



DEVELOPMENT AND EVALUATION OF SESAMOL LOADED *LINUM USITATISSIMUM* SEED MUCILAGE BASED MICROSPHERES

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Abstract

The mucilages are polysaccharide obtained from various seeds. Thus, present study is started with aim to formulate *Linum usitatissimum* seed mucilage based microspheres of sesamol. The drug loaded microspheres were formulated using ionic gelation method and evaluated for physicochemical properties. The mucilage showed acceptable colour, odour and taste. The microspheres showed good swelling ability, mucoadhesive potential and sustained drug release. Thus, *linseed* mucilage could be promising alternative for fabrication of gastroretentive drug delivery system.

Keywords: Sesamol, *Linum usitatissimum*, Natural Mucilage, Microspheres, Antihyperlipidemic

1. INTRODUCTION

The oral route is most common, safe and convenient route of drug administration. The solid oral dosage form like tablet is most popular oral dosage form because of ease of handling, large scale production and stability [1]. About 80% oral dosage forms are available in the form of tablet. However these dosage forms suffer with number of limitations like; the daily administration of dosage form is require which is difficult to monitor and greater chance of missing dose. The dosage form like tablet is available with fixed strength thus careful calculation is required to prevent overdosing. It is difficult to calculate exact dose of drug required for a child and geriatric patients.

Extensive researches have been conducted to minimize the limitations associated with conventional drug delivery systems. The fruitful outcome of these researches is developed modified drug release systems. The desirable characteristic of such system is the duration of drug action. The controlled release system should provide therapeutic drug concentration for prolonged period of time. This can be achieved by controlled release of drug from system. The controlled release is possibly achieved by combining drug with the release modifying polymer. Gastroretentive drug delivery system is a novel approach to prolong gastric residence time, these dosage forms can retain in the gastric region for long periods and hence significantly prolong the gastric retention time (GRT) of drugs [2]. Another

important approach to prolonged gastric residence time of drug delivery system is the use of bioadhesive/mucoadhesive polymers [3].

The use of natural excipients as carriers in drug delivery systems is recent trend of oral drug delivery. Environmental concerns are also playing considerable role and contributing to the growing interest in natural polymers due to their biocompatibility, biodegradability and low processing cost [4]. Various natural polymers can be classified as proteins-based natural polymers like collagen [5], gelatin, silk fibroin, fibrin and natural polysaccharides like chitosan, starch, alginate, gellan gum, pectin, gum acacia, gum tragacanth, guar gum. These polysaccharides have some excellent water solubility as well as swelling potential, which eventually useful for oral controlled drug delivery.

Mucilages are the substances which have high water absorbing and swelling capability on contact with water. Several species of mucilaginous species of plants have been used in traditional system of medicine in the world since last 4000 year. Mucilage found in seed endosperms, roots and rhizomes may act primarily as energy reserves. Chemically these are high molecular weight (approx. 200,000 Da) compounds consisting of sugar and uronic acid units. These are generally sulphuric acid esters and have a complex structure of polysaccharide. The high-water absorbing capability of mucilage is due to presence of hydroxyl groups in sugar structure of mucilages. However, upon addition of alcohol, mucilages are precipitated in the form of amorphous or granular mass [6].

Many scientific investigators have utilized plant derived mucilage for development of nano and microcarrier based systems. Thus present study has started with aim to formulate *Linum usitatissimum* seed mucilage based microspheres.

2. MATERIALS AND METHODS

Linum usitatissimum seeds were purchased locally. Sodium alginate and calcium carbonate were purchased from S. D. Fine Chemicals Ltd., India. All other reagents, chemicals and solvent were laboratory grade and purchased locally.

2.1 Isolation and characterization of *Linum usitatissimum* mucilage

Mucilage of linseed was isolated with hot water. Briefly, 100 gram of linseed seeds were soaked in 500 ml of water for 10 hours for hydration of seeds. The hydrated mucilage along with seeds were dried in hot air oven at 50°C. The dried mucilages were sieved through sieve 18 for separation from seeds. The isolated mucilage from seeds was characterized with respect to colour, odour and taste.

2.2 Design of *Linum usitatissimum* mucilage-alginate microspheres

Sesamol loaded microspheres were formulated using ionic gelation technique. Briefly appropriate quantities of *linseed* mucilage and sodium alginate were dissolved in distilled water with continuous stirring to polymeric solution. The weighed quantity of sesamol was dissolved in polymeric solution with continuous stirring. The resulting medicated polymeric solution was injected in 100 ml of 7% w/v calcium chloride solution using 24-G needle with continuous stirring at 500 rpm using magnetic stirrer. The resulting polymeric dispersion was stirred for 30 minutes for crosslinking of alginate in presence of calcium ions. After stirring continuous stirring for specified time, the dispersion was kept in standing for 1 hour for complete crosslinking of polymer. After 1 hour the microspheres were collected by filtration, washed with double distilled water and finally dried in hot air oven at 40°C for 10 hours.

2.3 Evaluation of *Linum usitatissimum* mucilage-alginate microspheres

2.3.1 Assessment of particle size

Particle size of sesamol loaded mucilage-alginate microspheres was assessed by optical microscopy using calibrated eyepiece micrometer. Briefly, 50 mg of drug loaded microspheres were spread over the clean glass slide and observed under compound microscope under the 10X scale. The particle diameter of 100 particle was measured randomly and arithmetic mean diameter was calculated.

2.3.2 Measurement of entrapment efficiency

The entrapment of sesamol in mucilage-alginate microspheres was quantitatively measured in percentage using UV spectrometric measurement. The dried drug loaded microspheres were finely ground using mortar pestle to obtain fine powder. The 40 mg of powder was weighed and dispersed in phosphate buffer pH 6.8. The resulting dispersion was stirred on 12 hours and filtered. The filtrate was diluted ten times using phosphate buffer and subjected to spectrometric measurement. The entrapment efficiency of sesamol in microspheres was then calculated using following equation.

$$\text{Percent entrapment of sesamol} = \frac{W_p}{W_t} \times 100$$

Where, W_p is practical content of sesamol in dispersion and W_t is theoretical content of sesamol in microspheres.

2.3.3 Assessment of sesamol release behavior

The dialysis membrane drug diffusion method was used for assessment of sesamol release. Dialysis membrane (Mol. weight: 12–14 kDa) was soaked in distilled water overnight. The sesamol encapsulated microspheres were dispersed in 5 ml of distilled water. The resulting dispersion was filled in membrane and closed at both ends using dialysis bag locks. The microspheres equivalent to 10 mg of sesamol was taken for drug release study. The weight of dried microspheres required was calculated based on entrapment efficiency study. The resulting dialysis membrane was fixed on USP type II dissolution apparatus. The drug release study was carried out in 500 ml of 0.1N HCl for first 2 hours. After 2 hours the release medium was change to phosphate buffer pH 6.8 for next 8 hours. The temperature of the both release mediums was adjusted to $37^\circ\text{C} \pm 0.5^\circ\text{C}$. The rotational speed of the paddle was fixed at 50 rpm. At fixed time intervals from start of study, the 2 mL of release medium was withdrawn and subjected to UV-spectrophotometry for assessment of extent of sesamol release in medium.

2.3.4 In vitro mucoadhesive behavior

The mucoadhesion potential of formulated microspheres was assessed on goat intestinal mucosa (64). The intestine was obtained from a local slaughterhouse. The isotonic saline solution was used to wash the intestine and pieces of dimension 2×4 cm were made. The piece of intestine was mounted on a glass slide separately and slide was fixed at an angle of 45° [7].

The 50 mg of dried microspheres were accurately weighed and sprinkled over the surface of each piece of intestinal mucosa. The isotonic solution was sprinkled over the microspheres and kept for 15 minutes for hydration and swelling of microspheres. After hydration, the 50 ml of isotonic saline (37°C) was passed through the mucosa at a flow rate of 5 ml/min and collected in pre-weighed petri plate. Finally, the collected saline solution was subjected to evaporation and weight of petri plate was recorded after complete evaporation of saline solution. Based on initial weight of microspheres applied on mucosa and weight of dried microspheres collected in petri plate, the weight of microspheres adhere to mucosa was calculated. The percentage mucoadhesion was calculated using following formula.

$$\% \text{ Mucoadhesion} = \frac{\text{Wt. of microspheres adhere to mucosa}}{\text{Wt. of microspheres initially added}} \times 100$$

3. Results and Discussion

3.1 Isolation and characterization of linseed mucilage

The mucilage from *linseed* seeds were isolated with distilled water. The extracted mucilage was dried in hot air oven at 50°C [8]. The resulting dried mucilage was transferred through sieve to obtain dried free flowing powdered mucilage. Initially mucilage was checked for organoleptic properties like colour, odor, taste and texture. The results are highlighted in table 1. The odorless mucilage was brownish in colour. The taste of mucilage was mucilaginous with smooth texture [9].

3.2 Design of *linseed* mucilage-alginate microspheres

The matrix of microsphere was prepared by combination of sodium alginate and *linseed* mucilage. The crosslinked polymeric microspheres were collected by filtration and dried at 40⁰C. [11]. The microspheres were spherical in shape.

3.3 Evaluation of *linseed* mucilage-alginate microspheres

3.3.1 Assessment of particle size

The particle size of formulated mucilage-alginate based microspheres was measured using optical microscopy. The particle size distribution was assessed by plotting particle size distribution curve as highlighted in figure 1 [12].

3.3.2 Measurement of entrapment efficiency

Percent entrapment of sesamol in dried microspheres was assessed using UV spectrometric measurement. Formulated microspheres showed percent entrapment 69.71%.

3.3.3 Assessment of sesamol release behavior

In vitro sesamol release behavior from formulated mucilage-alginate microspheres was assessed using dialysis diffusion technique [13]. The release study was performed in both acidic as well as basic buffers. The 0.1 N HCl was selected as an acidic medium and Phosphate buffer pH 6.8 was selected as basic medium for assessment of drug release behavior. The drug release profile has highlighted in figure 2. The initial burst release of sesamol was observed in first two hours, with almost 35 % of drug release. The initial burst release of drug could be due initial release of drug loaded at the surface of microsphere matrix. After two hours, the sustained drug release was observed for next 14 hours. The sustained drug could be due to slow penetration of drug across mucilage-alginate microsphere matrix.

3.3.4 *In vitro* mucoadhesive behavior

Assessment of mucoadhesion potential and swelling ability of microspheres is essential evaluation parameter governing *in vivo* performance of microspheres based systems [14]. The swelling behavior of microsphere in presence of phosphate buffer pH 6.8 has represented in figure 3. The microspheres showed increase swelling capability up to 8 hours with almost 49.96 % swelling index. After the 8 hours swelling behavior of microspheres was progressively decline up to 12 hours. The reduction in swelling of microspheres after 8 hours could be due to slow erosion of polymer. The percent mucoadhesion of mucilage-alginate microspheres on porcine intestinal mucosa was found to be 72.19 ± 1.8%. The formulated microspheres showed acceptable swelling and mucoadhesion capabilities.

CONCLUSION

The present investigation was initiated to utilize natural mucilage for controlled mucoadhesive delivery of sesamol. The mucilage extracted from *linseeds* was used in present investigation. The mucilage was then utilized for development of sesamol loaded microspheres. The mucilage and alginate combination was used as polymeric matrix for entrapment of sesamol. The microspheres showed acceptable physicochemical properties and sustained drug release profile. The above results shows usefulness of *linseed* mucilage-alginate microspheres for sustained oral delivery of sesamol.

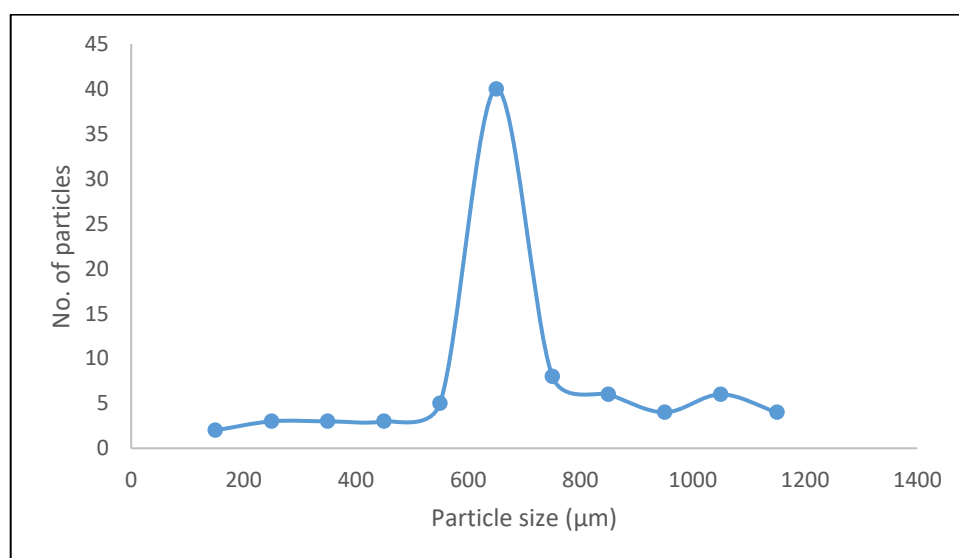
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Table 1 Organoleptic properties of *linseed* mucilage

Colour	Odour	Taste	Texture
Brownish	None	Mucilaginous	Smooth

**Figure 1** Particle size distribution of mucilage-alginate microspheres.

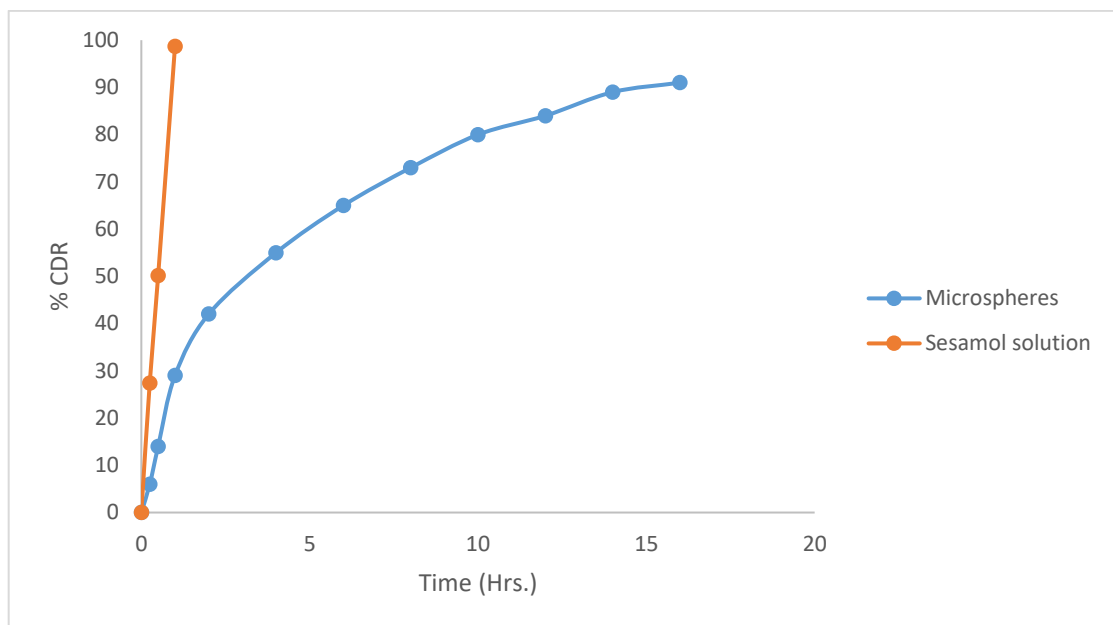


Figure 2 *In vitro* sesamol release profile of mucilage-alginate microspheres.

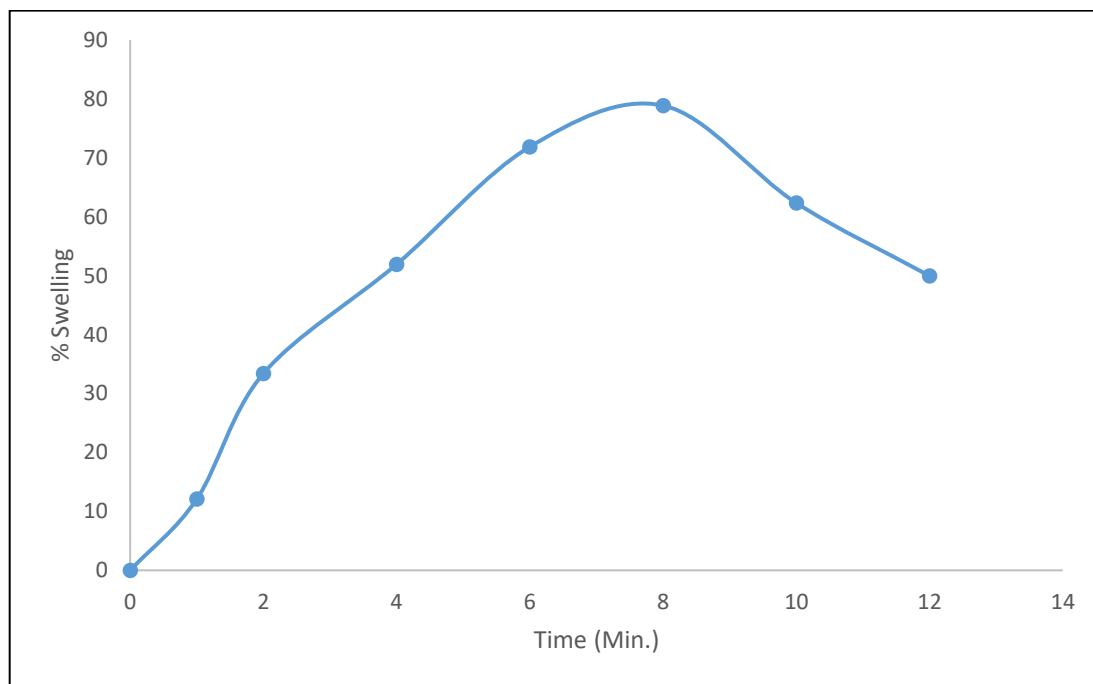


Figure 3 Swelling behavior of mucilage-alginate microspheres