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## Preparation and Characterization of Oral Mucosal Herbal Patch for Mouth Ulcer

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**ABSTRACT:** The study aims at development of patch from the herbal extracts (*G. glabra* & *A. catechu*), clove oil and other materials for oral mucosal drug delivery with more permeability and residence time. Materials and Methods: Oil i.e. clove oil, surfactant i.e. triethanolamine, co-surfactant i.e. propylene glycol was selected for the gel preparation. The gel was prepared using different combinations of surfactant, co-surfactant and polymer (HPMCK15M). Formulations were prepared in different batches (G1 to G4) and the prepared gel was evaluated in terms of physical appearance, acidity or basicity, nature with respect to viscosity, content of drug, spreadability and release of drug in in-vitro condition. Results and Discussion: Upto 6 hours the maximum in vitro release was shown by formulations whereas after 6 hours the in vitro drug release was static. The batch G4 have proved to be a better formulation than other batches with respect to in-vitro the profile of release of drug as well as their viscosity. Conclusion: Utilization of cold method for preparing oral mucosal herbal gel of *G. glabra* & *A. catechu* extract has proved to be potent method. Thus in view of uncertainties regarding oral mucosal delivery of drug, the results looked quite promising.

**KEYWORDS:** Gel, Bioadhesive, oral mucosal, Herbal, Carbopol, *in-vitro* release

### I. INTRODUCTION

*Glycyrrhiza glabra* drug consisting of the composition i.e. *Glycyrrhiza glabra* dried roots. Linn., Family *Fabaceae* [1]. The Classical Names of *Glycyrrhiza glabra* are Yashti, Yashtimadhu, Madhuyashtika, Yashtimadhuka [2]. It consists of few potential phytoconstituents, approximately 2-9 percent of glycyrrhizin, potassium and glycyrrhizinic acid calcium salts together as a mixture, coumarins, stigmaterol, umbelliferone, onocerin, herniarin,  $\beta$ - amyryl [1]. The expectorating property along with anti-inflammatory and demulcenting properties present in the drug is because of the presence of glycyrrhizin. Glycyrrhizin also have antiviral, antihepatotoxic, and antibacterial activities [3,4].

*Acacia catechu* (Fabaceae Family), The composition of the drug may be either finely coarse powder of dried bark or it may be dried powder of aqueous extract which is also known as Black catechu, basically which are produced from heartwood of *Acacia catechu* [5]. The Classical Names of *Acacia catechu* are Balpatra, Khadira, Bahushalya, Gayatri, Raktasara, Yadniya [6]. It consists of catechu red, catechutannic acid (25-30%), catechin (2-12%), epicatechin, quercitrin, quercetin [7]. The concentrated aqueous extract, have digestive, astringent and cooling properties, which has proven to have various health benefits viz., advantages in treatment of cough as well as diarrhoea, applied externally to ulcers, boils, and eruptions of the skin, and is used extensively in herbal preparations [8,9].

The most preferred route for delivery of drug is oral route because of its ease and convenience, also it is less expensive as well as versatile. But few reports have shown that there are few disadvantages of using drug delivery by oral route system, few of the drawbacks are degradation of the drug because of the enzymes present in gastrointestinal tract as well as first-pass metabolism by hepatic system. There are certain other transmucosal routes which may act as an

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alternative to the oral route of drug delivery system i.e. nasal system along with rectal way, genitourinary tract etc. These drug delivery routes may provide few new possibilities to overcome disadvantages occur due to conventional oral delivery system in the form of tablets, capsules, syrups, etc.

## II. RELATED WORK

With the advances in the emergence of new delivery routes, buccal oral mucosa route has emerged as an efficient delivery route for targeted delivery system for administration of drug as well as less enzymatic degradation. This drug route has wide variety of dosage forms, particularly for those drugs targeted for local delivery in the oral cavity. The noninvasive nature of administration, ease and convenience of administration, precise localization, and increased permeability of the buccal mucosa compared to other transepithelial routes makes this a promising route of delivery [10-12].

Several oral mucosal drug delivery system has been developed as bioadhesive dosage forms which are available in the market. Usually they are in tablets form, or in the form of patches and they are also in the form of ointments, powders or in the form of films. The recent advances in field is to develop dosage form (Gel) with the use of herbal extract and polymer, which is quite promising for oral mucosal delivery of drug.

## III. MATERIALS AND METHODS

The clove oil, carbopol 934P, Triethanolamine and Propylene Glycol was procured from N.S. Scientific Centre, Bhopal. The procurement of the components for therapy i.e. *Glycyrrhiza glabra* (*G. glabra*) and *Acacia catechu* (*A.catechu*) was done from Indian Scientific, Bhopal. After procurement, the sample was finely coarse and the powder preparation was done in laboratory followed by sieving through sieve no. 60. Procurement of other standard compounds, like 18- $\beta$ - glycyrrhetic acid and Catechin were done from Omkar Traders, Indore. All other chemicals and reagents used were of analytical grade. Distilled water was used throughout the study [13].

### Extraction

Fine coarse powder of *G. glabra* and *A. catechu* powder (approximately 100 gm) was allowed to mix with 500 ml of distilled water, followed by extraction using cold maceration for 24 hrs. The extraction procedure is followed by filtration and evaporation of the sample to dryness using rotary evaporator at 60 °C. The dessicator was then allowed to get dry in dessicator [14].

### Gel Formulations

By using cold method, from clove oil, *Glycyrrhiza glabra* and *Acacia catechu*, Carbopol-934P gel was prepared. Within a beaker, different formulation batch was prepared by placing weighed amount of carbopol-934P viz., 0.5%, 0.6%, 0.8% and 1.2 % respectively. For obtaining the homogenous mixture standard amount of water (approx 100 ml) is then added to the weighed amount of *Glycyrrhiza glabra*, *Acacia catechu* extract. Then for approximately 24 hours, it was kept at room temperature. In above dispersion the weighed amount of clove oil was then added, followed by continuous agitation. Agitation after a certain time may lead to formation of gel, which was then stored at ambient temperature, before its use [15].

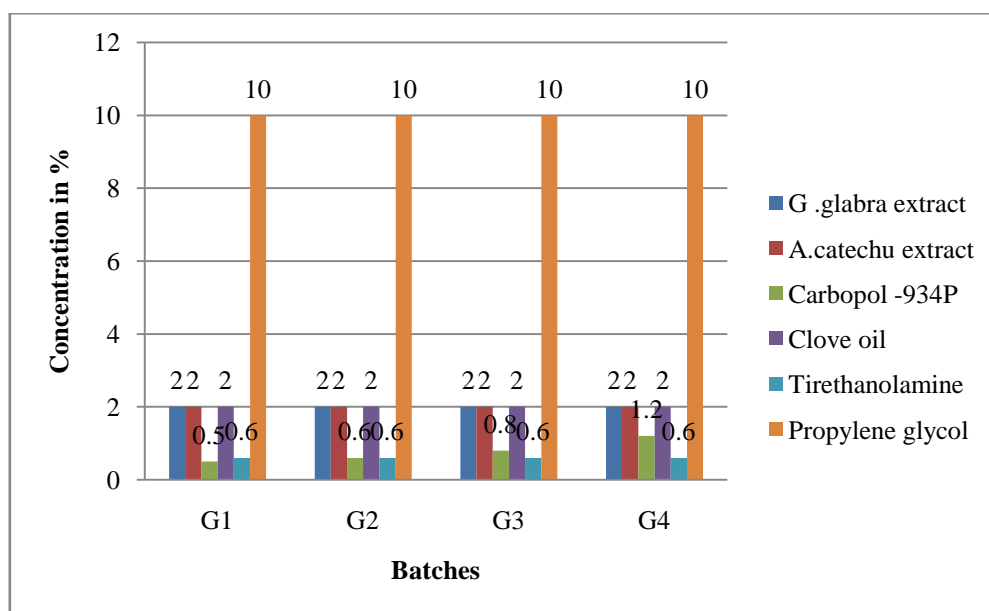


Fig. 1: Formulation of ingredients of mouth ulcer gel

### Characterization of gel

#### Appearance

The gel was visually inspected and appearance of gel was evaluated.

#### pH

The pH of gel was measured by accurately weighing 1 gm of gel, followed by dispersion of gel in approximately 10 ml of distilled water. After mixing pH reading was taken with the help of pH meter [16].

#### Drug Content Detection

In order to analyse drug content, cellulose membrane is used. Membrane was washed with running water for 3-4 hr to remove the irrelevant material. The acid is removed by treating the membrane with hot water (60°C) for 2 min followed by acidification with 0.04N sulphuric acid. Gel formulation (1g) was taken in the membrane, kept in 50ml beaker containing 50ml phosphate buffer of pH 6.8 and stirred with magnetic stirrer. At the end of 24 hr, sample was removed and estimated for drug content by HPLC [17].

#### Viscosity and Rheological studies

Viscosities of gel were determined using Brookfield Viscometer. Gels were also tested for their rheological characteristics using Brookfield Viscometer at 25°C. Over the entire range of speed setting of viscometer spindle, measurement was done. Where, time duration of 30 seconds was kept between two successive speeds i.e. 10 rpm to 100 rpm, followed by descending order [18].

#### In-vitro Drug Release study

*In-vitro* diffusion studies were carried out in Franz diffusion cell having a receptor compartment capacity of 10ml, through cellophane membrane (Table 1). In between the half-cells, the membrane mounting was done so as to allow an

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ease for that the membrane to make contact with receptor fluid (Phosphate buffer pH 6.8). Approximate area that was available for diffusion is 1.24 cm<sup>2</sup>. In order to prevent the evaporation of vehicle, the donor cells were covered with aluminium foil. The maintenance of fluid receiver compartment was done at 37 ± 0.5 °C. Into the donor compartment 1ml of gel was placed. The magnetic stirrer was used in order to keep the whole assembly and within the receiver compartment whole solution was stirred, with a constant rate of approximately 100rpm. A teflon coated magnetic bead was used for mixing purpose. At regular time interval a small sample from solution was withdrawn and the replaces volume was overcome with buffer to maintain the sink condition. The sample was then allowed to be assayed for the estimation of drug content. Using standard calibration curve of 18-β- glycyrrhithinic acid and catechin, unknown concentration of 18-β- glycyrrhithinic acid and catechin was detected in the gel [19].

Table 1. In-vitro drug release study conditions

<b>Apparatus</b>	Franz diffusion cell
<b>Diffusion medium (in receptor compartment)</b>	Phosphate buffer (pH 6.8)
<b>Diffusion medium volume</b>	10 ml
<b>Temperature</b>	37±0.5°C
<b>Sampling interval</b>	1 hour
<b>Sampling volume</b>	5 ml
<b>Speed</b>	100 rpm

## Spreadability

In the centre of the glass plate, approximately 1g of gel was placed in order to determine the spreadability of gel. An another glass plate of the same size was used to cover this glass plate. Further, on the upper side of the plate, for approximate 5 minutes weight of 1000g was carefully placed. This step is further followed by spreading of gel between the plates. Approximately 50 gm of weight was added to the pan. The time required to separate the two slides i.e. the time in which the upper glass slide moves over the lower plate was taken as measure of spreadability (S) [20].

$$S = m \times l/t$$

Where,

m = weight tide to upper slide

l = length moved on the glass slide

t = time taken

## IV. EXPERIMENTAL RESULTS

### Appearance

Gels prepared were found to be translucent and homogeneous with characteristics colour of extracts of *G. glabra* and *A. catechu*.

### Viscosity

Viscosity details are shown in Table 2. The Formulation batch G4 has viscosity 135.33 × 10<sup>4</sup> which was easy to spread among the other formulation batch.

### Drug content

Drug content details are shown in Table 2. Drug content of 18-β- glycyrrhithinic acid was within 79-82.65 and of catechin was 69-72.35 % in the formulation batch.

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Table 2. Viscosity and drug content parameters of gel

Formulation Batch	Viscosity (cps)	Drug Content	
		18-β- Glycyrrhetic acid	Catechin
G1	580.3 × 103	82.65	70
G2	744.3 × 103	81.0	72
G3	126 × 104	79.0	69
G4	135.33 × 104	82.1	72.35

### In-Vitro release profile

*In vitro* release details are shown in Figure 2. The formulation batch G4 has better release in 1 hour and 6 hour among other formulation batch.

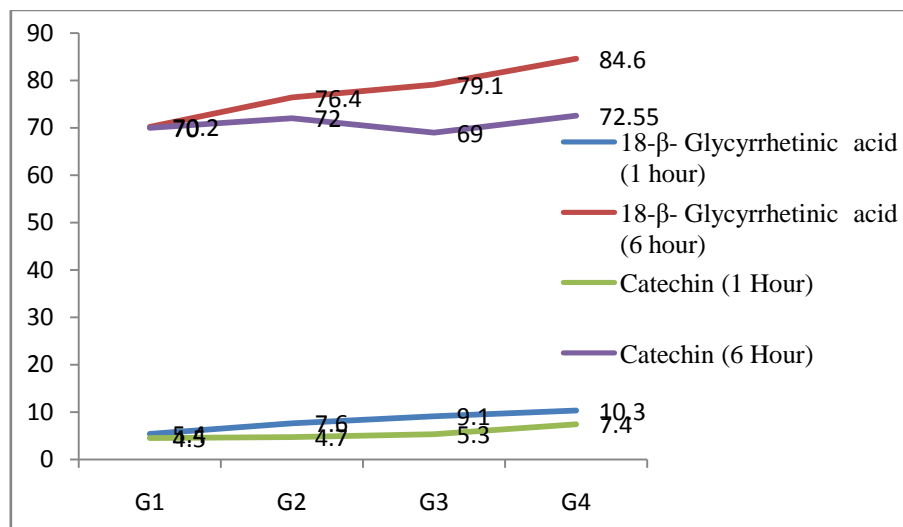


Fig. 2: Showing *in vitro* release profile of gel

### pH

The pH of the formulations was nearer to neutral as shown in Figure 3. This indicates the nonirritancy of the formulation in oral cavity.

### Spreadability

With increase in the concentration of the polymer, viscosity of formulation is increased. At the same time, spreadability of the formulation is reduced. This can be observed in Figure 3. Formulation G4 showed higher Spreadability compared to other formulations because viscosity of Formulation G4 was higher.

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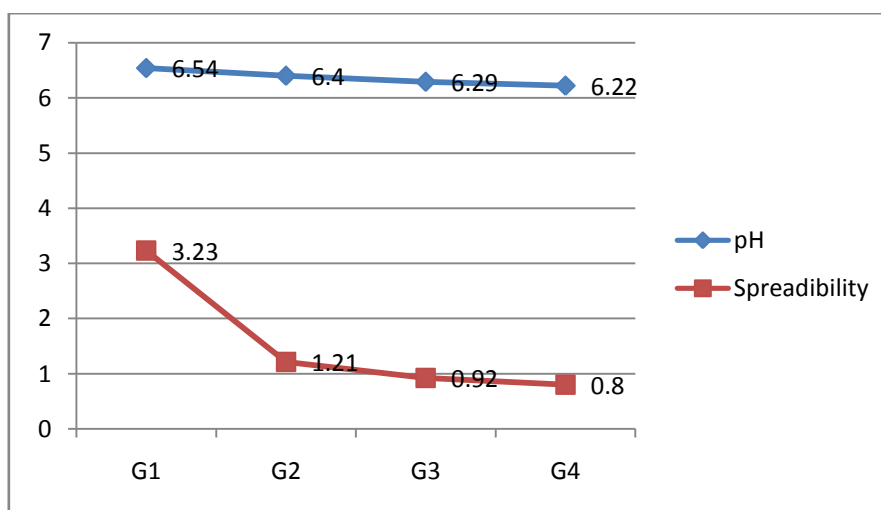


Fig. 3: pH and spreadability parameters of gel

## V. CONCLUSION

The oral mucosal herbal gel of *G.glabra* & *A.catechu* extract was successfully prepared by cold method. Polymer has significant effect on various parameters of formulation viz. viscosity, spreadability, pH, drug content and *in-vitro* release. The spreadability decreased whereas viscosity increased with increase in the concentration of polymer in the formulation. The various formulations shown maximum *in-vitro* release upto 6 hours and thereafter, release becomes constant. Overall results looked quite promising for oral mucosal delivery of drug.

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## CONFLICT OF INTEREST

There is no conflict of interest.

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