Larix Publications

Journal of Pharma Research

https://jprinfo.com/

Vol. 9, Issue 5, 2020 ISSN: 2319-5622

Original Article

Design and characterization of Glycyrrhiza glabra and Solanum lycopersicum extract bearing gel for topical delivery

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Received on: 06-03-2020; Revised and Accepted on: 31-05-2020

ABSTRACT

T*he demand of herbal medicine is rapidly growing in today's time. Now days, herbal medicines have existed with extensive recorded olden times as they were used in the ancient period for a variety of therapies. In Ayurveda, the use of single or multiple herbs (polyherbal) for the treatment of several diseases. The present study deals with development and evaluation of the polyherbal formulation comprising of the Glycyrrhiza glabra and Solanum lycopersicum extracts for their anti-oxidant activity. The gel was prepared by using polymer base Carbopol 934 gives better gel formation. The gel was prepared by using Carbopol 934, Glycyrrhiza glabra and Solanum lycopersicum extracts, Propylene glycol 400, Methyl paraban, Propyl paraben and required quantity of distilled water. Then maintenance of pH (6.8-7) was done with the help of tri-ethanolamine. The formulation was evaluated for physical appearance, viscosity, pH, washability, spreadability, stability and anti-oxidant activity. Prepared gel was found to be yellowish in colour, homogeneous, good in appearance and consistency. The anti-oxidant activity was performed using DPPH scavenging activity and the values for Glycyrrhiza glabra showed significant DPPH activity with the IC50 value of 21.81 µgmL−1, and for Solanum lycopersicum IC50 value was 17.62.*

Keywords: *Polyherbal gel, Glycyrrhiza glabra, Solanum lycopersicum, anti-oxidant activity.*

INTRODUCTION:

In the development of the modern-day civilization, herbal medicine is one of the oldest forms of health care recognized to mankind being an essential division [1]. One-fourth of the world's population depends on herbal components for their basic medicinal needs every day, and they have been considered as alternatives to other regular medications. The choice of herbal medicine is deemed to be a healthier option for the patients because of their least side effects compared to that of modern medicines [2]. 80% of the world's population additional to this utilizes herbs to extravagance skin-based diseases [3] including fungal, viral, hypertensive disorders, diabetes, cancer, immunomodulators etc. [4, 5].

Polyherbals are the formulations having two or more than two herbs are called polyherbal formulations (PHF). The demand of polyherbal formulation is due to its high efficiency towards several diseases. Drug formulation in Ayurveda is by and large based on two principles as: a) single drug use b) additional to single drug use which are now known as PHF[6].

Through the skin, the delivery of a number of drugs is an effectual and targeted as for local disorders connected to dermatological. The advantages of this route of drug delivery has gained because of avoidance of first-pass effects, gastrointestinal irritation, and metabolic degradation associated with oral administration of drugs.

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DOI: https://doi.org/10.5281/zenodo.3881578

Topical gel formulations are homogeneous, semisolid preparations consisting of solutions or dispersions of one or more medicaments in suitable hydrophilic or hydrophobic bases which provide a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin. They are applied to the skin or certain mucous membranes for protective, prophylactic or therapeutic purposes [7].

In this research,Glycyrrhiza glabra and Solanum lycopersicum extracts were used which shows the anti-oxidant activities which to delays or inhibits oxidative damage to a targeted molecule. In recent era, a lot of usual natural antioxidants have gained huge significance for their function in obviating the auto-oxidation of oils, fats and allied food products. Antioxidant compounds named phenolic acids, polyphenols and flavonoids scavenge free radicals such as lipid peroxyl, peroxide, hydroperoxide slow down the oxidative mechanisms that lead to diseases that are degenerative. As a good antioxidant herbal plants mostly considered seeing as ancient times [8].

Glycyrrhiza glabra (Licorice)and Solanum lycopersicum **(**tomato) both possess anti-oxidant property. Glycyrrhizic acid, has the good number studied constituent (active) of Glycyrrhiza glabra (liquorice); sweet property in taste. The ingredient is sweeter (50 times) than sugar, making it extensively as a sweetening additive entity in the food industry. GA is used as the most important therapeutic agent in lots of countries to treat allergic dermatitis addition to this chronic viral hepatitis. It is also known to have anti- oxidative, anti-inflammation, anti-ulcer, anti-hepatotoxic and antivirus activities. It also affects inflammation, melanogenesis, low-density lipoprotein oxidation as well as the defence of mitochondrial functions on or after oxidative stresses [9]. Lycopene including its antioxidant activity utilized to delocalize free radical species lies in the company of carbon-carbon conjugated double bonds makes it fairly helpful for the individual. Owing to this, its demand is quite high in food, feed, pharmaceutical and cosmetic industries. Tomatoes in addition to its pulp or paste both are regarded as one of the richest sources of lycopene.[10]

MATERIAL AND METHOD

Collection of plant material

Glycyrrhiza glabra (Licorice) and Solanum lycopersicum **(**tomato) were purchased from the local market and authenticated.

Preparation of extract

The shade Dried and coarsely powdered liquorice (7gm) extracted using 300ml ethanol and water (3:7) extract was prepared by soxhlet apparatus [13] and lycopene was obtained directly from fresh tomato.

Fig 1: Extracts of Glycyrrhiza glabra (Licorice) and Solanum lycopersicum (Tomato)

Phytochemical screening of plant extract (Glycyrrhiza glabra) [14]

Tests for flavonoids: With concentrated sulphuric acid: Extract was mixed with concentrated sulphuric acid. The yellow-orange colour indicates the presence of anthocyanins, orange to red colour indicates the presence of flavones.

Test for Saponins: Take Aq. as well as Alc. extract in little quantity separately to this add 20 ml of distilled water. After addition of water shake the formed solution lengthwise in a graduated cylinder for a time period of 15 minutes. The presence of Saponins is indicated by a 1 cm layer of foam.

Test for terpenoids: (Trichloroacetic acid test); to the extract trichloroacetic aid was added. The presence of terpenoids indicated by the development of yellow colour.

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Test for carbohydrates: Fehling's test: On the water bath, Extract was kept. To which Fehling solution A and B were mixed. Brick red precipitate showed the presence of reducing sugars.

Analysis using Thin Layer Chromatography (TLC)

Standard solution and developing a solvent system for Thin layer chromatography, were set. For pr test solution preparation, 7 part of alcohol and 3 part of water be mixed with liquorice extract. The solution was then heated after that using a water bath for time interval up to 5 minutes, after that it was cooled followed by filtration. The standard solution was prepared by dissolving 5 gm of standard glycyrrhizic acid in 1ml of a mixture of alcohol and water previously mentioned 7:3 respectively. Developing solvent system contains the mixture of butyl alcohol; glacial acetic acid; water (7:2:1). TLC plates were prepared using silica gel solution and the retention value (Rf) was calculated. The plates were kept in developing solvent system and examined under UV light at 254nm. [17]

For the purity of the precipitated lycopene, TLC system was developed with toluene-hexane (1:19 v/v) on the TLC plates prepared by silica gel. Authentic lycopene (Sigma L9879) was also developed.

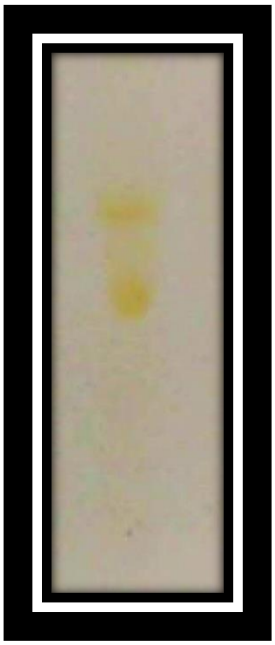

Fig 2: TLC of liquorice

Preparation of polyherbal gel

The formulation was prepared which was comprised of ethanolic extract of Glycyrrhiza glabra and lycopene in a concentration of (8%)and (2%)respectively. Carbapol- 940(1gm) was dissolved in a small amount of distilled water then stir on the magnetic stirrer. Methylparaben (0.5), propyl paraben (0.2) were added and then extracts were incorporated in it. After that Propylene glycol 400 (5%) was added to the mixture and triethanolamine (1.2 ml) was added drop wise to obtain the gelly consistency. It was stirred to obtain a homogeneous gel. The prepared gel formulation was kept at room temperature for 24 hours.

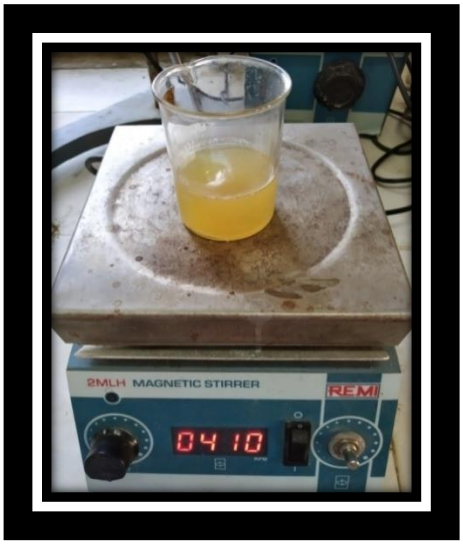

Fig 3: Preparation of polyherbal gel

Table 1: Formulation table of Polyherbal gel

Ingredients	Quantity taken in (%) for Gel	Role
Carbopol 940	1gm	Gelling agent
Extract of Liquorice and tomato	8%-2%	Anti-oxidant activity
Propylene glycol 400	5	Base
Methyl paraben	0.5	Preservative
Propyl paraben	0.2	Preservative

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Triethanolamine	1.2 ml	pH adjustment
Rose oil	q.s.	Perfume
Water	100 ml	Aqueous base

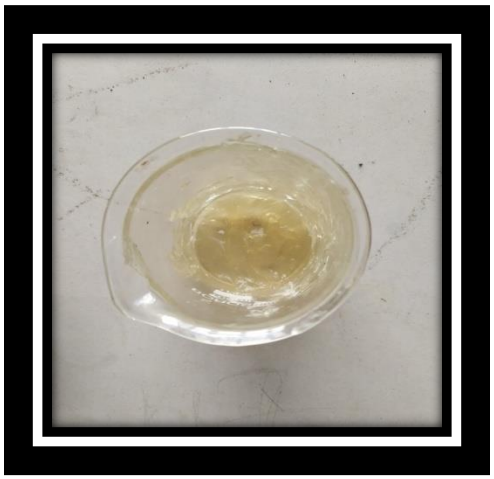

Fig 4: Prepared Polyherbal Gel

Phytochemical analysis: The tests performed for Phytochemical screening showed the presence of flavonoids, saponins, terpenoids and carbohydrates in the extract of Glycyrrhiza glabra.

Table 2: Phytochemical screening of Glycyrrhiza glabra

S.no.	Phytoconstituents	Glycyrrhiza glabra
1	Test for Flavonoids	+
2	Test for Saponins	+
3	Test for terpenoid	+
4	Test for carbohydrates	+

Note:"+ Sign indicates the presence of constituents"

Thin layer chromatographic analysis
Rf value was obtained through TLC analysis by dividing the distance travelled by solute from the distance travelled by a solvent.
Rf = Distance travelled by solute/ Distance travelled by solvent

For liquorice: 3.0/ 6.5 = 0.4cm
For lycopene: 2.5 / 6.5 =0.38 cm
Evaluation of poly herbal gel

Appearance and homogeneity: Physical analysis of the prepared polyherbal gel was observed for colour, consistency, odour, and homogeneity.[11]

pH: Digital pH meter (Systronics digital-DI-707) was used to determine the pH of the prepared formulation. 3 gm of the gel was accurately weighed and dispersed in 30 ml of distilled water and stored for two hours, then pH was measured. [11]

Viscosity test: The viscosity determinations were carried out using a Brookfield Viscometer (RV series) using spindle number 7 at a 100 rpm at a temperature of 250C. The determinations were carried out in triplicate and the average of three readings was recorded. [11]

Fig 5: Brookfield viscometer

Spreadability Studies: The formulation of gels was positioned in between the two glass plates, of size having 5 cm x 2 cm, all the formulation was sandwiched between the slides; placing in a weight of 100 gm consistently on the slides. After removal of weight, the excess of the gel was scraped off. Two slides in a position were fixed to a stand at a 45° angle without the slightest disturbance so that only the lower slide was held firmly by the clamp, allowing the upper slide to slip off freely with the help of 20 gm weight tied to the upper slide. The time taken for the upper slide is to separate away from the lower glass plate was noted.

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The experiment was done in triplicate, and spreadability was calculated as follows:

$$S = W \times L/T$$

Where, S = Spreadability,
L =Length of the glass plate,
W=Weight tied to the upper plate,
T = Time taken (sec).[12]

Washability: Formulations were applied on the skin and then ease and extent of washing with water were checked manually. The formulation exhibited good washability and left no traces over the skin on washing with water due to non-greasy properties. [12]

Irritancy Test: Skin irritation is one of the most common adverse effects in humans depend on many factors, including the concentration, duration and frequency of exposure, exposed skin site, rate of penetration and intrinsic toxic potential of the substance. In order to determine skin irritation mark, an area (1sq.cm) on the left-hand dorsal surface and the gel was applied to the specified area and time was noted. Irritancy, erythema, oedema, was checked if any for regular intervals up to 72hrs and reported.

Centrifugation: Centrifugation test for base and formulation kept at different storage conditions were performed for 30 days. The phase separation after centrifugation was recorded for formulation. [12]

Stability of polyherbal gel: Short term stability (for 30 days) of control (base) and formulation were verified at 8±0.1 and 40±0.1 C storage conditions (an incubator) with 75% relative humidity (RH) as mentioned by Pandey et al. by checking for their physical characteristics like colour, appearance, odour and centrifugation test[11].

Table 3: Physicochemical evaluation

Parameters	Observation/Values
Appearance	Good
Colour homogeneity	Uniform
pH	7.2
Viscosity	16800cps
Spreadability	71.38 (g.cm/sec)

Antioxidant activity of polyherbal gel

The scavenging ability of DPPH (2,2-diphenyl-1- picrylhydrazy) free radical was used to analyze the antioxidant activity of the extracts. DPPH scavenging activity of the extract was carried out according to the method of koleva et al. and Mathiesen et al. [14,15] ethanol solution of plant extracts at different conc. was carried. Vitamin C was used as an antioxidant standard.

A stock solution of DPPH was prepared by 100mg of extract dissolved in 100 ml methanol to get 1000 µg/ml solution. The test solution was diluted to prepare 10, 20, 30, 40, 50 µg/ml solution. The absorbance of the resulting solution was measured at 517 nm for each concentration by UV- Spectrophotometer.

A decrease in the absorbance in the presence of sample extract at different conc. (10-50 µg/ml) was noted after 15 min.IC_{50} was calculated from % inhibition. The absorbance of the resulting solution was measured at 517 nm by UV- Spectrophotometer.

$$\% \text{ Reduction} = \frac{\text{Control absorbance- Test absorbance} \times 100}{\text{Control absorbance}}$$

Table 4: DPPH free radical scavenging activity of alcoholic extract of Glycyrrhiza glabra

Concentration	Absorbance	% Reduction	IC_{50} value (µg/ml)
10	1.011	27.22	21.81
20	0.970	35.90	
30	0.901	38.87	
40	0.872	41.48	
50	0.751	59.20	

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Table 5: DPPH free radical scavenging activity of alcoholic extract of Solanum lycopersicum (lycopene)

Concentration	Absorbance	% Reduction	IC 50 Value (µg/ml)
10	0.875	31.84	17.62
20	0.784	39.56	
30	0.713	41.09	
40	0.698	43.18	
50	0.694	60.37	

Result and Discussion

Phytochemical Screening: Phytochemical analysis revealed the presence of flavonoids, saponins, triterpenoids, carbohydrates in the crude extract of liquorice plant.

Thin layer chromatography analysis: The Rf value for liquorice and lycopene was found to be 0.4 cm and 0.38 cm respectively.

The polyherbal gel was prepared and was evaluated for their physical appearance, pH, viscosity, spreadability, and its anti-oxidant acitivity. Prepared gel was found to be yellowish in colour, homogeneous, good in appearance and consistency. The pH of the formulation was found to be 7.2 hence it causes no skin irritation. The viscosity value of the formulation was found to be 16800 cps. There is no phase separation after centrifugation was recorded for the formulation.

The spreadability was measured on the basis of the slip and drag approach. The spreadability of polyherbal gel formulation was 71.38 gm.cm/sec.

Stability studies were done to check the stability of dosage form for its drug potency, any changes at the physical and chemical basis. By following WHO-ICH guidelines gel formulation was kept in accelerated stability conditions at 40ºC ± 2ºC/ 75% RH± 5% for a period of 30 days and studied for appearance, pH, viscosity and drug content. This result showed that the polyherbal gel formulation was stable at accelerated stability conditions as there were very slight changes in the observations. The anti-oxidant activity of ethanolic extracts of Glycyrrhiza glabra and Solanum lycopersicum was measured by the ability to scavenge DPPH free radicals comparing with vitamin C. Vitamin C is usually used as a standard antioxidant and it has a strong DPPH scavenging property.

The scavenging effects of both plant extracts and the standard on the DPPH radical we're expressed as half-maximal inhibitory concentration (IC_{50}) values; the results are reported in Table 4 and 5 for both extracts. Lower IC_{50} value reflects higher DPPH radical scavenging activity. According to the results obtained, the ethanolic extract of Glycyrrhiza glabra showed significant DPPH activity with theIC_{50} valueof21.81μgmL−1, and for Solanum lycopersicum IC_{50} value was 17.62. DPPH is a free radical compound which has scavenging ability for antioxidants samples and shows good absorbance at517nm.

Conflict of interest: There is no conflict of interest.

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Article Citation

Authors Name. Deepshikha Kukde. Design and characterization of Glycyrrhiza glabra and Solanum lycopersicum extract bearing gel for topical delivery. JPR 2020; 9 (5):42-48.
DOI: https://doi.org/10.5281/zenodo.3881578

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