Academic Sciences Asian Journal of Pharmaceutical and Clinical Research

Vol 5, Suppl 3, 2012 ISSN - 0974-2441

Research Article

DEVELOPMENT OF NEW MUCOADHESIVE POLYMER FROM NATURAL SOURCE

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Received:19 July 2012, Revised and Accepted:2 August 2012

ABSTRACT

Mucoadhesive polymers that bind to the gastric mucin or epithelial cell surface are useful in drug delivery for the purpose of increasing the intimacy and duration of contact of drug with the absorbing membrane. Natural gums and mucilage have been extensively explored as pharmaceutical excipients. Several synthetic polymers are in use for mucoadhesive. Since the biodegradability of the synthetic polymers are questionable, in this exploration, an oral mucoadhesive polymer has been developed which is extracted from gum of *Azadirachta indica* and *Moringa oleifera b*y several evaluation such as measurement of viscosity, adhesive force and swelling property. The other parameters such as solubility, hydration capacity, viscosity, pH, preliminary phytochemical screening, physicochemical properties, were also evaluated. The result shows that mucoadhesive properties of both gums are comparable to synthetic polymers such as hydroxyl propyl methyl cellulose (HPMC) and carbopol 934 under the experimental conditions used in this study. Briefly, it could be concluded that the gum of *Azadirachta indica* and *Moringa oleifera* can be used as a pharmaceutical excipient in oral mucoadhesive drug delivery systems; it has the potential to also replace some synthetic mucoadhesive polymers upon further modifications.

Keywords: Mucoadhesive, Natural polymer, Neem gum, Moringa gum.

INTRODUCTION

Controlled release formulation describes sustained action along with its predictability and reproducibility of release of drug ingredients from the drug delivery system[1]. Out of drug delivery systems, the mucoadhesive drug delivery system is more reliable than traditional drug delivery systems. Mucoadhesion, an interfacial phenomenon, is based on two materials, one of which is mucus layer of mucosal tissue to which the drug is held together by means of interfacial forces for prolonged period of time. Control release system ensures localization of drug in a particular site to improve and increase the bioavailability. The contact time is also enhanced due to interaction between polymers and mucus lining of tissue for sustained action[2]. Advance polymer systems in controlled delivery systems maintain the release rate as well as the concentration in the biological system by increasing its localization and avoiding first pass metabolism[3]. Several polymeric bioadhesive drug delivery systems have been developed and studied in the past. Different types of bioadhesive synthetic polymers such as acrylic-based hygrogels[4]. Including carbopol 934 and hydroxyl propyl methyl cellulose (HPMC) are used to prepare oral mucoadhesive formulations[5]. However, the adhesiveness and drug delivery capabilities of these devices can continue to be improved, as presently known bioadhesive materials, and more bioadhesive materials are discovered[6-9]. Since the biodegradability of the synthetic polymers is questionable, some natural mucoadhesive materials extracted from edible fruits and vegetables having good mucoadhesive properties are used for the purpose of mucoadhesive formulation[10].

MATERIALS AND METHODS

Moringa gum and Neem gum (Omji herbs, Barnala) HPMC-K4M and Carbopol 934 (Central drug house, New Delhi), were employed in the present study. All other chemicals were of analytical grade and were freshly prepared.

Physicochemical properties of mucoadhesive materials

Solubility, pH, Viscosity, Bulk density, angle of repose, Housner's ratio and Carr's index were determined according to Indian pharmacopoeia[11].

Study of swelling property of mucoadhesive materials

Natural mucoadhesive material obtained from *Azadirachta indica* gum and *Moringa oleifera* gum, each 250 mg of natural bioadhesive materials and HPMC and Carbopol 934 synthetic materials was allowed to hydrate in 25 ml of distilled water at 25^{0}C in a 25 ml graduated cylinder. The volume of the natural bioadhesive materials, Carbopol 934 and HPMC measured at 5 min intervals until there was no further hydration observed. Swelling property of different mucoadhesive polymer and materials were checked in different pH[4].

Shear Stress Measurement

The shear stress measure the force that cause a mucoadhesive to slide with respect to the mucus layer in directional parallel to their place of contact of adhesion. The test was performed by using different concentration of mucoadhesive agent solution likes 1%, 2%, 3% w/v using Carbopol 934, HPMC, neem gum and moringa gum was prepared. A specified amount of prepared solution was spread on 3 glass plate. Another clean slide was placed over the first plate and made to spread the polymer solution uniformly in between two glass plates by placing 100g weight on the glass plates. It was allowed undistributed for 15, 30 and 60 min then one side of glass plate was fixed in a hook and the other was collected to a twin passing over a pulley and at the end of pan was attached, Illustrated in figure 1. After the said times 15, 30 and 60 min weight was placed in an increasing manner till the plates attached with polymer got detached. The weight which just detaches, were noted and the average values were tabulated as per methods official method[12,13].

Falling sphere method

To characterize the mucoadhesive strength, the falling sphere method was used for that a clean burette was taken and filled with 10% mucus solution and fixed in a stainless steel tube. Mustard grain which retained on sieve size # 12 were taken and dipped in polymer solutions (Carbopol , HPMC, neem gum and moringa gum) of various concentrations (1.0, 2.0 and 3.0% w/v) and then each grain were slowly placed at the top of the mucus layer. Time taken by the grain to fall 50 divisions in the burette was noted and values were tabulated[14,15].

Determination of mucoadhesiveness by Wilhelmy plate method

In this method small glass plates were coated uniform by synthetic polymer and natural bioadhesive material solution to be tested and dried at 60^{0}C. The prepared coated plates were immersed in goat intestinal mucus solution (pH=5.5), or USP simulated intestinal fluid (pH=6.0), or USP simulated gastric fluid (pH=1.2), for 5, 10, 15, and 30 min, at room temperature. The force required to pull the plate out of the solution was determined under constant experimental conditions[16].

RESULTS

Table 1: Solubility Studies of Natural Mucoadhesive Agent

Solvent use	Neem gum	Moringa gum
*Cool water (8^0C-25^0C)	+	+
Warm water (30^0C-40^0C)	+	+
Di methyl sulfoxide	-	-
Ethanol	-	-
Methanol	-	-
Cyclohexane	-	-
Dichloromethane	-	-
Chloroform	-	-
Carbon tetrachloride	-	-
Acetonitrile	-	-
Benzene	-	-
Ether	-	-
Ethyl acetate	-	-

+ Present, - Absent, *partially soluble

Table 2: Physicochemical Property of Natural Mucoadhesive Agent

Sl No.	Parameter	Neem gum	Moringa gum	HPMC	Carbopol 934
1	pH (1% w/v)	6.7±0.5	6.6±0.5	6.7±0.5	6.8±0.5
2	Viscosity(1%w/v) At,				
	37^0C	1.1032 Poise	1.1112 Poise	1.1172 Poise	1.1194
	45^0C	0.8928 Poise	0.9008 Poise	0.9105 Poise	0.9211
	60^0C	0.4982 poise	0.5071 poise	0.5098 poise	0.5126
3	Bulk density (gm/ml)	0.611±0.018	0.518±0.043	0.479±0.053	0.462±0.059
4	Tapped density(gm/ml)	0.710±0.054	0.754±0.064	0.778±0.068	0.792±0.074
5	Carr's Index (%)	12.983±0.581	18.981±0.603	21.943±0.651	22.216±0.671
6	Haunser's Ratio	1.074±0.074	1.193±0.085	1.205±0.093	1.223±0.098
7	Angle of Repose	28.711±1.431	24.917±1.513	22.674±1.901	23.812±1.871

Table 3: Shearing Stress Measurment of Selected Mucoadhesive Agent

Polymer	Concentration (%w/v)	Weight required to detach glass plate (gm) At the time interval (n=3)		
		15 min	30 min	60 min
Neem gum	1	1.10	1.18	1.31
	2	1.16	1.29	1.52
	3	1.86	1.91	2.09
Moringa gum	1	1.03	1.11	1.22
	2	1.05	1.20	1.43
	3	1.67	1.81	2.01
HPMC	1	1.09	1.11	1.28
	2	1.15	1.27	1.46
	3	1.79	1.88	2.07
Carbopol 934	1	1.01	1.03	1.21
	2	1.08	1.18	1.35
	3	1.63	1.76	1.98

Table 4: Falling Sphere Analysis of Selected Mucoadhesive Agent

Polymer	Polymer concentration (%w/v)	Average time taken (sec.) (n=3)
Neem gum	1	10.21
	2	10.46
	3	10.98
Moringa gum	1	10.03
	2	10.38
	3	10.84
HPMC	1	10.16
	2	10.42
	3	10.86
Carbopol 934	1	10.01
	2	10.24
	3	10.71

Table 5: Mucoadhesive Strength by Wihelmy's Method of Selected Mucoadhesive Agent

Polymer	Time (min)	Wihelmy's method (gm) (n=3)
Neem gum	05	0.91
	10	1.24
	15	1.41
	30	1.68
Moringa gum	05	0.84

	10	1.09
	15	1.28
	30	1.57
HPMC	05	0.76
	10	0.98
	15	1.27
	30	1.48
Carbopol 934	05	0.68
	10	0.92
	15	1.12
	30	1.34

Table 6: Swelling Property of Selected Mucoadhesive Agent

Polymer	Contact time (min)	Volume changes in pH 5.5 (ml)	Volume changes in pH 6.5 (ml)	Volume changes in pH 7.5 (ml)
Neem gum	00	0.6	0.6	0.6
	05	0.7	0.7	0.7
	10	0.8	0.8	0.8
	15	0.9	0.9	0.9
	20	1.0	1.0	1.0
	25	1.0	1.1	1.1
	30	1.0	1.1	1.1
Moringa gum	00	0.7	0.7	0.7
	05	0.8	0.8	0.8
	10	0.9	0.9	0.9
	15	1.0	1.0	1.0
	20	1.1	1.1	1.1
	25	1.2	1.2	1.2
	30	1.2	1.2	1.2
HPMC	00	0.8	0.8	0.8
	05	0.9	0.9	0.9
	10	1.0	1.0	1.0
	15	1.1	1.1	1.1
	20	1.2	1.2	1.2
	25	1.3	1.3	1.3
	30	1.3	1.3	1.3
Carbopol 934	00	0.9	0.9	0.9
	05	1.0	1.0	1.0
	10	1.1	1.1	1.1
	15	1.2	1.2	1.2
	20	1.3	1.3	1.3
	25	1.4	1.4	1.4
	30	1.4	1.4	1.5

DISCUSSION

The pH, swelling index, viscosity and solubility (as per IP) tests for the selected natural mucoadhesive agents are shown in Table 1 and 2. The pH was found to be neutral indicating that the selected natural mucoadhesive agent may not irritate the epithelium and mucus membrane of oral route and was found to be suitable for oral dosage forms. The water absorption of the polymers was inversely related to the pH of the medium. The viscosity studies 1.0%w/v solution of isolated natural mucoadhesive agent shows decrease in viscosity with increase of temperature. The natural mucoadhesive agent was soluble only in warm water and partially soluble in cool water. In case of shear stress measurement and Falling sphere analysis the natural agent from gum of *Azadirachta indica* and *Moringa oleifera* showed more adhesiveness than HPMC and Carbopol 934 from the comparable of adhesiveness. Result is tabulated in Table 3, 4. The initial measurement values for shear stress, (time 15 mins) normalized and the values at 30 and 60 mins reported as increase in ratio compared to time 15 mins. The results obtained from Wilhelmy plate method result is tabulated in Table 5 confirmed that the mucoadhesive materials obtained from gum of *Azadirachta indica* and *Moringa oleifera* showed better adhesive and mucoadhesive property than the synthetic polymer HPMC and Carbopol 934. The adhesive and mucoadhesive strength of this synthetic polymer and natural mucoadhesive materials was increased with time and it was maximum in case of material extracted from gum of *Azadirachta indica* and minimum in case of Carbopol 934. The swelling property of HPMC and mucoadhesive materials obtained from gum of *Azadirachta indica* and *Moringa oleifera* tabulated in Table 6, from these results, it was confirmed that swelling property of Carbopol 934 is maximum followed by HPMC, the material obtained from gum of *Moringa oleifera* and it was minimum for the materials obtained from gum of *Azadericta indica*.

The polymers are playing an important role in field of controlled or sustained release drug delivery system. The selected natural mucoadhesive agent from gum of *Azadirachta indica* and *Moringa oleifera* was successfully tested against their adhesive characteristic in the available physical studies like shear stress method, wihelmy's method, falling spheres method along with some synthetic polymer such as HPMC and Carbopol 934. The results were comparable to that of same synthetic polymer. The mucilage obtained from gum of *Azadirachta indica* and *Moringa oleifera* was having mucoadhesive character which may replaces the synthetic mucoadhesive polymer.

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