

Formulation and Evaluation of Natural Excipient-based Mucoadhesive Salbutamol Sulphate Tablets

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ABSTRACT

When creating a mucoadhesive sustained-release formulation for oral consumption, aquaphilic matrices are a captivating option to consider. These aquaphilic matrices are used to release water-soluble and water-insoluble drugs. Gums and mucilages used in the current study are linseed mucilage (LM) and tamarind seed polysaccharide (TSP). The present work aims to focus on the possibilities of using these polysaccharides to prepare a new medication delivery system. The aim of the research was to make a salbutamol sulfate mucoadhesive tablet for the treatment of asthma. The wet granulation method was adopted for the formulation of the salbutamol sulfate mucosal adhesive tablet. Mucosal adhesive tablets were assessed for multiple parameters. The drug release is low as the amount of gums and mucilages is high. A mucoadhesive tablet containing linseed mucilage and chitosan exhibits good mucoadhesive performance and *in-vitro* drug release. Optimized formulation FM1 fits the Higuchi plot of release kinetics.

Keywords: Salbutamol sulfate, Mucoadhesive, Linseed mucilage, Chitosan, Asthma, Tamarind seed polysaccharide.

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INTRODUCTION

The field of drug delivery has noticed a paradigm shift in the past few years in the direction of the exploration of natural polymers as excipients in pharmaceutical formulations. Among these, mucoadhesive tablets have come up as a promising platform for sustained drug delivery, offering advantages such as prolonged dwell time at the target of action, enhanced bioavailability, and improved patient compliance. Utilizing these extracted gums and mucilages in mucoadhesive tablet formulations presents an innovative approach that addresses the limitations associated with synthetic polymers and aligns with the growing demand for sustainable and biocompatible pharmaceutical products.¹

The research paper seeks to investigate the potential of natural polymers in the formulation of mucoadhesive tablets for sustained medication delivery applications. By utilizing the inherent properties of natural polymers, like biodegradability, biocompatibility, and mucoadhesive properties, this approach aims to overcome the challenges associated with conventional synthetic polymers while offering additional therapeutic benefits.^{2, 3}

The natural polymers are derived from renewable sources like plants, animals, and microorganisms and offer a diverse range of physicochemical functions that involve disintegrating,

suspending, binding, emulsifying, gelling and mucoadhesive properties.⁴⁻⁷ In mucoadhesive tablet formulation, examples of commonly utilized polymers include chitosan, alginate, gum arabic, pectin, and carrageenan. These polymers have intrinsic mucoadhesive properties because they interact with mucin glycoproteins, which are present on the mucosal surfaces, facilitating intimate contact and sustained drug release.⁸⁻¹⁰

One of the most important advantages of natural polymers is their biocompatibility and safety profile, making them preferable for mucosal drug-delivery systems. Unlike synthetic polymers, natural polymers are often recognized as biologically inert or even beneficial to physiological systems, minimizing the risk of adverse reactions or tissue irritation. Moreover, natural polymers offer the potential for enhanced patient acceptance and compliance, as they are perceived as more environmentally friendly and sustainable alternatives to synthetic counterparts.¹¹⁻¹³

Here, in our research paper, our main objective is to provide an overview of the latest advancements in the technology of mucoadhesive tablet technology utilizing natural polymers like linseed mucilage, tamarind seed mucilage, and salbutamol sulphate as a model drug. We seek to highlight the versatility and promise of natural polymer-based mucoadhesive tablets

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in sustained drug delivery. By advancing our understanding of this novel approach, we hope to contribute to developing safer, more effective, and environmentally sustainable drug administration techniques for efficient patient treatment.

MATERIAL AND METHODS

Materials

The major components, such as linseeds and tamarind seeds, were collected from the district Buldhana located in the Maharashtra state, India, and verified by the Shri Shivaji Science and Arts College, Chikhali, dist. This is located in the Buldana district, Maharashtra. Salbutamol sulfate has been collected as a gift sample from Leben Lab which is located in the Akola district, Maharashtra. Lactose monohydrate (IP grade), talc (AR grade), starch, and acetone (AR grade) have been collected from Loba Chemie Pvt. Ltd, Which is located in Mumbai (India), Chitosan (AR grade) was collected from the Rajesh Chemical Industries, Which is located in Mumbai, Maharashtra.

Extraction of Mucilage

Linseed

Linum usitatissimum seed was taken and soaked for 12 hours in the water, which was distilled, and then the mixture was kept boiling at 70 to 80°C for the next 30 minutes; as the heat increased the rate of mucilage extraction and inactivation enzymes. After 2 to 3 hours, a maximum percentage of mucilage is extracted in distilled water, which develops a thick glue-like mass. To reduce viscosity, this thick glue-like mass was diluted with water, and then it passed through several folds of the muslin cloth. Around three times the amount of acetone was mixed to the thick glue, which help carry out the precipitation of dissolved mucilage from the glue. Precipitated mucilage was taken out. Mucilage was heated at 50°C in a device named as hot air oven and gave a yield of 45 to 50 g mucilage/Kg linseed, kept in a desiccator for subsequent use.

Tamarind seed

The *Tamarindus indica* seeds have been cleaned with distilled water to remove the adhesive ingredients. The red color testa from the seeds has been extracted by providing heat to the seeds in the sand. The testa has been removed. The pulverized seed of the *T. indica* were kept in water individually for the next 24 hours, boiled for an hour, and retained by side for 2 to 3 hours for the removal of mucilage in the water. The saturated seeds have been taken out and passed through the sieve to clear the marc from the filtrate. Then, around 3 times acetone has been added to the mucilage. The separated mucilage was kept for drying at 50°C in an oven and gave yield of 35 to 40 g mucilage/Kg tamarind seed, kept in a desiccator for subsequent use.

Chemical Test of Mucilages¹⁴⁻¹⁶

Extracted mucilages have been analyzed for multiple chemical tests. Molisch's test has been used to develop a violet-green color between the first & second layers, showing the availability of carbohydrates in it. The nonavailability of starch was confirmed by performing the iodine method called the iodine test, which showed no change in color when the

iodine solution was mixed. The availability of mucilage was substantiated by the ruthenium present solution which showed the formation of a pink color.

Physiochemical, Derived and Microbiological Properties of Mucilages¹⁷⁻¹⁹

Separated mucilages have been evaluated for multiple physiochemical properties like solubility, swelling index, water retention capacity, pH, melting point, microbial load, and particle size distribution for multiple derived functions like, tapped density, bulk density, comprehensibility index, Hausner in proportion, and inclination angle.

Microbial load¹⁹⁻²¹

The test was performed to estimate the number of viable aerobic microorganisms present in pharmaceutical substances. The plate count method has determined the total viable aerobic microbial count.

Agar-plate method

Agar medium two, casein soya bean digest agar has been added to each petri dish and kept for solidification. Then, pre-treated sample preparation was spread on the medium solidified in a petri dish and incubated at 37°C for 72 hours. The result was examined after a period of 24 hours.

Particle size distribution^{22,23}

A few particles of linseed mucilage and tamarind seed polysaccharide powder were taken separately on a glass slide, uniformly spread by a brush, such that individual particles could be seen and particle size distribution was measured by Microscope Image Analyzing System (Vision plus-5000).

Rheology study^{20,21,24}

Rheological measurements have been carried out using the apparatus named rotational viscometer (Brookfield R/S plus rheometer) equipped with C25 measuring spindles and for each test, approximately 0.2 to 0.5 mL of the sample has been poured to the compartment of cone and plate viscometer.

Determination of viscosity at different concentrations of mucilage

The viscosity has been determined for the linseed mucilage and tamarind seed polysaccharide solutions with a concentration of 1, 2, and 3% (which has been prepared in distilled water) at a shear rate of 30 1/s, and the graph have been plotted between by considering the concentration of the sample on X-axis and viscosity of the sample on Y- axis.

Determination of viscosity at different pH

The viscosity was determined for 1, 2, and 3% linseed and tamarind seed polysaccharide solutions with the pH range between 2.0 to 10.0 (kept by using 0.1N NaOH and 0.1N HCl) at various rates of shears and under the room thermal condition.

Drug-Excipient Interactions

Measuring the different types of interaction between drugs and mucilage is very important. It has been confirmed by considering fourier transform infrared spectroscopy and differential thermal analysis methods.

Fourier transform infrared spectroscopy

Separate IR spectra have been obtained for pure salbutamol sulphate and mucilage. Also, a physical mixture of the drug and the mucilage was stored at room thermal temperature one month before conducting Fourier transform infrared spectroscopy (FTIR) analysis to assess potential interactions between the drug and mucilage.

Differential scanning calorimetry

Temperature analysis of drug, excipients, and their physical mixture has been performed by using a differential scanning calorimeter (DSC) method. The drug and excipients have been sieved through a sieve no. 60. The drug and its mixture also, the excipient, was weighed into the pierced DSC aluminum pan (Aluminum Standard 40 μ L). Then the sample was scanned over a temperature between 20 to 300°C at a high-temperature speed of 10°C/min in a nitrogen atmosphere with a flow velocity of 50 mL per minute. The obtained thermo grams were performed to detect interactions.

Preparation of Granules and Tablet

In order to achieve the uniform particle size, we weighed the drug and other excipients and crushed them to make it powdered with mortar and pestle as per the composition given in Table 1. Preparation & testing of mucous-adhesion tablets of salbutamol sulfate by the use of linseed mucilage tamarind seed polysaccharide and chitosan as shown in Table 1.

The powder was thoroughly mixed to ensure uniform mixing of drug and excipients. Some starch paste was added to form a moist mixture. Then, the prepared bulk-damp mass was transferred from sieve no #16/22. The small granules that transferred through sieve no #16 and kept on sieve no. #22 was used. The prepared granules were set for drying in a hot air oven at 50 to 60°C. Then, the remaining dried granules were collected and differentiated from fines using the sieving method. The separated granules were kept for weighing and examined for bulk density, true density, angle of repose, and Carr's index. Prepared granules are kept for weighing and commonly mixed with lubricants and fines followed by compression method.

Assessment of Tablets

The formulations were assessed for weight differentiation to check the hardness, friability, thickness and diameter, and amount of drug.²⁵

Outer/Surface pH

pH of the surface on the formulation was determined by keeping the formulation in 5 mL of purified water (pH 7.0 \pm 0.05) at the thermal condition of the room for 2-hour period of time. The formulation gets swelled and the pH value of the tablet was calculated by retrieving the electrode of the device named as pH meter at the surface of the formulation and letting it constant to stabilize and allow for 60 seconds.^{26, 27}

Mucous Adhesion properties

The advanced physical balance method determined the tablets' mucous adhesion capability. The balance apparatus included

Table 1: Composition of salbutamol sulphate tablets

Ingredients (mg)	ML ₁	ML ₂	ML ₃	MT ₁	MT ₂	MT ₃
Salbutamol sulphate	4.8	4.8	4.8	4.8	4.8	4.8
Lactose monohydrate	81.2	71.2	61.2	41.2	31.2	21.2
Linseed mucilage	70	80	90	-	-	-
Tamarind seed polysaccharide	-	-	-	110	120	130
Chitosan	40	40	40	40	40	40
Magnesium stearate	02	02	02	02	02	02
Talcum	02	02	02	02	02	02

*Weights are given for one tablet

Tablets with Linseed mucilage: ML₁, ML₂, ML₃

Tablets with tamarind seed polysaccharide: MT₁, MT₂, MT₃

a two-arm structure balance, the physical balance apparatus having two glass plates, the bottom plate was connected strongly to the base, and the upside plate were attached to the bottom of one of the balances. Covering use for mucous-adhesion goat intestinal mucous was sicked to the lower plate of the physical balance apparatus using adhesive. The physical balance apparatus attached the precisely weighed tablet to the upper side. Then, the up side plate kept over the lower side plate, and pressurized by tip of finger for a five-minute period of time. Increasing weight was implemented on the second side of the balance apparatus by adding some water using the burette until the plates separated from each other's surface. The amount of weight required for the removal of the glass plates was measured and the mucous-adhesion strength of formulated tablet was measured. By taking the mucous - adhesion values (in grams), the force by the adhesion in the parameters (Newton/meter²) were measured. Mucous-adhesion will be determined as follows:

$$\text{Mucous-adhesion strength} = \frac{\text{the mass (in grams)}}{\text{area}}$$

Necessary to separate the polymer from the mucus area.

The goat intestinal mucous layer is considered a mucous layer in this process. Goat intestinal mucous was cut in to multiple slices and cleaned with a phosphate buffer solution (pH 6.8). Both pans kept balancing by adding some weight to the left side pan. At the same time, the weighed beaker was kept on the left-sided pan along with the water and was poured with a constant speed until the tablet detached from the mucous surface. The specific amount of weight to detach the tablet from the surface of the mucous gave the mucous adhesion.^{28,29}

$$\text{Force of adhesion (N)} = \frac{\text{Mucous-Adhesion strength}}{1000} \times 9.81$$

Measuring of Swelling Behavior of Sustained Release Mucoadhesive Tablet

The swelling index was calculated based on the percentage of weight the tablet increased. The swelling indexes of all formulations were performed. One tablet was taken from each preparation and put in a petri dish with phosphate buffer solution 6.8 pH for the next eight hours of time. At the result of 0.5 and 1 hour, the tablet was taken out, soaked using tissue

paper for a particular period, and weighed. Then, after every 1-hour, the total weight of the tablet were taken and the cycle continued till the last of 8 hours. Swelling (%) was determined according to the following formula.^{20,21,25}

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

Where,

W_t = Matrix weight followed by swelling

W_0 = Matrix weight initially

W_r = Dissolved matrix weight

Dissolution Studies

In-vitro studies were performed to release salbutamol sulfate from tablets, which were formulated into a phosphate solution with a pH value of 6.8 for the next 12 hours. The dissolution studies were done in USP Dissolution apparatus II with 50 rotation per minute speed. The thermal condition was maintained at $37 \pm 0.5^\circ\text{C}$ and analyzed for Salbutamol sulphate at 276 nm using the UV-visible spectrophotometer method.³⁰

Kinetic Treatment

The value of 'n' of formulation ML1 from the Korsmeyer-Peppas was calculated as 0.845 and the release mechanism was non-diffusion based ($0.5 < n < 1$). R2 value (i.e., 0.980).

Stability Study

The refined batches of ML1 were kept for stability study, and results show insignificant differences in drug release and another evaluation parameter for 6 months at $40^\circ\text{C}/75\% \text{ RH}$.

RESULTS AND DISCUSSION

Microbial Load

The results of microbial load are presented in Table 2.

Particle Size Distribution

Some linseed and tamarind seed mucilage powder particles were kept on a glass slide and constantly dispersed using a brush to make sure the individual particles were visible to the naked eye. The Microscope Image Analyzing System (Vision plus-5000) measured particle size distribution distribution. (See Tables 3 and 4, Figures 1 and 2)

Viscosity

The viscosity of a 1% weight/volume solution of linseed mucilage was measured at 10.20 Pa.s, while tamarind seed polysaccharide calculated a viscosity of 21.33 Pa.s. Detailed

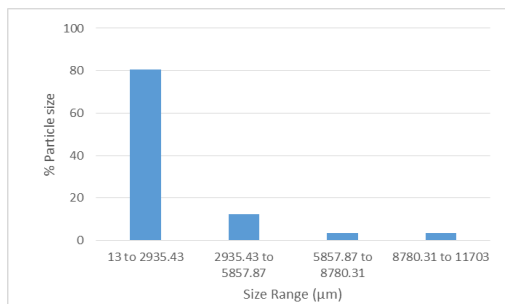


Figure 1: Particle size distribution for linseed mucilage

Table 2: Results of pathogenic microbial load

Mucilage	Number of CFU per mL	Microbial count (Number of CFU per gm mucilage)
Linseed mucilage	60	6000
Tamarind seed Poly-saccharide	80	8000

Table 3: Particle size distribution for linseed mucilage

S. No.	Particle size range (µm)	Percentage
1	13–2935.43	80.7
2	2935.43–5857.87	12.28
3	5857.87–8780.31	3.51
4	8780.31–11703	3.51

Table 4: Particle size distribution for tamarind seed polysaccharide

S. No.	Particle size range (µm)	Percentage
1	12–2725.61	83.48
2	2725.61–5548.05	10.97
3	5548.05–8396.95	3.01
4	8396.95–10207	2.54

Table 5: Effect of concentration on viscosity of linseed mucilage and tamarind seed polysaccharide

S. No.	Concentration (%)	Viscosity (Pa.s)	
		Linseed mucilage	Tamarind seed mucilage
1	1	10.20	21.33
2	2	14.44	24.18
3	3	18.63	27.96

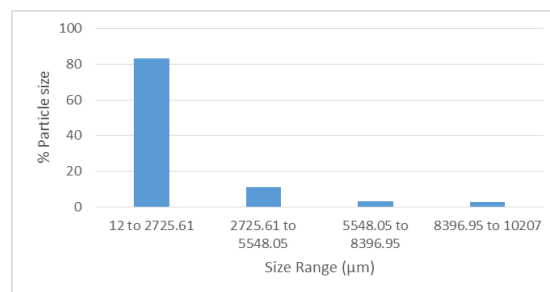


Figure 2: Particle size distribution for tamarind seed polysaccharide

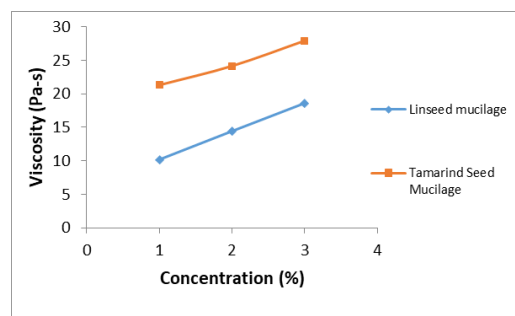


Figure 3: Effect of concentration on viscosity of linseed mucilage and tamarind seed polysaccharide

effects of concentration and pH on viscosity for linseed mucilage and tamarind seed polysaccharide are presented in Tables 5 and 6, and illustrated in Figures 3, 4, and 5. Viscosity and pH are noted as crucial physical parameters, offering valuable data into the properties of granules and tablets derived from different substances.

Table 6: Effect of pH on viscosity linseed mucilage and tamarind seed polysaccharide

pH	Viscosity of linseed mucilage (Pa.s)			Viscosity of tamarind seed polysaccharide (Pa.s)		
	1%	2%	3%	1%	2%	3%
2	16.11	22.66	26.96	28.37	32.88	36.30
4	22.18	28.48	32.13	33.71	38.84	43.71
6	29.09	35.72	37.81	39.09	44.27	48.63
8	33.56	41.92	45.08	44.85	50.62	55.24
10	35.82	43.35	46.15	46.60	53.05	57.08

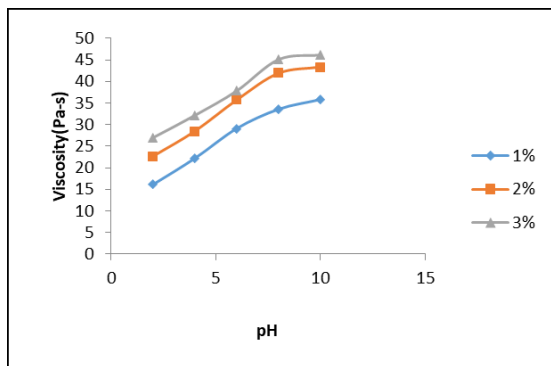


Figure 4: Effect of pH on the viscosity of linseed mucilage

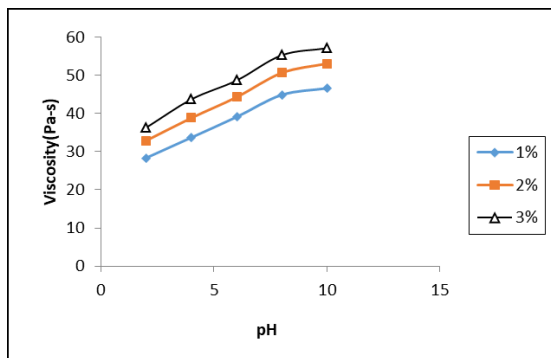


Figure 5: Effect of pH on viscosity of tamarind seed polysaccharide

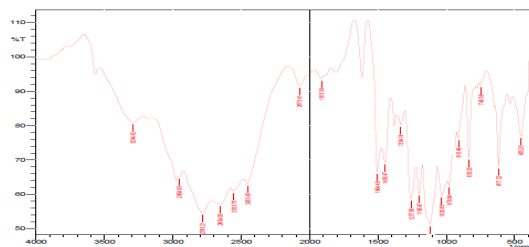


Figure 6: FTIR of salbutamol sulphate

Drug Excipient Compatibility Studies

FTIR analysis of the drug finalizes the presence of all distinguished peaks, with no disturbance in the functional groups. The important peaks of the Salbutamol sulfate remained the same in the drug-mucilage mixture. Also, the thermographic analysis showed no change in the melting point

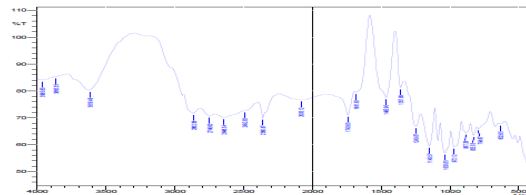


Figure 7: FTIR of linseed mucilage

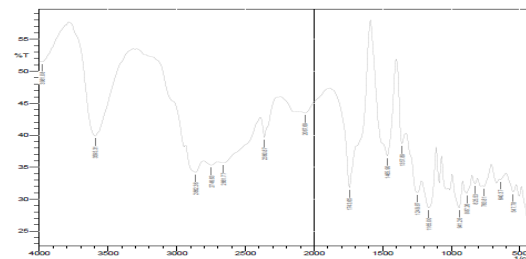


Figure 8: FTIR spectra of tamarind seed mucilage

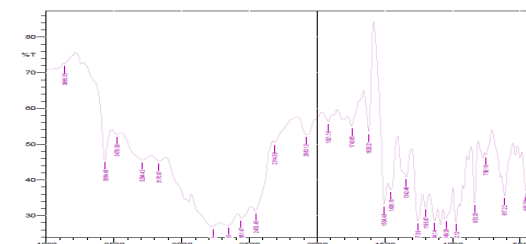


Figure 9: FTIR of mixture of salbutamol sulphate and linseed mucilage

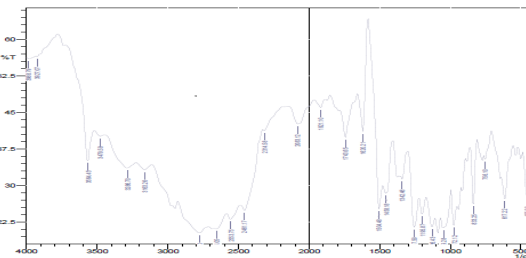


Figure 10: FTIR of mixture of salbutamol sulphate and tamarind seed mucilage

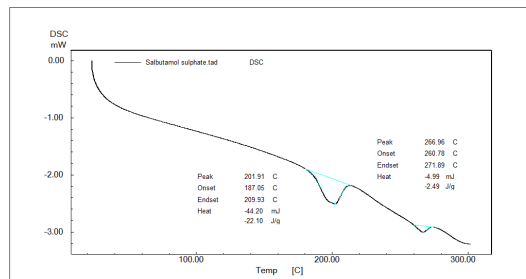


Figure 11: DSC thermograph of salbutamol sulphate

of salbutamol sulfate, resulting in no changes in its crystalline or any interaction with linseed or tamarind seed mucilage. It inferred that there was no interaction between Salbutamol sulfate and mucilage components use in tablet preparation. FTIR and DSC studies showed the harmony between the drug and the extracted mucilages (Figures 6-13)

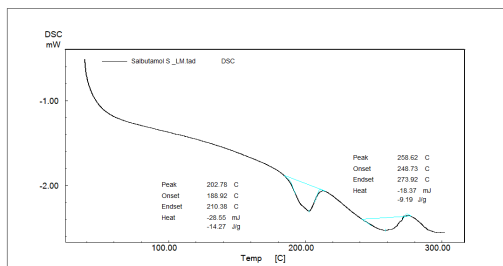


Figure 12: DSC thermograph of salbutamol sulphate and linseed mucilage

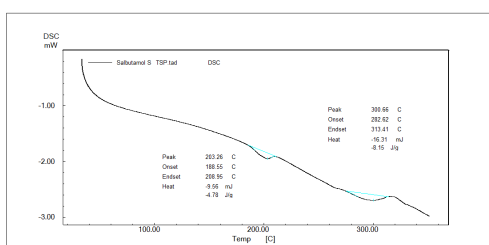


Figure 13: DSC thermograph of salbutamol sulphate and tamarind seed mucilage

Post-compression Parameter of Salbutamol Sulphate Tablets

The batches undergo various assessment tests, including friability, hardness, and *in-vitro* drug release, which are protocols outlined in the Indian Pharmacopoeia. Results demonstrate that all batches exhibited correct physical attributes with acceptable limits. Table 7 presents the results obtained from tablet evaluations. Tablet hardness ranged from 9.00 to 12.00 kg/cm². Drug content analysis shows that the tablets contained between 95.91 and 98.21% of the intended drug, showing consistency in drug content. Individual tablet weights varied between ± 7.5% of the average weight, and friability test values ranged from 0.23 to 0.39% across all formulations.

Swelling Studies

From the swelling studies, it was measured that the matrix swelling occurred in both radial and axial directions. Tablets containing linseed mucilage and chitosan exhibited an increase in the swelling index, albeit less compared to those containing tamarind seed mucilage and chitosan, due to the lower viscosity of linseed mucilage. Tablets containing tamarind seed mucilage with chitosan gave a higher swelling index which is attributed to the high hydrophilicity of tamarind seed mucilage. Over time, all tablets showed an increase in swelling index, resulting in dominant chain relaxation being the prevailing phenomenon.

Tablet weight gain is proportional to the rate of hydration up

Table 7: Post-compression parameter of salbutamol sulphate tablets

Formulations	Hardness* (kg/cm ²)	Friability* (%w/w)	Thickness* (mm)	Diameter* (mm)	%Drug content*
ML ₁	10.18 ± 0.03	0.23 ± 0.01	2.60 ± 0.044	8.01 ± 0.02	98.21 ± 0.33
ML ₂	9.39 ± 0.01	0.32 ± 0.06	2.61 ± 0.035	8.02 ± 0.07	96.73 ± 0.81
ML ₃	10.82 ± 0.04	0.27 ± 0.02	2.59 ± 0.036	8.01 ± 0.01	95.91 ± 0.64
MT ₁	10.37 ± 0.07	0.39 ± 0.08	2.63 ± 0.033	8.04 ± 0.04	98.53 ± 0.82
MT ₂	11.71 ± 0.02	0.37 ± 0.05	2.56 ± 0.051	8.01 ± 0.02	96.78 ± 0.80
MT ₃	9.89 ± 0.03	0.28 ± 0.02	2.68 ± 0.037	8.02 ± 0.08	97.82 ± 0.57

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

Table 8: Percentage swelling indices of formulations containing linseed mucilage and tamarind seed polysaccharide

Time (min)	% Swelling index*					
	ML ₁	ML ₂	ML ₃	MT ₁	MT ₂	MT ₃
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
30	14.28 ± 1.23	16.34 ± 1.15	19.98 ± 1.68	21.24 ± 1.75	24.63 ± 1.46	26.98 ± 1.06
60	25.10 ± 1.56	31.25 ± 1.97	34.57 ± 1.34	32.37 ± 1.98	36.07 ± 1.90	39.83 ± 1.42
90	38.69 ± 1.62	42.86 ± 1.03	47.82 ± 1.66	40.97 ± 1.17	43.58 ± 1.04	48.15 ± 1.65
120	50.81 ± 1.91	55.98 ± 1.71	59.06 ± 1.27	52.49 ± 1.45	57.52 ± 1.82	60.93 ± 1.48
180	59.27 ± 1.50	67.32 ± 1.63	69.86 ± 1.90	60.84 ± 1.72	69.08 ± 1.88	72.84 ± 1.56
240	66.13 ± 1.45	71.83 ± 1.81	76.53 ± 1.17	68.42 ± 1.55	74.77 ± 1.63	79.75 ± 1.74
300	71.35 ± 1.63	76.93 ± 1.49	79.05 ± 1.22	74.33 ± 1.81	81.62 ± 1.49	83.35 ± 1.20
360	74.97 ± 1.22	79.08 ± 1.61	82.71 ± 1.89	69.05 ± 1.66	70.06 ± 1.27	86.82 ± 1.42
420	62.36 ± 1.35	65.83 ± 1.47	68.14 ± 1.09	51.93 ± 1.83	52.84 ± 1.85	65.92 ± 1.56
480	48.09 ± 1.81	51.28 ± 1.90	56.43 ± 1.06	43.17 ± 1.06	47.65 ± 1.05	50.61 ± 1.95

*Values represent the mean ± standard deviation (n=3)

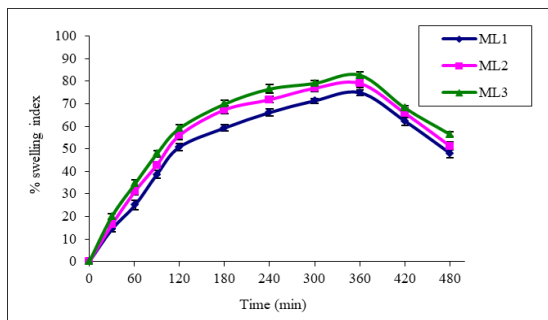


Figure 14: Percentage swelling indices of formulations ML₁ – ML₃

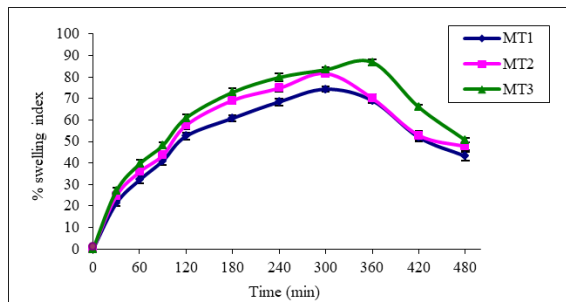


Figure 15: Percentage swelling indices of formulations MT₁ – MT₃

Table 9: Surface pH of tablet, mucous-adhesion strength and mucoadhesive force

Formulations	Surface pH	Mucous-adhesion strength (gm)	Mucous-adhesion force (N)
ML ₁	6.7	0.54	0.0053
ML ₂	6.8	0.67	0.0066
ML ₃	6.7	0.87	0.0085
MT ₁	6.9	0.66	0.0065
MT ₂	6.9	0.74	0.0073
MT ₃	6.8	0.88	0.0086

to a limit, after which it continuously decreases because of the mixing of the last layer of the formulated tablet into the prepared medium (Table 8, Figures 14 and 15).

The swelling index of natural mucilage in increasing order is as follows:

Linseed mucilage < Tamarind seed mucilage

Assessment of Mucous-Adhesion Strength in Mucous-Adhesion Tablets

The concentration of mucous-adhesion polymers altered the mucoadhesive features of salbutamol sulfate tablets. These

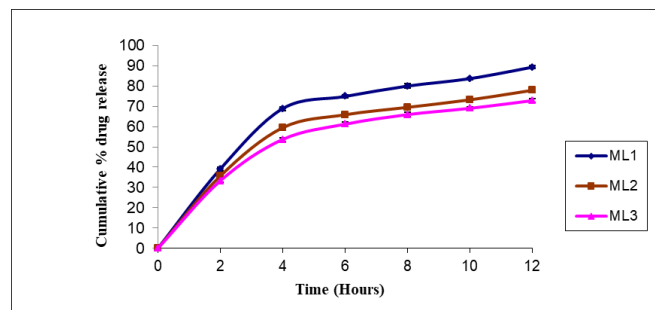


Figure 16: In-vitro drug release profiles of formulations ML₁–ML₃ for 12 hours

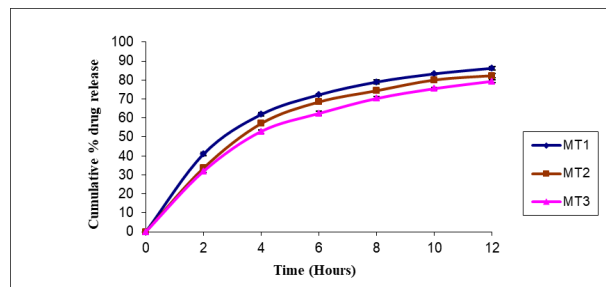


Figure 17: In-vitro drug release profiles of formulations MT₁–MT₃ over 12 hours

Table 10: In-vitro dissolution profiles of salbutamol sulphate tablets

Time (hr)	Cumulative %drug release					
	ML ₁	ML ₂	ML ₃	MT ₁	MT ₂	MT ₃
0	0	0	0	0	0	0
1	35.34 ± 0.76	31.98 ± 0.26	27.87 ± 0.55	32.15 ± 0.48	28.45 ± 0.54	25.98 ± 0.56
2	39.06 ± 0.83	35.64 ± 0.57	33.28 ± 0.78	40.94 ± 0.82	33.56 ± 0.73	31.83 ± 0.72
3	53.76 ± 0.09	49.09 ± 0.03	45.81 ± 0.91	54.60 ± 0.99	42.73 ± 0.95	40.01 ± 0.75
4	68.87 ± 0.62	59.45 ± 0.66	53.69 ± 0.35	61.85 ± 0.43	57.07 ± 0.80	52.89 ± 0.46
5	71.19 ± 0.78	62.35 ± 0.90	58.36 ± 0.18	69.09 ± 0.62	63.81 ± 0.50	59.47 ± 0.17
6	74.89 ± 0.43	65.87 ± 0.18	61.19 ± 0.37	72.17 ± 0.19	68.42 ± 0.42	62.34 ± 0.63
7	77.02 ± 0.32	67.77 ± 0.82	63.51 ± 0.48	75.56 ± 0.98	71.17 ± 0.75	67.48 ± 0.49
8	79.98 ± 0.13	69.51 ± 0.59	65.92 ± 0.90	78.92 ± 0.56	74.35 ± 0.19	70.24 ± 0.24
9	81.37 ± 0.92	71.20 ± 0.42	67.48 ± 1.14	80.91 ± 0.76	78.61 ± 0.93	72.71 ± 0.99
10	83.65 ± 1.08	73.21 ± 0.55	69.03 ± 0.22	83.24 ± 0.87	80.01 ± 0.37	75.43 ± 0.63
11	87.58 ± 0.66	75.94 ± 0.49	70.22 ± 0.87	84.35 ± 0.19	81.62 ± 1.09	78.50 ± 0.39
12	89.29 ± 0.50	77.89 ± 1.03	72.81 ± 0.63	86.19 ± 0.82	82.27 ± 0.09	79.31 ± 0.28

*Values represent the mean ± standard deviation (n=3)

Table 11: Linseed mucilage tablets as release retardant ML₁ at 40°C /75%RH

Parameter	0 month	1 month	2 month	3 month	4 month	5 month	6 month
Appearance	Cream	Cream	Cream	Cream	Cream	Cream	Cream
Thickness (mm)	2.61	2.59	2.60	2.59	2.61	2.61	2.60
Hardness (Kg/cm ²)	10.24	10.18	10.47	10.28	10.51	10.89	10.63
Friability (%)	0.29	0.35	0.27	0.28	0.38	0.31	0.29
Drug content (%)	97.98 ± 0.72	97.10 ± 0.52	98.62 ± 0.50	97.91 ± 0.81	97.19 ± 0.19	96.08 ± 0.90	98.49 ± 0.93

Table 12: *In-vitro* drug release study of formulation FL1 at 40°C/75% RH.

Time (hr)	Cumulative %drug release*						
	month	1 month	2 month	3 month	4 month	5 month	6 month
0	0	0	0	0	0	0	0
1	34.70 ± 0.03	33.37 ± 0.27	34.08 ± 0.93	34.27 ± 1.08	33.16 ± 0.10	34.32 ± 1.13	35.11 ± 0.56
2	40.18 ± 0.65	41.87 ± 0.09	40.82 ± 0.78	40.64 ± 0.34	39.07 ± 0.73	39.90 ± 0.90	41.19 ± 0.71
3	51.09 ± 0.27	50.73 ± 0.26	49.90 ± 0.64	50.94 ± 0.81	50.53 ± 0.28	51.24 ± 0.37	52.98 ± 0.37
4	65.91 ± 0.78	65.09 ± 1.87	64.56 ± 0.77	65.23 ± 0.98	64.49 ± 0.35	64.82 ± 0.82	67.35 ± 0.84
5	70.09 ± 0.29	71.76 ± 0.89	69.76 ± 0.29	70.88 ± 0.45	69.90 ± 0.70	70.25 ± 0.45	71.48 ± 0.89
6	75.01 ± 0.10	74.87 ± 0.63	73.12 ± 0.71	75.53 ± 0.50	74.71 ± 0.92	75.34 ± 0.76	76.73 ± 0.08
7	76.82 ± 0.82	75.41 ± 0.78	74.71 ± 0.09	76.98 ± 0.67	75.57 ± 0.44	76.55 ± 0.56	77.99 ± 0.46
8	78.89 ± 0.90	79.09 ± 0.02	76.69 ± 0.81	78.11 ± 0.71	77.79 ± 0.62	79.21 ± 0.61	79.81 ± 0.71
9	81.05 ± 0.54	82.06 ± 0.76	80.96 ± 0.18	82.01 ± 0.54	80.95 ± 0.71	82.56 ± 0.09	82.91 ± 0.85
10	84.73 ± 0.06	85.88 ± 0.43	83.29 ± 0.46	84.37 ± 0.84	83.50 ± 0.59	83.89 ± 0.27	85.68 ± 1.05
11	86.92 ± 0.76	86.06 ± 0.33	85.88 ± 0.73	86.47 ± 0.82	85.11 ± 0.09	86.37 ± 0.23	87.75 ± 0.86
12	88.89 ± 0.81	87.98 ± 0.58	87.99 ± 0.34	88.15 ± 0.09	87.90 ± 0.12	88.66 ± 0.04	89.52 ± 0.63

tablets contain different concentrations of linseed mucilage, including chitosan, tamarind seed mucilage, and chitosan. The salbutamol sulfate tablet with tamarind seed polysaccharide with chitosan exhibited the highest mucous-adhesion strength of 0.88 gm with the goat intestinal mucous, attributed to the higher content of tamarind seed polysaccharide. However, the optimized formulation ML1 demonstrated good mucoadhesive strength of 0.87 gm with goat intestinal mucosa due to swelling (Table 9).

***In-vitro* Release Studies**

Phosphate buffer with a value of pH 6.8 was used to perform the dissolution study. The *in-vitro* studies vary in the release of Salbutamol sulfate based on the concentration of mucilage used. When the concentration of mucilage increased simultaneously, drug release decreased. The *in-vitro* drug release profiles of salbutamol sulphate formulations are presented in Table 10 and Figures 16, and 17. The result shows that the drug was released in a controlled manner with an increase in the concentration of polymers. Preparation ML1 exhibited not only slow but also complete drug release of 89.29% throughout 12 hours (Table 10, Figures 16 and 17).

The drug releases of salbutamol sulfate from various formulations containing natural mucilage followed the order mentioned:

Tamarind seed mucilage < Linseed mucilage.

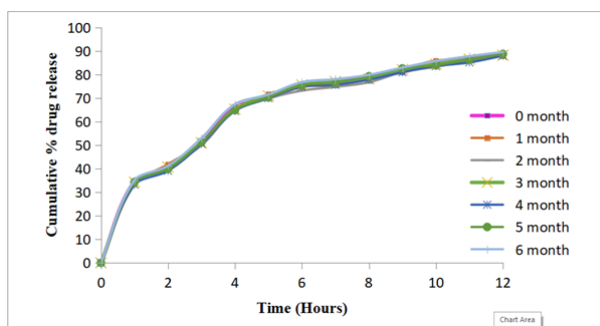


Figure 18: *In-vitro* drug release study of formulation ML1 under stability conditions at 40°C/75% RH.

Kinetic Treatment

The ‘n’ value derived from the Korsmeyer-Peppas equation for formulation ML1 was 0.845, indicating an anomalous mechanism of release (0.5 < n < 1). This indicates that drug diffusion and polymer erosion affect the drug release. The highest R² value (0.980) was observed for the Higuchi plot, in results the release kinetics checked well to the Higuchi model.

Stability Study

Formulation ML1, confirmed as the ideal preparation because of its drug liberation profile, was chosen for stability testing. The formulated tablets were covered in aluminum foil and kept

at a temperature of $40 \pm 2^\circ\text{C}$ along with a humidity level of $75 \pm 5\%$. Sample analysis was performed monthly, and results were calculated for drug content, thickness, hardness, friability, and % drug release. The results are summarized in Tables 11 and 12, and depicted in Figure 18.

CONCLUSION

In pharmaceutical applications use of natural gums is more due to their cost-effectiveness, easy accessibility, non-toxicity, potential for chemical modification, and biodegradability. The mucoadhesive sustained-release matrix tablet (MLI), prepared with linseed mucilage and chitosan, exhibited effective control over drug release for 12 hours of time even at very low concentrations, good mucoadhesion, demonstrating good practical yield and economical. This study suggests that linseed mucilage and tamarind seed polysaccharide could serve as alternatives to costly synthetic mucous adhesion sustained-release additives.

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