AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Evaluation of Modified Gum From Pistacia Lantiscus As A Release Retardant Matrix In The Tablet Dosage Form

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ABSTRACT

In the current investigation we formulated and evaluates matrix tablet using modified gum of *Pistacia lantiscus* gum (PLMG) as natural matrix forming agent used in various successively increasing concentration. The pre-compression study of the powder blends of drug, PLMG and other excipients were done by calculating bulk density, tapped density, angle of repose and carr's index (% compressibility) and hausner's ratio. The tablets using PLMG as matrix forming agent were prepared by direct compression method and prepared tablets were evaluated for thickness, hardness, weight uniformity, friability and content uniformity and were found according to the official guidelines by pharmacopoeia. The swelling behavior of prepared matrix tablets was studied using for 12 hours at 37 ±0.2 ^{0}C, it was fond that the drug to modified gum ratio of 1:2 was found to be optimum swelling with the sustained release of model drug up to 97.12 in matrix tablet formulation. The results revealed, that modified fraction of *Pistacia lantiscus* gum can be used as a drug release modifier to delay as the rate of drug release of which depended on the amount of gum composition, as the concentration of gum was increased there was sustain the drug release.

Keywords: Pistacia lantiscus, tablet, modified gum, diclofenac potassium, hausner's ratio.

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Received 19 January 2023, Accepted 10 February 2023

Please cite this article as: Fegade TD *et al*., Evaluation of Modified Gum From Pistacia Lantiscus As A Release Retardant Matrix In The Tablet Dosage Form . American Journal of PharmTech Research 2023.

INTRODUCTION

Sustained drug delivery systems can improve patient compliance and provide extended periods of effective blood levels. In an approach, polymers and their blend are used in various formulations to achieve sustained drug release. The authors investigated various natural, semisynthetic and synthetic polymeric materials. Most thoroughly investigated and used synthetic polymers for sustained release drug delivery are methylcellulose, ethyl cellulose, methacrylic acid copolymer[1], hydroxypropylmethylcellulose[2], polyoxyethyleneglycol[3], sodium carboxymethylcellulose.[4]

The natural gums have been well studied and 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, sealant, binding media and waterproofing. Most commonly used resins for paint and varnishes are Rosin, Sandarac, Mastic, Copal and Dammar.[5-8] Characterization of gums is an essential step in establishing their suitability as pharmaceutical excipients.

In the present research work the alcohol soluble fraction of gum have been 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 drug, to establish alcohol soluble derivative of *Pistacia lantiscus* gum as excipient in drug delivery application.

Because of its 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 concentration of gum through phase separation or exclusion, viscosity decreases can be observed. Examples of this unusual behavior are shown for blends of with polyelectrolytes and with cold swelling starches.[7-8]

The recovery of viscosity on subsequent dilution has potential in a number of 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 showing excellent dispersibility and a strong degree of swelling with less or no characteristic smell of resin gums. Under appropriate conditions the viscosity development of *Pistacia lantiscus* 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.

The gum slowly hydrated in water, dispersing and swelling to form a highly viscous dispersion exhibiting pseudoplastic flow behavior. In view of this, it is apparent that natural gums and their derivatives are promising candidates to design the sustain drug delivery systems. Increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of sustained or controlled release drug delivery systems.[9]Matrix system is widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed. In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. [9, 10]

Pistacia lentiscusgum contains α-Pinene, β-myrcene, β-pinene, limonene, and β-caryophyllene were found to be the major components of it.[11]In the current study modified gum from Pistacia lantiscus was physically characterized and formed matrix tablet was evaluate.

MATERIALS AND METHOD

Collection and authentication

Plant material was authenticated from the department of botany with specimen no DNM/SR/2017-18/45 and all the excipients were purchased 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 *Pistacia lantiscus*. The *Pistacia lantiscus* gum obtained was shade dried and grinded; the powder gum was passed through sieve, and used for further modification. The 20 g of gum was then dissolved in 100 ml chloroform in 500 ml beaker stirred using a mechanical stirrer for 4h. The supernatant liquid was collected and kept in evaporating dish at room temperature. The resultant yellow colour product after evaporation was collected and used as chloroform soluble fraction of gum (PLMG) and fractional crystallization was done to get purified and modified form of PLMG and chloroform insoluble fraction of *Pistacia lantiscus* gum all the further tests will be carried on PLMG that is crystallized and modified soluble fraction. The precipitate was separated and dried in a vacuum decicator 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 air tight container. [12]

Physiochemical characterization of PLMG

The soluble fraction of *Pistacia lantiscus* PLMG was evaluated for physicochemical properties as, colour, solubility, viscosity[13-15] ,swelling index, softening point, glass transition temperature (Tg) , acid value, ash value[16,17] and pH.[14,18]

Preparation of powder blend

All the ingredients were weighed accurately and passed through the 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 drug, polymer, lactose and other excipients were done by calculating bulk density, tapped density, angle of repose and carr's index (% compressibility) and hausner's ratio.[19]

Formulation of matrix tablets of diclofenac potassium using VIMG.

Formulation of preliminary batches of matrix tablets

The various preliminary batches coded as PLMG-1 to PLMG-9 were prepared by using drug (50 mg) to polymer ratios ranging from 1:0.5, 1:1 upto 1:4.5 in serial in increasing concentrations of PLMG from 25 to 225 mg with 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 PLMG. The tablets were prepared direct compression on 8 station tablet compression machine (Jaguar JMD08) using flat-faced 10 mm diameter punch.

Evaluation of matrix tablets

All the different formulations of matrix tablets prepared by PLMG with diclofenac potassium as a model drug were subjected for evaluation for various parameters like thickness, hardness, weight uniformity, friability as per I.P. method. Also along with all these parameters content uniformity, swelling index and *in- vitro* drug release patterns of the prepared batches of matrix tablets was studied. [20, 21]

Thickness

Thickness in mm was measured by vernier caliper. Tablets from each type of formulation were used and average values were calculated.

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 minutes. The tablets were then dusted

and reweighed. A loss of less than 1 % in weight in generally considered acceptable. Percent friability was calculated as follows,

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

Weight uniformity

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Shimadzu), average weight was calculated and individual tablet weight was then compared with 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 next 10 hours at 37±0.2 ^{0}C.At the time interval of 1,2, 3 hrs tablets are removed from the Petri dish and excess water is removed carefully using the filter paper.[22] The swollen tablets are then reweighed (W2) and the percent Swelling index is calculated using the following formula.[23]

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

Content uniformity

For drug content, 20 tablets were weighed accurately and powdered. Powder equivalent to 50 mg of Diclofenac potassium was shaken with 60 ml of solvent in 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 volumetric flask and drug contents were determined by UV– Vis spectrophotometer (UV-1800, Shimadzu, Japan) at 276 nm using calibration curve based on the prepared standard solutions.[24]

***In-vitro* drug release**

In vitro drug release profile of PLMG formulations was studied using USP TDT dissolution apparatus type II (paddle method; Elecrtolab, India. The release of 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^{0}C. The paddles are rotated at 75rpm. Aliquots (10 ml) of the release medium were removed at predetermined time intervals and analyzed spectrophotometrically (Shimadzu 1800 Double beam) for the release amount of Diclofenac potassium using spectrophotometric detection.[25]

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

On the basis of 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 selected as optimized formulations and further subjected to the accelerated stability studies according to ICH guidelines.

Accelerated stability testing of optimized formulations of matrix tablets

Accelerated stability testing of selected formulation was carried out to determine the stability of drug and carrier and also to determine the physical stability of formulations under accelerated storage condition at various temperatures using programmable environmental tester. The prepared tablets were placed in borosilicate screw capped glass containers. The samples were kept at condition of 40 ±2 ^{0}C and 75 ±5% RH and were analyzed at interval of 0, 30, 60 and 90 days for their physical changes and in drug content.[26-30]

RESULTS AND DISCUSSION

Physiochemical characterization of PLMG

Various physiochemical properties of PLMG was been studied. They were found to be optimum for formation of matrix tablet.

Evaluation of powder blends:

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

Angle of repose was found to be in the range of 15.21± 0.12 to 21.67 ±0.26 for powder blends prepared by using PLMG. Bulk density was found to be in the range of 0.33 ±0.021 to 0.39±0.074 g/ml for the powder blends prepared with PLMG. Tapped densities were found to be in range for PLMG0.40±0.032 to 0.45 ±0.078 gm/ml. Compressibility index was found in the range of 11.36 ±0.82 to 21.42 ±0.31 for matrix tablet powder blend prepared by using PLMG. Hausner's ratio was found in the range of 1.12 to 1.27 for the powder blends prepared by PLMG.

The bulk density, angle of repose results indicated that the powder has good flow characteristics and suppose to be good compressibility hence good candidate to form 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. Hardness of the tablet was found 4.9±0.28 to 5.8 ±0.78kg/cm^2 for the tablets containing PLMG. Friability was found in the range of 0.24±0.020 to 0.52 ±0.012 % for the tablets prepared using PLMG. Weight variation was found to comply with official limits. Uniformity of content was found 98.40 ±0.72 to 99.78 ±0.32 % for the tablets prepared by PLMG and within the standard limits. As the concentrations of polymers get increases ultimately the hardness of matrix tablets were increases and simultaneously the friability of matrix tablets was decreases.

Swelling index:

The swelling behavior of prepared matrix tablets were studied using 0.1 N HCl, pH 1.2 for two hours and then phosphate buffer pH 6.8 for next 10 hours at 37±0.2 ^{0}C. Swelling index of matrix tablet of different batches prepared by using *PLMG* as showed in Figure No. 1.It was fond that the drug to modified gum ratio of 1:2 was found to be good swelling index of 218.43 as compare with other ratios.

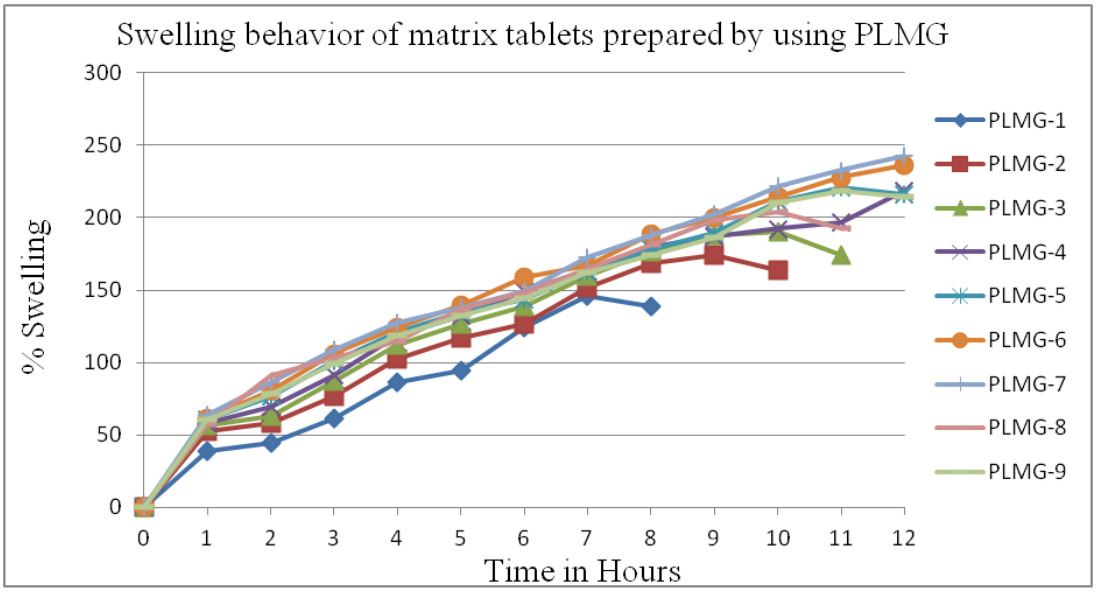

Figure 1: Swelling behavior of matrix tablets prepared by using PLMG

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

***In-vitro* dissolution study of matrix tablets prepared by using PLMG**

Drug released profiles were determined for all the batches of matrix tablets prepared by using PLMG 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 PLMG.

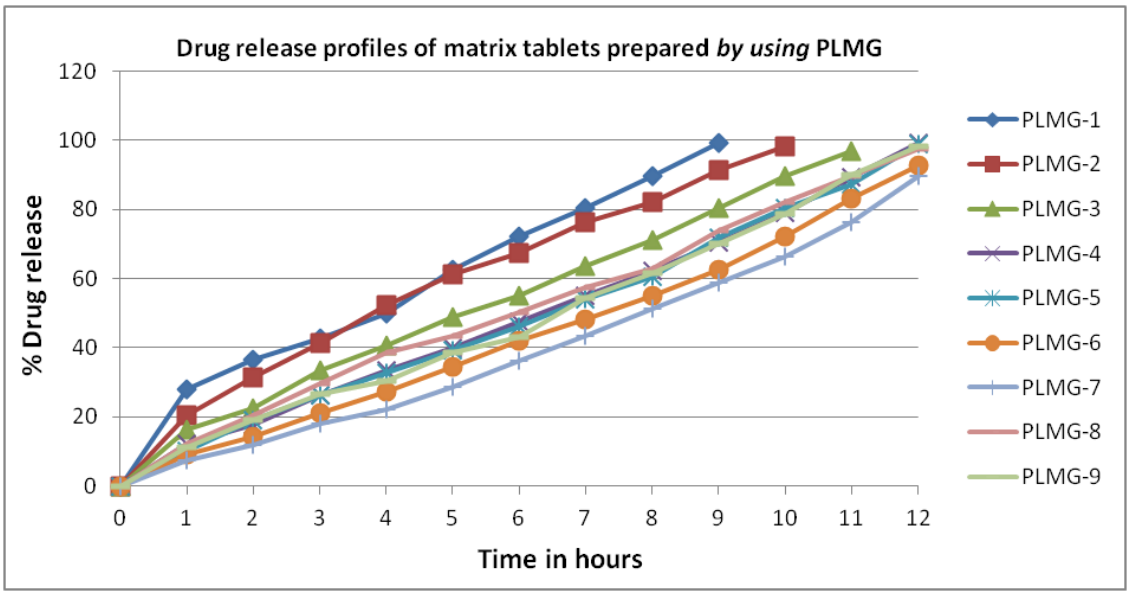

Figure 2: Cumulative drug release data of various formulations of PLMG Matrix tablets

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

From the results formulation PIMG-1 to PIMG -3 had showed the nearly complete drug release in 9 to 11 hrs. Whereas formulation PIMG -4, PIMG -5 and PIMG -6 showed drug release i.e. 97.12 ±1.53, 96.89 ±1.64, 93.12 ±1.52 %respectively among of these PIMG -4 showed better release and that contains drug: polymer ratio 1:2had showed the 97.12 ±1.53 % drug release in 12 hrs, which was in perfect for matrix forming agent which was used in the present study. Formulations PIMG -7 to PIMG -9 had showed the incomplete drug release i.e. 92.67 ± 1.24, 90.35 ±1.41, 89.14 ± 1.36 % in 12 hrs.

From the overall results of in-vitro drug release studies the matrix tablets prepared in various drug to polymers ratios like 1:0.5, 1:1.upto1:4.5 by using PLMG. The matrix tablets prepared by using VIMG in the ratio of 1:2(i.e., formulation PLMG-4) had showed best results. Thus, finally in concern to in vitro drug release studies VIMG was better.

Selection of performing formulations of matrix tablets prepared by using PLMG:

In concern to the micromeritic evaluation of powder blend prepared for the compression of matrix tablets of Diclofenac potassium containing PLMG gum formulation PLMG-4 had showed the angle of repose 17.31 ±0.01, bulk density 0.38 ±0.015, tapped density 0.44 ± 0.071, compressibility index 13.63 ± 0.36 and Hausner's ratio 1.15which were within the official limits and this indicates that formulation PLMG-4 was best in case of micromeritic properties among all formulation's matrix tablets of PLMG gum.

In concern to post compression evaluation of matrix tablets of VIMG formulation VIMG-5 had showed hardness 5.4±0.26, friability 0.49±0.024, uniformity of weight 515 ±0.16& uniformity of

content 99.80±084were within the official limits and this indicates that formulation PLMG-4was best in case of post compression evaluation parameters among all formulations of matrix tablets of PLMG.

In concern to swelling index of matrix tablets formulations prepared using PLMG formulation PLMG-4 had showed swelling index 218.43 and matrix tablets formulations prepared using PLMG.

In concern to *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 PLMG, the matrix tablets prepared by using PLMG in 1:2 ratio (i.e., formulation PLMG-4) had showed drug release 97.12 % which was selected for further study.

From above observation, VIMG in lower drug to polymer ratio was found effective as *gums had* showed successful sustained release of Diclofenac potassium more than 12 hours from the matrix tablets.

From the overall results of micrometric evaluation of powder blends, post compression evaluations, % swelling index determination & in-vitro drug release studies of matrix tablets evaluations formulation PLMG-4 amongst from all PLMG 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 Optimized Formulations of Matrix Tablets Prepared by Using PLMG.

The overall accelerated stability of selected best formulation on the basis of evaluation parameters shown to be stable on the basis of hardness, friability, weight uniformity and content uniformity when compared with original formulation with SD and RSD below 2,hence unaffected by stored in harsh environment as 40 ±2 ^{0}C and 75 ±5% RH.

Formulation PLMG-4 showed 96.97% drug released in 12 hrs after 90 days of storage in prescribed conditions for accelerated stability and the yield was found to be in acceptance range, with good preformulation, micromeritic study parameters.

The pre and post stability IR graphs data indicate that the various characteristic peaks were obtained in the FTIR spectrum of formulation there were no shifting in the frequencies of above said functional groups and there was no additional peaks observed in the pre and post stability optimized formulations and it didn’t showed any signs of incompatibility in between drug and the excipients including PLMG. Hence, above results concluded that there were no chemical

interactions were occurred in these formulations which were subjected to the accelerated stability studies as per the ICH guidelines. After the overall accelerated stability studies PLMG-4 formulation were found physically as well as chemically stable in nature.

CONCLUSIONS

In the present investigation the novel biomaterial modified gum from *Pistacia lantiscus* (PLMG) successfully characterized for various physicochemical properties and further studied as novel matrix forming material by direct compression method using diclofenac potassium as model drug. The PLMG tablets have shown to sustained the *in vitro* drug release up to 12hrs. Thus from the above studies, it could be proposed that, the novel matrix forming material PLMG would be used for sustaining the release characteristics of the drug. The overall accelerated stability of selected best formulation showed statistically promising results on the basis of evaluation parameters.

ACKNOLEDGEMENT

The authors are thankful to institution for providing research facility for this research work and further the authors are extend their gratification to Kalash Pharmachem Pvt. Ltd. Jalgaon for providing generous gift sample.

REFERENCES

1. Pandey VP, Manavalan R, Rajan S andGanesh KS. Formulation and release characteristics of sustained release diltiazem hydrochloride tablet. Indian J. Pharm. Sci, 2003; 651:44–48.
2. Yan G, Li H, Zhang R and Ding D. Preparation and evaluation of a sustained release formulation of nefidipine HPMC tablets. Drug Dev. Ind. Pharm, 2000; 266:681–686.
3. Ishikawa T, Watanabe Y, Takayama K, Endo H and Matsumoto M. Effect of HPMC on the release profiles and bioavailability of poorly water soluble drug from tablets prepared using macrogol and HPMC. Int J Pharm, 2021; 2:173–178.
4. Rao YM, Veni JK, and Javasagar G. Formulation and evaluation of Diclofenac sodium using hydrophilic matrices. Drug Dev Ind Pharm, 2021; 278:759–766.
5. Gayathri R and Ganapathy R.S., Preliminary characterization and in-vitro cytotoxic studies of the polysaccharaide from Araucaria heterophylla, International Journal of Recent Scientific Research, 2017; 8(5): 17200-17203.
6. Deb A and Das B, Isolation, purification and characterization of natural polymer obtained from plant Baheda (Terminella bellarica), World Journal of Pharmacy and Pharmaceutical Sciences Pharmacy and Pharmaceutical Sciences, 2016; 5(6): 1118-1129.
7. Deb A, Das B and Barua S: Pharmacological activities of Baheda (Terminella bellarica), A review. Journal of Pharmacognosy and phytochemistry, 2015; 4(4): 1-4.

8. Rahim H, Khan MA, Sadi A, Khan S, Chishti KA, Comparative studies of binding potential of Prunus armeniaca and Prunus domestica gums in tablets formulations. Pak. J. Pharm. Sci, 2015; 23(3): 909-914.
9. Gwen MJ and Joseph RR, In Banker GS and Rhodes CT, Eds. Modern Pharmaceutics, Marcel Dekker Inc. New York , 1996; 72(3): 575.
10. Salsa T, Veiga F and Pina ME. Oral controlled release dosage form of cellulose ether polymers in hydrophilic matrices. Drug Develop. Ind. Pharm. 1997; 23: 929-938.
11. Koutsoudaki C, Martin K, and Alison R.Chemical Composition and Antibacterial Activity of the Essential Oil and the Gum of Pistacia lentiscus Var. chia, J. Agric. Food Chem. 2005; 53, (20):7681–7685.
12. Gayathri R and Ganapathy RS. Extraction And Characterization Of The Gum Isolated From Araucaria Heterophylla, International Journal of Recent Scientific Research**.** 2018; Vol. 9(3): 1062-1067.
13. Government of India. Indian Pharmacopoeia. The Controller of Publication: New Delhi, Vol. III, Ministry of Health and Family Welfare. Indian Pharmacopoeia Commission, Ghaziabad; 2010: 746-758.
14. Beckett AH and Stenlake JB. Practical Pharmaceutical Chemistry, Part II. 4th ed., New Delhi: CBS Publisher and Distributors;2004: 199-205.
15. Sinko, P. J., Martin's Physical Pharmacy, 5th ed.,New Delhi: Wolters Kluwer Health (India) Pvt. Ltd; 2007: 570-571.
16. Nep EI, Conway BR, Characterization of Grewia Gum, a Potential Pharmaceutical Excipient, J. Excipients and Food Chem. 2010; 1 (1):30-40.
17. Subhryamanyam, CVS, Physical Pharmacy, IInd ed, Vallbh Prakashan; 2000: 215-217.
18. British Pharmacopoeia, Her Majesty's Stationey Office, British Pharmacopoeia Commission London, UK: 2007: 340-346.
19. Martin A, Patrick N and Sinko JP, Martin's Physical Pharmacy and Pharmaceutical Sciences, Physical Chemical and Biopharmaceutical Principles in the Pharmaceutical Sciences. Phila: Lippincott Williams and Wilkins; 2006: 533–560.
20. Government of India, Ministry of health & welfare. Indian Pharmacopoeia Vol. II, The Indian Pharmacopoeia Commission, Ghaziabad; 2007:402-404.
21. Lachman L, Liberman HA and Kanig JL: The Theory and Practice of Industrial Pharmacy, 3rd ed., Mumbai: Varghese Publishing House; 1991: 88.

22. Shekar BC, Kiran RS, Design and Evaluation of Sustained Release Monolithic Matrix Tablets of Tramadol Hydrochloride. IJPI's Journal of Pharmaceutics and Cosmetology 2010; 1(1): 1-11.
23. Wadher KJ and Kakde RB, Development of a sustained-release tablet of Metformin hydrochloride containing hydrophilic eudragit and ethyl cellulose polymer. International Journal of Comprehensive Pharmacy, 2011; 5(7): 1-4.
24. Beckett AH and Stenlake JB. Practical Pharmaceutical Chemistry, Part II. 4th ed. New Delhi: CBS Publisher and Distributors; 2004: 85-100.
25. The United States Pharmacopoeia (USP/NF). Physical tests/ dissolution. The U. S. Pharmacopoeial Convention, Rackville MD. 24/19;2000: 1941–1943.
26. ICH Guideline Guidelines for industry - Q1-B: Photostability testing of New drug substance & product; 1996: 1-25.
27. ICH Q1A (R2). Stability testing guidelines: Stability testing of new drug substances and products. ICH Steering Committee; 2003: 1-70.
28. Yoshioka S., and Stella VJ., Stability of drugs and dosage forms, New York: Kluwer Academic/Plenum Publishers; 2000: 139-150.
29. Chow SC, In: Statistical Design and Analysis of Stability Studies, Imprint Chapman and Hall/CR, Vol. I, 2007; 28.
30. Bajaj S, Singla D and Sakhuja N, Stability testing of pharmaceutical products. Journal of Applied Pharmaceutical Science 2012; 2(3):129-138.