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Formulation, Evaluation and Comparison of Sustained Release Matrix Tablets of Diclofenac Sodium Using Natural Polymers as Release Modifier

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ABSTRACT

In the present investigation, an attempt was made to formulate sustained release matrix tablets of Diclofenac sodium using gum acacia and tamarind gum as release modifier. Six batches of sustained release matrix tablets of Diclofenac sodium were prepared by using different drug: polymer ratios viz. 1:1, 1:1.5, 1:2, 1:2.5, 1:3, and 1:3.5 for both gum acacia and tamarind gum. The tablets were analyzed for their hardness, friability, weight variation, and an *In-vitro* release was performed in phosphate buffer saline (PBS) pH 7.4 for twenty four hours. Swelling study was also carried out to study dispersibility of gums at different concentrations. The physical characters of the fabricated tablet were within acceptable limits. Gum acacia showed better swelling than tamarind gum. A better sustained drug release (98.7%) was obtained with the matrix tablet (Batch F) of the tamarind gum. Results showed that the drug release from matrix tablets prepared by using natural polymers can be sustained for more than 12 hrs and the drug release vary with concentration of polymer in matrix tablets.

KEY WORDS

Sustained release matrix tablet, gum acacia, tamarind gum, Diclofenac sodium, swelling index.

INTRODUCTION

Drug products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years [1]. Regular research is going on for the use of natural occurring biocompatible polymeric material in designing of dosage form for oral controlled release administration. Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media, so these have been used for the preparation of dosage form [2]. Plant polysaccharide, has been shown to be useful for the construction of drug delivery systems for specific drug delivery [3]. Gum acacia is often used as plasticizer and tablet binder. The gum acacia has been recognized as an acidic polysaccharide containing D-galactose, L-arabinose, L-rhamnose and D-glucuronic acid [4]. Tamarind gum was xyloglycon present in tamarind seed. Both of these are hydrophilic polymer and had been limited for use as gelling, thickening, suspending

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and emulsifying agents [5, 6, 7, 8]. Diclofenac sodium is sodium 2-[(2, 6-dichlorophenyl)-amino] phenyl acetate. Diclofenac is an acetic acid nonsteroidal antiinflammatory drug (NSAID) with analgesic property. Diclofenac is used to treat pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic keratosis [9, 10]. The present investigation is aimed to formulate the matrix tablet of Diclofenac sodium with tamarind gum and gum acacia using no other varying parameter.

MATERIAL AND METHODS

Isolation of gum from Tamarind Seed

The crushed seeds of *Tamarindus indica* were soaked in water for 24 h, boiled for 1 h, and kept aside for 2 h for the release of gum into water. The soaked seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, to the filtrate, equal quantity of absolute ethyl alcohol was added to precipitate the gum. The gum was separated by filtration. The marc was not discarded but it was sent for multiple extractions with decreasing quantity of extracting solvent, i.e., water with the increase of number of extractions. The isolation was continued until the material was free of gum. The separated gum was dried in hot air oven at temperature 40°C. The dried gum was powdered and stored in airtight containers at room temperature [11, 12, 13].

Procurement of drug and other excipients

Diclofenac sodium was obtained as gift sample from Alchem Laboratories, Baddi India. The Pharmacopoeial grade of gum acacia was obtained from RFCL Limited, New Delhi, India and microcrystalline cellulose was procured from RANKEM Limited, New Delhi, India.

Preparation of SR matrix tablets

According to Table 1 and Table 2 sustained release (SR) matrix tablets of Diclofenac sodium were prepared by using different drug: polymer ratios viz. 1:1, 1:1.5, 1:2, 1:2.5, 1:3, 1:3.5 for various batches Batch A, Batch B, Batch C, Batch D, Batch E and Batch F respectively.Tamarind gum and gum acacia were used as matrix forming material, while microcrystalline cellulose was used as filler to maintain the tablet weight. All ingredients were passed through a # 20 sieve, weighed and blended. The granules (which were obtained after wet granulation) were compressed by a direct compression technique, using KBr press (IR Press), with the help of 8mm flat faced punches [14, 15].

Table 1.
Formulation composition of matrix tablets.

Ingredients	Formulations					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Diclofenac sodium	50mg	50mg	50mg	50mg	50mg	50mg
Polymer [a]	50mg	75mg	100mg	125mg	150mg	175mg
Microcrystalline cellulose	200mg	175mg	150mg	125mg	100mg	75mg

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Total weight	300mg	300mg	300mg	300mg	300mg	300mg

[a] *gum acacia and tamarind gum for their respective batches.*

Evaluation of Fabricated Matrix Tablets

Weight variation: All prepared matrix tablets were evaluated for weight variation as per USP XXIV monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and standard deviation was calculated [16, 17].

Friability: Tablets of all batches were used to evaluate friability as per USP XXIV monograph. Friability testing was done by Roche friabilator with triplicate readings [16, 17].

Hardness: Hardness of all batches was determined using Digital Force Gauge (Model:EL=500N, Electrolab). The test was carried out in triplicate for all batches as per USP XXIV monograph for uncoated tablets [16, 17].

Thickness: Thickness was measured by vernier caliper as per USP XXIV monograph. The readings were carried out in triplicate and average value was noted [16, 17].

Drug content: The tablets were powdered, and 50 mg equivalent weight of Diclofenac sodium in tablet powder was accurately weighted and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH6.6) was added and shaken for 10 min. then, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 276 nm using UV-visible spectrophotometer (Shimadzu UV-2450, Japan). The drug content of the each sample was estimated from their standard curve [18, 19].

Swelling behavior of sustained release matrix tablets: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of all formulation was studied. One tablet from each formulation was kept in a petridish containing pH 7.4 phosphate buffer. At the end of 0.5 h and 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 1 h, weights of the tablet were noted, and the process was continued till the end of 8 h. Percentage weight gain by the tablet was calculated by formula;

$$S.I = \{(M_t - M_o) / M_o\} \times 100,$$

Where, S.I = swelling index, M_t = weight of tablet at time t (h) and M_o = weight of tablet at zero time [20, 21].

***In vitro* drug release study:** *In vitro* drug release was studied using LabIndia Dissolution Apparatus, with 900 ml of dissolution medium (phosphate buffer pH 7.4) maintained at 37±1°C for 24 h, at 50 rpm. 5ml of sample was withdrawn after every hour, and was replaced by an equal volume of fresh dissolution medium of same pH (phosphate buffer pH 7.4). Collected samples were analyzed spectrophotometrically at measured wavelength of 276nm, and cumulative percent drug release was calculated [22, 23].

The data obtained in the in-vitro dissolution study is grouped according to two modes of data treatment as follows:

1. Percentage drug released Vs time (h).
2. Cumulative percentage drug released Vs time (h)

In these two methods, drug release profile can be better studied using cumulative percentage drug release Vs time (h) plot.

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RESULT AND DISCUSSION

Infrared spectra of drug and polymers were used to study the compatibility between them. No change in peak shows that there was no interaction between drug and polymers.

As per the Table 3 and Table 4, the formulated matrix tablets met the Pharmacopoeial requirement of uniformity of weight. All the tablets confirmed to the requirement of assay, as per USP. Hardness, percentage friability and thickness were all within acceptable limits [16, 17].

Table 2.
Various evaluation parameters for fabricated gum acacia tablets.

Parameter	Guar acacia					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Weight variation(gm)	0.301 ±0.01	0.293 ±0.02	0.299 ±0.01	0.298 ±0.01	0.301 ±0.01	0.302 ±0.01
Friability (%)	0.03 ±0.01	0.02 ±0.01	0.02 ±0.01	0.02 ±0.01	0.01 ±0.01	0.01 ±0.01
Hardness (N)	20.07 ± 0.06	20.20 ± 0.0	20.37 ±0.06	20.53 ±0.06	20.63 ± 0.06	20.83 ±0.06
Thickness(mm)	3.503 ±0.02	3.560 ±0.08	3.740 ±0.04	3.683 ±0.03	3.777 ±0.04	4.04 ±0.07

Table 3.
Various evaluation parameters for fabricated tamarind gum tablets.

Parameter	Tamarind Gum					
	Batch A	Batch B	Batch C	Batch D	Batch E	Batch F
Weight variation(gm)	0.299 ±0.01	0.300 ±0.01	0.291 ±0.01	0.293 ±0.01	0.298 ±0.01	0.293 ±0.01
Friability (%)	0.05 ±0.01	0.03 ±0.01	0.03 ±0.01	0.03 ±0.01	0.02 ±0.01	0.02 ±0.01
Hardness (N)	20.24 ± 0.12	20.27 ± 0.15	20.40 ±0.1	20.53 ±0.06	20.77 ± 0.06	20.80 ±0.1
Thickness(mm)	3.623 ±0.01	3.727 ±0.02	3.790 ±0.03	3.677 ±0.18	3.777 ±0.19	3.707 ±0.05

Sustained drug release was displayed by all formulations in phosphate buffer (pH 7.4). Figure 1 and Figure 2 showed the swelling characteristics of gum acacia and tamarind gum respectively. The swelling index was calculated with respect to time. As time increases, the swelling index was increased, because

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weight gain by tablet was increased proportionally with rate of hydration up to certain limit. Later on, it decreases gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The direct relationship was observed between swelling index and polymer concentration, and as polymer concentration increases, swelling index was increased [20, 21].

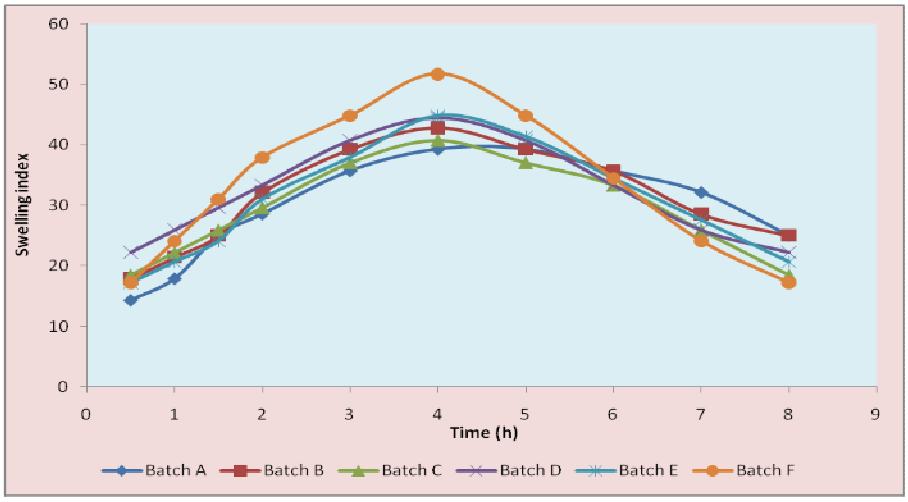

Figure 1. ***Swelling Index profile of tablet containing gum acacia as polymer***

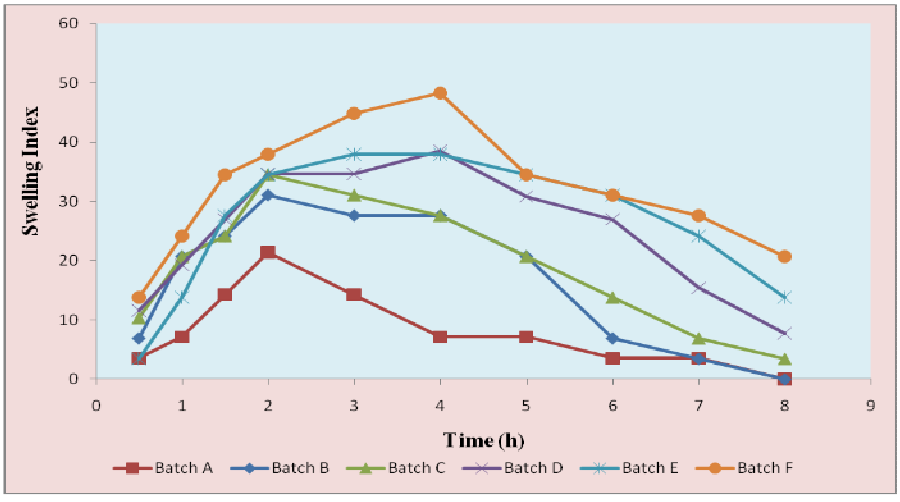

Figure 2. ***Swelling index profile of tablets containing tamarind gum as polymer.***

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Figure 3. ***Figure showed dispersion of tablet containing tamarind gum.***

It has been observed that the cumulative percent drug release decreases with increasing concentration of polymer and swelling index. The reason attributed to this fact is slow erosion of the gelled layer from the tablets containing higher amount of natural polymer. This slow release is because of the formation of a thick gel structure that delays drug release from tablet matrix [22, 23, 24, 25, 26].

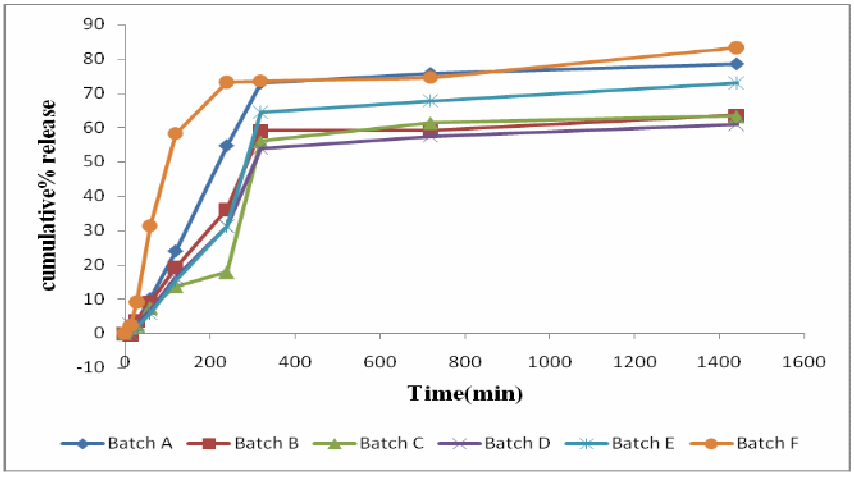

Figure 3. ***Drug release profile of tablets containing gum acacia as polymer***

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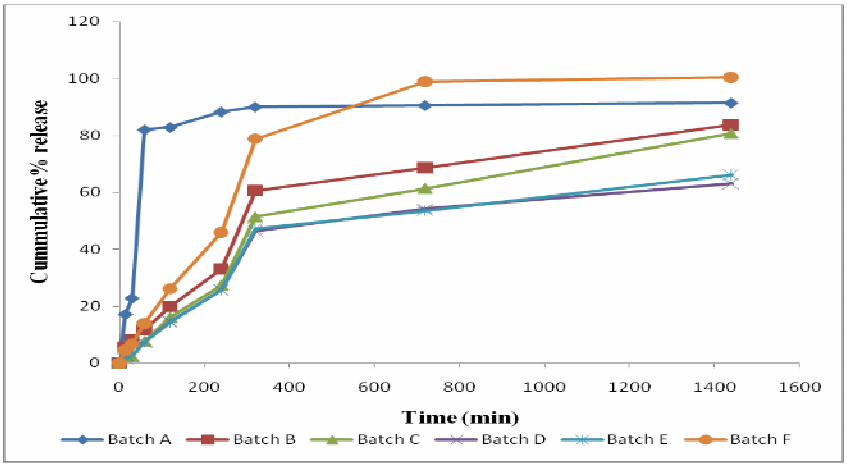

Figure 4. ***Drug release profile of tablets containing tamarind gum as polymer***

The *in vitro* release of Diclofenac sodium from gum acacia and tamarind gum were showed in Figure 3 and Figure 4 respectively. From the findings, obtained so far it can be concluded that Batch F of tamarind gum in the concentration ratio of 1:2.5 was promising concentration for oral sustained release tablet of Diclofenac sodium.

CONCLUSIONS

Natural polymers when used as release retardent exhibits uniform release over longer period of time. Hence it can be concluded that, the tamarind gum which is a natural polymer can be used as a promising drug release retardent in comparision to the estabilized gum acacia in a particular cocentration range.

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REFERENCES

1. Ansel H.C., Loyyd V.A., Pharmaceutical dosage forms and Drug Delivery System. Lippincott's Williams and Wilking, Hong Kong, 8: 275-280, (1999).
2. Gwen M.J., Joseph R.R., Rhodes C.T. Modern Pharmaceutics, Marcel Dekker, Inc., New York, 72(3): 58, (1996).
3. Langer R.S., Peppas N.A., Present and future application of biomaterials in controlled drug delivery systems. Biomaterials, 2(10): 201-213, (1981).
4. Arthur H.K. Handbook of Pharmaceutical Excipients. 3rd ed. American Pharmaceutical Association, London, 271, 297, 463-464, (2000).
5. Rao P.S., Srivastav H.C., Tamarind. In Indusrtial Gums, (Ed.) R.L. Whistler, Academic Press, 2nd Ed, New York, 369-411, (1973).
6. Nandi R.C., A Process for preparation of polyose from the seeds of Tamarindus indica. Ind. Pat, 142092, (1975).
7. Rao P.S., Extraction and purification of tamarind seed polysaccharide. J Sci Ind Research, 4: 705, (1946).

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8. Kulkarni D., Ddwivedi D.K., Sarin J.P.S., Singh S., Tamarind seed polyose: A potential polysaccharide for sustained release of verapamil hydrochloride as a model drug. Indian J Pharm Sci, 59(1): 1-7, (1997).
9. Indian Pharmacopoeia. Ministry of health. The controller of publications, New Delhi, 4ed; 432, (1996).
10. Sujja-areevath J., Munday D.L., Cox P.J., Khan K.A., Release characteristics of diclofenac sodium from encapsulated natural gum mini-matrix formulations. Int J Pharm, 139: 53-62, (1996).
11. Kulkarni G.T., Gowthamarajan K., Rao B.G., Suresh B., Evaluation of binding properties of selected natural mucilages. Journal of Scientific and Industrial Research (India), 61: 529-532, (2002).
12. Kulkarni G.T., Gowthamarajan K., Rao B.G., Suresh B., Evaluation of binding properties of *Plantago ovata* and *Trigonella foenum* graecum mucilages. Indian Drugs, 39: 422-425, (2002).
13. Baveja S.K., Rangarao K.V., Arora J., Examination of natural gums and mucilages as sustaining materials in tablet dosage forms. Indian Journal of Pharmaceutical Sciences, 50: 89-92, (1988).
14. Nokano M., Ogata A., *In vitro* release characteristics of matrix tablets: Study of Karaya gum and Guar gum as release modulators. Ind J Pharm Sc, 68(6): 824-826, (2006).
15. Gwen M.J., Joseph R.R., Rhodes C.T., Modern Pharmaceutics, Marcel Dekker, Inc, New York, 72(3): 581, (1996).
16. USP30-NF25, The official compendium of standards. The United States Pharmacopoeial Convention, 2007.
17. Lantz R.J., Schwartz J.B., Tablets. In: Lieberman HA, Lachman L, editors. Pharmaceutical dosage forms. 2nd Ed. New York, USA: Marcel Dekker, Inc, 15-20, 69, (2005).
18. Khullar P., Khar R.K., Agarwal S.P., Evaluation of guar gum in the preparation of sustained-release matrix tablets. Drug Dev Ind Pharm, 24: 1095-1109, (1998).
19. Krishnaiah Y.S.R., Rama Rao T., Ushasree M., Satyanarayana S., A study on the *in vitro* evaluation of guar gum as a carrier for oral controlled drug delivery. Saudi Pharm J, 9: 91-98, (2001).
20. Sujja-areevath J., Munday D.L., Cox P.J., Khan K.A., Relationship between swelling, erosion and drug release in hydrophilic natural gum mini-matrix formulations. Eur J Pharm Sci, 6: 207-217, (1998).
21. Abrahamsson B., Alpsten M., Bake B., Larsson A., Sjogren J., *In vitro* and *in vivo* erosion of two different hydrophilic gel matrix tablets. Eur J Pharm Biopharm, 46: 69-75, (1998).
22. Sujja-areevath J., Munday D.L., Cox P.J., Khan K.A., Release characteristics of diclofenac sodium from encapsulated natural gum mini-matrix formulation. Int J Pharm, 139: 53-62, (1996).
23. Ei-Arini S.K., Leuenberger H., Modelling of drug release from polymer matrices: Effect of drug loading. Int J Phar, 121: 141-148, (1995).
24. Harland R.S., Gazzaniga A., Sanagalli M.E., Colombo P., Peppas N.A., Drug/polymer matrix swelling and dissolution. Pharm. Res., 5(8): 488-494, (1998).
25. Ritger P.L., Peppas N.A., A simple equation for description of solute release II Fickian and anomalous from swellable devices. J Control Rel, 5: 37-42, (1987).
26. Munday D. L., Cox P. J., Compressed xanthan and karya gum matrices: hydration, erosion and drug release mechanisms. Int J Pharm, 203: 179-182, (2000).