Research Article

Formulation and Evaluation of Natural Polymer-Based Sustained Release Matrix Tablets Containing Salbutamol Sulphate

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ABSTRACT

Using hydrophilic matrices offers an intriguing option for the creation of oral sustained-release formulations. They can be used for controlled release of both water-soluble and water-insoluble drugs. The present study explores the potential of linseed mucilage (LM) and fenugreek seed mucilage (FSM) as excipients in drug delivery systems. The main aim of proposed work is to focus on the possibilities of using these polysaccharide in industries with particular reference to its physical properties, chemical properties for the formation of new drug delivery systems. This study aimed to develop and characterize sustained release matrix tablets of Salbutamol Sulphate to treat asthma. Matrix tablets containing Salbutamol Sulphate were prepared using the wet granulation method and subsequently assessed for their drug release profiles. The drug release was decreased with the increase in LM, FSM concentration. Drug release kinetics was explained by Higuchi's equation. Testing of the optimized formulation for stability revealed that the drug degradation was not appreciable. The results suggest that the LM and FSM can be used in the formulation of Sustained release tablets.

Keywords: Tablet, sustained-release formulation, Salbutamol Sulphate, linseed mucilage, fenugreek seed mucilage, treatment of asthma, hydrophilic matrix.

INTRODUCTION

Hydrophilic matrices are an interesting option when developing an oral sustained release formulation. The drug release from such matrices can be controlled through their physical properties. Since Polysaccharides are nontoxic and acceptable by the regulating authorities they are the preferred hydrophilic polymers [1].

Gums and Mucilages are polysaccharide complexes formed from sugar and uronic acid units. They can absorb large quantity of water and swell[2].

Synthetic hydrophilic polymers are used more often than natural polymers[2]. Today the whole world is interested in natural drugs and excipients. As a non-toxic, cheaper and readily available alternative to synthetic materials, natural material has many advantages over synthetic ones. Furthermore, they can be modified to obtain tailor made materials for drug delivery system allowing them to compete with the synthetic product that are commercially available. Many kinds of natural gum and mucilages are used in the food industry and are regarded as a safe for human consumption[3].

In recent times, increasing attention has been given to the application of gums and mucilages of various sources as pharmaceutical excipients. They possess a variety of pharmaceutical properties, which include binding, disintegrating, suspending, emulsifying, gelling, and sustaining properties[4-12].

Present work reports extraction of gum/mucilage of *linum ussitatissimum* and trigonella foenum-graecum using water and precipitation by acetone. Mucilage yield is dependent on the temperature. Physicochemical characteristics of gum/mucilage such as solubility, swelling index, loss on drying, pH were studied. Salbutamol Sulphate was as a model drug in the evaluation of mucilage's release retarding properties in tablets.

MATERIALS AND METHODS

Materials

The linseeds and fenugreek seeds were collected from local area of Buldhana, Maharashtra, India and authenticated by Shri Shivaji Science and Arts College, Chikhali, dist. Buldana. Salbutamol sulphate was obtained as a gift sample from Leben Lab Akola. Lactose Monohydrate (IP grade), Talc (AR grade), Starch and Acetone (AR grade) were obtained from Loba Chemie Pvt. Ltd, Mumbai (India).

Isolation of mucilage:

Linseed:

Seeds of *Linum usitatissimum* were taken and soaked for 12 h in distilled water, then this mixture was boiled at 70-80° C for around 30 min, heating increases rate of mucilage extraction and inactivates enzymes. After 2-3 hours maximum amount of mucilage was extracted in water, which results in formation of thick glue-like mass. To reduce viscosity this thick glue-like mass was diluted with water, then passed through the several folds of muslin cloth. Around three times volume of acetone was added to the thick glue to carry out precipitation of dissolved mucilage from glue. Precipitated mucilage was separated. Mucilage was dried at 50°C in hot air oven and gave a yield

of 45g-50g mucilage/Kg linseed, stored in desiccator for further use.

Fenugreek seed mucilage:

Seeds of trigonella foenum-graecum were taken and soaked for 12 h in distilled water. This mixture was boiled at 70-80° C for 30 min, heating increases rate of mucilage extraction, which results in formation of thick glue like mass. Then thick glue like mass was passed through the several folds of muslin cloth. Around two times volume of acetone was added to the thick glue to carry out precipitation of dissolved mucilage from glue. Precipitated mucilage was separated. Mucilage was dried at 45-50°C in hot air oven and gave a yield of 45g-50g mucilage/Kg fenugreek, stored in desiccator for further use.

Chemical Test for Mucilages:[13-15]

Extracted mucilages were analyzed for various chemical tests, Molisch's test developed violet green color at the junction of the two layers showed presence of carbohydrate in it. The absence of starch was confirmed by iodine test, showed no color change on addition of iodine solution. The presence of mucilage further substantiated by Ruthenium solution which showed development of pink color.

Physiochemical, Derived and Microbiological Properties of Mucilages: [16-18]

Separated mucilages was evaluated for various physiochemical properties such as solubility, swelling index, water retention capacity, loss on drying, pH, melting point, microbial load, particle size distribution as well as for various derived properties such as bulk density, tapped density, compressibility index, Housner ratio and angle of repose.

Microbial Load:[19-21]

The test is designed for the estimation of the number of viable aerobic micro-organisms present in pharmaceutical substances. Total viable aerobic microbial count was determine by plate count method.

Pour – Plate Method:

Casein soya bean digest agar such as medium 2 was added in each petri dish and allowed to solidify. Then pre treated sample preparation was spread on the solidified medium in a petri dish and it was incubate at 37° for 72 hour. Result was examined after 24 hours.

Particle Size Distribution: [22]

Few particles of Linseed mucilage and Fenugreek seed mucilage powder were taken separately on a glass slide, uniformly spread by a brush, such that individual particle can be seen and particle size distribution was measured by Microscope Image Analyzing System (Vision plus-5000).

Rheology Study: [19, 20, 23]

Rheological measurements were carried out using a rotational viscometer (Brookfield R/S plus rheometer) equipped with C25 measuring spindles and for each test, approximately 0.2-0.5 ml sample was transferred to sample compartment (cone and plate).

A. Determination of Viscosity at Different Concentration of Mucilage:

The viscosity was measured for linseed and Fenugreek seed mucilage solutions with concentration of 1 %, 2 % and 3 % (which were prepared in distilled water) at shear rate 30 1 / s and the graph was plotted between by taking concentration on X- axis and viscosity on Y- axis.

B. Determination of Viscosity at Different pH

The viscosity was measured for 1%, 2% and 3% linseed and Tamarind seed mucilage solutions with pH ranging from 2.0 to10.0 (adjusted using 0.1N NaOH and 0.1N HCl) at different shear rates and at room temperature.

Drug-Excipient Interactions:

It is important to check any kind of interaction between drug and mucilage. It was done by using Fourier transformed infrared spectroscopy and Differential Scanning Calorimetry**.**

A. Fourier Transform Infrared Spectroscopy:

IR spectra of pure Salbutamol Sulphate and mucilage were taken separately and physical mixture of drug and mucilage were kept for a month at room temperature and then their FTIR were taken to know any possible interaction between drug and mucilage.

B. Differential Scanning Calorimetry:

A differential scanning calorimeter was used for thermal analysis of drug, excipient and their physical mixture. The drug and excipients were passed through sieve no. 60. Drug alone and its mixture with excipient was weighed directly in the pierced DSC aluminium pan (Aluminium Standard 40µl) and scanned from temperature range of 200^0 to 300°C and at heating rate of 10°C/min in nitrogen atmosphere at flow rate 50 ml/min. the thermogram obtained were observed for any interaction.

EXPERIMENTAL METHODS

Preparation of Granules and Tablet:

Drug and excipients were weighed accurately as per composition given in Table 2 and powdered to obtained uniform particle size using mortar and pestle. In order to ensure uniform mixing of dug and excipients, the powder was thoroughly mixed. To form damp mass required amount of starch paste was added to the above mixture. Then prepared damp mass was passed through sieve no # 16/22. The granules which passed through sieve no #16 and retained on sieve no. #22 were used. The prepared granules were kept for drying in hot air oven at 50-60°. Then dried granules were collected, separated from fines by sieving. Separated granules were weighed and analyzed for bulk density, true density, angle of repose, and Carr's index. Weighed amount of prepared granules were taken,

lubricants and fines were added to it and uniformly mixed. Compression was performed on the prepared mixture.

Evaluation of Tablets:

Prepared tablet was evaluated for weight variation, hardness, friability, thickness and diameter, drug content[24].

Determination of Swelling and Erosion Behavior of Sustained Release Matrix Tablet:

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 petri dish containing pH 1.2 for 2 h and pH 6.8 phosphate buffer for 6 h. At the end of 0.5 h and 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed. Then after every 1 h, weights of the tablet were noted, and the process was continued till the end of 8 h. To determine matrix erosion, tablet was introduced into the dissolution apparatus under the standard set of conditions as specified for determination of *in vitro* drug release. The tablets were removed using a small basket at hourly intervals and swollen tablets were placed in a oven at 40°C and after 48 h tablets were removed and weighed. The same tablet was subjected for erosion study up to 12 h. Swelling (%) and erosion (%) was calculated according to the following formula[19, 20, 24].

$$\% \text{ Swelling} = (W_t - W_0) / W_0 \times 100$$

$$\% \text{ Erosion} = (W_0 - W_r) / W_0 \times 100$$

Where,

W_t = the weight of the matrix after swelling

W_0 = the initial weight of the matrix

W_r = the weight of the eroded matrix

Dissolution Studies:

The *in vitro* release of Salbutamol Sulphate from formulated tablets was carried out in acid buffer pH 1.2 for 2 h and then phosphate buffer pH 6.8 for remaining 10 h. The studies were performed in USP dissolution apparatus II, at 37 ± 0.5° C and 50 rpm speed. Samples were taken at 1 hour interval and analyzed for Salbutamol Sulphate content at 276 nm by using UV–visible spectrophotometer, (Model. UV 2401 PC, Shimadzu Corporation, Singapore). [25]

Stability Study:

The optimized batches FL_1 was kept for stability study, results shows insignificant difference for drug release and other evaluation parameter for the period of 3 months at 40^0C/75% RH.

RESULT AND DISCUSSION

The mucilages were isolated from the seeds of *Linum ussitatissimum* and *Trigonella foenum-graecum* using aqueous extraction followed by precipitation using acetone as non-solvent (Fig. 1 and 2). The yield of the mucilage was calculated with respect to the weight of dried seeds and was found to be 45g-50g and 45g-50g respectively. Extracted mucilages were analyzed for various chemical tests, Molisch's test developed violet green color at the junction of the two layers showed presence of carbohydrate in it. The absence of starch was confirmed by iodine test, showed no color change on addition of iodine solution.

Table 1: Characterization of Mucilages

Property of mucilage	Result	
	Linseed mucilage	Fenugreek seed Mucilage
Bulk density (g/cc)	0.488 ± 0.02	0.583 ± 0.01
Tapped density (g/cc)	0.541 ± 0.04	0.698 ± 0.03
Compressibility Index (%)	18.85 ± 0.05	22.2 ± 0.05
Housner Ratio	1.18 ± 0.06	1.22 ± 0.09
Angle of repose (°)	35°20' ± 0.12	40°85' ± 0.16
Swelling Index (%)	1000 ± 0.32	1400 ± 0.18
Water Retention (%)	8.00 ± 1.02	11.00 ± 1.09
Loss on drying (%)	5.2 ± 0.16	5.6 ± 0.30
pH	6.32 ± 0.19	7.12 ± 0.12
Melting point (°C)	260° - 280°	270° - 290°
Practical yield (g/Kg)	45g-50g	45g-50g

*Each value represents the mean ± standard deviation (n=3)

The presence of mucilage further substantiated by Ruthenium solution which showed development of pink color. In the microbial load testing, the polysaccharide showed 6000 and 7000 colony forming unit per gram of bacteria for linseed mucilage and Fenugreek seed Mucilage respectively which was in acceptable limits for the natural products. The above results indicated that the selected polysaccharide can be used as an excipient in dosage forms. The viscosity of 1% w/v solution of the Linseed mucilage and Fenugreek seed mucilage was found to be 10.20 Pa.s. and 17.24 Pa.s respectively. Viscosity and pH are important physical properties, which can contribute significantly to the understanding of the granule and tablet properties of various substrates. The pH of the isolated mucilage was found to be 6.32 ± 0.19 and 7.12 ± 0.12 respectively. The compatibility between the drug and the isolated mucilages were found to be good by the FTIR and DSC studies. The matrix tablets of Salbutamol sulphate using linseed mucilage and fenugreek seed mucilage were prepared by wet granulation method. Table 3 shows the data obtained from the evaluation of tablets. The hardness of the tablets was found to be in the range of 10.00 – 12.00 kg/cm^2. The tablets showed 95.90- 98.52 % of the labeled amount of drug, indicating uniformity in drug content. The individual weight variation was found to be within ±7.5% of the average tablet weight and the friability values were found to be in the range of 0.23 - 0.43% for all the formulations. The swelling index increased with the increase in concentration of mucilage wherein Fenugreek seed mucilage have more swelling than Linseed mucilage and the matrices underwent both water uptake and

erosion simultaneously immediately after placement in the dissolution medium shown in Table 4. The drug release decreased as the concentration of mucilage in the matrix increased. The in-vitro drug release profile of Salbutamol sulphate from all the formulations is shown in Table 5 and Fig. 3, 4. The results indicated retardant release of drug from all the formulations with increase in the polymer concentration. The Formulation FL_1 showed a slow and complete drug release of 91.30±0.91 over a period of 12 hr. as that of marketed formulation. The 'n' value of formulation FL_1 from korsmeyer-peppas equation was found to be 0.829 indicating that the release mechanism was non-Fickian or anamolous release (0.5 < n < 1). It showed that the release was dependent on both drug diffusion and polymer erosion. R^2 value (i.e., 0.978) was maximum for Higuchi plot. Therefore, release kinetics fits Higuchi plot.

Table 2: Composition of Salbutamol Sulphate Tablets:

Ingredients (mg)	FL_1	FL_2	FL_3	FF_1	FF_2	FF_3
Salbutamol sulphate	4.8	4.8	4.8	4.8	4.8	4.8
Lactose monohydrate	120.7	110.7	100.7	110.7	100.7	90.7
Linseed mucilage	20	30	40	-	-	-
Fenugreek seed Mucilage	-	-	-	30	40	50
Magnesium stearate	3	3	3	3	3	3
Talc	1.5	1.5	1.5	1.5	1.5	1.5

*Weights are given for one tablet; Tablets with Linseed mucilage: **FL_1, FL_2, FL_3**; Tablets with Fenugreek seed Mucilage: **FF_1, FF_2, FF_3**

Table 3: Post Compression Parameter of Salbutamol Sulphate Tablets:

Formulations	Hardness* (kg/cm^2)	Friability* (%w/w)	Thickness* (mm)	Diameter* (mm)	%Drug Content*
FL_1	11.45±0.09	0.37±0.05	3.13±0.044	6.03±0.08	**97.95± 0.29**
FL_2	11.13±0.05	0.24±0.04	3.19±0.035	6.02±0.06	**95.90± 0.30**
FL_3	10.31±0.03	0.31±0.07	3.11±0.036	6.03±0.09	**98.52± 0.53**
FF_1	10.75±0.04	0.43±0.02	3.18±0.045	6.02±0.04	**96.87± 0.45**
FF_2	11.32±0.08	0.32±0.06	3.12±0.037	6.02±0.01	**95.95± 0.62**
FF_3	11.48±0.01	0.36±0.05	3.05±0.031	6.03±0.05	**97.46± 0.15**

*Each value represents the mean ± standard deviation (n=3).

Table 4: Percentage Swelling Indices and Percentage erosion of Formulations containing Linseed mucilage and Fenugreek seed Mucilage:

	Time (min)	FL_1	FL_2	FL_3	FF_1	FF_2	FF_3
% Swelling *	0	0±0	0±0	0±0	0±0	0±0	0±0
	30	11.82±1.80	14.27±1.27	17.72±1.49	18.08±1.75	20.09±1.05	24.28±1.46
	60	23.47±1.79	30.15±1.56	33.80±1.28	24.33±1.82	28.36±1.74	30.84±1.22
	90	34.58±1.73	47.28±1.61	49.08±1.67	30.91±1.67	36.66±1.53	38.12±1.63
	120	50.23±1.76	53.07±1.30	55.63±1.35	38.17±1.55	40.17±1.66	42.87±1.92
	180	58.17±1.29	60.19±1.76	60.98±1.77	47.23±1.61	49.97±1.03	53.23±1.51
	240	65.92±1.72	66.22±1.43	67.77±1.29	53.15±1.36	56.31±1.83	59.38±1.38
	300	70.08±1.80	72.54±1.05	74.82±1.91	61.28±1.49	65.48±1.91	68.09±1.74
	360	74.18±1.61	76.15±1.59	77.01±1.57	49.82±1.21	50.22±1.57	79.21±1.82
	420	51.15±1.23	56.63±2.01	60.02±1.83	40.30±1.77	40.50±1.10	63.33±1.68
	480	39.27±1.92	43.37±1.35	49.13±0.78	35.16±1.04	38.26±1.99	42.40±1.00
% Erosion*	0	0±0	0±0	0±0	0±0	0±0	0±0
	1	5.13±1.67	4.03±1.56	3.87±1.36	7.72±1.72	6.09±1.73	5.87±1.55
	2	8.48±1.75	6.28±1.60	5.15±1.08	14.28±1.67	13.97±1.22	11.98±1.63
	3	12.40±1.37	9.97±1.39	8.23±1.09	20.15±1.74	19.23±1.53	17.22±1.11
	4	15.98±1.89	13.24±1.71	11.17±1.61	25.87±1.36	24.17±1.52	21.45±1.05
	5	20.63±1.90	16.82±1.03	14.81±1.79	31.09±1.78	29.54±1.91	25.38±1.56
	6	24.22±1.52	20.84±1.24	18.26±1.82	38.33±1.56	35.22±1.80	31.72±1.79
	7	29.37±1.09	25.50±1.80	23.82±1.17	42.18±1.50	40.98±1.51	35.49±1.64
	8	34.14±1.25	29.36±1.45	27.35±1.42	45.28±1.61	44.36±1.33	42.50±1.13
	9	38.46±1.13	35.72±1.71	32.23±1.50	47.39±1.11	46.03±1.50	43.37±1.47
	10	46.17±1.61	42.10±1.38	38.15±1.24	49.81±1.42	48.88±1.89	45.08±1.95
	11	54.08±1.38	46.69±1.83	43.07±1.72	51.23±1.90	50.92±1.77	47.90±1.88
	12	62.84±1.71	53.18±1.29	47.89±1.91	54.95±1.01	53.13±1.64	50.80±1.63

*Each value represents the mean ± standard deviation (n=3)

Table 5: *In vitro* dissolution profiles of Salbutamol Sulphate tablets:

Time (hr)	Cumulative % drug release					
	FL_1	**FL_2**	**FL_3**	**FF_1**	**FF_2**	**FF_3**
0	0	0	0	0	0	0
1	17.07±0.53	12.21±0.98	13.46±0.63	13.35±0.78	12.86±1.03	11.25±0.87
2	24.95±0.61	19.46±1.07	20.16±0.76	20.09±0.88	19.68±0.98	15.49±0.52
3	39.44±0.76	43.84±0.53	32.67±0.81	39.99±0.65	47.43±0.52	37.99±0.65
4	46.18±0.50	52.24±0.84	42.71±0.59	46.83±0.86	50.88±0.61	43.37±0.71
5	54.32±0.84	58.06±0.68	54.40±0.28	50.04±0.91	59.00±0.82	48.40±0.91
6	60.37±0.72	65.04±0.37	58.93±0.64	58.90±0.59	63.35±0.74	53.08±0.32
7	69.20±0.63	71.68±0.42	63.33±0.39	68.75±0.93	66.96±0.35	62.66±1.03
8	74.34±0.97	77.36±0.67	69.70±0.71	73.29±0.64	70.59±0.49	66.29±0.93
9	82.50±1.05	80.05±0.51	73.61±0.03	79.87±0.17	73.50±0.92	69.19±0.72
10	86.96±0.82	82.64±0.82	76.12±0.72	81.87±0.85	76.79±0.89	72.48±0.58
11	89.94±0.74	86.37±1.21	79.93±0.59	84.41±0.13	81.22±0.71	76.92±0.65
12	91.30±0.91	88.49±0.93	83.62±0.27	89.50±0.65	83.80±1.10	80.89±0.55

*Each value represents the mean ± standard deviation (n=3)

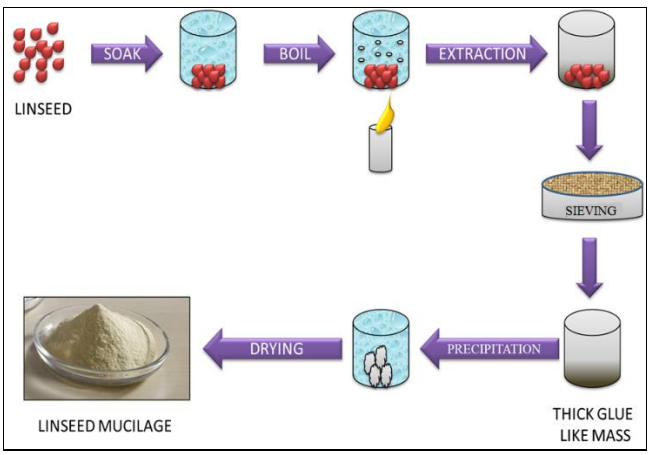

Figure 1: Separation of Linseed Mucilage

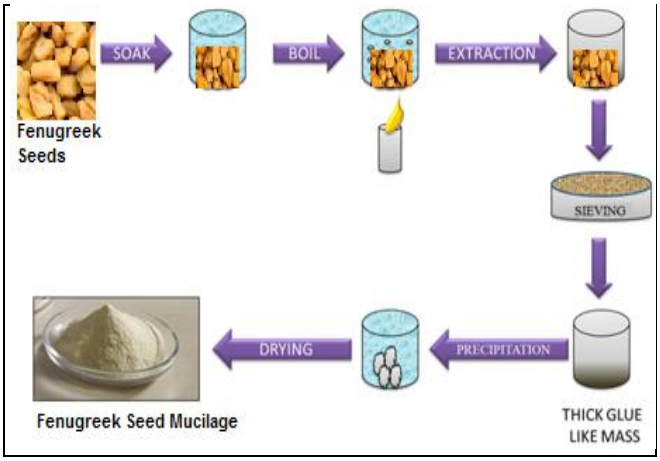

Figure 2: Separation of Fenugreek seed Mucilage

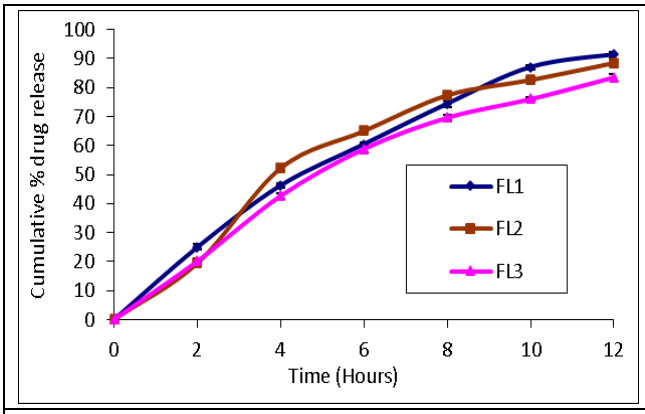

Figure 3: *In Vitro* Drug Release Profiles of Formulations FL_1–FL_3 for 12 h

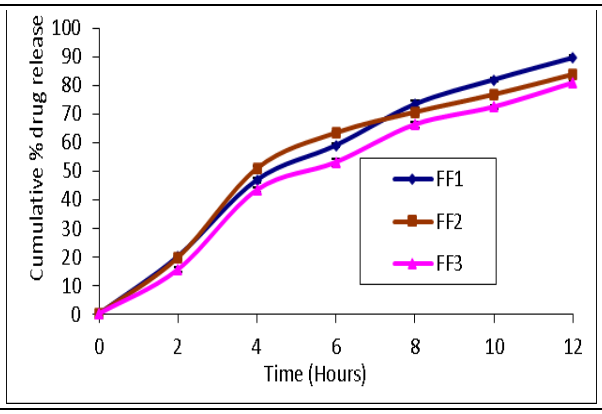

Figure 4: *In Vitro* Drug Release Profiles of Formulations FF_1–FF_3 for 12 h

CONCLUSION

Utilizing natural gums for pharmaceutical purposes holds significant appeal due to their cost-effectiveness, widespread availability, non-toxic nature, capacity for chemical alteration, and potential for biodegradability. The sustained release matrix tablet (FL1), formulated with linseed mucilage, exhibited effective control over drug release for 12 hours at a remarkably low concentration. This formulation demonstrated excellent practical yield, making it economically advantageous. The findings of this study suggest that linseed mucilage could serve as a more cost-

effective alternative to expensive synthetic sustained release additives.

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REFERENCES

1. Bonferoni MC, Rossi S, Tamayo M, Pedraz JL, Dominguez Gil A, Caramella C., On the employment of l-Carrageenan in a matrix system I. Sensitivity to dissolution medium and comparison with Na carboxymethyl cellulose and Xanthan gum, J.Control Release.,1993, 26, 119.
2. Sachinkumar Vasantrao Patil, Tamarind Gum: A Pharmaceutical Overview. https://www.researchgate.net/publication/26575572. 2008; 6(4): 1-8.
3. Shah DP, Jani GK, Prajapati VD, Jain VC. Gums and mucilages: versatile excipients for pharmaceutical formulation. Asian J.Pharm.sci. 2009**;** 4(5): 309-323.
4. Monif T, Malhotra AK, Kapoor VP. *Cassia fissula* seed galactomanan: potential binding agent for pharmaceutical formulation. Indian. J. Pharm. Sci. 1992; 54: 234–240.
5. Mylangam CK, Beeravelli S, Medikonda J, Pidaparthi JS and Kolapalli V. Badam gum: a natural polymer in mucoadhesive drug delivery. Design, optimization, and biopharmaceutical evaluation of badam gum based metoprolol succinate buccoadhesive tablets. Drug Deliv, 2016; 23(1): 195–206.
6. Baveja SK, Gupta BM. Rheology of Aqueous dispersion of *Plantago ovata* seed husk. Indian. J. Pharma. Sci. 1968; 30: 187-194.
7. Baveja SK, Gupta BM. Rheology of Aqueous dispersion of *Plantago ovato* seed husk. Indian. J. Pharm. Sci. 1968; 30: 247-251.
8. Mithal BM, Kasid JL. Evaluation of emulsifying properties of *Plantago ovata* seed husk. Indian. J. Pharm. Sci. 1964; 26: 316-319.
9. Mithal BM, Kasid JL. Evaluation of the suspending properties of *Plantago ovata* seed husk. Indian. J. Pharm. Sci. 1965; 27: 331-335.
10. Madan M, Bajaj A, Lewis S, Udupa N, Baig AG. *In Situ* Forming Polymeric Drug Delivery Systems. Indian J. Pharm. Sci., 2009; 71(3): 242-251.
11. Nirmal HB, Bakliwal SR, Pawar SP. In-Situ gel: New trends in Controlled and Sustained Drug Delivery System. International Journal of PharmTech Research. 2010; 2(2): 1398-1408.
12. Taylor M, Paul T, Sahota T. Thermoresponsive gels. Gels 2017; 3(4): 1-31.
13. Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare, Controller of Publication, New Delhi, 2007; vol-1:36-37.
14. Pelczer MJ, Chan ECS, Krieg NR. Microbiology Tata MC Graw Hill, 5th ed., 2009; 128-129.
15. Koocheki A, Mortazavi SA, Shahidi F, Razavi SMA, Taherian AR. Rheological properties of mucilage extracted from *Alyssum homolocarpum* seed as a new source of thickening agent. J Food Eng. 2009; 91: 490-496.
16. Gesinde AF, Oyawoye OM, Adebisi A. Comparative studies on the quality and quantity of soymilk from different varieties of soybean. Pak J Nut. 2008; 7: 157-160.
17. Sharjel L, Andrew BCY. Applied Biopharmaceutics and Pharmacokinetics, 4th ed. Prentice Hall International, New York. 1999; 437.
18. Kuksal A, Tiwary AK, Jain NK, Jain S. Formulation and *in vitro-in vivo* evaluation of extended release matrix tablet of Zidovudine: influence of combination of hydrophilic and hydrophobic matrix formers. AAPS Pharm Sci Tech. 2006; 1: E1-E9.
19. Bashar, M, Taani AL, Tashtouch L. Effect of microenvironment pH of swellable and erodible buffered matrices on the release characteristics of diclofenac Sod. AAPS Pharm Sci Tech. 2003; 4 (3):43,1-6.
20. Sung-Hyun Park, Myung-Kwan Chun, Hoo-KyunChoi. Preparation of an extended release matrix tablet using chitosan /carbopol interpolymer complex. Int J Pharm, 2008; 347: 39-44.
21. Nakano M, Nakamura Y, Juni K. Sustained release of sulfamethizole from agar beads after oral administration to humans. Chem Pharm Bull. 1980; 28: 2905-2908.
22. Polli JE et al. Methods to compare dissolution profiles and a rational for wide dissolution specifications for metoprolol tartrate tablets. J Pharm Sci. 1997; 86, 690.
23. Higuchi T. Mechanism of sustained action medication, J Pharm Sci. 1963; 52 (12): 1145.
24. Kuksal A, Tiwary AK, Jain NK, Jain S. Formulation and *in vitro-in vivo* evaluation of extended release matrix tablet of Zidovudine: influence of combination of hydrophilic and hydrophobic matrix formers. AAPS Pharm Sci Tech. 2006; 1: E1-E9.
25. Indian Pharmacopoeia. Controller of publications, Delhi, India. 2007; Vol-II, p. 241-243, 736.