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Development of in-situ gel containing phytoconstituents for the treatment of mouth ulcer

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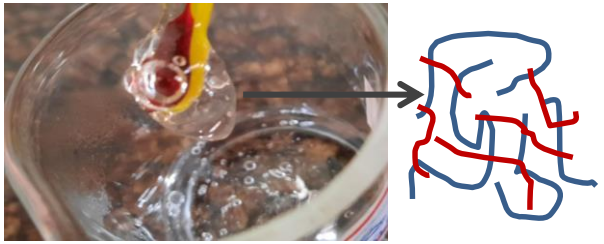
Graphical Abstract

Polymeric solution containing Phytoconstituents (at 25 °C)

- Ease of applicability
- Reduction of pain

Temperature change



In situ gel formed (at body temperature)

- Prolong the retention time
- Improved the bioavailability

Abstract

An ulcer that develops on the mucosal surface of the oral cavity is known as a mouth ulcer, also known as an oral ulcer or a mucosal ulcer. The most typical type of oral ulcer is aphthous stomatitis. This investigation focuses on temperature-sensitive in-situ gel formulations, which change their phase on response to body heat from liquid to semisolid gel. These are easily administered into the buccal cavity at the ulcer site and are a free-flowing liquid at room temperature. Utilizing various polymers, a temperature -sensitive *in-situ* gel comprising phytoconstituents was developed utilising the cold technique. To optimise various types and concentrations of polymers, including carbopol, Poloxamer 188 (P 188), Poloxamer 407 (P 407), and others, preliminary research was conducted. For the formulation, 20% P 188 and 15% P 407 were employed because there is a correlation between the amount of poloxamers and thermogelling transition temperatures (Tsol-gel). A blend of phytoconstituents found in the extracts of *Glycyrrhizin glabra* and *Psidium guava* are used in the formulation because, as we know, they have less negative effects than synthetic chemicals. The outcomes demonstrated improved homogeneity, stability, gelation temperature, and spreadability for the developed product, which was lessen dose variation and treat oral ulcers in the most effective way with improved patient compliance.

Keywords: Aphthous stomatitis; *In-situ* gel; Phytoconstituents

Introduction

A mucus membrane ulcer is an open sore that is distinguished by the removal of inflammatory dead tissue. Although they can occur everywhere, ulcers are frequently found on the skin of the lower extremities and in the digestive system. There are numerous different types of ulcers, including vaginal, oesophageal, and mouth ulcers. They are painful round or oval sores that typically develop on the inside of the cheeks or lips and the buccal cavity.

Currently available topical delivery for the treatment of mouth ulcer is gel or cream base, and necessary to apply with figure which is painful and, many times, not possible to access the ulcer easily. The goal is to formulate liquid formulation, therefore, it can directly delivered through container and spread easily on affected part where than liquid film is converted into semisolid. This semisolid layer remains on ulcer for longer period of time as compared to liquid film, hence will improve the therapy in terms of longer duration of action.

Additionally, in contrast to the semisolid dosage forms, spreading of formulation is spontaneous and hence not required force to apply on ulcer which ultimately improves the patient compliance.

Introduction

Herbs used in Treatment of Mouth ulcer

- *Glycyrrhiza glabra L.,* is a sweet, moist, soothing, flavouring herb commonly known as Liquorice belonging to the family *Fabaceae*.
  - It contains triterpenoid saponins (4–20%), mostly glycyrrhizin, a mixture of potassium and calcium salts of glycyrrhizic acid.
  - Anti-ulcer properties of saponins have been reported.

- *Psidium Guava* - The biological source of Guava is *Psidium guajava*. It belongs to family *Myrtaceae*.
  - It contains carotenoids and polyphenols like gallocatechin and leucocyanidin.

Method of *in situ* gel preparation

- Different grades of polymers were used for the preparation of *in situ* gel by cold method.
- This method involved slow addition of polymer in deionized cold water with continuous stir.
- Add required amount of extracts of *Glycyrrhiza glabra L.* and *Psidium guajava*.
- The formed mixtures were stored overnight at 4°C and studied for their gelation temperature to select type and optimum concentration of polymer for effective *in situ* gel formulation.

Evaluation of *in situ* gel

- Physical appearance
- Clarity
- Homogeneity
- pH
- Gelation temperature
- Spreadability

  $S = M \times L / T$

  where, M = weight tide to upper slide

  L = length moved on the glass slide

  T = time taken to separate both slides

- Stability

Results and discussion

Selection of polymers

- For the creation of the in situ gel formulation, different grades of Poloxamer, including Poloxamer 188, Poloxamer 407, Gellan gum and carbopol were employed.
- Poloxamer 188 and Poloxamer 407 were the only polymers to form viscous clear solutions and gel at high temperatures.
- Due to its gel formation during formulation, gellan gum was not used to make the formulation.
- In order to produce an in situ gel, the polymers Poloxamer 188 and Poloxamer 407 were chosen based on visual inspection and gelation temperature.

Results and discussion

Selection of polymers concentration

- As the temperature of the periodontal cavity is nearest 37°C, this study aimed at preparing the liquid formulations that may gel below 37°C.

Optimization of different polymer concentration

Concentration (%w/v)	Gelation temperature (°C)	
	Poloxamer 188	Poloxamer 407
5	69	51
10	64	45
15	60	40
20	54	33
25	48	26

Results and discussion

Selection of polymers concentration

- As the temperature of individual polymer was not suitable so we combine both Poloxamer for getting desired gelation temperature.

Optimization of different polymer concentration

Concentration(%w/v)		Gelation temperature (°C)
Poloxamer 188	Poloxamer 407	
15	5	40
10	10	41
5	15	39
20	15	34
15	20	37

Results and discussion

Results of evaluation parameter

Sr. No.	Evaluation parameter	Results/observation
1	Physical appearance	Good
2	Clarity	Transparent
3	Homogeneity	No aggregates found
4	pH	6.67
5	Gelation temperature	34
6	Spreadability	32.24 gm.cm/sec
7	Stability study	Stable

Conclusions

- *Glycyrrhizin glabra* and *Psidium guava* anti-ulcerative and anti-inflammatory agent used in the treatment of mouth ulcer was successfully formulated as temperature-sensitive *in situ gel* by cold method. The physical appearance, pH, spreadability, homogenity, gelation temperature, stability study, clarity of formulation containing 20% of Poloxamer 407 and 15% Poloxamer 188 was found to be satisfactory.
- The prepared formulation minimize the dose variation and heal the mouth ulcer in best effective way with better patient compliance.

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