)	Compressibility Index± SD (%)	Hausner's Ratio ± SD
F1	29.67 ± 0.03	0.50 ± 0.01	0.44 ± 0.03	13.5 ± 0.01	1.26 ± 0.01
F2	28.36 ± 0.03	0.49 ± 0.03	0.43 ± 0.01	13.94 ± 0.04	1.28 ± 0.23
F3	27.47 ± 0.02	0.51 ± 0.03	0.44 ± 0.01	15.90 ± 0.03	1.25 ± 0.02
F4	28.30 ± 0.03	0.45 ± 0.03	0.39 ± 0.01	15.38 ± 0.02	1.27 ± 0.20
F5	27.30 ± 0.03	0.49 ± 0.04	0.43 ± 0.03	13.95 ± 0.01	1.26± 0.10
F6	26.40 ± 0.04	0.46± 0.02	0.41 ± 0.02	12.36 ± 0.04	1.25 ± 0.10
F7	25.50 ± 0.03	0.49 ± 0.01	0.43 ± 0.01	14.40 ± 0.01	1.26 ± 0.01
F8	26.60 ± 0.03	0.48 ± 0.03	0.42 ± 0.02	14.28 ± 0.03	1.28± 0.03
F9	28.40 ± 0.04	0.50 ± 0.04	0.44± 0.03	13.5 ± 0.01	1.30 ± 0.21

Table: 3 Evaluations of compressed tablets

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Wt. variation (mg)	Friability (%)	Drug content (%)
F1	5.4 ± 0.06	6.0 ± 0.01	500 ± 0.15	0.205	97.96
F2	5.4 ± 0.07	6.1 ± 0.01	498 ± 0.16	0.185	95.04
F3	5.5 ± 0.04	6.1 ± 0.03	498 ± 0.17	0.235	98.26
F4	5.4 ± 0.06	6.3 ± 0.04	501 ± 0.15	0.456	95.56
F5	5.5 ± 0.06	6.0 ± 0.01	505 ± 0.14	0.127	97.03
F6	5.4 ± 0.07	6.0 ± 0.05	500 ± 0.15	0.354	98.01
F7	5.4 ± 0.06	6.0 ± 0.01	500 ± 0.15	0.235	94.04
F8	5.4 ± 0.06	6.2 ± 0.02	496 ± 0.17	0.274	95.54
F9	5.4 ± 0.07	6.1 ± 0.03	498 ± 0.16	0.135	95.23

Table: 4 Kinetic treatments to dissolution data for sustained release tablet

Formulations	Regression Coefficient (R^2)					Best fit Model
	Zero order Plot	First order Plot	Korsmeyer- Peppas Plot		Higuchi plot	
			(R^2)	n (release exponent)		
F1	0.9736	0.8916	0.8208	0.602	0.9960	Higuchi
F2	0.9785	0.9985	0.8126	0.633	0.9816	Higuchi
F3	0.9784	0.8675	0.8126	0.654	0.9941	Higuchi
F4	0.9776	0.8718	0.8336	0.608	0.9822	Higuchi
F5	0.9874	0.9161	0.8106	0.632	0.9732	Zero order
F6	0.9785	0.8983	0.8050	0.661	0.9812	Higuchi
F7	0.9747	0.9114	0.8357	0.586	0.9876	Higuchi
F8	0.9863	0.9103	0.8139	0.614	0.9938	Higuchi
F9	0.9947	0.9734	0.8390	0.583	0.9763	Zero order

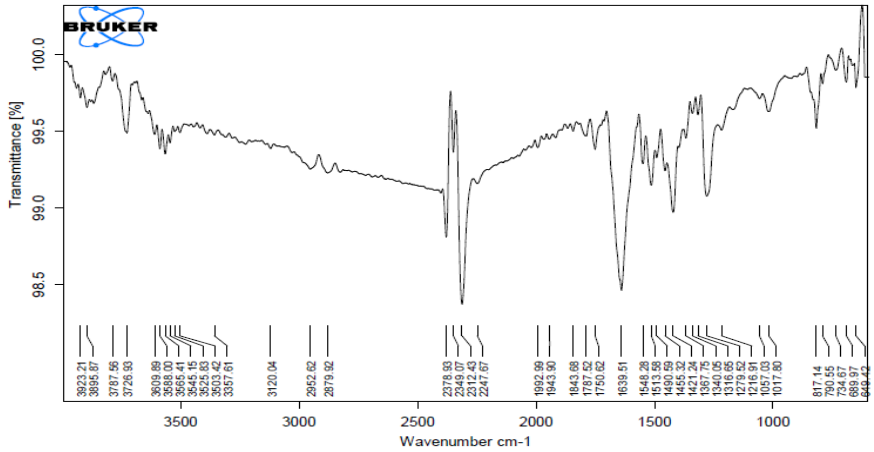

Figure 1:FTIR spectra of Nifedipine

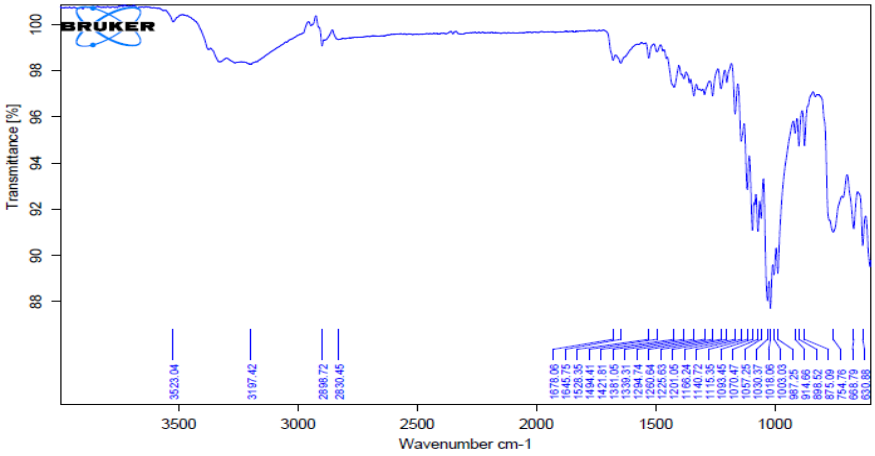

Figure 2: FTIR spectra of Nifedipine with excipients to be used in the formulation of sustained release tablets

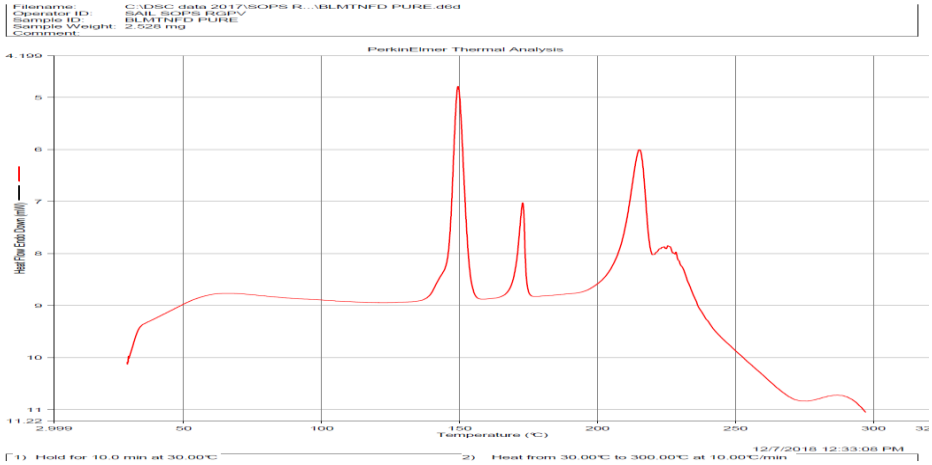

Figure 3: DSC spectra of Nifedipine pure

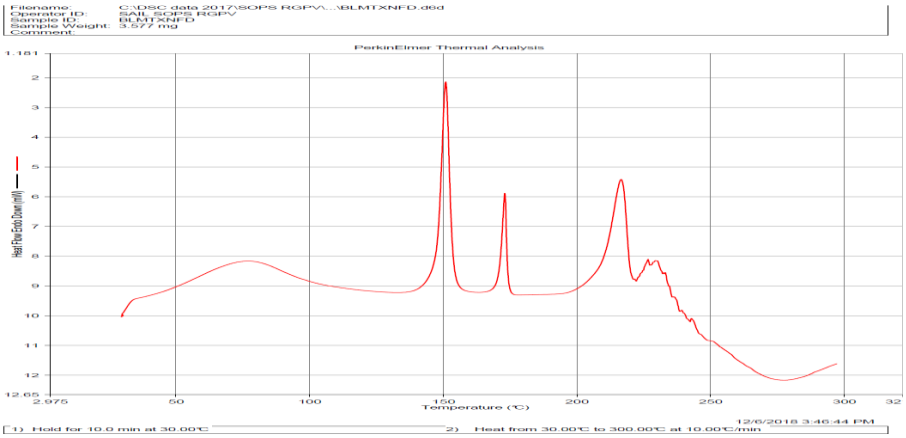

Figure 4: DSC spectra for Nifedipine drug and excipient to be used in formulation of sustained release tablets

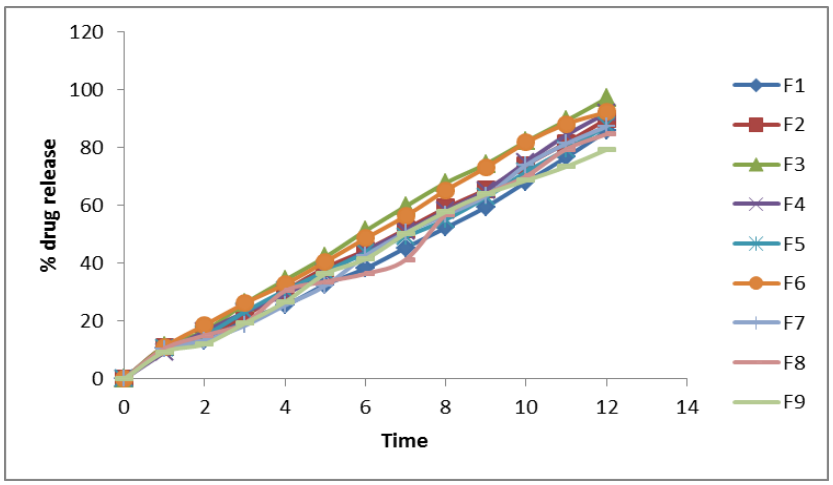

Figure 5: Dissolution profile for all formulation

CONCLUSION

The current study may lead to the conclusion that formulations made with xanthan gum, tamarind seed gum, and fenugreek mucilage polymer delayed drug release for 12 hours. The formulations with optimized drug natural gum ratios may delay the drug's release for the desired amount of time. Because both of these swellable polymers are present in the hydrophilic matrix tablets' polymer blend of xanthan gum, tamarind seed gum, and fenugreek mucilage, they slow the rate at which drugs are released from their bodies. The release study revealed that the rate at which the drug was released was decreased as the concentration of xanthan gum, tamarind seed gum, and fenugreek mucilage polymer was raised. The increased viscosity of tamarind seed gum and the slower rate of xanthan gum erosion may have contributed to the stability of the hydrated gel and the drug's 12-hour release. Among these formulations, F3 contains a ratio of xanthan gum, tamarind seed gum, and fenugreek mucilage, which showed a 95.8611% release in 12 hours and a release profile that adheres to Higuchi kinetics.

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