Formulation and evaluation of ficus benghalensis emulgel for its anti- rheumatoid arthritis effect
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Abstract
The current study focuses on the development and characterization of ficus benghalensis powdered aerial roots emulgel to avoid the first-pass effect and strengthen bioavailability while reducing dosage intervals and dose related deleterious reactions. three formulations with same concentration and different polymers were formulated. Ethanolic and petroleum ether extract of dried aerial roots of ficus benghalensis were prepared by using different gelling agents like Carbopol 934, Carbopol 940 and Xanthane gum were formulated. The prepared formulations were evaluated for their qualitative as well as quantitative tests, physical appearance, pH, viscosity, spreadability, consistency, homogeneity, moisture loss and finally in vitro anti-arthritic activity. Depending on the outcomes, it was observed that to all the formulation, F1 formulation containing Carbopol 940 with 4.6% moisture loss, 3780.3±5.0 viscosity and 6.1±0.1 PH and 43.7±1.53 spreadability shows better activity then all the other. Herbal emulgel of ethanolic extract of dried aerial roots of ficus benghalensis linn when compared with diclofenac emulgel confirms the anti-arthritic activity through invitro release method.

Keywords:
Ficus benghalensis, Herbal emulgel, anti-arthritic activity, invitro release method.

Introduction
Rheumatic diseases that cause locomotor vulnerability and impairment in the adult population are known as arthritic dysfunction. Osteoarthritis and Rheumatoid arthritis are the most dominant articular disorders [1]. Rheumatoid arthritis is an autoimmune condition, caused by pro-inflammatory cytokines such as TNF-a, IL-6, IL-1b, and induces joint and organ inflammation [2]. The most common symptom in patients with Rheumatoid Arthritis is joint pain, which is broadly linked to physical impairment, reduced mobility, exhaustion, sleep disruptions and elevated medical expenses, resulting in a depletion in life quality and a significant socio-economic effect [3].

The topical drug delivery system can be used in conditions where other drug delivery systems have failed [4,5]. Skin is the largest organ in the human body, accounting for about 10% of a person's body mass and covering an average of 1.7m2. Emulgels are novel dosage forms and it is the combination of emulsion and gel [6]. It is considered as one of the best formulations for topical usage as the presence of gelling agent in the water phase transforms the classical emulsion into an emulgel [7].

Ficus benghalensis is a laticiferous, moraceaeous, tremendous evergreen tree that belongs to the Moraceae family and ficus genus, which has over 800 species and 2000 sub-varieties [8]. Throughout many regions of India, this tree is recognized as sacrilegious [9]. The parts of the tree has been reported to segregate glucoside, 20-tetra triaconthene-2-one, 6-heptatriacontene-10-one, pentatriacontane-5-one, beta sitosterol-alpha- D-glucose, and meso-inositol [10, 11].

Materials and Methods
Collection of Plant Material
The crude drug (aerial roots) of the plant were collected from the nearby garden, Goel campus Lucknow authenticated by O.P Verma. The aerial roots were washed under tap water and dried in sunlight for 1-2 months and then were finely ground into powder. The aerial roots were divided into two equal parts. One of the parts was used for the chemical analysis and the other was used for the formulation.
powdered in a grinder. The physiochemical parameters of powdered material was done as per the procedure of Saurabh Chaudhary et, all (2016).

Chemicals
Carbopol 940, triethanolamine, petroleum ether, ethanol, propylene glycol, etc. were purchased from Star Micronics Devices and Chemicals.

Preparation of Plant Extract
Around 500g of powder was subjected to Soxhlet extraction with petroleum ether (60o-80o C) to defeat the powder and also with ethanol (50o-60o C) for 8 hours, separately. Then, each extract were filtered and filtrate were evaporated to dryness. The extracts were optimized among other physicochemical specifications in terms of purity, pH, and extractive value.

Phytochemical screening
Qualitative and quantitative chemical tests had been performed on the extracts to identify the constituents by following the procedure of Nathan Harris et al (2005) and Sampat Navale et, all (2018) [12, 13].

Preparation of gel
To the 200ml water, 1% w/w Carbopol 940 was added and dispersed uniformly, and add 2.1ml of glycerin ensuring no lumps. A 0.5 N NaOH solution was added drop wise, until a gel was formed. The prepared gel was weighed and stored in air-tight containers [14].

Preparation of Ficus benghalensis Emulgel
At first, o/w emulsion having 0.01g aerial roots extracts of ficus benghalensis was formulated by dissolving it in a mixture of 0.5ml of Span 20 in 4.5ml of liquid paraffin, this acts as oil phase, and the aqueous solution was formulated by dissolving 0.5% Tween 20 in a purified water. Both the phases of emulsion were heated separately at 60o-70o C followed by mixing of the two with continuous stirring until the product cooled to room temperature resulting in the formation of ficus benghalensis emulsion. The prepared o/w emulsion was added with continuous stirring to the prepared gel in 1:1 weight ratio to produce homogeneous [15]. (Table.1)

Characterization of Ficus Benghalensis Emulgel
Optimization of emulgel
The prepared gel formulations were visually examined for their texture, color, clarity and existence of particle [16].

Consistency of emulgel [17]
To determine the consistency of the prepared gel, a small amount of gel was squeezed between the thumb and the index finger and the consistency of the gel was observed.

Homogeneity of emulgel [18]
All formulated gels were visually inspected for homogeneity after they were stored in the container. They were examined for their appearance and availability of any aggregates.

Determination of pH [19]
Accurately weighed 1.0g of various prepared gel and dispersed in 100ml purified water. The pH was measured by using digital pH meter. In order to ensure that the formulation can be used without the harm of skin irritancy, the pH of the preparation has been determined.

Spreadability [20]
0.5g gel was mounted within a circle of 1 cm diameter pre-marked on a glass plate of 20*20cm and another glass plate was mounted over it. A mass of 100g was placed on the upper glass slide. The change in diameter due to the expansion of gel was reported.

Viscosity [21]
Viscosity of gel was carried out by using Brookfield Viscometer at 25oC, having spindle speed at 12rpm.

Percentage moisture loss [22]
Precisely weighed films were put in a Desiccator containing fused anhydrous calcium chloride for 24 hours to verify the level of moisture loss from freshly prepared films. After 24 hours, films were again weighed and moisture loss has been calculated by using following formula:

\[
\% \text{ Moisture loss} = \frac{\text{Initial wt.} - \text{Final wt.}}{\text{Initial wt.}} \times 100
\]

In vitro Anti-arthritis activity [23]
The drug release analysis was carried out in a Franz diffusion cell apparatus. It is having two compartments, the receptor and the donor compartment. For filling of receptor compartment, phosphate buffer with 7.4 pH was used and temperature maintained at 37± 5oC. Magnetic stirrer was used for continuous agitation. In the donor compartment, 2g of cell was applied and cellulose membrane was placed in between the donor and receptor compartment. The drug release from prepared formulation was analyzed by collecting samples of 0.5ml from the diffusion cell at eight hours intervals. Every time, as 0.5ml of sample was withdrawal, the same amount of sample was filled in the receptor compartment for the maintenance of initial volume. The samples that has been taken out from the receptor compartment has been analyzed in UV. The amount of drug released was calculated by using calibrate curve.

Results
The quantitative physiochemical parameters have been performed to determine the authenticity and purity of plant part. The evaluated result has been listed in table 2. The qualitative phytochemical screening of aerial roots of ficus benghalensis has been investigated and summarized in table 2. The prepared emulgel was evaluated by various parameters like optimization, weight, consistency, homogeneity, pH, spread ability, viscosity. The evaluated data has been given in table 3 (i) and (ii).

The aerial roots extract fractions of Ficus benghalensis used are ethanol and petroleum ether. These extracts showed positive response as compared to std. diclofenac sodium for its anti-arthritis property using in-
vitro release of prepared formulation shows the maximum release of 85% drug in 8 hours. (Table.4)

Table 1: Composition of Various Formulations of Ficus bengalensis Emulgel

| Ingredients             | Types of formulation | Sn.  |
|-------------------------|----------------------|------|
| F. bengalensis Extract  | 0.01g, 0.01g, 0.01g | F1   |
| Polymer (0.8g)          | Carbopol 940         | F2   |
| Glycerin                | 2.1 ml               | F3   |
| Ethanol                 | 0.1ml                |      |
| Water                   | 0.8ml                |      |
| Triethanolamine         | 2%                   |      |

Table 2: Quantitative Physiochemical Parameters

| Parameters                        | Results          |
|-----------------------------------|------------------|
| Ash Value                         | 5.0%             |
| Water soluble Ash                 | 2.0%             |
| Acid insoluble Ash                | 1.0%             |
| Water soluble extractive values   | 1.74%            |

| % Yield                           | Pet-ether 0.48%  |
| Hydro alcholol                    | 1.68%           |

Table 2: Qualitative Physiochemical Parameters

| S.no | Phytochemicals | Extracts | Hydro alcohol | Petroleum ether |
|------|----------------|----------|---------------|-----------------|
| 1.   | Carbohydrates  | ++       | ++            | ++              |
| 2.   | Proteins       | --       | --            | --              |
| 3.   | Amino acids    | --       | --            | --              |
| 4.   | Steroids       | ++       | ++            | ++              |
| 5.   | Glycosides     | --       | ++            | ++              |
| 6.   | Saponins       | --       | ++            | ++              |
| 7.   | Flavonoids     | ++       | --            | --              |
| 8.   | Alkaloids      | --       | --            | --              |
| 9.   | Tannins        | --       | ++            | ++              |
| 10.  | Phenolic       | --       | ++            | ++              |

Table 3 (i): Evaluation Parameters

| Parameters          | Types of Formulations | F1 | F2 | F3 |
|---------------------|-----------------------|----|----|----|
| Texture             | Smooth                | Smooth | Smooth | Smooth |
| Color               | Light                 | Light | Dark |
| Clarity             | Brown                 | Brown | Brown |
| Consistency         | Good                  | Poor | Good |
| Clarity             | Clear                 | Clear | Clear |
| Grittiness          | Present               | Absent | Absent |
| Homogeneity         | Present               | Present | Present |

Table 3 (ii): Evaluation Parameters

| Sn. | Formulations | pH (Mean±SD) |
|-----|--------------|--------------|
| 1   | Carbopol 940 (F1) | 6.1±0.1  |
| 2   | Carbopol 934 (F2) | 5.8±0.1  |
| 3   | Xanthane gum (F3) | 5.2±0.1  |

Table 3: Individual Data of Spread ability

| Sn.  | Formulations     | Spread ability |
|------|------------------|----------------|
| 1    | Carbopol 940 (F1)| 42             |
| 2    | Carbopol 934 (F2)| 41             |
| 3    | Xanthane gum (F3)| 35             |

Fig. 1: pH data of different formulation
Table 4: Group Data of Spread ability

| Sn. | Formulations     | Spread ability (Mean ± SD) |
|-----|------------------|-----------------------------|
| 1   | Carbopol 940 (F1)| 43.7±1.53                   |
| 2   | Carbopol 934 (F2)| 39.3±1.53                   |
| 3   | Xanthane gum (F3)| 35.3±0.6                    |

Fig. 2: Spreadability data of different formulation

Table 5: Individual Data of Viscosity

| Sn. | Formulations     | Viscosity         |
|-----|------------------|-------------------|
| 1   | Carbopol 940 (F1)| 3785              |
|     |                   | 3781              |
|     |                   | 3775              |
| 2   | Carbopol 934 (F2)| 3902              |
|     |                   | 3908              |
|     |                   | 3911              |
| 3   | Xanthane gum (F3)| 4001              |
|     |                   | 4002              |
|     |                   | 3999              |

Table 6: Group Data of Viscosity

| Sn. | Formulations     | Viscosity (Mean±SD) |
|-----|------------------|---------------------|
| 1   | Carbopol 940 (F1)| 3780.3±5.0          |
| 2   | Carbopol 934 (F2)| 3907.0±4.6          |
| 3   | Xanthane gum (F3)| 4000.7±1.5          |
Table 2: In vitro Drug Release group formulations (Mean ± SD)

| Sn. | Time | F1       | F2       | F3       |
|-----|------|----------|----------|----------|
| 1   | 0    | 0±0      | 0±0      | 0±0      |
| 2   | 1    | 7.24±0.53| 6.5±0.35 | 6.13±0.19|
| 3   | 2    | 14.47±0.66| 13.34±0.31| 13.34±0.56|
| 4   | 3    | 22.52±0.60| 21.69±0.29| 22.38±0.22|
| 5   | 4    | 45.07±0.90| 43.64±0.33| 42.31±0.48|
| 6   | 5    | 51.44±0.55| 50.53±0.40| 52.11±0.54|
| 7   | 6    | 70.73±0.77| 69.35±0.31| 68.48±0.68|
| 8   | 7    | 78.7±1.65| 77.23±1.68| 74.67±0.57|
| 9   | 8    | 85.29±0.42| 84.11±0.89| 82.55±0.12|

Conclusion
This study was the scientific report that proves convincing phytochemical studies and also observed that, to all the three formulations, the F1 formulation containing Carbopol 940 was best suited with the parameters of the standard diclofenac formulation. The F1 formulation established greater spread ability and consistency when compared with other developed gels. The formulated F1 gel demonstrated good homogeneity, an excellent pH, minimal skin irritation and great stability. The maximum percentage of moisture loss was found to be 4.6% after 24 hrs in F1 formulation. Anti-arthritic efficacy of the aerial roots of Ficus benghalensis has been demonstrated giving empirical support to its conventional use by the native people in South India.

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