EXPLOITATION OF GUM OLIBANUM AS NOVEL NATURAL BINDING AGENT IN THE DESIGNING OF ORAL FUROSEMIDE FORMULATIONS

*BAHLUL Z. AWEN[1], BABU RAO CHANDU[1], PRAKASH KATAKAM[1] , VARUN DASARI[2] AND RAMALINGAM PERAMAN[3]

[1]Faculty of Pharmacy, 7th April University, Zawia, Libya

[2]Hindu College of Pharmacy, Guntur, AP, India

[3]Raghavendra Institute of Pharmaceutical Education and Research, Ananthapur, AP India

ABSTRACT

Current work reports extraction of mucilage of Olibanum from *Boswellia serrata* by maceration technique using water and chloroform, precipitated by absolute Ethanol (40% w/w yield).Physicochemical characteristics of mucilage, such as solubility, swelling index, loss on drying, pH and viscosity were studied and also microbial load was determined. The mucilage was evaluated for its granulating and binding properties in tablets, using furosemide as a model drug. Mucilage was used in different concentrations of 5, 7 and 10% w/v.The granules were prepared by wet granulation technique. The prepared granules were evaluated for percentage of fines, average particle size, total porosity, compressibility index and flow properties. The properties were compared with starch, which was used as standard binder at 10% w/v concentration. The tablets were prepared and evaluated for content uniformity, hardness, friability, disintegration time and *in vitro* dissolution profiles. The tablets had good physicochemical properties and the drug release was more than 75% within 2 h. The tablets prepared by using 10% mucilage as binder exhibited more hardness than by using 5% and 7% concentrations. Hence, 5 and 7% concentrations can be considered as ideal concentrations for preparation of tablets of Furosemide.

1.INTRODUCTION

Mucilages are polyuronides consisting of sugar and uronic acid units. They are usually formed from the cell wall or deposited on it in layers. They swell in water and form a gel (Trease, 1983). The usefulness of mucilages as emulsifying, gelling and suspending agents has been well furnished. Some of the mucilages have also been used in tablet formulations as binding agents also to sustain the drug release (Tilak,2000). Natural mucilages are nontoxic, non-irritant and act as stabilizers, emollients and stiffening agents(chowdary,2006). Olibanum is a gum obtained from *Boswellia serrata (B. serrata), Roxburgh* and other species of *Boswellia.* Olibanum consists chiefly an acid resin (56-60%), gum (30-36%) and volatile oil (3-8%)(Chowdary, 2006;Chowdary,2008). The resin contains mainly a resin acid (boswellic acid) and a resene (Olibanoresene) in equal proportions (Indian Pharmacopoeia, 1996). The current work was attempted to evaluate the binding properties of mucilage extracted from Gum Olibanum. The main objective of the current study is to exploit the use of Gum Olibanum as natural binding agent in development of oral tablet formulations taking Furosemide as model drug.

***For correspondence**

Email: bahlulawen@yahoo.com

Tele/Fax : +218-23-7631775

2.MATERIAL AND METHODS

Plant Material:

Crude form of Gum Olibanum was procured from Girijan Corporation Ltd, Visakhapatnam, A.P., India. Furosemide was a gratis sample obtained from Organ Care Pvt Ltd, Hyderabad, India. All the chemicals and other reagents used in the study were of AR grade purchased from Loba Chemie, Mumbai, India.

Isolation of Mucilage:

The gum was treated with a mixture of chloroform and water in the ratio of 5:95 for 5 days with occasional mixing. Any extraneous materials are then filtered and the gum is then precipitated by adding absolute ethanol. The precipitated gum was filtered, washed with ether and air dried. The dried gum was powdered and passed through 100 mesh for further use.

Physicochemical and microbiological characterization of mucilage:

The physicochemical properties such as solubility, swelling index, loss on drying, viscosity and microbial load of the mucilage were determined according to the Indian Pharmacopoeial Procedures(Indian Pharmacopoeia, 1996). The pH of the mucilage was determined using an Elico® digital pH meter.

Preparation and Evaluation of granules:

Furosemide, which has basically a poor binding property, was used as a model drug to formulate granules. Starch was used as disintegrating agent, whereas lactose and talc were used as diluent and lubricant respectively. The binder solution was prepared by dissolving the mucilage of gum olibanum of *B.serrata* in water at 5, 7 and 10% w/v concentrations. The granules were prepared by wet granulation process. The batch size was 250 g. Drug, lactose, talc and starch were mixed thoroughly and a sufficient volume of 5, 7 and 10% w/v of mucilage were added slowly to the powder blend and kneading was performed for 12 h until formation of wet mass with enough cohesiveness. The wet mass was passed through No.16 sieve. The prepared granules were then evaluated for percentage of fines, particle size and flow properties by measuring the angle of repose(gordon, 1999;Banker,1987). The bulk and tapped densities of granules were assessed in accordance with tapped volumetric apparatus. Compressibility index of the granules was determined by Carr's index(Shah,1997;Auldon,1998; Martin,1991;Reddy,2003). Total porosity was also determined by measuring the volume occupied by selected weight of a powder and the true volume of granules taken.

Preparation and evaluation of Tablets:

The tablets were compressed by using single punch machine (Cadmach®, India) using flat-faced punches. A batch of 100 tablets was prepared. The prepared tablets were evaluated for content uniformity, hardness, friability, disintegration time and *in vitro* dissolution profile using methods specified in Indian Pharmacopoeia.

3. RESULTS AND DISCUSSION

The dried and coarsely powdered gum of *B.serrata* yielded high percentage (40% w/w) of mucilage using ethanol as mucilage-precipitating solvent. The physicochemical and microbiological properties of mucilage were determined and summarized in Table-1. The extracted and purified mucilage was evaluated for bacterial load and pH. The microbial count was found to be less than 120 CFU (colony forming units) per gram of mucilage. The pH of the mucilage was found to be 6.8. Since the pH value of this mucilage is near to neutral, it may be less irritating on gastrointestinal tract and hence was suitable for uncoated tablets.

The prepared granules were evaluated for percentage of fines, particle size and flow properties as shown in Table 2. It was observed that the percentage of fines was reduced as the concentration of mucilage was increased. The percentage of fines was little higher in granules prepared using 5% w/v mucilage as binder. The flow property of granules was determined by determining the angle of repose, which was found to be 28° to 31°. The mean particle size was found to be in the range of 0.32 and 0.38 mm and found to be satisfactory for preparation of tablets. Hence all the granules exhibited good flow properties. Table 2 indicates that the bulk densities of the prepared granules decreased slightly by increasing concentrations of olibanum mucilage. This result may be due to the formation of larger agglomerates and the decrease in fines in the granules which is attributed to increased olibanum mucilage concentrations that provide more binding to the granules. The results of compressibility index (Table 2) indicate a decrease in flowability with increasing olibanum mucilage concentrations. However, all formulations showed good flow properties. The porosity of the granules ranged from 29.32% to 36.35% indicating that the granules are loosely packed and that the particles did not vary in size range. This is in conformity with the general phenomena of percentage porosity value below 26% which indicates that the particles in the powder are of different sizes and a value greater than 45% shows that particles in the powder are in the form of aggregates or flocculates. All these results confirm that the granules possessed satisfactory flow properties, compressibility and porosity.

Three batches of 100 tablets were prepared using mucilage of olibanum at three different concentrations, viz., 5, 7 and 10% w/v. Starch mucilage (10% w/v) was used as standard binder for the comparison. The prepared tablets were evaluated for content uniformity, hardness, friability, disintegration time and *in vitro* dissolution profiles and the results are shown in Table 3. All the batches of tablets exhibited good uniformity of furosemide content. The hardness of tablets increased with increase in percentage of binding agent used. The tablets prepared with 10% w/v olibanum mucilage of *B.serrata* showed more hardness when

compared to tablets prepared with 10% starch mucilage indicating that olibanum mucilage has more binding power compared to that of the starch mucilage. The percentage friability values were constant in all the batches of tablets prepared by using different concentrations of mucilage. The olibanum mucilage has shown an increase in disintegration time with increase in concentration, but all the values were within pharmacopoeial limits. At 10% w/v concentration, the disintegration time was higher when compared to that of the tablets prepared by using 10% w/v starch mucilage.

The *in vitro* dissolution profiles of the prepared formulations were shown in Fig. The drug release was inversely proportional to the concentration of the mucilage. The drug release from the tablets prepared using the mucilage at three different concentrations was more than 75% in 2 h. These tablets have shown reduced diffusion of drug which was due to the formation of hydrogel in the form of thick sticky film of hydration on the surface of the tablets. This may be the reason for the reduced dissolution of the drug with increased mucilage concentration.

From the present investigation, it can be concluded that olibanum mucilage of *B.serrata* may be used as binding agent in tablet formulations. The study explores the potential for the identification of new natural materials as excipients in pharmaceutical formulations which can be replaced by synthetic excipients in future.

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Table 1: Physicochemical and microbiological evaluation of gum olibanum mucilage.

Parameter (s)	Result (s)
Solubility	Insoluble in water and produces viscous solution. Soluble in alcohol, acetone, ether and chloroform
Swelling index	13%
Loss On Drying	9.2%
pH	6.8
Bacterial Load (No. of CFU/g of mucilage)	103

Table 2: Characterization of granules prepared using gum olibanum mucilage as binder

Parameter	Olibanum mucilage as binder (% w/v)			Starch 10% w/v
	5	7	10	
Percentage of fines	19.86	16.30	14.27	18.19
Mean particle size (mm)	0.32	0.32	0.38	0.45
Angle of repose (°)	28°	31°	29°	28°
Loose bulk density (g/cm^3 ±sd)	0.523±0.02	0.530±0.05	0.512±0.03	0.486±0.04
Tapped bulk density (g/cm^3 ±sd)	0.586±0.05	0.602±0.02	0.569±0.04	0.576±0.02
Compressibility index (%±sd)	8.17±0.85	10.37±0.69	11.85±0.91	12.09±1.17
Total porosity (±sd)	29.32±2.15	34.92±2.29	36.35±3.34	37.51±2.59

Table 3: Evaluation of tablets prepared using olibanum mucilage as binder

Property	Olibanum mucilage as binder (% w/v)			Starch 10% w/v
	5	7	10	
Content Uniformity (mg ±sd)	96.75±0.36	97.92±0.51	97.21±0.44	98.12±0.70
Hardness (Kg/cm^2 ±sd)	5.83±0.08	6.48±0.15	7.16±0.09	6.62±0.07
Friability (%)	0.35	0.32	0.35	0.20
Disintegration time (sec)	290	310	330	250

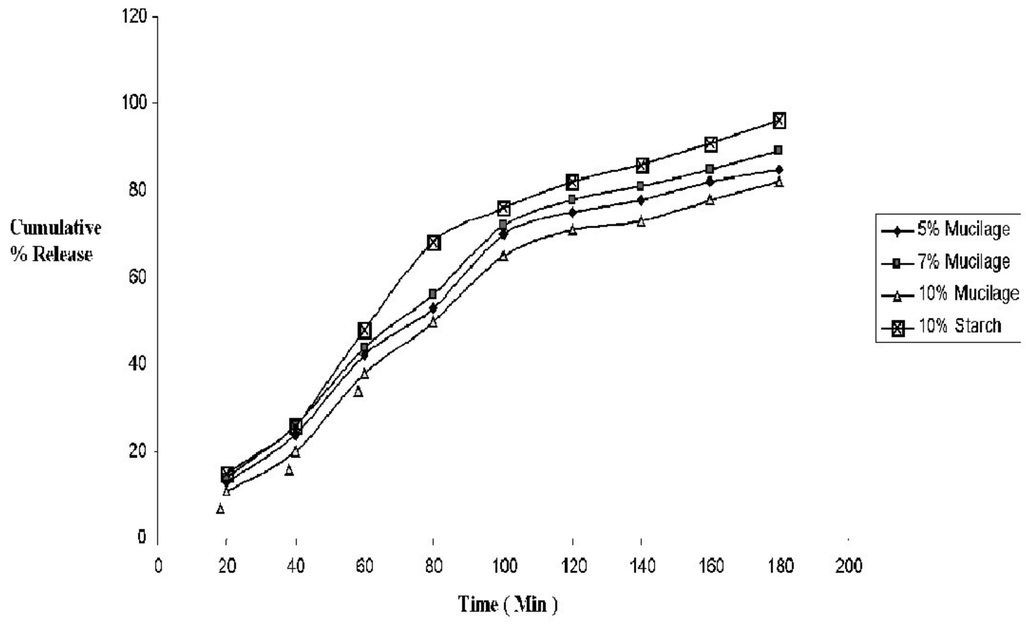

Fig : *In vitro* dissolution profile of Furosemide tablets prepared with Olibanum of *Boswellia serrata* as binding agent

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