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Isolation and characterization of novel mucoadhesive biomaterial from *Phoenix dactylifera*

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ABSTRACT

Phoenix dactylifera belongs to the family Arecaceae. The current aim of our research work is to isolate bio-material from the fruit pulp of *Phoenix dactylifera* and evaluate its mucoadhesivity. The bio-material was isolated by simple economical process. The isolated biomaterial was subjected for determination of solubility, colour changing point, viscosity, surface tension, pH and chemical tests. The mucoadhesivity of the biomaterial was assessed by shear stress method and rotating cylinder method using *Capra aegagrus* labium and intestine as mucosal substrates. The results were compared with HPMC and sodium CMC. The research study revealed that the biomaterial from *Phoenix dactylifera* exhibits promising inbuilt mucoadhesivity. So it can serve as a powerful natural mucoadhesant and may be used to develop mucoadhesive transmucosal drug delivery systems.

Key Words: Mucoadhesive polymers, Novel drug delivery, Mucoadhesion, Labial mucosa, *Phoenix Dactylifera*, Bioadhesion.

INTRODUCTION

The term bioadhesion can be defined as the state in which two materials, at least one biological in nature, are held together for an extended period of time by interfacial forces (Smart, 2005). The biological surface can be epithelial tissue or the mucus coat on the surface of a tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion (Tangri and Madhav Satheesh 2011) Mucosal drug delivery technologies are expanding exponentially with applications in every imaginable route of administration because of its indisputable therapeutic benefits like site-specific targeting, less frequent dosing, and maintaining effective plasma concentration without increased consumption (Shaikh *et al.*, 2011). *Phoenix dactylifera* belongs to the family Arecaceae. The dried fruit is more than 50 percent sugar by weight and contains about 2 percent of protein, fat and mineral matter. The infusion, decoction, syrup or paste of *Phoenix dactylifera* is

administered for sore throat, cold and for relieving fever (Shahib and Marshall, 2003). The objective of this study is to isolate the biomaterial from the fruit pulp of *Phoenix dactylifera* and evaluate its intrinsic mucoadhesive and mucoadhesive properties.

MATERIALS AND METHODS

Phoenix dactylifera was obtained from the local market. Acetone was purchased from CDH Pvt. Ltd. Sodium dihydrogen phosphate, potassium dihydrogen phosphate, 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. IR spectral analysis was done in Laureate Institute; Himachal Pradesh and SEM analysis was performed in Wadia Institute; Dehradun.

Isolation

The fruit pulp of *Phoenix dactylifera* was collected and minced with water. It was filtered through muslin cloth. The biomaterial was recovered from the filtrate via precipitation with 3 volumes of acetone. The precipitated biomaterial was washed repeatedly with acetone, collected, purified by

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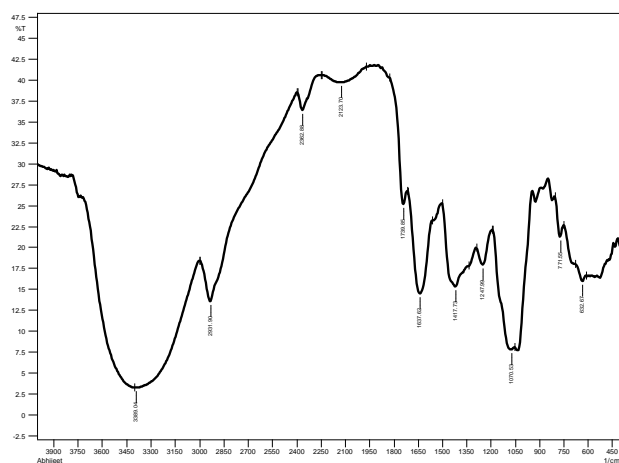


Figure 1: IR Spectra of *Phoenix dactylifera* biomaterial.

dialysis, and naturally dried. The dried biomaterial was pulverized, passed through a 120 mesh sieve and stored in a desiccator.

Physicochemical Characterization

The isolated biomaterial was subjected for various physical tests like solubility, colour changing point, viscosity, surface tension, pH (Martin, 2001; Subrahmanyam and Thimma Setty, 2002). It was also subjected for chemical tests, IR spectral analysis and SEM analysis.

Evaluation of Mucoadhesive Properties

The mucoadhesive property of isolated material was evaluated by Shear Stress method and Rotating cylinder method. 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, 15, 20, 25 and 30 minutes with concentrations ranging from 1 to 5% w/v (Rao *et al.*, 1998). It was compared with the standard polymer sodium CMC and HPMC.

In Rotating cylinder method, the mucoadhesive property was evaluated by *Capra aegagrus* (goat) labial and intestinal mucosa (Chen and Cyr, 1970). The biomaterial film was prepared by casting method. The film was placed on labial and intestinal mucosa and subjected for rotation at 100 rpm. The detachment and dislodgement of film from mucosal substrate was noted at regular intervals and data was compared with standard film of HPMC and sodium CMC polymer.

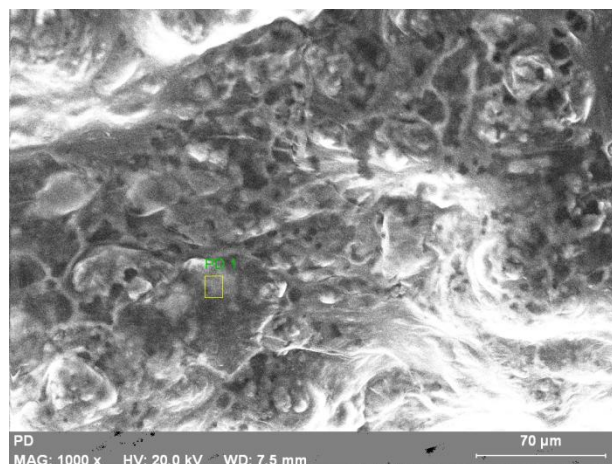


Figure 2: SEM image of *Phoenix dactylifera* biomaterial.

Acute Toxicity Study

The biomaterial was evaluated for acute toxicity study. The study protocol was approved by the Institutional Animal Ethical Committee (Registration No. 1156/AC/07/CPCSEA). The procedure followed was as per OECD 423 guidelines. Two groups of 6 albino rats, one for test and other for control, were used for the study. The study was performed by administering the biomaterial at 5g/kg body weight for the test group animals. 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, behavioural patterns, and convulsions and compared with the control group animals (Madhav Satheesh and Uma Shankar 2011).

RESULTS AND DISCUSSION

Our experimental results revealed that the isolated biomaterial was brown in colour with colour changing point of 214°C. It was soluble in water,

Table 1: Physical evaluation parameters of *Phoenix dactylifera* biomaterial.

Sl. No.	Conc. (%w/v)	pH	Viscosity (cp)	Surface tension (dyne/cm)
1	1	7.4	1.12	76.38
2	2	7.4	1.21	72.24
3	3	7.1	1.42	70.2
4	4	7.2	1.63	69.14
5	5	6.9	1.72	67.91

Table 2: Mucoadhesive property determination by Shear Stress method.

Contact time	05 min	10 min	15 min	20 min	25 min	30 min
Water	8.0	10.5	11.1	13.2	16.6	22.2
Biomaterial 1%	9.3	10.5	13.2	17.4	20.0	30.3
Biomaterial 2%	15.6	19.1	26.2	29.0	37.0	45.0
Biomaterial 3%	19.0	26.2	34.1	37.0	49.0	59.3
Biomaterial 4%	30.0	39.0	49.0	66.0	79.0	92.0
Biomaterial 5%	48.4	58.0	69.1	92.0	118.3	164.0
HPMC 3%	58.0	58.4	72.2	97.3	115.0	160.0
Na CMC 3%	52.2	58.3	73.9	98.2	117.0	164.2

Values are indicating the weight (gm) required for breaking adhesive bonds between water/biomaterial/standard polymer and glass plate at specified intervals

insoluble in alcohol, chloroform and ether. It gave positive Benedict's test, Fehling's test, Molisch test and Ninhydrin test. Its 1% solution had the pH value 7.4. Its 1 to 5% w/v concentration solution showed viscosity ranging from 1.1 to 1.72 cps and surface tension 76.38 to 67.91 dyne/cm (Table 1).

IR spectroscopy (Figure 1) revealed 3389 cm^{-1} (OH stretching), 2931 cm^{-1} (C-H stretching), 2362 cm^{-1} (C=C stretching alkene), 1637 cm^{-1} (C=O stretching of carboxyl group), 771 cm^{-1} (CH bending aromatic ring) (Figure 1). SEM image of the biomaterial revealed that particles were ovoid to irregular in shape with larger surface area, so it is amorphous in nature (Figure 2).

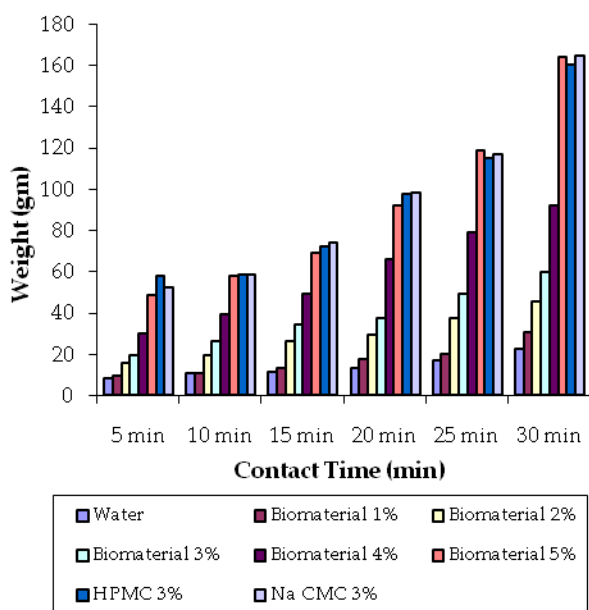


Figure 3: Mucoadhesive property determination by Shear Stress method.

Table 3: Dislodgement time determination by Rotating Cylinder method in *Capra aegagrus* labial mucosa.

Sl. No.	Polymer	Dislodgement time (min)
1	<i>Phoenix dactylifera</i>	22
2	HPMC	27
3	Sodium CMC	20

Table 4: Dislodgement time determination by Rotating Cylinder method *Capra aegagrus* intestinal mucosa.

Sl. No.	Polymer	Dislodgement time (min)
1	<i>Phoenix dactylifera</i>	35
2	HPMC	45
3	Sodium CMC	41

The shear stress study revealed that 5% concentration showed promising mucoadhesivity comparable to standard HPMC and sodium CMC polymer (Figure 3, Table 2). The *ex-vivo* release study with *Capra aegagrus* labial mucosa revealed that the biomaterial had film dislodgement time of 22 min which was comparable with HPMC (27 min) and sodium CMC (20 min) (Figure 4, Table 3). Similarly film dislodgement time of biomaterial in intestinal mucosa was 35 min which was potentially similar to HPMC and sodium CMC (Figure 5, Table 4). The plausible mechanism of the mucoadhesive property of biomaterial 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 for the mucoadhesive strength exhibited by the biomaterial of *Phoenix dactylifera* (Peppas and Buri, 1985; Lehr *et al.*, 1992).

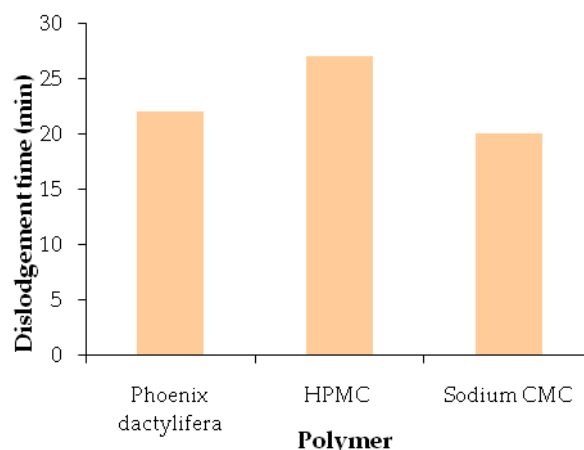


Figure 4: Dislodgement time determination by Rotating Cylinder method in *Capra aegagrus* labial mucosa.

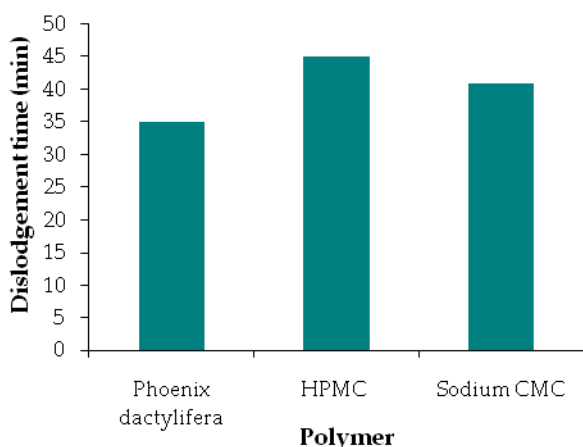


Figure 5: Dislodgement time determination by Rotating Cylinder method *Capra aegagrus* intestinal mucosa.

Acute toxicity study of the biomaterial showed that no change was found in body weight or physical behaviour of animals after the administration of biomaterial. This may be due to the edible nature of the *Phoenix dactylifera*.

CONCLUSION

Finally conclusion can be drawn that the isolated biomaterial shows promising inbuilt mucoadhesive and mucoretentive properties. Since this natural mucoadhesive agent is edible, it is easily biodegradable and may provide an alternative to conventional synthetic/semisynthetic mucoadhesive agents.

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