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A novel smart mucoadhesive biomaterial from *Lallimantia royalena* seed coat

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ABSTRACT: Our aim was to isolate a novel biomaterial from the seed coat of *Lallimantia royalena*, a member of the Labiatae family widely available in the western part of Uttar Pradesh, India. The seed coat was isolated by the non-solvent addition method and its colour, texture, solubility, and chemical and IR spectral properties were determined. The biomaterial swelling index, colour change point, and acute animal toxicity were also studied. The mucoadhesivity of the biomaterial was determined by the shear stress, Park and Robinson, and rotating cylinder methods, and the results were compared with those of the standard polymers sodium carboxymethyl cellulose and hydroxypropylmethyl cellulose. The research study revealed that the biomaterial from *L. royalena* seed coat exhibits promising inbuilt mucoadhesion and good mucoretentability. The mucoadhesion of the biomaterial was also confirmed by IR spectra showing carboxyl and hydroxyl groups. Hence the isolated biomaterial from the *L. royalena* seed coat can serve as a powerful natural mucoadhesant and may be used to develop mucoadhesive transmucosal drug delivery systems.

KEYWORDS: transmucosal delivery, Labiatae

INTRODUCTION

Mucoadhesive materials from natural sources are nowadays gaining more importance for spatial placement of mucoadhesive dosage devices. If they are biocompatible and biodegradable this provides added advantages for formulating various controlled release pharmaceutical formulations and avoids patient non-compliance, especially for chronically ill patients. The advantages of such materials include their natural origin, ready availability, low cost, biodegradability, and capability of a multitude of chemical modifications. The majority of natural mucoadhesive agents are polysaccharides or proteins. *Lallimantia royalena* (Labiatae) seeds are oval shaped. When soaked in water, the biomaterial coat covering the outer surface of the seed gets swollen, becomes sticky, and forms a gel when removed from the seed[1]. The plant has been traditionally used as a remedy against ulcers, wounds, insect bites, toothaches, and used as an astringent. The objective of this study is to isolate the biomaterial from the seed coat and to determine its intrinsic mucoadhesive and mucoretentive properties.

MATERIALS AND METHODS

L. royalena seeds were obtained from the local market. Acetone, sodium dihydrogen orthophosphate, potassium dihydrogen orthophosphate, and sodium hydroxide were purchased from Qualigen Chemicals Pvt. Ltd. Double distilled water was prepared from the institutional laboratory. All chemicals used were of analytical grade.

Extraction of mucoadhesive biomaterial from *L. royalena*

Extraction of the biomaterial was performed by first soaking 100 g of seeds with 500 ml of distilled water for 8 h in a refrigerator at 5 °C. The mixture was mechanically stirred at 1250g to shred the seed coat and dissolve it in the water. The mixture was strained through muslin cloth. The seeds were washed with water and the washings were mixed with the filtrate. The biomaterial was recovered from the extract via precipitation with 3 volumes of acetone. The precipitated biomaterial was washed repeatedly with acetone, collected, purified by dialysis, and dried at 50–60 °C under vacuum for 12 h. The dried biomaterial was pulverized and passed through a 100 mesh sieve and stored in a desiccator.

Physicochemical characterization

The texture, solubility, pH of 1% biomaterial solution, swelling factor[2,3], viscosity, colour changing point[2,3], and UV and IR spectra for the biomaterial were measured. Elemental analysis and thin layer chromatography were also performed.

Assessment of mucoadhesive properties

The mucoadhesive property of *L. royalena* seed coat extract was determined in vitro by the shear stress method[4], ex vivo by the Park and Robinson method[5], and rotating cylinder method[6]. The biomaterial was subjected to a shear stress study for in vitro assessment of its adhesive strength in terms of weight required for breaking adhesive bonds between polymer and glass plate in a specified contact time of 5, 10, 20, or 30 min period with concentrations of 0.5%, 1%, 2%, 3%, or 5% w/v of the natural mucoadhesive extract and compared with the standard polymer NaCMC 1%.

With the Park and Robinson method, the biomaterial was punched into a small circular bioplate of thickness 0.2 mm using a hydraulic pelletizer and the force required to detach the bioplate from the mucosal surface was determined and compared with that of the standard polymers sodium carboxymethyl cellulose (NaCMC) and hydroxypropyl methyl cellulose (HPMC). The average of 6 readings was registered. With the rotating cylinder method, the stainless steel rotating baskets were covered with a thin layer of aluminium foil. A freshly excised goat soft palate tissue was secured onto the aluminium foil surface around the rotating cylindrical basket. The compressed bioplate was placed on the mucosal surface. It was then put in a flask containing 900 ml of phosphate buffer at pH 6.8 at $37 \pm 2\,^{\circ}\mathrm{C}$. The cylindrical baskets were rotated at 100 rpm. Every 30 min the machine was stopped and checked for dislodgement or disintegration of the bioplate from the mucosal surface. The results were compared with the standard polymers NaCMC and HPMC. The average of 6 readings was registered.

Acute toxicity study of the seed coat extract

The biomaterial was evaluated for acute toxicity study. The study protocol was approved by the Institutional Animal Ethical Committee. The procedure followed was as per OECD 423 guidelines. Two groups of 6 albino unisex rats, one for test and other for control, were used for the study. The animals were provided with free water ad libitum. The study was performed by administering the dried biomaterial at 2 g/kg body weight for the test group animals and the acute toxicity study was evaluated for a period of 14 days by observing body weight, changes in the skin, corneal reflex, respiratory rate, autonomic symptoms, salivation, diarrhoea, lethargy, sleep, somatomotor, behavioural patterns, and convulsions.

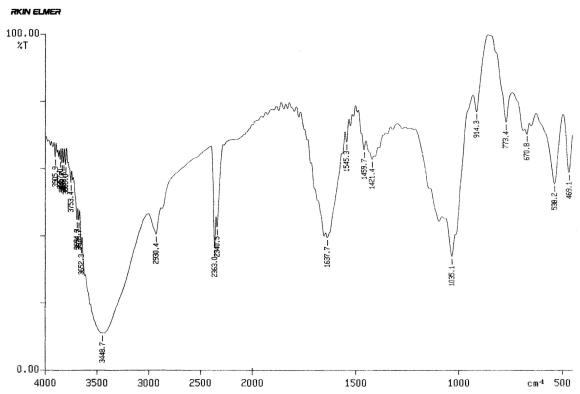

Fig. 1 IR spectra of the natural mucoadhesive extract of *Lallimantia royalena*.

RESULTS AND DISCUSSION

The biomaterial was isolated by a simple extraction procedure and 0.9 g of biomaterial was obtained for 100 g of *L. royalena* seeds. The *L. royalena* seed coat was white, smooth, amorphous, partially soluble, swelled in water, insoluble in alcohol, and around pH 6.8 (1% solution). It gave a positive Molisch's test for carbohydrate nature of the extract, and the functional groups test showed the presence of ketone, aldehyde, and alcoholic hydroxl groups. Swelling factor (1 g) was 2 ml, and the colour changing point was at 200 °C. UV spectra showed a $\lambda_{\max}$ of 241 nm. IR spectroscopy revealed 3448 cm^{-1} Hb(OH), 2930 cm^{-1} C−H (str), 2363.0 cm^{-1} C=C (str), 1637.6 cm^{-1} C=O (str), 1459.7 cm^{-1} C−H (def), 1035.1 cm^{-1} C−O (str), 772 cm^{-1} C−H (def) (Fig. 1). The presence of carboxyl and hydroxyl groups in the biomaterial is the key to its mucoadhesive properties. Elemental analysis showed the presence of carbon 28.60%, hydrogen 4.70%, and nitrogen 1.32%. Thin layer chromatography showed the presence of galactomannan.

Assessment of mucoadhesive property

A 0.5% w/v solution of the mucoadhesive extract of exhibited excellent bioadhesive strength (Fig. 2). Further increment in the biomaterial concentration did not affect its bioadhesiveness. This is probably due to loss of hydration by evaporation that increases the mucoadhesive strength. The macromolecules containing numerous hydrogen bond forming groups (e.g., hydroxyl, carboxyl groups) show the most promising mucoadhesivity.

The ex vivo mucoadhesivity of the extracted biomaterial of *L. royalena* by Park and Robinson method showed that the biomaterial possesses a promising

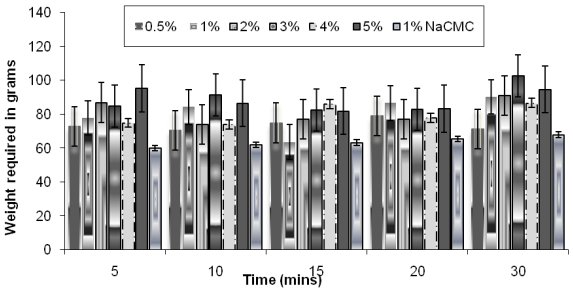

Fig. 2 Bioadhesive property of the natural mucoadhesive extract and the synthetic polymers 1% NaCMC as determined by shear stress method.

mucoadhesivity in comparison to NaCMC and was found to be similar to that of HPMC. The process of mucoadhesion has been proposed to begin with the establishment of an intimate contact between the mucoadhesive polymer and mucus gel[7,8]. The plausible mechanism of its mucoadhesive property may be the interaction of mucus with carboxyl or hydroxyl groups of the biomaterial. The role of surface energy thermodynamics in mucoadhesion has been considered vital[9,10] for the mucoadhesive strength exhibited by the biomaterial extract of *L. royalena*.

The rotating basket method revealed that the biomaterial had a promising mucoretentability which was found to be higher than that of HPMC or NaCMC. This is due to the fact that *L. royalena* having high molecular weight exhibited higher adhesion and better mucoadhesion than the synthetic polymers (HPMC and NaCMC) at the same concentration. This may be due to the presence of numerous disulphide bridges and carboxyl and hydroxyl groups, which adopt more favourable macromolecular conformation, and accessibility of its hydrogen-binding groups. HPMC and NaCMC, being cellulose derivatives, form weaker bonds with mucus, which may be due to either a decrease in available hydrogen binding sites or unfavourable entanglement with the mucus.

Acute toxicity study of the seed coat extract

The biomaterial was devoid of signs of toxicity in animals tested. This may be due to the edible nature of the *L. royalena* seeds.

CONCLUSIONS

It can be concluded that *L. royalena* seed coat extract is a better mucoadhesive agent than HPMC and NaCMC with respect to inbuilt mucoadhesive and mucoretentive properties. Since this natural mucoadhesive agent is edible, it is easily biodegradable and not an allergen and may provide an alternative to conventional synthetic and natural mucoadhesive agents.

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