RESEARCH ARTICLE

Formulation and Evaluation of Polyherbal Gel containing Ethanolic Extract used as Local Anesthetics in Oral Cavity

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ABSTRACT

Conventional dosage forms frequently produce leakages and drip. There is a need for the development of innovative formulation technology that fulfills certain criteria such as desirable product dispersion throughout the system, retention for intended intervals, and adequate release of drug. These features can be achieved using bioadhesives based novel delivery systems. *In-situ* gelation is a process of gel formation at the site of application after the composition or formulation has been applied the site. Formulation and evaluation of one such bioadhesive based novel drug delivery system for an effective and patient friendly use of drug to formulated In-situ polyherbal gel. *Piper betel* L. (Pan, leaves) fam. Piperaceae; *Spilanthesacmella* Murr. (Akarkara, fruit), fam. Asteraceae; *Foeniculum vulgare* Mill. (Fennel, fruits) fam. (Umbelliferae); *Eugenia caryophyllus* (Spreng.) Bullock & S.G. Harrison (Clove, clove bud) fam. (Myrataceae) and *Capsicum annum* L. (Capsicum, fruits) fam. Solanaceae is medicinally important and is used as local anesthetics in oral cavity and these herbs were taken for formulation of polyherbal gel using Carbopol 934 & HPMC. The prepared formulation was evaluated, and the results were presented. The results indicate that the PHG-3 have satisfactory results when compared with other formulated PHG.

Keywords: Herbal Extract, Oral cavity, Polyherbal gel.

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INTRODUCTION

The conventional dosage forms such as preformed gel and solutions have limitations that they do not remain for long time at the site of application and needs frequent dosing. Direct application of gels onto the infected sites might be difficult, inconvenient as well as have frequent dosing because the conventional gels do not remain for long time at the site of application. A new and recent approach is to try to combine advantages of both gels and solution so that an accurate dose can be administered with ease of administration. These formulations remain to a solution state before administration but transforms to gel after administration into cavity.[1,2] *In situ* polyherbal gel has broad drug absorption peak and a longer drug residence time as compared to conventional dosage form. For a better therapeutic efficacy and patient compliance, mucoadhesive, thermosensitive and prolonged release polyherbal gel was formulated. Nowadays, *in situ* gelling liquids have also proved as more convenient dosage forms for local applications because they are easy to administer into desired body cavities. To achieve desirable therapeutic effect, delivery systems need to reside at the sites of infection for a prolonged period. The conventional formulations such as solutions, suspensions, ointments, etc. show some constraints such as increased elimination, high variability in efficiency which reduces their bioavailability. Polyherbal *in situ* activated gel forming systems are liquid upon instillation and undergo phase transition in the cavity to form a viscoelastic gel in response to environmental changes such as change in temperature and pH.[1,2] Hence, it offers higher efficacy and bioavailability as compared to other conventional dosage form.

Polyherbal are the formulations containing two or more than two herbs are called polyherbal formulations. The popularity of polyherbal formulation is due to its high effectiveness towards a number of diseases. Traditional medicine, since ages have been an important source of potentially useful new compounds to develop chemotherapeutic agents and nature is contributing to an impressive number from which numbers of modern drugshave been isolated.[3] Thus the aim of the study was to develop a topical polyherbal formulation consisting of ethanolic extract of the part material of *Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *Foeniculum vulgare* Mill.

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fruits; *Eugenia caryophyllus* clove bud and *Capsicum annum* L. fruits and to evaluate polyherbal gel.

MATERIAL AND METHODS

Extract

The dried ethanolic extract of the part material of *Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *F. vulgare* Mill. fruits, *E. caryophyllus* clove bud and *C. annum* L. fruits were taken after extraction for formulation of polyherbal gel.

Formulation of Polyherbal Gel

Carbopol 940 & HPMC K 100 M was dispersed in 50 mL of distilled water. It was kept aside to swell, which was further stirred to form a gel. Required quantity of methyl paraben was dissolved in distilled water with the aid of heat on water bath. Solution was cooled and propylene glycol was added to it. Further required quantity of ethanolic extract of *Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *F. vulgare* Mill. fruits; *E. caryophyllus* clove bud and *C. annum* L. fruitsat different concentration was mixed to the above mixture and volume made up to 100 mL by adding remaining distilled water. All the ingredients were mixed properly and with continuous stirring. Triethanolamine was added drop wise to the formulation for the adjustment of skin pH (6.8–7) and also to obtain a gel at required consistency.[4,5] The formula was mentioned in Table 1.

Evaluation of Polyherbal Gel[6,7]

Physical Evaluation

The appearance of the formulation was observed which included clarity and transparency was determined visually.

Determination of pH

The pH of the gel was determined using a calibrated pH meter at 4°C. The readings were taken for an average of 3 samples.

Gelling Capacity

The gelling capacity was measured by visual method. 100 µL sample was placed in a vial containing 2 mL of artificial tear fluid freshly prepared and equilibrated at 35 °C and then visually assessing the gel formation and noting the time taken for gel formation.

Gelation Temperature

The gelation temperature was determined using the test-tube-inverting method. A volume of 2 mL of the *in-situ* gel was placed in a test tube, which was then immersed in a water bath at 15°C. The temperature of the water bath was then gradually increased, samples were examined every 2 minutes, and the gelation temperature was recorded when the gel stops flowing upon test tube inversion at 90°. The readings were taken for an average of 3 samples

Viscosity

Viscosity of sols was measured using Brookfield viscometer (model DVII, Engineering Laboratories, Middleboro, MA) spindle no 01 at 20 r.p.m. at temperature 4°C and 37°C. The experiment was conducted in triplicate.

Syringeability Study

The ability of the prepared formulations to flow easily through a syringe of 21 gauge needle was assessed using the method employed by Maheshwari. One ml of the cold gel was filled in 21 gauge needle syringe and the ability of the gel to flow under normal handling pressure was assessed.

Extrudability

A closed collapsible tube containing about 20 g of gel was pressed firmly at the crimped end and a clamp was applied to prevent any roll back. The cap was removed, and the gel was extruded. The amount of the extruded gel was collected and weighed. The percentage of the extruded gel was calculated.

Spreadability

Two sets of glass slides of standard dimensions were taken. The herbal gel formulation was placed over one of the slides. The other slide was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 7.5 cm along the slides. Hundred g weight of gel was placed on the upper slides so that the gel was between the two slides was pressed uniformly to form a thin layer.

Table 1: Formulation of polyherbal gel containing ethanolic extract of Indian herbal drugs

	Formulation code					
Ingredients	*PHG-1*	*PHG-2*	*PHG-3*	*PHG-4*	*PHG-5*	*PHG-6*
EEPBL (mg)	500	500	500	1000	1000	1000
EESAF (mg)	500	500	500	1000	1000	1000
EEFVF (mg)	500	500	500	1000	1000	1000
EEECB (mg)	500	500	500	1000	1000	1000
EECAF (mg)	500	500	500	1000	1000	1000
Carbopol 934	0.25 mg	0.50 g	0.75 mg	1 gm	1.25 gm	1.5 gm
HPMC	0.25 mg	0.50 g	0.75 mg	1 gm	1.25 gm	1.5 gm
Polyethylene glycol (mL)	0.2	0.2	0.2	0.2	0.2	0.2
Methyl paraben (mg)	0.08	0.08	0.08	0.08	0.08	0.08
Triethanol amine (mL)	1	1	1	1	1	1
Distilled water (qs 100 mL)	100	100	100	100	100	100

The weight was removed and the excess of gel adhering to the slides was scrapped off. The two slides in position were fixed to a stand without slightest disturbance and in such a way that only upper slides to slip off freely by the force of weight tied on it. A 20 g weight was tied to the upper slide carefully. The time taken for the upper slide to travel the distance of 7.5 cm and separated away from the lower slide under the influence of the weight was noted. The experiment was repeated for three times and the mean time was taken for calculation.

Spreadability was calculated by using the following formula:

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

where, S= spreadability, m-weight tied to upper slides (20 g), l- length of the glass slide (7.5 cm), t- time taken in sec (Table 2).

Drug Content

Each formulation (1 g) was taken in a 50 mL volumetric flask and made up to volume with methanol and shaken well to dissolve the active constituents in methanol. The solution was filtered through Whatman filter paper and 0.1 mL of the filtrate was pipetted out and diluted to 10 mL with methanol. The content of active constituents was estimated spectrophotometrically by using standard curve plotted at 280 nm (Graph 1).

In-vitro Release Studies

A sample of 1-mL of gel was placed into a dialysis membrane 7 cm long. Bags were then suspended in 50 mL of (ethanol: water 1:1) preheated at 37 ± 0.5°C in shaking water bath at 37°C and 25 strokes per min. At predetermined time intervals, one milliliter sample was withdrawn and replaced with an equal volume of fresh medium. The whole release media were changed and replaced with fresh media every day (24 hours) during the release studies duration (up to one week). Samples were diluted and analyzed using an UV spectrophotometer for tannins concentration at λ 280 nm. The cumulative amount of drug released was calculated based on a calibration curve. All experiments were done in triplicate (Table 3, Graph 2).

RESULTS AND DISCUSSION

The dried ethanolic extract of plant material viz., *Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *F. vulgare* Mill. Fruits, *E. caryophyllus* clove bud and *C. annum* L. fruitswere used to formulate polyherbal gel using carbopol 934 and HPMC K 100 M using different concentration of extract and polymers. Six different batches were prepared and was evaluated for physical appearance, pH, gelling capacity, gelation temperature, viscosity, Syringeability study, Extrudability, Spreadability and drug content.

From the results observed it was concluded that all the prepared polyherbal gel has good clarity and transparency. The pH so obtained was within the limit as for most of the preparation indented to be used. The pH values of all the formulations were in the close range of neutral pH and hence it caused no skin irritation. The gelling capacity and gelation temperature were found within the limit. Polymers were included in the designed topical formulations in order to provide a prompt release of drug and to achieve as well as

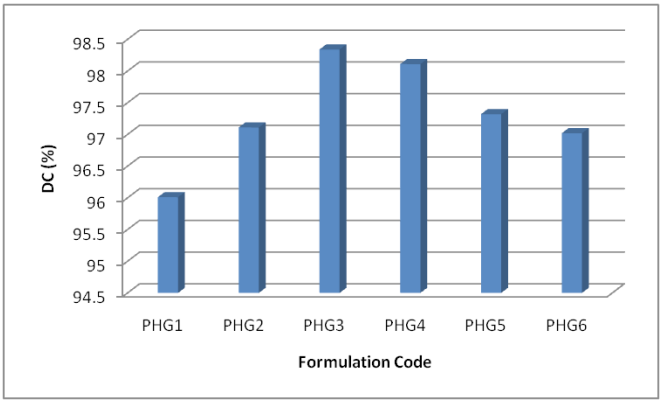
Table 2: Evaluation parameters of poly herbal gel containing ethanolic extract of Indian herbal drugs

	Formulation code					
Evaluation parameters	*PHG-1*	*PHG-2*	*PHG-3*	*PHG-4*	*PHG-5*	*PHG-6*
Clarity	C	C	C	C	C	C
Transparency	T	T	T	T	T	T
pH	7.18	7.23	7.20	7.10	7.21	7.11
Gelling capacity	-	+	++++	+++	++++	+
Gelation temperature	26.2	28.3	31.2	37.4	39.2	40.6
Viscosity (Poise)	0.3811	0.3781	0.3922	0.3721	0.3520	0.3622
Syringeability study	E	E	E	E	E	E
Extrudability (%)	94.32	96.16	98.11	97.18	96.20	94.12
Spreadability (gcm/sec)	59.22	66.18	75.09	69.11	68.11	60.30
Drug content (%)	96.01	97.11	98.34	98.11	97.32	97.02

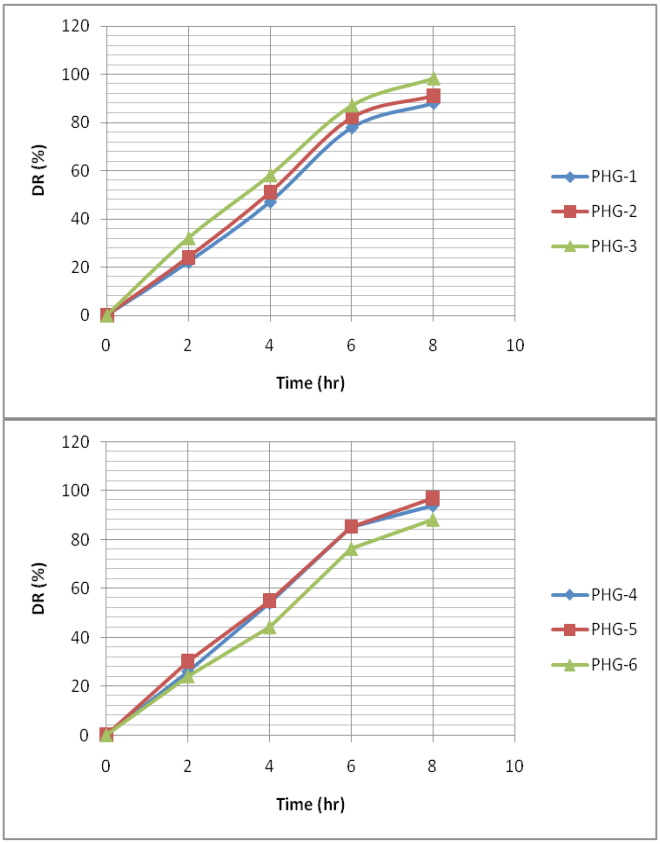
Abbr:- :No gelation, + : Gel forms after some time, ++ : Gel forms immediately, +++: Immediate gelation remains for 8 hrs, ++++ : Immediate gelation remains for more than 10 hours. T : Translucent, C: Clear, E: Easily syringeable through 21-gauge needle at cold temperature.

Table 3: *In-vitro* drug release of poly herbal gel containing ethanolic extract of Indian herbal drugs

Time	*Formulation code*					
(hours)	*PHG-1*	*PHG-2*	*PHG-3*	*PHG-4*	*PHG-5*	*PHG-6*
0	0	0	0	0	0	0
2	22.19	24.16	32.11	26.04	30.20	24.11
4	47.18	51.07	58.21	54.09	55.09	44.21
6	78.02	82.09	87.09	85.11	85.32	76.30
8	88.18	91.11	98.34	94.01	97.10	88.21



Graph 1: Drug content of poly herbal gel



Graph 2: %Drug release of poly herbal gel

to maintain the drug concentration within the therapeutically effective range. As the concentration of the polymer was 0.25 to 1.25 in all gel formulations no major variation in viscosity was observed. Values of the spreadability indicated that the gel formulations are easily spreadable. The drug content was found to be maximum of 99.11 (PHG-3). From the data obtained it was concluded that the polyherbal gel formulated using ethanolic extract of *Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *F. vulgare* Mill. fruits; *E. caryophyllus* clove bud and *C. annum* L. fruits was found to be more potent and efficacious at equal concentration of Carbopol 934 and HPMC. Further the same conclusion has been confirmed by the results of *in-vitro* drug release studies.

CONCLUSION

From the results of drug content and drug release it was found that the formulation code PHG-3 was found to maximum therefore further this formulation was found to be suitable as compared to other tested PHG and is considered as potent and may be investigated as biological activity is concerned to prove the efficacy of polyherbal gel.Hence, it was concluded from the present investigation that PHG-3 i.e., ethanolic extract of*Piper betel* L. leaves; *Spilanthesacmella* Murr. fruits; *F. vulgare* Mill. Fruits, *E. caryophyllus* clove bud and *C. annum* L. fruits is beneficial in the form of polyherbal gel as local anesthetic in oral cavity. Moreover, further detail clinical trial may be carried in respect of its safety and efficacy profile.

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