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Original Article

FORMULATION AND *IN VITRO* EVALUATION OF VENLAFAXINE MATRIX TABLETS USING GUM KONDAGOGU AS EXCIPIENT

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ABSTRACT

Objective: A naturally obtained Gum Kondagogu (GK) investigated as a novel matrix-forming material for sustained drug delivery using Venlafaxine HCl (VH) as a model drug.

Methods: The VH tablets were prepared with different concentrations of GK along with other excipients such as sodium alginate and zinc acetate. The compressed tablets were then evaluated for pre-compression parameters, including flow properties and post-compression parameters, such as hardness, friability, and drug content uniformity. Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) studies were conducted to assess potential interactions between the excipients and the drug. Additionally, the lead formulation underwent accelerated stability studies at 40±2 °C/75±5% RH for 3 mo to evaluate the stability and consistency of drug release.

Results: The compressed tablets of VH with GK were found to have acceptable pre-and post-compression parameters. Among the various formulations tested, the one containing 0.25%w/v of GK, 0.3% of sodium alginate, and 0.3% of zinc acetate demonstrated a release profile closely matching that of a commercial tablet dosage form. FTIR and DSC studies confirmed that there were no interactions between the excipients and the drug. The lead formulation maintained stability over 3 mo of accelerated stability studies, with no significant changes in drug release observed during this period.

Conclusion: GK has shown potential as a controlled release agent for oral dosage forms, particularly for drugs like VH. The formulation containing 0.25%w/v of GK, 0.3% of sodium alginate, and 0.3% of zinc acetate exhibited a release profile similar to that of a commercial product and maintained stability under accelerated conditions. These findings suggest that GK could be a viable option for developing control-release oral formulations.

Keywords: Gum Kondagogu, Venlafaxine HCl, Sodium Alginate, Zinc Acetate, Matrix Tablets, Controlled release

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INTRODUCTION

Oral route is the most preferred route for administration of drugs. Tablets are the most popular oral formulations available in the market and preferred by patients and physicians alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses in a single day and, therefore, have several disadvantages. Oral controlled-release matrix tablets represent a significant advancement in pharmaceutical formulation, designed to optimize drug delivery by providing sustained and controlled release [1] of active ingredients over an extended period. They offer extended duration of action, better patient compliance, maintain stable drug levels systemic circulation, reduce dose and dosing frequency and side effects, and enhancing therapeutic efficacy and safety for high potency drugs. The key advantage of controlled-release matrix tablets lies in their ability to modulate the release of the API, ensuring a constant and predictable plasma concentration over an extended duration [2, 3].

Pharmaceutical scientists utilize various techniques to achieve controlled release from matrix tablets, such as altering the composition of the matrix, incorporating polymers with specific release-modifying properties [4-6], or employing coating technologies to further refine the release kinetics. In clinical practice, oral controlled-release matrix tablets have been successfully employed across a wide range of therapeutic areas, including cardiovascular diseases, pain management, psychiatric disorders (like depression and anxiety), and chronic conditions requiring sustained drug therapy.

Venlafaxine Hydrochloride (VH) extended-release tablets are for oral administrations that contain VH, a structurally novel antidepressant. VH is a white to off-white crystalline solid with a solubility of 572 mg/ml in water (adjusted to ionic strength of 0.2 M with sodium chloride). Its octanol: water (0.2 M sodium chloride) partition coefficient is 0.43. Maximum daily dose for VH range of 75 to 450 mg/d. Maximum commercially available strength is 250 mg. based on the pharmacokinetics studies, to maintain study state concentration patients should take 75 mg tablet every 4 h interval. So, it is essential to develop a control/extended-release formulation to allow consistent drug release for 24 h to increase patient compliance [7].

Hence, the aim of present study was to develop a matrix control/extended-release formulation using different natural gums with combinations of natural gums for 24 h release. Further the formulated blend converted to tablets and evaluated for *in vitro* release studies.

Matrix systems are also called monoliths since the drug is homogeneously dispersed throughout a rate-controlling medium. They are very common and employ waxes such as beeswax, carnauba wax, hydrogenated castor oil, etc., which control drug dissolution by controlling the rate of dissolution fluid penetration into the matrix by altering the porosity of tablet, decreasing its wettability or by itself getting dissolved at a slower rate. This research works focused matrix diffusion controlled systems [8-11].

Here, the drug is dispersed in an insoluble matrix of rigid, non-swellable hydrophobic materials or swellable hydrophilic substances. The material generally used for matrix formulations are hydrophilic gums [12-14] and may be of natural origin (guar gum, tragacanth), semisynthetic (HPMC, CMC, Xanthan Gum) or synthetic (Polyacrylamides).

Materials

VH soured from Yarrow Chemicals Private Limited, Mumbai, India, Sodium Alginate, Zinc acetate sourced from Ashland India, GK sourced from Alfa Chemicals Ltd, Lactose and magnesium stearate gift samples received from Hetero labs limited.

Methods

Preformulation studies for GK

Solubility

Solubility test was performed for the GK in various organic solvents like Water, Methanol, ethanol, Acetone, and Dichloro methane. The solvents were taken in different test tubes, and to these test tubes small amount of VH drug was added and shake vigorously and kept aside for a while. GK was freely soluble in the solvents like Water [15-17].

Swelling index

Swelling index test was performed for the GK, by taking measured quantity of gum taken in a measuring cylinder and water was added to the measuring cylinder. The initial volume of GK measured. After adding water to the measuring cylinder, and it was kept aside for 24 h. and the swelling property evaluation. And the final percentage of swelling index was calculated by using the following formula [18-20].

$$\text{Swelling index} = \frac{\text{Initial volume} - \text{Final volume}}{\text{Initial volume}} \times 100$$

Analytical method development

U. V Spectrophotometric method developed for the analysis of VH in pure form and in pharmaceutical formulations. VH exhibited maximum absorbance at 222.00 nm with an apparent molar absorptivity of 1.2399 x 105. Beer's law was obeyed in the concentration range of 2-26 µg/ml, results of the analysis were validated statistically and by recovery studies. This method is successfully employed for the determination of VH in various pharmaceutical preparations [23-27].

In view of the above fact, some simple analytical methods are in need for quantitative estimation. The objectives of the present work were to develop a simple Spectrophotometric method with greater precision and accuracy that can be used for the routine Q. C analysis of the formulations containing VH in which the drug dissolved in phosphate buffer of pH 6.8, and then the absorbance is measured at 222.0 nm.

Standard and sample solution of VH

About 10 mg of VH (bulk or formulation) was weighed accurately and dissolved in 100 ml of phosphate buffer of pH 6.8 in a volumetric flask to give a stock solution having 0.1 mg/ml concentration. Aliquots of stock solution were suitably diluted with buffer to give final concentrations of 2-26 µg/ml, the absorbance of the diluted solutions measured at 222.0 nm against blank.

Assay procedure

20 tablets were weighed and ground to form fine powder. Tablet powder equivalent to 10 mg of drug was transferred to 100 ml volumetric flask and it is dissolved and made up to mark with buffer. The solution was filtered through Whatman filter paper no: 41 and it is suitably diluted to obtain a solution having a concentration of 10 µg/ml. Now this solution was analyzed by the method described above. The amount of VH was computed from the calibration curve [28, 29].

Preparation of matrix tablets

Formulating controlled-release matrix tablets involves several key steps, which are generally followed to achieve the desired drug release profile. Controlled drug delivery is a topic of current interest in pharmaceutical research and industry. Excipients play a crucial role in the formulation of matrix tablets. Polymers have vital role in the control release mechanism, for this investigation, GK, Sodium alginate and Zinc acetate selected as control release polymers, Lactose selected as diluent/filler and magnesium stearate selected as glidant to increase the flow properties of prepared blend [30-34].

Wet granulation process selected for preparation matrix tablets; calculated quantities of API and polymers were dry mixed/blended for 5 min to make homogeneous blend, add required amount of purified water and knead the wet mass for uniformity, and pass the wet mass through the sieve no 20 to make granules, then the granules were dried at 50 °C for about 10 to 15 min in hot air oven. Dried granules further processed through sieve no 40 to make then uniform size. Add calculated amount of magnesium stearate to the blend and blend for 10 min [35].

The final blend was compressed into tablets by direct compression technique using embossed C25 concave punches in multi-station tablet compression machine (Rimek).

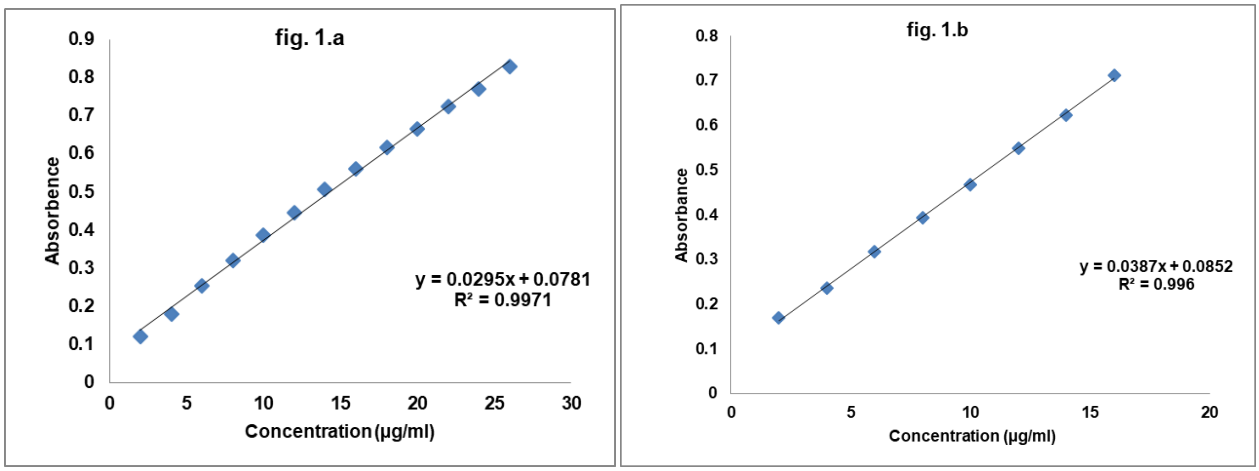

Fig. 1: a. Calibration curves estimation 6.8 pH buffer of VH (a), estimation of 0.1 N pH buffer for VH (b)

Table 1: Formulation table

Ingredients	DG1	DG2	DG3	DGS1	DGS2	DGS3	DGSZ1	DGSZ2	DGSZ3
Venlafaxine	100	100	100	100	100	100	100	100	100
Gum kondagogu	25	50	100	25	25	25	25	25	25
Sodium alginate	-	-	-	10	20	30	30	30	30
Zinc acetate	-	-	-	-	-	-	20	30	40
Lactose*	171	146	96	161	151	141	121	111	101
Mg. Stearate	4	4	4	4	4	4	4	4	4
Total tablet weight	300	300	300	300	300	300	300	300	300

*Lactose acts as a bulking agent, based on composition lactose quantity compensated to get uniform tablet weight.

Precompression parameters

Bulk density

Bulk density is determined by graduated cylinder containing a known mass of powder whose initial volume is noted. Cylinder is fixed on the mechanical tapper apparatus. Then the final volume is noted, and this bulk volume. Then bulk density is calculated is using.

$$\text{Bulk density}(\rho) = \frac{\text{Mass of powder(w)}}{\text{Bulk volume}}$$

Angle of repose (θ)

These are the simple and related techniques for measuring the resistance to particle moment. Angle of repose is defined as the maximum angle possible between the surface of a pile of powder and horizontal plane,

$$\text{Tan}\,\theta = \frac{h}{r}$$

$$\theta = \frac{\tan^{-1}h}{r}$$

Where h =height of pile, r =radius of base of pile, θ =angle of repose

Carr's consolidation index

It is defined as

$$\text{Consolidation index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's Ratio

It is defined as the ratio of the tapped density to bulk density it can also be calculated by using the formula by using Carr's consolidation index [36, 37].

$$\text{Hausner's ratio} = \frac{\text{Ptapped}}{\text{Pbulk}}$$

$$\text{Hausner's ratio} = \frac{100}{100 - C}$$

Where C is Carr's consolidation index value

Post compression parameters

Hardness

The tablet crushing load which is the force required to break a tablet into halves by compression. Three tablets were taken from each batch and the hardness was determined using Monsanto hardness tester.

Thickness

The thickness of prepared matrix tablets was measured using Vernier calipers.

Friability test

Twenty tablets were weighed initially ($W_{initial}$) and transferred into the friabilator. The friabilator was operated at 25rpm for 4 min or 100 revolutions. The tablets were dusted using a soft muslin cloth and reweighed (W_{final}). The friability (F%) was then calculated by the formula given below.

$$\%\ \text{Friability} = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

***In vitro* release studies**

In vitro dissolution studies were conducted for tablets was performed in an electro-lab dissolution apparatus using paddle apparatus (USPII) with acid stage and buffer stage.

The dissolution studies of different formulations of VH are performed in eight station dissolution apparatus by using phosphate buffer of pH 6.8 (900 ml) as the dissolution medium. The temperature was maintained at 37±2 °C with a paddle stirrer at 50 rpm is maintained5 ml of samples were withdrawn at different time intervals over 12 h. period through 0.45µ membrane filter and were assayed at 222 nm for VH using systronics U. V. visible spectrophotometer. The sample (5 ml) taken at each sampling time was replaced with fresh dissolution medium (5 ml). The release experiments were conducted in triplicates. For comparison VH release from EFFEXOR XR tablets (a commercial controlled release formulation of VH) was also studied [38].

Dissolution profile comparison using similarity and dissimilarity factor

A dissolution profile can characterize the product more precisely than a single-point dissolution test. It helps to assure similarity in product performance and signals bioequivalence. The factor f_1 is proportional to the average indifference between two profiles, whereas factor f_2 inversely proportional to the average squared indifference between two profiles. The factor f_2 measures the closeness between two profiles; FDA has set a public standard of f_2 values range 50-100 to indicate similarity between two profiles [18].

$$F_1\ (\text{Difference factor}) = \frac{\sum_{j=1}^{n} |Rj - Tj|2}{\sum_{j=1}^{n} |Rj}$$

$$F_2\ (\text{Similarity factor}) = 50 \times \log\{[1 + \left(\frac{1}{n}\right)\sum_{j=1}^{n} |Rj - Tj|2]^{0.5} \times 100$$

For comparison, f_1 should be less than 15.

For comparison, f_2 should be more than 50.

***In vitro* release kinetics**

The rate and mechanism of release of VH from the prepared matrix tablets were analyzed by fitting the release data into following [39-40]

i) The zero-order equation can be represented as

$$C = C_0 - K_0 t$$

Where C is the amount of drug released at time t.

K_0 is the release rate

ii) The first-order equation can be represented as

$$L_n C = L_n C_0 - K_1 t$$

Where K_1 is the release rate constant

iii) The Higuchi equation can be represented as

$$Q = K_2 t^{1/2}$$

Where K_2 is the diffusion rate constant

iv) The peppas equation can be represented as

$$M_t/M_\infty = Kt^n$$

Where $M_t/M_\infty$is the fractional release of the drug

K is the constant incorporating structural and geometrical characteristics of release device

n is the release exponent indicative of mechanism of release, and it is estimated from the linear regression of log M_t/M_∞ vs. log t.

Stability studies

The tablets were packaged (triplicate) in a clear glass bottle with a screw cap and subjected to stability testing at 40±2 °C and 75 %±5% RH for 3 mo. The drug content, color, and dissolution (tablet formulation) were evaluated for 3 mo period [41].

RESULTS AND DISCUSSION

Solubility studies for GK

Solubility test was performed for the GK in various organic solvents like Methanol, ethanol, Acetone, and Dichloro methane, and in purified water. Based on the observation GK soluble in water but not soluble in organic solvents.

Swelling index

Swelling index was performed for GK with purified water. The initial volume of GK was 1.8 ml; after 24 h the swelling property of GK was increased to 6.4 ml. The swelling index increased to 255.55 %. This is one of the good properties of the controlled-release polymer.

Evaluation of precompression parameters for power blends

The prepared blends were evaluated for precompression parameters like angle of repose, compressibility index, Hausner ratio, taped density and bulk density. The results were shown in table 2.

The powder flow is influenced by so many interrelated factors which includes physical, mechanical, and environmental factors. Therefore, in our study, three flow measurement types were employed. The angle of repose (ɵ) is a measure of the internal friction and cohesion of the particles, the value of the angle of repose will be high if the powder is cohesive and low if the powder is non-cohesive. All the formulations showed in the range of 23.25± 0.024 to 28.08±0.016. These ranges are acceptable flowability according to the pharmacopeial limits. This was due to the less cohesion of powder particles.

Carr's consolidation index up to 21% is considered to have acceptable flow properties. Hausner ratio was related to the inter particle friction, the powders with low interparticle friction, had ratios of approximately 1.25 indicating good flow. The VH matrix formulated blends have Carr's index in the range of 6.74±0.064 to 14.71±0.07%. The Hausner ratio of VH matrix formulated blends was found to be 1.10±0.037 to1.14±0.043. Based on these evaluations the prepared VH matrix-formulated blends showed good flowing properties.

Evaluation of post-compression parameters

The prepared VH matrix tablets were evaluated for post-compression parameters like hardness, thickness, friability, weight variation, assay, disintegration, and *in vitro* dissolution studies. The results were shown in table 3.

Table 2: Precompression parameters

Formulation	Angle of repose±SD	BD±SD	TD±SD	Carr's index±SD	Hausners ratio±SD
DG1	23.54±0.032	0.456±0.0048	0.554±0.0094	14.51±0.086	1.13±0.044
DG2	23.47±0.044	0.465±0.0036	0.527±0.01	10.39±0.055	1.14±0.043
DG3	25.22±0.043	0.452±0.0048	0.560±0.008	13.51±0.086	1.12±0.032
DGS1	26.22±0.016	0.458±0.0052	0.572±0.0071	14.62±0.057	1.13±0.037
DGS2	27.19±0.016	0.461±0.0085	0.583±0.0069	6.74±0.064	1.14±0.032
DGS3	25.24±0.029	0.434±0.0078	0.575±0.0075	14.23±0.083	1.13±0.043
DGSZ1	24.18±0.016	0.455±0.0041	0.528±0.0063	14.71±0.07	1.12±0.016
DGSZ2	23.25±0.024	0.460±0.0074	0.531±0.0078	14.45±0.077	1.10±0.037
DGSZ3	28.08±0.016	0.468±0.0045	0.564±0.018	14.63±0.093	1.11±0.069

The obtained results were an outcome of 3 successive experiments (mean±SD, n=3)

Table 3: Evaluation of post-compression parameters of compressed tablets

Formulation	Hardness kg/cm²±SD	Thickness Mm±SD	Friability±SD	Weight variation %±SD	Drug content±SD
DG1	4.15 ±0.032	3.56±0.102	0.71±0.06	1.019±0.005	99.16±0.057
DG2	4.08±0.021	3.61±0.077	0.73±0.02	1.040±0.007	97.23±0.049
DG3	4.08±0.053	3.08±0.040	0.82±0.01	1.034±0.009	98.69±0.098
DGS1	4.11±0.032	3.60±0.114	0.61±0.02	1.028±0.003	98.24±0.049
DGS2	4.05±0.021	3.17±0.057	0.58±0.03	1.033±0.006	99.25±0.041
DGS3	4.08±0.024	3.14±0.049	0.47±0.04	1.030±0.001	98.39±0.057
DGSZ1	4.12±0.024	3.13±0.036	0.49±0.02	1.039±1.008	99.33±0.049
DGSZ2	4.12±0.048	3.11±0.053	0.33±0.04	1.084±0.008	99.48±0.046
DGSZ3	4.19±0.048	3.16±0.029	0.35±0.04	1.077±0.01	98.58±0.040

The obtained results were an outcome of 3 successive experiments (mean±SD, n=3)

Tablet requires a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packing and shipping. The hardness of the VH matrix tablets is uniform with 4.05±0.021to4.19±0.048 kg/cm², which is required to maintain mechanical strength. Percentage friability of VH matrix tablets ranged from 0.33±0.04 to0.82±0.01%. All the formulations showing acceptable friability loss.

The thickness of VH matrix tablets ranged between 3.08±0.040to3.61±0.077 mm. All the formulated tablets showed uniform thickness.

The %weight variation of various prepared VH matrix tablets ranged from 1.019±0.005 to 1.084± 0.008%. The weight variation of all the formulated tablets was within acceptable Pharmacopoeia limits.

The fundamental quality attribute for all pharmaceutical preparations is to maintain constant dose of drug between individual tablets. It was observed that all the formulations of VH matrix tablets were ranged between 98.24±0.049 to99.48±0.046%. It complies with the assay specifications mentioned in the USP.

***In vitro* dissolution studies**

Based on *in vitro* dissolution profiles of VH matrix tablets and marketed tablets were shown in fig. 2. As the concentration of GK increased in composition, controls the rate of release, DG1 formulation 95.6%±0.94 drug released at 12 h' time point, DG2 and DG3 formulations released 78.5%±0.74 and 72.9%±0.72 respectively. DG2 and DG3 not able to release 100% VH in terminal time point of 24 h, DG1 composition selected, and further dissolution rate controlled by adding sodium alginate.

Based on the results concentration of sodium alginate is inversely proportional to the % drug release. DGS1 formulation 98.2%±0.94 drug released at 16 h' time point, DGS2 and DGS3 formulations released 96.4%±0.93 and 87.4%±0.84, respectively. DGS1 composition selected, and further dissolution rate controlled by adding Zinc acetate.

Based on the results concentration of Zinc acetate is inversely proportional to the % drug release. DGSZ1 formulation 100% drug released at 16 h' time point, DGSZ2 and DGSZ3 formulations released 92.8%±0.9 and 87.1%±0.85 respectively at terminal time point (24 h.). DGS1 composition selected, and further dissolution rate controlled by adding Zinc acetate.

***In vitro* release kinetics**

From the kinetic data it was found that the correlation coefficient values of first order kinetics are more than the zero-order kinetics it indicates that the drug release from the VH matrix tablets are following first order kinetics [19]. So, the first order release rate K1 is calculated and reported. The results were shown in table 4.

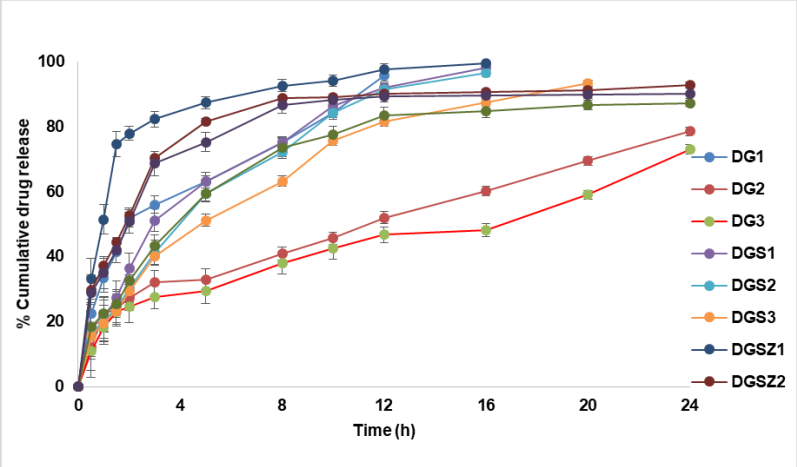

Fig. 2: Release profiles of different formulations of VH in combination with GK, Sodium Alginate and Zinc Acetate (Note: The obtained results was an outcome of 6 successive experiments (mean±SD, n=6))

Table 4: Release kinetics for venlafaxine matrix tablets

Formulation code	Correlation coeffecient (r^2)				Release rate Ko (mg/h)	$K_1(h^{-1})$	T_{50} (h)	T_{90} (h)
	Zero-order	First order	Higuchi	Peppas				
DG1	0.849	0.915	0.973	0.973	6.28	0.184	2	11.5
DG2	0.926	0.924	0.980	0.964	2.71	0.046	12	-
DG3	0.915	0.940	0.968	0.962	2.39	0.023	17	-
DGS1	0.891	0.971	0.985	0.972	5.89	0.207	2.5	11.5
DGS2	0.921	0.986	0.987	0.988	5.99	0.184	4	12
DGS3	0.899	0.995	0.989	0.987	4.50	0.115	4.5	17
DGSZ1	0.526	0.921	0.932	0.800	4.23	0.234	1	7
DGSZ2	0.588	0.784	0.816	0.866	2.90	0.103	1.5	16
DGSZ3	0.769	0.897	0.762	0.946	3.39	0.089	4	-
Commercial	0.604	0.769	0.829	0.876	2.90	0.096	2	15

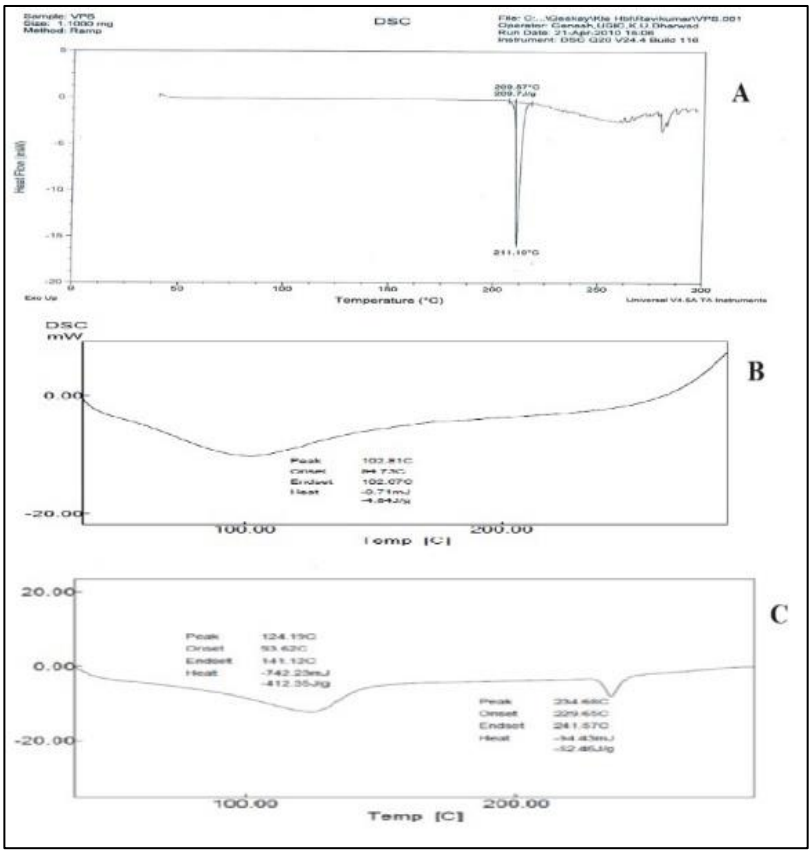

Fig. 3: DSC thermo g of pure venlafaxine (A), Placebo (B) and DGSZ2 formulation (C)

The release data was analyzed as per Peppas equation the release exponent 'n' was>0.5 with all the matrix tablets indicating the anomalous non fickian diffusion as the release mechanism. Based on the results, an increase in the polymer concentration shows a good, controlled release and the combination of gum and polymers shows more controlled release than the individual gum concentrations. Finalized formulation further assessed for difference factor f1 and similarity factor f2 for the comparison of drug release profile of the formulation DGSZ2 with that of commercial formulation and found to be f1 2.73, f2 79.14; this is one of the pieces of evidence that finalized formulation is similar to the commercially available formulation.

Drug and excipients compatibility studies

DSC studies

DSC scans of about 5 mg using an automatic thermal analyzer system performed accurately weighed VH and tablet containing the same amount of drug. Sealed and performed aluminum pans were used in the excipients for all the samples. Temperature calibration was performed using indium as standard. An empty pan sealed in the same way as the sample was used as a reference. The entire samples were run at a scanning rate of 10 °C/min from 25-250 °C [22].

DSC thermogram of pure VH showed endothermic peak at 211.1 °C and formulation showed endothermic peak at 209.080 °C. From the obtained results the drug and excipients were compatible.

ATR spectral studies

The Infra-red studies were performed by the instrument BRUKER ALPHA-E with the wave number of region 400-2000 cm^{-1}. In this, enough samples are placed on the crystal area, and the pressure arm should be positioned over the sample area. Force is applied to the sample, pushing it onto the diamond surface and scanned over a scanning range of 400-2000 cm^{-1}1. The same procedure is repeated for analysis of pure drug, excipients, and mixture [21].

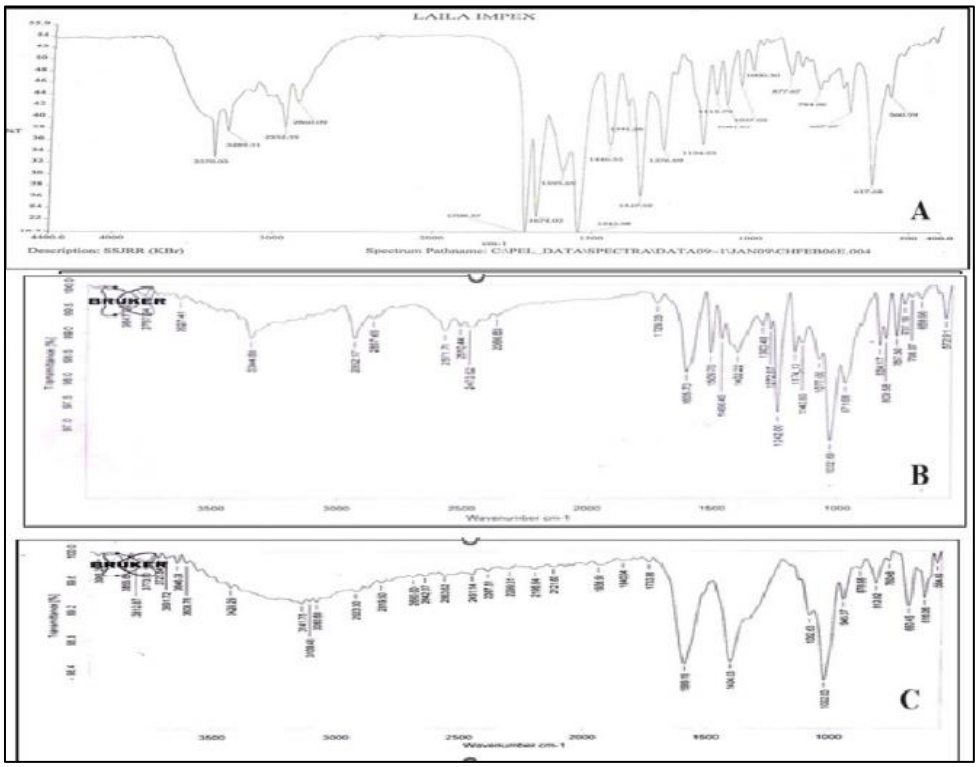

Fig. 4: ATR spectrum of pure venlafaxine (A), Placebo (B) and DGSZ2 formulation (C)

Table 5: Comparison of confirmatory groups in pure sample and physical mixtures

S. No.	Functional group	Wave number (cm^{-1})	
		Pure drug	Drug+Placebo
1.	Tertiary amine Stretching	3527.64	3519.69
2.	Hydroxyl stretching	3339.20	3420.37
3.	Aromatic C-H Stretching	3119.05	3109.48
4.	C-H Stretching	2916.95	2923.53
5.	Methoxy stretching	1027.17	1022.68
6.	O – H stretching	2573.49	2563.63

The ATR spectra of pure VH and drug+excipients mixtures are showed in fig. 4a–4c. The peaks obtained in the spectra of each formulation correlates with the peaks of the drug spectrum. This indicates that the drug was compatible with the formulation components. The functional groups of VH like Tertiary amine stretching 3257.64, Hydroxyl Stretching 3339.20 cm^{-1}, Aromatic C – H Stretching 3119.05 cm^{-1}, C-H Stretching 2916.95 cm^{-1}, Methoxy stretching 1027.17 cm^{-1}, O – H Stretching 2573.49 cm^{-1}, were found in the final formulation.

Stability studies

The optimized VH matrix tablets are packed in 40cc HDPE bottles with Child Resistance Caps (CRC) and induction sealed, then loaded in an accelerated stability chamber (40±2 °C/75±% RH) for 3 mo as per ICH guidelines. After stability studies tablets were evaluated for appearance, hardness, assay and dissolution profile.

Table 6: Stability data of optimized formulation (DGSZ2) at the accelerated temperature of 40±2 °C/relative humidity of 75±5%

Formulation code	DGSZ2	
	Before storage	After storage
Appearance	Brownish White	Brownish White
Hardness (kg/cm²)	4.12±0.048	4.09±0.073
Assay %	99.04±0.16	98.39±0.93

The obtained results were an outcome of 6 successive experiments (mean±SD, n=6)

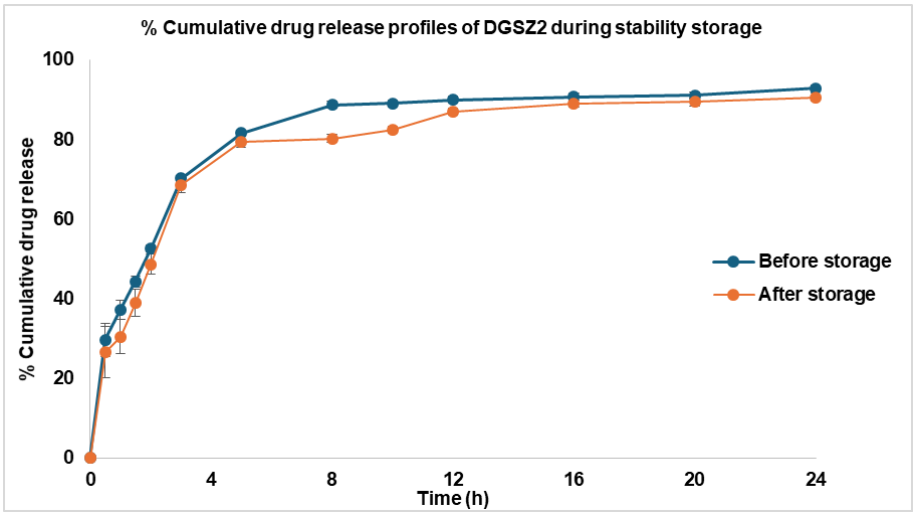

Fig. 5: % Cumulative drug release profiles of DGSZ2 during stability storage, the obtained results were an outcome of 6 successive experiments

CONCLUSION

The coontrolled release (bidning effect) property of GK has been studied using VH as a model drug. The lead matrix table formulation showing similar controlled release profile compared with commercially avaialnle dosage form. Further, the lead formulation stable for three months at AST tetsing conditions. DSC and FTIR confirms no incompatibility of VH with GK and other excipeints used in the formulation development. Future stuides will be needed to confirm the *in vivo* behavior of GK as conbtrolled release agent containing tablets.

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Nil

AUTHORS CONTRIBUTIONS

Anil Kumar Dindigala was responsible for conceptualization, methodology, formal analysis, and writing the original draft. Suryaprakash Reddy Chappidi contributed to conceptualization, supervision, and review and editing. Anantha Makineni also played a role in writing review and editing.

CONFLICT OF INTERESTS

Declared none

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