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Original Article

EVALUATION OF VATERIA INDICA MODIFIED GUM AS A RELEASE RETARDANT MATRIX IN THE TABLET DOSAGE FORM

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ABSTRACT

Objective: A natural gum from *Vateria indica* was investigated as a novel matrix-forming material for sustained drug delivery using diclofenac potassium as a model drug.

Methods: In the current investigation, we formulated a matrix tablet using chloroform soluble gum portion of *Vateria indica* modified gum (VIMG) as a natural matrix-forming agent. It was used with a drug-polymer ratio ranging from 1:0.5 to 1:4.5. The pre-compression study of the powder blends was done by calculating bulk density, tapped density, angle of repose, and carr's index, compressibility, and hausner's ratio. The tablets were prepared by direct compression method and prepared tablets were evaluated and were found according to the official guidelines by pharmacopeia. The *in vitro* drug release was carried out using USP paddle type II apparatus and the release was found to be sustained.

Results: The formulation VIMG-5 containing drug: polymer ratio 1:2.5 showed the 96.26%±1.73 drug release in 12 h. The results showed that chloroform soluble fraction of *Vateria indica* can be used as a drug release modifier to delay the rate of drug release, which depended on the amount of gum composition, as the concentration of gum was increased, there was sustained the drug release with promising accelerated stability.

Conclusion: The evaluation studies on sustained release matrix tablets using *Vateria indica* chloroform soluble portion of gum as natural material demonstrate the multivariate applications such as matrix forming, binder, and release retardant of the gum in tablet formulation.

Keywords: *Vateria indica*, Matrix tablet, Modified gum, Diclofenac potassium, Sustained release

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INTRODUCTION

The merits of natural gums have been well acknowledged in the past many years, they are readily available, cost-effective, eco-friendly, fairly degradable and biocompatible. They can be modified and converted into useful semi-synthetic and synthetic materials for pharmaceutical applications. Natural resins have been used since ancient times for a wide range of applications like, varnishes, sealants, binding media, waterproofing and most commonly used resins for paint and varnishes are rosin, sandarac, mastic, copal, and dammar [1-4].

Gums are characterized by several techniques such as gas chromatography (GC), gel permeation chromatography (GPC), scanning electron microscopy (SEM), differential scanning calorimetry (DSC), x-ray diffraction crystallography (XRD) and thermo-gravimetric analysis of the sample [2-6].

In some research work the *Vateria indica* gum haven investigated for various pharmaceutical applications such as film forming, coating, matrix forming, and microencapsulating properties as well as their biodegradation, biocompatibility, and interaction studies with various drugs, to establish chloroform soluble fraction of *Vateria indica* gum as an excipient in drug delivery application.

The high chain stiffness gum resins will form an anisotropic liquid crystalline phase at lower concentrations than other food hydrocolloids. The appearance of this phase can result in a decrease in viscosity with increasing concentration. A consequence of this is that on the concentration of gum through phase separation or exclusion, viscosity decreases can be observed. Examples of this unusual behavior are shown for blends of polyelectrolytes and with cold swelling starches [7, 8].

The recovery of viscosity on subsequent dilution has potential in several applications including a liquid product for thickening foods for consumers with swallowing difficulties. A new form of gum can be prepared by modification. These modified form show excellent dispersion and a strong degree of swelling with less or no characteristic smell of resin gums. The viscosity development of *Vateria indica* gum on heating is similar to starch thus gum can be produced which combines the desirable dispersibility and heat transfer properties of starch, with the end-use advantages it [9].

The gum slowly hydrated in water, dispersing and swelling to form a highly viscous dispersion exhibiting pseudo plastic flow behavior. Increased complications and expenses involved in marketing of new drug entities have focused greater attention on the development of sustained or controlled release drug delivery systems. The matrix system is widely used for sustained or controlled release, in prolonged resident time of drug in the body is believed to prolong the duration of action [9, 10].

It is the release system that prolongs and controls the release of the drug that is dissolved or dispersed. A matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers [7, 11]. The *Vateria indica* gum resin contains triterpene, hydrocarbons, phenols, ketones, alcohols and acids as well as small amounts of sesquiterpenes were found to be the major components of it [12, 13]. In the current study an attempt made to evaluate modified gum from *Vateria indicaas* matrix forming material in tablet dosage form.

MATERIALS AND METHODS

Collection and authentication

Plant material was collected from ranges of the Satpuda region in Maharashtra and authenticated from the department of botany with specimen no DNM/SR/2017-18/46 and all the other excipients were procured from Sigma Aldrich, diclofenac potassium was gifted by Kalash Pharmachem Pvt Ltd Jalgaon, Maharashtra. The solvents used

were of analytical grade, freshly prepared double distilled water was used throughout the experiment and all other chemicals used were of analytical grade.

Purification and modification of gum

The gum exudates were collected from the incisions made on the bark of *Vateria indica*. The *Vateria indica* gum obtained was shade-dried and ground then the powder gum was passed through a sieve and used for further modification. The 20 g of gum was then dissolved in 100 ml chloroform in a 500 ml beaker and stirred using a mechanical stirrer for 4h. The supernatant liquid was collected and kept in an evaporating dish at room temperature. The resultant yellow color product after evaporation was collected and used as a chloroform soluble fraction of gum (VIMG) and fractional crystallization was done to get a purified and a modified form of VIMG and chloroform insoluble fraction of *Vateria indica* gum all the further tests will be carried on VIMG that is crystallized and modified soluble fraction. The precipitate was separated and dried in a vacuum desiccator at 50 °C for 48 h. The dried precipitate was pulverized using a laboratory blender, passed through sieve number 80 to get uniform particles and stored in an airtight container [14].

Physiochemical characterization of VIMG

The soluble fraction of *Vateria indica* VIMG was evaluated for physicochemical properties such as color, solubility, a viscosity [15-17], swelling index, softening point, glass transition temperature (Tg), acid value, ash value [18, 19] and pH [16, 20].

Preparation of powder blend

All the ingredients were weighed accurately and passed through sieve no. 100. Then all the ingredients were mixed according to decreasing order of their weight (geometrical dilution). The prepared powder blend was subjected to various parameters as follows.

Evaluation of powder blends

The pre-compression study of the powder blends of the drug, polymer, lactose and other excipients done by calculating bulk density, tapped density, angle of repose and carr's index (% compressibility) and hausner's ratio [21].

Formulation of matrix tablets of diclofenac potassium using VIMG

Formulation of preliminary batches of matrix tablets

To study the release pattern of diclofenac potassium from the gum, the various preliminary batches were prepared by using VIMG in various concentrations from 25 to 225 mg with a constant weight of the tablet 515 arranged with filler lactose, magnesium stearate, and talc. The formulations of the matrix tablets of diclofenac potassium which was selected as a model drug for VIMG. The tablets were prepared by direct compression on 8 stations tablet compression machine (Jaguar JMD08) using a flat-faced 10 mm diameter punch.

Evaluation of matrix tablets

All the different formulations of matrix tablets prepared by VIMG with diclofenac potassium as a model drug were subjected to evaluation for various parameters like hardness, weight uniformity, and friability as per the Indian pharmacopeia method. Also, along with all these parameters, content uniformity, swelling index and *in vitro* drug release patterns of the prepared batches of matrix tablets were studied [22, 23].

Hardness

For each formulation, the hardness of tablets was determined using the Monsanto hardness tester.

Friability

Friability is the measure of tablet strength. A sample of pre-weighed tablets was placed in Roche Friabilator, which was then operated for 100 revolutions i.e. 4 min. The tablets were then dusted and reweighed. A loss of less than 1 % in weight is generally considered acceptable. Percent friability was calculated as follows,

$$\% \text{ Friability} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \text{ X } 100$$

Weight uniformity

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Shimadzu), the average weight was calculated and individual tablet weight was then compared with the average value to find the deviation in weight.

Swelling behavior of tablets

Selected tablets are individually weighed (W1) and placed separately in petri dishes with 0.1 N HCl, pH 1.2 for two hours and then phosphate buffer pH 6.8 for the next 10 h at 37±0.2 °C. At the time interval of 1, 2 and 3 h, tablets are removed from the petri dish, and excess water is removed carefully using filter paper [24]. The swollen tablets are then reweighed (W2) and the percent swelling index was calculated using the following formula [25].

$$SI = [(W2-W1)/W1] \times 100$$

Content uniformity

The drug content, 20 tablets, were weighed accurately and powdered, the powder equivalent to 50 mg of diclofenac potassium was shaken with 60 ml of solvent in a 200 ml volumetric flask and the volume was further adjusted with solvent to 200 ml. Then 5 ml of this solution was diluted to 100 ml in a volumetric flask and drug contents were determined by UV spectrophotometer (UV-1800, Shimadzu, Japan) at selected wavelength using a calibration curve based on the prepared standard solutions [26].

***In vitro* drug release**

In vitro drug release profile of VIMG formulations was studied using USP TDT dissolution apparatus type II (paddle method; Elecrtolab, India). The release of the drug from the tablets was tested in 900 ml of 0.1 N HCl pH 1.2 solution for two hours later in phosphate buffer and pH 6.8 for further hours as a dissolution medium at 37±0.5 °C. The paddles are rotated at 75 rpm. Aliquots of 10 ml of the release medium were removed at predetermined time intervals and analyzed for the release amount of diclofenac potassium using spectrophotometric detection [27].

Selection of better-performing formulations of matrix tablets based on evaluation parameters

Based on data obtained from the evaluation of diclofenac potassium matrix tablets prepared using individually for various official as well as non-official parameters like micromeritic properties, various tablet evaluation parameters. The formulation which showed the best results was selected as best performing formulation and further subjected to accelerated stability studies according to ICH guidelines.

Accelerated stability testing of optimized formulations of matrix tablets

Accelerated stability testing of the selected formulation was carried out to determine the stability of the drug and carrier and also to determine the physical stability of formulations under accelerated storage conditions at various temperatures using a programmable environmental tester. The prepared tablets were placed in borosilicate screw-capped glass containers. The samples were kept at conditions of 40±2 °C and 75±5% RH and were analyzed at intervals of 0, 30, 60, and 90 d for their physical changes and drug content [28-32].

RESULTS AND DISCUSSION

Physiochemical characterization of VIMG

Various physiochemical properties of VIMG was been studied and they were found to be optimum for the formation of matrix tablets.

Evaluation of powder blends

Sustained released tablets were prepared by direct compression method using VIMG as a matrix forming agent in various drug-to-polymer ratios ranging from 1:0.5, 1:1 to 1:4.5 in serial increments. The blends of different batches of the matrix tablets prepared by using VIMG were evaluated in the current research paper.

Table 1: Powder blend properties of formulation of matrix tablets prepared by VIMG

Formulations code	Angle of repose (°) (±SD)*	Bulk density (g/ml) (±SD)*	Tapped density (g/ml) (±SD)*	Compressibility index (%) (±SD)*	Hausnar's ratio
VIMG–1	28.14±0.32	0.32±0.016	0.40±0.022	11.06±0.34	1.25
VIMG–2	27.93±0.12	0.34±0.018	0.41±0.015	11.54±0.57	1.20
VIMG–3	27.31±0.31	0.33±0.015	0.42±0.023	11.90±0.47	1.27
VIMG–4	26.82±0.21	0.34±0.024	0.43±0.016	12.63±0.29	1.26
VIMG–5	26.12±0.19	0.35±0.020	0.43±0.028	13.12±0.21	1.22
VIMG–6	25.91±0.22	0.39±0.018	0.46±0.024	13.22±0.29	1.17
VIMG–7	25.05±0.29	0.38±0.032	0.43±0.027	12.63±0.65	1.13
VIMG–8	24.85±0.24	0.38±0.016	0.46±0.035	12.22±0.42	1.21
VIMG–9	24.21±0.31	0.37±0.026	0.45±0.015	12.12±0.22	1.21

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

The results show angle of repose in the range of 24.21±0.31 to 28.14±0.320°, bulk density was found to be in the range of 0.32±0.016 to 0.39±0.018 g/ml for the powder blends prepared with VIMG. The tapped densities were found to be in the range of VIMG 0.40±0.022 to 0.46±0.035 g/ml compressibility index was found in the range of 11.06±0.34 to 13.22±0.29 % and hausner's ratio was found in the range of 1.13 to 1.27 for the powder blends prepared with VIMG comparable with the procedures and results as per Rahim H *et al.*, 2015 [4] and Das B *et al.*, 2014 [5].

The bulk density and angle of repose shown in table 1 indicated that the powder has good flow characteristics and suppose to be good compressibility; hence good candidate to form a directly compressible matrix tablet.

Evaluation of matrix tablets

The different batches of the matrix tablets were prepared and evaluated for the various post-compression evaluation parameters. The hardness of the tablet was found 5.3±0.30 to 5.9±0.48 kg/cm², and friability was found in the range of 0.24±0.020 to 0.52±0.012 % for the tablets prepared using VIMG. The weight variation was found to comply with official limits, uniformity of content was found to be 98.48±0.37 to 99.88±0.37 % for the tablets prepared by VIMG and all the data was found to be within the standard limits.

As the concentrations of polymers get increased the hardness of matrix tablets ultimately increased and simultaneously the friability of matrix tablets was decreased.

Swelling index

The swelling behavior of prepared matrix tablets was studied using 0.1 N HCl, pH 1.2 for 2 h, and then phosphate buffer pH 6.8 for the next 10 h at 37±0.2 °C. The swelling index of matrix tablets from different batches was measured as per the Shekar BC *et al.*, 2010 [24] and Wadher KJ *et al.*, 2011 [25] and the results are as shown in fig. 1.

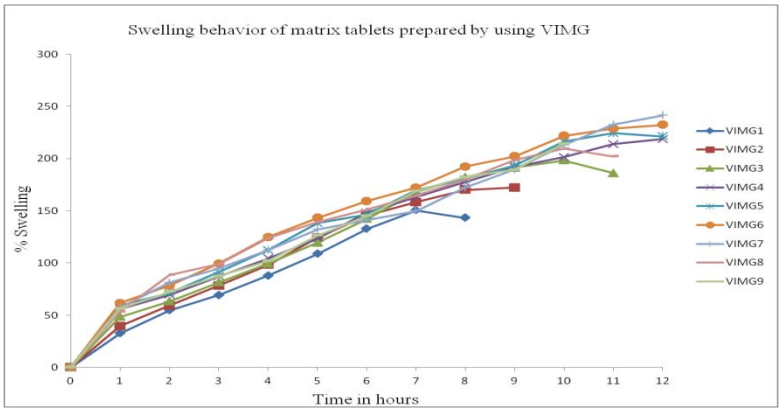

Fig. 1: Swelling behavior of matrix tablets prepared by using VIMG, The obtained results were outcome of 3 successive experiments (n=3)

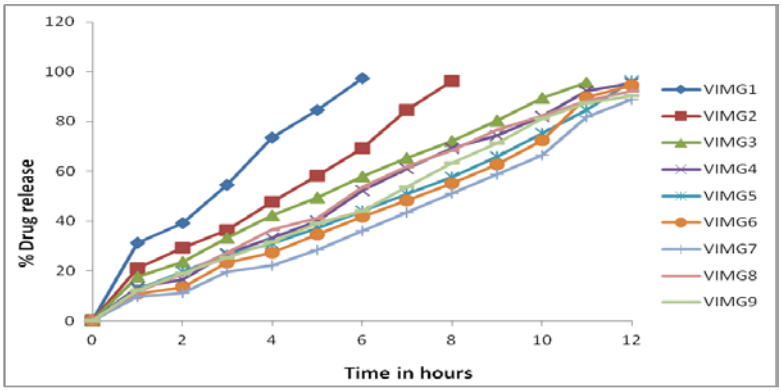

Fig. 2: Cumulative drug release data of various formulations of VIMD matrix tablets, the obtained results are the outcome of 3 successive experiments (n=3)

***In vitro* dissolution study of matrix tablets prepared by using VIMG**

Drug-released profiles were determined for all the batches of matrix tablets prepared by using VIMG in 0.1 N HCl, pH 1.2 for two hours and then further in Phosphate buffer pH 6.8. The drug released data of matrix tablets prepared by using VIMG.

The results from formulations VIMG-1 to VIMG-3 showed nearly complete drug release within 6 to 11 h, whereas formulations VIMG-4, VIMG-5 and VIMG-6 showed drug release of 95.26±1.34, 96.26±1.73, 94.62±1.41% respectively among of these, VIMG-5 showed better release with the drug: polymer ratio of 1:2.5 and showed 96.26±1.73% drug release in 12 h. Formulations VIMG-7 to VIMG-9 showed incomplete drug releases i.e. 88.89±1.18, 92.35±1.23 and 90.23±0.35 % in 12 h. The data was shown that VIMG has perfect as matrix forming agent, which was used in the present study.

The overall results of *in vitro* drug release study the matrix tablets prepared in various drug to polymers ratios like 1:0.5, and 1:1 up to 1:4.5 by using VIMG. The matrix tablets prepared by using VIMG in the ratio of 1:2.5 (i.e., formulation VIMG-5) showed best results. Thus, finally in concern to *in vitro* drug release studies, VIMG was better.

Selection of best-performing formulations of matrix tablets prepared by using VIMG

The micromeritic evaluation of the powder blend prepared for the compression of matrix tablets of diclofenac potassium containing VIMG gum formulation VIMG-5 showed the angle of repose 26.12±0.19 °, bulk density 0.35±0.020g/ml, tapped density 0.43±0.028 g/ml, compressibility index 13.12±0.21 % and hausner's ratio 1.22 which were within the official limits and this indicates that formulation VIMG-5 was best in case of micromeritic properties among all formulated matrix tablets of VIMG gum.

The post-compression evaluation of matrix tablets of VIMG formulation VIMG-5 showed hardness of 5.6±0.20 kg/cm^2, friability 0.39±0.034 %, uniformity of weight 515±0.34and uniformity of content 99.54±0.47 were within the official limits and this indicates that formulation VIMG-5 was best in case of post compression evaluation parameters among all formulations of matrix tablets of VIMG. The swelling index of matrix tablets formulations prepared using VIMG formulation VIMG-5 showed the swelling index of 221.32±1.32 and matrix tablets formulations prepared using VIMG.

The *in vitro* drug release studies the matrix tablets prepared in various drug to polymers ratios like 1:0.5, 1:1, upto 1:4.5 by using VIMG, the matrix tablets prepared by using VIMG in 1:2.5 ratio (i.e., formulation VIMG-5) had shown drug release 96.26±1.73 % which was selected for further study. From the above observations, VIMG in a lower drug-to-polymer ratio was found effective as gums had shown successful sustained release of diclofenac potassium more than 12 h from the matrix tablets.

The overall results of the micromeritic evaluation of powder blends, post-compression evaluations, % swelling index determination and *in vitro* drug release studies of matrix tablets evaluations formulation VIMG-5 amongst all VIMG formulations showed the best results amongst their all formulations hence both these formulations were selected as optimized formulation and which were further subjected to the accelerated stability studies as per the ICH guidelines.

Accelerated stability study of best-performing formulations of matrix tablets prepared by using VIMG

The overall accelerated stability of the selected best formulation based on evaluation parameters as per Bajaj S *et al.*, 2012 [32] and the result data shown to be stable based on hardness, friability, weight uniformity, and content uniformity when compared with the original formulation with SD and RSD below 2, hence unaffected by stored in harsh environment as 40±2 °C and 75±5% RH.

The formulation VIMG-5 showed 96.12 % drug released in 12 h after 90 d of storage in prescribed conditions for accelerated stability and the yield was found to be in the acceptance range, with good preformulation and micromeritic study parameters.

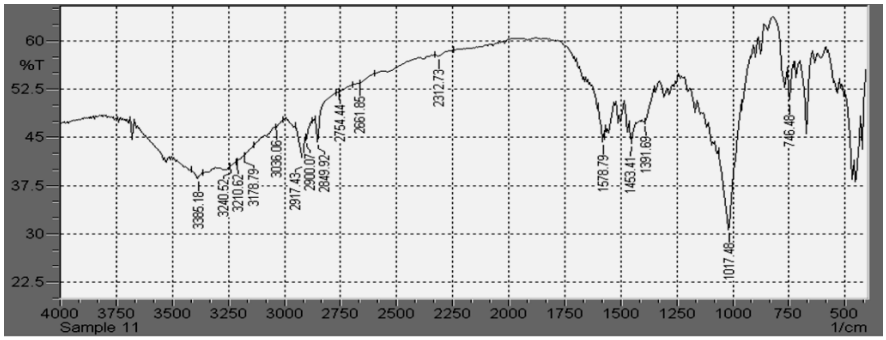

Fig. 3: Pre-stability IR spectrum of matrix tablets formulation VIMG-5

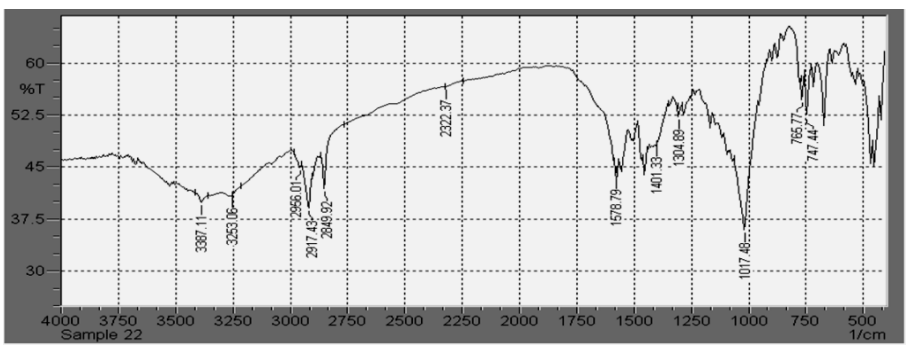

Fig. 4: Post-stability IR spectrum of matrix tablets formulation VIMG-5

The pre and post-stability IR spectrum data indicate that the various characteristic peaks were obtained in the FTIR spectrum of Diclofenac potassium at 1602 cm-1 for (-C=C Alkene), 3203 cm-1 for-COOH (Carboxylic acid), 3258 cm-1 for O-H and N-H stretching

and 3387 cm-1–N-H (Amine group) there was no shifting in the frequencies of above said functional groups and there were no additional peaks observed in the pre and post stability optimized formulations and it didn't show any signs of incompatibility in between drug and the excipients including VIMG. As per the results, one should conclude that there were no chemical interactions occurred in these both optimized formulations, which were subjected to the accelerated stability studies as per the ICH guidelines; after the overall accelerated stability studies VIMG-5 formulation was found physically as well as chemically stable nature.

CONCLUSION

In the present investigation, the novel biomaterial-modified gum from *Vateria indicia* (VIMG) was successfully characterized for various physicochemical properties and further studied as a novel matrix-forming material. The evaluation studies on sustained release matrix tablets using *Vateria indica* chloroform soluble portion of gum as natural material demonstrate the multivariate applications such as matrix forming, binder, and release retardant of the gum in tablet formulation. The significant reduction in the release of drug and proportionate enhancement in sustained release characteristics provided by VIMG could make it a good natural material for its applications in dosage forms.

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AUTHORS CONTRIBUTIONS

The coauthors Dr. Vijay R. Patil and Dr. Tushar A. Deshmukh have made a substantial contribution to the conception, acquisition of data, interpretation of results and in the drafting of the article.

CONFLICTS OF INTERESTS

No conflicts of interest are reported by authors.

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