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Formulation And Evaluation Of Xanthan Gum Based Extended Release Tablets Of Venlafaxine Hcl

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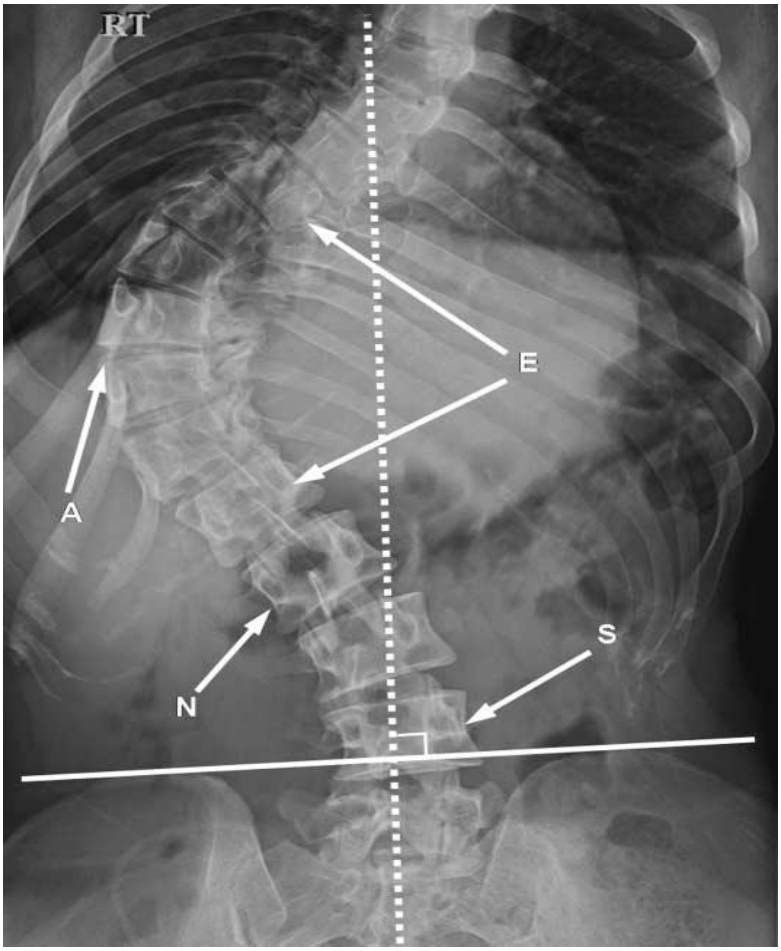
ABSTRACT

The present study aimed to formulate and evaluate Venlafaxine extended release matrix tablets using Xanthan gum as a natural release-retarding polymer. Extended release tablets were prepared by the wet granulation method using different concentrations of Xanthan gum to achieve sustained drug release. The prepared powder blends were evaluated for pre-compression parameters including angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio, which indicated good flow and compressibility characteristics suitable for tablet compression. The compressed tablets were further evaluated for post-compression parameters such as thickness, hardness, friability, weight variation, drug content, and swelling index. All formulations showed satisfactory physical characteristics within acceptable pharmacopeial limits. In vitro dissolution studies demonstrated that all formulations exhibited an initial burst release followed by sustained drug release behavior. The release rate decreased with increasing concentration of Xanthan gum due to the formation of a hydrophilic gel matrix that controlled drug diffusion and matrix erosion. Formulation F4 showed an optimized drug release profile with 18.42% drug release during the first hour and 97.62% cumulative drug release at the end of 12 hours. The optimized formulation exhibited satisfactory mechanical strength, good swelling behavior, and effective sustained release characteristics. The study concluded that Xanthan gum can be effectively utilized as a natural polymer for the development of extended release matrix tablets of Venlafaxine HCl with prolonged drug release and improved therapeutic performance..

Keywords: *Venlafaxine HCl, Extended release matrix tablets, Xanthan gum, Natural polymer, setc*

INTRODUCTION

Depression is one of the most common psychiatric disorders affecting millions of people worldwide and is associated with significant emotional, social, and economic burden. Effective management of depression often requires long-term pharmacotherapy to maintain therapeutic drug levels and improve patient compliance. [1] Venlafaxine is a serotonin–norepinephrine reuptake inhibitor widely used in the treatment of major depressive disorder, generalized anxiety disorder, panic disorder, and social anxiety disorder. Venlafaxine HCl possesses good water solubility and is rapidly absorbed after oral administration; however, its relatively short biological half-life of approximately 5 hours necessitates frequent dosing, which may lead to fluctuations in plasma drug concentration and reduced patient compliance. Extended release drug delivery systems have gained considerable attention due to their ability to maintain uniform plasma drug concentrations, reduce dosing frequency, minimize side effects, and improve therapeutic efficacy.[2] Matrix tablet systems are among the most widely used approaches for developing extended release formulations because of their simplicity, cost-effectiveness, ease of manufacturing, and ability to control drug release effectively.[3] In hydrophilic matrix systems, polymers play a critical role in controlling the release of the drug through swelling, diffusion, and erosion mechanisms. Natural polymers are increasingly preferred in pharmaceutical formulations because of their biocompatibility, biodegradability, non-toxicity, cost-effectiveness, and environmental friendliness. [4,5] Among the various natural polymers, Xanthan gum has gained significant importance as a release-retarding agent in controlled drug delivery systems. [6] The present study was therefore aimed at the formulation and evaluation of Xanthan gum-based extended release matrix tablets of Venlafaxine HCl using the wet granulation technique. Different concentrations of Xanthan gum were incorporated to investigate their effect on tablet properties and drug release behavior.



MATERIALS AND METHODS

Venlafaxine Hcl was received as a gift sample from Cipla Ltd, Mumbai, India. Xanthan gum was obtained from Rajesh Chemicals Mumbai. All other materials used was of analytical grade and procured from commercial sources.

Preparation of Extended Release Tablets

The extended release matrix tablets of Venlafaxine were prepared by the wet granulation method using Xanthan gum as a natural release-retarding polymer. Accurately weighed quantities of Venlafaxine HCl, Xanthan gum, and microcrystalline cellulose (MCC PH101) were passed through sieve no. 60 separately to ensure uniform particle size distribution. The sieved ingredients were blended thoroughly in a mortar for approximately 15 minutes to obtain a uniform powder mixture. A binder solution of PVP K30 was then added gradually to the powder blend with continuous mixing until a coherent damp mass was formed. The wet mass was then passed through sieve no. 16 to obtain granules of uniform size. The prepared granules were dried in a hot air oven at 45–50°C until suitable moisture content was achieved. After drying, the granules were again passed through sieve no. 20 to break aggregates and obtain uniform granules. Finally, talc and magnesium stearate were added as glidant and lubricant, respectively, and mixed gently for 3–5 minutes. The lubricated granules were compressed into tablets using a rotary tablet compression machine equipped with 8mm concave punches to obtain extended release matrix tablets. [7,8]

Table 1. - Formulation Venlafaxine Hcl Extended Release Tablets

Ingredients (mg/tablet)	F1	F2	F3	F4	F5
Venlafaxine HCl	75	75	75	75	75
Xanthan Gum	30	45	60	75	90
MCC PH101	183	168	153	138	123
PVP K30	6	6	6	6	6

Talc	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3
Total Weight	300	300	300	300	300

Evaluation of Extended Release Tablets

Pre-compression Evaluation

Bulk Density and Tapped Density

Bulk density of the prepared powder blend was determined by the loose bulk volume method. Accurately weighed quantity of powder blend was transferred into a clean and dry 100 mL graduated measuring cylinder without compacting the material. The initial volume occupied by the powder was noted as bulk volume. Bulk density was calculated by dividing the weight of the powder by the bulk volume. While tapped density was determined by transferring an accurately weighed quantity of powder blend into a graduated measuring cylinder. The cylinder was tapped mechanically using a tapped density apparatus until no further change in volume was observed. The final tapped volume was recorded and tapped density was calculated using equation. [9]

Angle of Repose

The angle of repose was determined by the fixed funnel method. The funnel was fixed at a suitable height above the graph paper placed on a flat surface. The powder blend was allowed to flow freely through the funnel until a conical heap was formed. The height (h) and radius (r) of the powder cone were measured, and the angle of repose was calculated using the following equation:

$\tan \theta = h/r$

where, θ is the angle of repose, h is the height of the powder cone, and r is the radius of the cone.

Hausner Ratio

Hausner ratio was determined using the values of bulk density and tapped density obtained experimentally. It indicates the flow characteristics of the powder blend. Hausner ratio was calculated. A Hausner ratio less than 1.25 indicates good flow properties of the powder blend.

Compressibility Index (Carr's Index)

Compressibility index was determined from the bulk density and tapped density values of the powder blend. It provides information regarding compressibility and flowability characteristics of the granules. Carr's compressibility index was calculated using the equation. Lower values of Carr's index indicate good flowability and compressibility of the powder blend.[10,11]

Post Compression Evaluation

Hardness

The hardness of the prepared tablets was determined using a Monsanto hardness tester. Randomly selected tablets from each formulation batch were placed individually between the anvils of the hardness tester, and pressure was applied until the tablet fractured. The force required to break the tablet was recorded in kg/cm². The average hardness value of three tablets was calculated and reported. [12]

Thickness

The thickness of the prepared tablets was measured using a Vernier caliper. Randomly selected tablets from each formulation were individually placed between the jaws of the caliper, and the thickness was recorded in millimeters (mm). The average value was calculated to determine uniformity in tablet dimensions.

Friability

Friability of the tablets was determined using a Roche friabilator. Pre-weighed tablets equivalent to approximately 6.5 g were placed in the friabilator and rotated at 25 rpm for 4 minutes (100 revolutions). After completion of the test, the tablets were dedusted and reweighed. The percentage friability was calculated using the following equation: [13]

$$Friability\ (\%) = \frac{W1 - W2}{W1} X\ 100$$

where, W1 is the initial weight of tablets and W2 is the final weight after friabilization.

Weight Variation

Twenty tablets from each formulation batch were selected randomly and weighed individually using a digital weighing balance. The average tablet weight was calculated, and individual tablet weights were compared with the average weight to

determine weight variation. The test was performed according to pharmacopeial specifications to ensure uniformity of dosage units.

Drug Content

Ten tablets from each formulation batch were weighed and finely powdered. A quantity of powder equivalent to 75 mg of Venlafaxine HCl was accurately weighed and transferred into a 100 mL volumetric flask containing suitable solvent such as methanol or phosphate buffer. The solution was shaken thoroughly to dissolve the drug completely and filtered through Whatman filter paper. Appropriate dilutions were prepared and analyzed using a UV-visible spectrophotometer at 224 nm. The drug content was calculated using the calibration curve of Venlafaxine HCl. [14]

Swelling Index

The swelling behavior of the prepared matrix tablets was evaluated by determining the swelling index. Tablets were weighed individually and placed in a Petri dish containing phosphate buffer pH 6.8 maintained at room temperature. At predetermined time intervals, the tablets were removed carefully, excess surface liquid was blotted using filter paper, and the swollen tablets were reweighed. The swelling index was calculated using the following equation [15]

$$Swelling\ Index\ (\%) = \frac{Wt - W0}{Wt} X\ 100$$

where, W_0 is the initial weight of the tablet and Wt is the weight of the swollen tablet at time t.

In Vitro Drug Release Study

In-Vitro drug release studies were carried out using USP tablet dissolution test apparatus) at 50 rpm. The dissolution medium consisted of 900 ml phosphate buffer pH 6.8. During the study the temperature of the medium was maintained at 37±0.5^{0}C. The sample of 5 ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. After suitable dilution, the diluted samples were assayed at 224 nm against blank and cumulative percent drug release was calculated. [16,17]

RESULTS AND DISCUSSION

Extended release tablets of venlafaxine Hcl were prepared by using natural xanthan gum as a rate controlling polymer. (Table 1). Six formulations were prepared by wet granulation method using various concentration of xanthan gum. The pre-compression parameters of the prepared powder blends for Venlafaxine matrix tablets were evaluated to determine their flow and compressibility characteristics. The angle of repose values ranged from 25.86 ± 0.29° to 28.14 ± 0.42°, indicating good flow properties of the powder blends. Bulk density and tapped density values were found in the range of 0.42 ± 0.01 to 0.46 ± 0.03 g/cm³ and 0.49 ± 0.04 to 0.53 ± 0.02 g/cm³, respectively, demonstrating satisfactory packing ability of the granules. Carr's index values ranged between 13.20 ± 0.44% and 14.28 ± 0.36%, while Hausner ratio values were found between 1.12 ± 0.02 and 1.16 ± 0.02. These values indicated good compressibility and excellent flowability of the powder blends suitable for tablet compression. The results confirmed that all formulations possessed acceptable pre-compression characteristics, ensuring uniform die filling and consistent tablet quality during compression (Table 2). IR spectroscopy was used to perform the the study of drug-excipient compatibility and it was found that the drug venlafaxine was compatible with natural xanthan gum showed no drug-excipient interaction.

Table 2. Precompression Parameters of Powder Blend

Formulation	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner Ratio
F1	28.14 ± 0.42	0.42 ± 0.01	0.49 ± 0.04	14.28 ± 0.36	1.16 ± 0.02
F2	27.62 ± 0.38	0.43 ± 0.04	0.50 ± 0.01	14.00 ± 0.41	1.15 ± 0.01
F3	26.84 ± 0.45	0.44 ± 0.02	0.51 ± 0.02	13.72 ± 0.52	1.14 ± 0.02
F4	26.25 ± 0.33	0.45 ± 0.02	0.52 ± 0.03	13.46 ± 0.48	1.13 ± 0.03
F5	25.86 ± 0.29	0.46 ± 0.03	0.53 ± 0.02	13.20 ± 0.44	1.12 ± 0.02

The post-compression parameters of the prepared Venlafaxine extended release matrix tablets were evaluated to assess the quality, mechanical strength, and uniformity of the compressed tablets (table 3). The results demonstrated that all formulations exhibited satisfactory physical characteristics and complied with acceptable pharmacopeial limits. The thickness of the tablets was found to be in the range of 4.18 ± 0.05 mm to 4.40 ± 0.07 mm, indicating uniform die filling and

consistent compression during tablet manufacturing. A slight increase in tablet thickness was observed with increasing concentration of Xanthan gum, which may be attributed to the higher swelling and compressibility characteristics of the polymer. The hardness of the formulations ranged between 5.48 ± 0.21 kg/cm² and 5.86 ± 0.22 kg/cm², indicating adequate mechanical strength to withstand handling, packaging, and transportation. Formulation F2 showed the highest hardness value, whereas F4 exhibited comparatively lower hardness among all batches. Friability values of all formulations were found between 0.56 ± 0.03% and 0.78 ± 0.04%, which were below the official limit of 1%, demonstrating good mechanical resistance and satisfactory tablet integrity. The decrease in friability with increasing polymer concentration suggested improved cohesiveness and binding properties of Xanthan gum within the tablet matrix. The average tablet weight of all formulations ranged from 298.6 ± 2.42 mg to 301.2 ± 1.96 mg, indicating minimal weight variation and uniform distribution of the powder blend during compression. The obtained values were within acceptable pharmacopeial limits, confirming reproducibility of the formulation process. Drug content analysis showed values between 98.12 ± 0.84% and 99.54 ± 0.58%, indicating uniform drug distribution throughout the formulations and absence of significant drug loss during processing. Among all formulations, F4 exhibited the highest drug content, demonstrating efficient blending and content uniformity. The swelling index of the formulations increased progressively from 118.42 ± 3.24% for F1 to 188.92 ± 5.02% for F5 with increasing concentration of Xanthan gum. This increase in swelling behavior may be attributed to the hydrophilic nature and high water uptake capacity of Xanthan gum, resulting in formation of a viscous gel layer around the tablet matrix. The enhanced swelling behavior is advantageous for sustaining drug release over an extended period by controlling drug diffusion and matrix erosion. The post-compression evaluation results confirmed that all formulations possessed satisfactory physical properties, good mechanical strength, acceptable drug content uniformity, and significant swelling characteristics suitable for the development of extended release matrix tablets of Venlafaxine HCl.

Table 3. Evaluation of Extended Release Venlafaxine Hcl Tablets

Formulation	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Weight Variation (mg)	Drug Content (%)	Swelling Index (%)
F1	4.18 ± 0.05	5.52 ± 0.18	0.78 ± 0.04	298.6 ± 2.42	98.12 ± 0.84	118.42 ± 3.24
F2	4.22 ± 0.04	5.86 ± 0.22	0.72 ± 0.03	300.4 ± 2.18	98.84 ± 0.76	136.84 ± 3.68
F3	4.28 ± 0.06	5.54 ± 0.16	0.68 ± 0.05	301.2 ± 1.96	99.26 ± 0.64	154.26 ± 4.12
F4	4.34 ± 0.05	5.48 ± 0.21	0.62 ± 0.04	299.8 ± 2.04	99.54 ± 0.58	171.48 ± 4.54
F5	4.40 ± 0.07	5.82 ± 0.19	0.56 ± 0.03	300.6 ± 1.88	99.18 ± 0.62	188.92 ± 5.02

* All values are expressed as mean ± SD, n=3

In Vitro Drug Release Study

The in vitro drug release study of the prepared Venlafaxine extended release matrix tablets was carried out for 12 hours to evaluate the effect of varying concentrations of Xanthan gum on drug release behavior. All formulations showed an initial burst release during the first hour followed by sustained drug release over the remaining study period. The initial burst effect may be due to the rapid dissolution of drug particles present on the surface of the tablet before complete hydration of the polymer matrix. Formulation F1 exhibited the fastest drug release, releasing 96.24% drug within 8 hours due to the lower concentration of Xanthan gum, which formed a weaker gel barrier. As the concentration of Xanthan gum increased from F2 to F5, the drug release rate gradually decreased because of enhanced swelling and formation of a more viscous hydrophilic matrix that retarded drug diffusion. Formulation F4 showed an optimized release profile with 18.42% drug release during the first hour and 97.62% cumulative drug release at the end of 12 hours. The sustained release behavior of F4 may be attributed to the formation of a strong gel layer by Xanthan gum, which effectively controlled drug diffusion and matrix erosion. In contrast, F5 showed release retardation copare to batch F4 due to higher polymer concentration, resulting in incomplete drug release within 12 hours. The results demonstrated that increasing the concentration of Xanthan gum significantly prolonged the release of Venlafaxine HCl from the matrix tablets. Among all formulations, F4 was considered the optimized formulation as it provided a desirable balance between initial burst release and sustained drug release over 12 hours, making it suitable for extended release drug delivery applications. The results are shown in figure 1.

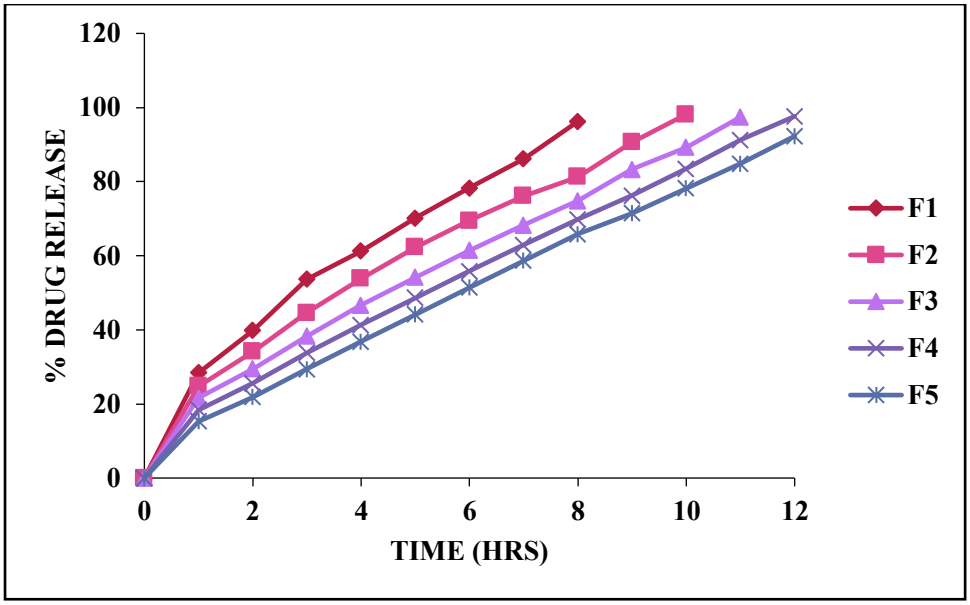


Fig.1- In Vitro Dissolution Profile of Venlafaxine Hcl Extended Release Tablets

CONCLUSION

The present study successfully formulated Venlafaxine extended release matrix tablets using Xanthan gum as a natural release-retarding polymer. All formulations exhibited satisfactory pre-compression and post-compression characteristics with acceptable mechanical strength and drug content uniformity. The in vitro drug release study demonstrated that increasing the concentration of Xanthan gum effectively prolonged drug release by forming a hydrophilic gel matrix. Among all formulations, batch F4 showed an optimized release profile with controlled initial burst release and sustained drug release for up to 12 hours. Therefore, Xanthan gum was found to be an effective natural polymer for the development of extended release matrix tablets of Venlafaxine HCl.

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