EVALUATION OF *PROSOPIS AFRICANA* GUM IN THE FORMULATION OF JELLIES

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ABSTRACT

Prosopis gum has been evaluated for use in the formulation of jellies. The percentage of salicylic acid released from jellies prepared from prosopis gum was investigated. The percentage of permeation of the drug through the jelly was also evaluated. Surfactants were incorporated into the gels and the effect on the release and permeation also investigated.

The release of salicylic acid from the jellies was low. Similarly, the quantity of the drug that permeated through the jelly was also low. Incorporation of surfactants did not enhance the release of the drug. The low release and permeation rates may be due to the poor water solubility of the incorporated drug.

Correlation of the quantity of drug released with viscosity shows that drug release was dependent on the viscosity of the jellies, the highly viscous jellies showing lower release.

Keywords: *Prosopis gum, prolong release, permeation, poor water solubility*

INTRODUCTION

Plant gums have wide and varied applications. Historical records show the utilization of various seaweed gums for food and medicinal purposes by many coastal inhabitants of Africa, Asia, Australia as well as Western Europe [1]. Recently, the use of natural gums has achieved wider dimension and the economic value enhanced despite competition from semi and synthetic gums.

Various gums are used to formulate jellies. They may be formulated from natural gums such as those of acacia, chondrus, gelatin, tragacanth, pectin, and alginates [2] or from synthetic derivatives of natural substances such as methyl cellulose and sodium carboxymethyl cellulose [3]. Currently many more drugs are being

PHARMACEUTICS

formulated as jellies and include such drugs as piroxicam, an anti arthritic drug marketed as Feldene Gel by Pfizer Pharmaceuticals [4], and etofenamate, another anti arthritic drug marketed as Buyrogel by Bayer Pharmaceuticals [5]. Many more examples abound and range from local anaesthetic to anti-infective agents. In this study, the potentials of Prosopis gum as an excipient in the formulation of gels is explored. Prosopis gum is a rapidly swelling polysaccharide from the seeds of *Prosopis africana* [6, 7].

MATERIALS AND METHODS

Materials

The following materials were used as purchased without further purification: sodium salicylate (Fluka A.G.), salicylic acid, sodium lauryl sulphate, Brij 35, tragacanth and methyl hydroxybenzoate (E. Merck), glycerol and ethanol (Buternchem). Prosopis gum was obtained from a batch processed in our laboratory.

Methods

Extraction of prosopis gum

The dried seeds of *Prosopis africana* were boiled for 3 hours after which the tegmen were removed manually and soaked in distilled water for 48 hours. The resultant jelly-like mass was passed through a muslin cloth. The filtrate was diluted with an equal volume of distilled water and precipitated with acetone. The precipitate was collected on a Buchner funnel with the aid of suction from a vacuum pump. The precipitate was dried in a vacuum desiccator and pulverised. The material was stored in well-capped bottles until used.

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PREPARATION OF GELS

Gels were prepared using the formula below:

Salicylic acid	- 5.0 gm
Gum	- X* GM
Methyl hydroxybenzoate	- 0.2 GM
Glycerol	- 2.0 GM
Ethanol	- 10.0 ml
Water to	- 100.0 GM

X* ranged from 3-5%

The gum mucilages were prepared according to the method described in the BPC [8]. The drug (salicylic acid) was dissolved in glycerol and a small quantity of water was then added to the mucilage and properly agitated. The volume was made to 100 ml in a wide-mouthed jar and shaken properly. Similar mucilages were also prepared but without drug, and used for permeation studies.

RELEASE STUDY

The assembly of the apparatus shown in Figure 1 was used for the release study. The arrangement is made of two compartments, the inner and outer compartments.

The inner compartment is made of glass cylinder with internal diameter of 75 mm. One end of the cylinder tapers down to an orifice of 40 mm diameter. This together with a polyvinyl chloride (PVC) ring, forms the support for a dialysing membrane impregnated with a small quantity of castor oil. The membrane was held in position between the supports with a stainless steel screw clamp so that only the diffusion area was exposed. The outer compartment was made of a 1-litre beaker containing a plastic support. The membrane assembly was mounted on this support. Constant stirring of the acceptor medium (0.1N HCl) was effected with a magnetic stirrer. A thermometer was also provided to monitor the temperature and ensure that it was maintained at 37 ± 0.5°C.

At the beginning of the release study, 5 gm quantity of the gel was placed in the inner compartment while the outer compartment containing 500 ml volume of 0.1 N HCl was

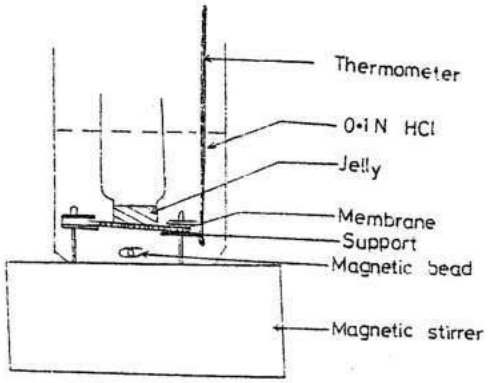

Figure 1: Diagram of the apparatus used for the release and permeation studies

constantly stirred at a rotational speed of 100 RPM with the aid of a magnetic bead. Five ml samples were withdrawn at 1-hour intervals and analysed for salicylic acid content. Each sample withdrawn was replaced with equal volume of 0.1 N HCl. Absorbance of each sample was measured at 540 mm in a colorimeter (model 254, Ciba-Corning), after addition of 2 ml of ferric chloride test solution. Actual drug content in each sample was determined from the slope of a standard plot of Beers law for salicylic acid.

Permeation Study

The same set-up of apparatus used for the release study was employed for the permeation study. In this study, a one per cent solution of the drug was placed in the inner compartment of the set up. The sample of the gel without the drug was placed inside the dialysing membrane to a thickness level of 2 mm. The outer compartment contained 500 ml of 0.1 N HCl. At regular time intervals 5 ml was withdrawn and analysed for the drug that had permeated through the gel into it.

Viscometry

The rheological properties of the gel were determined using a viscometer (Model RV11, Haake). The medium sensor was used and all determinations were done under room temperature.

RESULTS AND DISCUSSION

Figure 2 shows the release profiles of sodium salicylate from the gels. The release was affected by the concentration of the gum in the gels. Higher drug release was obtained with the formulation containing 3% prosopis gum than the 5% concentration of the gum. Similarly gels containing prosopis gum generally had better release than those containing equivalent concentrations of tragacanth. Within the first 3 hours of the experimental period the quantity of drug released was the same for all the formulations.

Generally the release of the drug from all the formulations was low. This may be associated with the poor water solubility of the incorporated drug as well as the castor oil which was used to impregnate the dialysing membrane. The castor oil/membrane is necessary to mimic actual life situations where drugs have to penetrate a lipoidal barrier. Before any drug applied topically can be absorbed, it must penetrate the barrier layer of the skin, the stratum corneum. This layer is now widely acknowledged to be essentially uniformly impermeable [8]. It behaves like a passive diffusion barrier with no evidence of metabolic transport processes. Penetration of water and low molecular weight non-electrolytes through the epidermis is proportional to their concentration, and to the partition co-efficient of the solute measured between tissue and vehicle [8]. Fick's Law describes steady state transport through the skin:

$$J = \frac{DP\ CV}{h}$$

where J = solute flux
D = solute diffusion co-efficient in the stratum corneum
P = solute partion co-efficient between vehicle and skin
h = thickness of the stratum corneum
CV = difference in solute concentration between vehicle and tissue

The above equation applies in a situation whereby the drug is being transferred by a passive mechanism involving simple diffusion driven by differences in drug concentration across the two sides of the membrane [9]. This passive diffusion is also applicable to non-living membranes as the type used in this study.

Figure 3 shows the permeation profiles of salicylic acid through the gels. More drug permeated through the gels containing 3% tragacanth than that with percentage of the gum as well as those prepared with prosopis gum. The quantity of drugs that permeated through the gels were rather low, not reaching 50% in 9 hours for all the formulations.

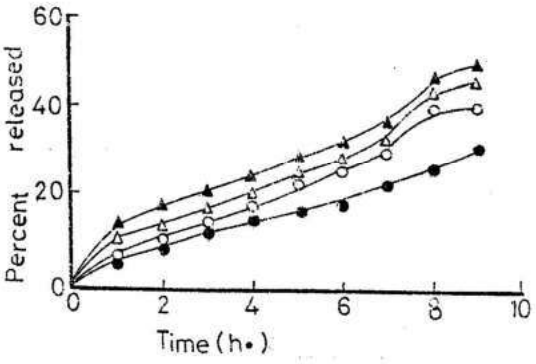

Figure 2: Release profiles of salicylic acid from the jellies: Prosopis gum ▲3gm, Δ5gm; tragacanth O 3gm, ● 5gm

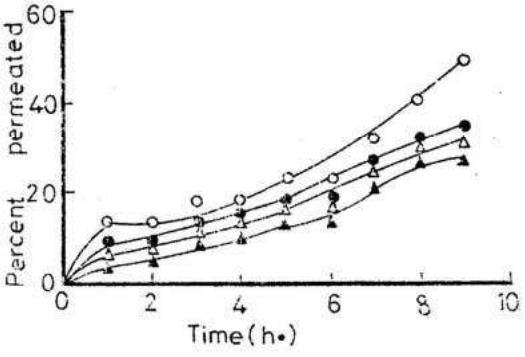

Figure 3: Permeation profiles of salicylic acid through the jellies: Prosopis Δ3gm, ▲5gm; tragacanth O 3gm, ● 5gm

Table 1: The effect of viscosity on the release of salicylic acid from and permeation through gels prepared with prosopis gum.

Conc	3%	5%	5% with 2% Brij 35	5% with 2% SLS
Apparent Viscosity (cps)	560.38	3170.11	3570.83	5200.47
% drug released in 9 hours	31.82	22.73	16.48	13.74
% drug permeated in 9 hours	31.82	27.27	21.07	18.21

Figure 4 shows the release of salicylic acid from gels containing 5% of the gums as well as 2% of surfactants: Brij 35 and sodium laurylsulphate (SLS). The surfactants did not enhance the release of the incorporated drug. Skin penetration of drug substances can be enhanced by the use of suitable vehicles. The affinity of the vehicle for the drug substance can influence the release of the active membrane from the vehicle. The epidermis has been said to be most permeable to substances with an ether/water partition co-efficient of about 9. By formulating certain oil-soluble drugs with surfactant, it is possible to move the ether/water partition co-efficient towards 1, as with Vitamin A which, when solubilised in water containing polysorbate 80, penetrates the skin more readily than when applied as a solution in oil [9]. Similarly, the emulgents in modern creams often have high surface activity, which helps to ensure good contact with hydrophobic surface of the skin and possibly increase the release rate. Contributory effects to an accelerated release rate include the absorption of water by the base from its aqueous environment and the formation of an emulsion at the base/environment interface.

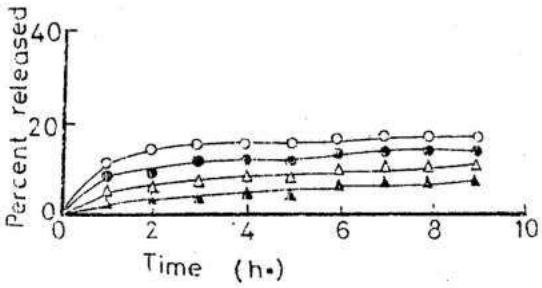

Figure 4: Release profiles of salicylic acid from the jellies containing 5% of the gums and 2% of surfactants: O Prosopis/Brij 35, ● Prosopis/SLS; Δ tragacanth/Brij 35, ▲ tragacanth/SLS

However, in this study, a decrease in release and permeation rates were observed as shown in Figures 4 and 5. Such retardation caused by inclusion of a surfactant may be due to an increase in the hydrophilic nature of the base which may have an adverse effect on the rate of partition of the medicament between the base and its aqueous surroundings [10].

Secondly, the surfactants increased the viscosity of the gels. Generally, Brij 35 increased the release and permeation rates than SLS. This is because the gels formulated with SLS had higher viscosity than those formulated with Brij 35.

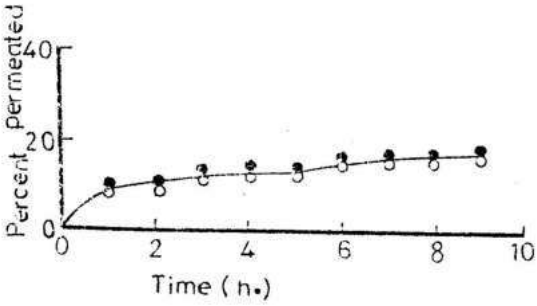

Figure 5: Permeation profiles of salicylic acid through jellies containing 2% of Brij 35 and 5% of the gums. ● tragacanth/Brij 35, O prosopis/Brij 35.

Figure 6 shows rheograms for some of the gel formulations. The viscosity of the gels containing 5% of prosopis gum was higher than those containing 3% of the gum. Similarly, the formulations containing the surfactants were more viscous than those without surfactants with that containing SLS showing a greater viscosity. The effects of the viscosity on release and permeation through the gels are clearly shown in Table 1.

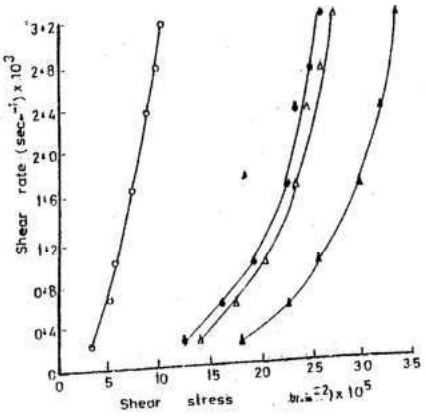

Figure 6: Rheogram of jellies formulated with prosopis gum
○ 3 gm without surfactant
● 5 gm without surfactant
Δ 5 gm with Brij 35
▲ 5 gm with SLS

The more the viscosity, the less the release of the drug from the gels. Similarly, since the gels containing the surfactants were more viscous than those without surfactants less drugs permeated through them.

CONCLUSION

Prosopis gum may find use as an excipient in the formulation of gels. Though the study showed that the release of the incorporated drug was low, other classes of drugs, especially the water-soluble drugs are being investigated and the use of other release enhancers in the gels are also being studied.

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