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Studies on the Development of Promising Herbal Emulgel of *Coccinia Grandis* Leaf Extract for Dermatalogical Complications

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Abstract:

Introduction: Now a days, there has been a boom in the field of herbal medicine and excipients. The aim of the present research work was to evaluate the current potential and future scope of emulgel formulation for enhancing the topical delivery of *Coccinia grandis* extract using gelling agents such as Carbopol 940, Carbopol 934.

Materials and methods: Emulgel formulation of herbal extract was prepared by using liquid paraffin/coconut oil/olive oil as oil phase, Carbopol 940/Carbopol 934 as gelling agents, tween 80/ span 80 as surfactants and methyl paraben/propyl paraben as preservatives. The emulsion was prepared and was gelled into the Carbopol gel base. The formulations were evaluated for physicochemical parameters, rheological studies, *in vitro* release studies and antibacterial activity.

Results and discussions: All the formulated emulgels were of acceptable physical properties such as colour, homogeneity, consistency, pH, spreadability, content uniformity and release studies. Stability studies of the formulated emulgels were carried out as per ICH guidelines for 3 months at different temperature and humidity conditions. The results showed that all the formulations were stable throughout the period. So, it can be concluded that topical emulgel of *Coccinia grandis* leaf extract can be used for the bacterial skin infections.

Key words: Emulgel, *Coccinia grandis* leaf extract, Carbopol 940, spreadability, topical drug delivery.

INTRODUCTION:

Emulgel is a combination of emulsion and gel, which is a new approach for topical delivery of drugs. It has a double control release like emulsion and gel[1]. Gel is new class of formulation, it releases the drug faster in comparison to ointment, cream and lotion. Incorporation of drug in emulgel formulation is suitable to treat skin disorders. Topical application of therapeutic agents provides various advantages over the other route of administration. The presence of a gelling agent in the aqueous phase converts a classical emulsion into an emulgel. Within the major group of semisolid preparations, like use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations[2]. Emulgels have several complimentary properties for dermatological use such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, long shelf life, bio-friendly, transparent and pleasing appearance[3].

Herbal medicine is still the main stay, about 75-80% of the whole population and the major part of traditional therapy involves the use of plant extract and their active constituents. Following the advent of modern medicine, herbal medicine suffered a setback, but during last two or three decades, advances in phytochemistry and in identification of plant compounds, effective against certain diseases have renewed the interest in herbal medicines[4]. *Coccinia grandis* belongs to the family Cucurbitaceae. It is growing wild throughout India and also cultivated in various parts of India. It is commonly known as kundru. The whole plant is traditionally used for various medicinal purposes. Leaves of this plant are used in Indian folk medicine for treatment of number of ailments including diabetes, wounds, ulcers, inflammation, in eruptions of skin, fever, asthma and cough. Earlier scientific investigation of *Coccinia grandis* showed that the crude extract has hepatoprotective [5,6] antioxidant [7,8] anti-inflammatory and anti-nociceptive [9,10] anti-diabetic [11,12] hypolipidemic [13] anti-bacterial [14,15] and antitussive activities [16]. There are several reports in the literature regarding the antibacterial activity of crude extract prepared form plants[17].

The aim of the present study was to formulate and evaluate novel herbal emulgel containing *Coccinia grandis* leaves extract by using liquid paraffin/ olive oil/ coconut oil as oil phase and Carbopol 934/ Carbopol 940 as gelling agent.

MATERIALS AND METHODS:

Leaves of the plant *Coccinia grandis* werecollected directly from the plant in and around Guntur, Andhra Pradesh, India from June to October. The shade dried leaves were grounded into a coarse powder. Dr. Ammani, Head, Department of Botany, Acharya Nagarjuna University, Guntur, Andhra Pradesh, India, confirmed the authentication of the plant. The ethanolic, Aqueous, Chloroform extract of the plant was prepared in the laboratory. Carbopol 934, Carbopol 940 were from Merck Labs, Mumbai. Methyl paraben, propyl paraben was from Fisher scientific, Mumbai. Liquid paraffin form LobaChemie, Mumbai. Olive oil and coconut oil were purchased from the local market. All the ingredients were of pure and of analytical grade.

Methods:

Extraction[18]

The extraction was carried out in a Soxhlet extractor with ethanol as menstruum for the coarsely grounded powder of the *Coccinia grandis* leaves free from the debris. The extract was concentrated by distillation process. Then the extract was dried under the shade for further evaporation of the solvent. The dried extract was labelled and stored in desiccators for further use. The extract was tested for

various phytochemical constituents and the data was given in Table 1.

Extract-excipient compatibility study[19]

The compatibility of the extract with the selected excipients was studied by FTIR spectroscopic studies by using physical mixture of extract with various excepients in the ratio 1:1. The physical mixture samples were subjected to spectroscopic studies by KBr pellet method. Spectra of drug and polymer were taken and analyzed for the major interactions.

Preparation of Emulgel[20]:

The various emulgel formulations of *Coccinia grandis* were prepared as per the formula given in Table 2. To formulate emulgels, first the gel was prepared by dispersing gelling agents viz., Carbopol940 andCarbopol934 in hot purified water (80ºC) and the dispersion was cooled and left aside overnight. The oil phase of the emulsion was prepared by dissolving span80 in light liquid paraffin while the aqueous phase was prepared by dissolving Tween 80. Simultaneously, methyl and propyl paraben were dissolving in Propylene glycol where drug was dissolving in water, both solutions were added to the aqueous phase. Both oily and aqueous phase were separately heated to 70-80ºC then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. The formed emulsion was mixed with gel in 1:1 ratio with gentle stirring to obtain emulgel. The pH of the emulgel was adjusted by using Triethanolamine

Evaluation of emulgels [21,22]:

1. Physical Examination: The prepared emulgel formulations were inspected visually for their colour, appearance, homogeneity, consistency and grittiness.

2. Measurement of pH [23]: The pH of emulgel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml of distilled water and it was kept aside for 2 hr. The pH of each formulation was measured in triplicate and average values were calculated.

3. Viscosity: The viscosity of various emulgel formulations of *Coccinia grandis* was measured at 25ºC by using Brookfield Viscometer.

4. Spreadability [26,27]: Spreadability of emulgel was measured 48 h after preparation of the emulgel. It is measured in terms of diameter of emulgel circle produced when emulgel was deposited between two glass plates of definite weight. A weighed quantity (350 mg) of emulgel was taken on one glass plate and another glass plate was dropped from a distance of 5cm. The diameter of the circle of spread emulgel was measured.

5. Extrudability [36]: The extrudability of the formulated emulgels was measured based on the quantity in percentage of the gel extruded from aluminium collapsible tube on application of weight in grams required to extrude at least 0.5cm ribbon of gel in 10s. If more quantity was extruded means the product having good extrudability. The measurement of extrudability of each formulation was performed in triplicate and the average value was calculated. The extrudability was calculated by using the formula;

$$\text{Extrudability} = \frac{\text{applied weight to extrude gel from tube (g)}}{\text{area (cm2)}}$$

6. Drug content determination [28-30]: Drug content from the emulgel formulations was measured by taking 1gm each of formulation containing approximately 40mg of extract in to a 50 ml volumetric flask and diluted with water and shaken to dissolve the extract in water. The dispersion was filtered through Whatman filter paper, 0.1 ml of the filtrate was diluted to10ml. The content of the drug was estimated spectrophotometrically at 215nm by using standard curve.

***7.* *In-vitro* Release/ Permeation Studies [31-34]:** The *in vitro* release study of the formulated emulgels was carried out by using Franz diffusion cell with dialysis membrane. The dialysis membrane was soaked in phosphate buffer pH 6.8 for 9-12h was clamped carefully between donor and receptor compartments of the diffusion cell. The emulgel was spread uniformly on the dialysis membrane. The receptor compartment was filled with 10ml of p^H 6.8 phosphate buffer maintained at 37ºC and stirred by using magnetic stirrer by using magnetic stirrer. 1ml of sample was collected at suitable time intervals (i.e., for every 30mins until completely drug was released) and replaced with fresh buffer. The collected samples were analysed by UV-Spectrophotometer at 215nm to measure the amount of drug release. The process was carried out in triplicate.

8. Antimicrobial activity: The microbial assay was performed to determine the activity of the prepared emulgel formulation with the strain of Bacillus subtillis. Agar well diffusion method was used for the evaluation of bacteriostatic activity of the emulgels. 500µl of optimized emulgel formulation was pipetted and then added into the well. The plates were incubated for 12h at 37ºC. The diameter of zone of inhibition was measured and the data was given in Table 3. The procedure was carried out in triplicate.

9. **Skin irritation test[35]:** Rabbits of each sex were used to study the skin irritation study. The animals were maintained on standard animal feed and had free access for water. Hair was shaved from back of rabbit with an area of 3cm^2 on both the sides, one side was served as control, while the other side as test. Formulated emulgel was applied twice a day for a period of 7 days and the site was observed for any sensitivity and the reaction if any. The data given in Table 4.

***10.* Stability Studies [18,36]:** Stability studies were carried out for the optimized emulgel formulation according to International Conference on Harmonization (ICH) guidelines. Short term accelerated stability studies were carried out for the period of 3months for the formulations. The samples were stored at different temperature conditions i.e., refrigeration temperature (4-8ºC), room temperature (25±2ºC) and oven maintained at (45ºC±2ºC). Samples were withdrawn on weakly interval and analysed for visual appearance, clarity, spreadability and drug content. At the end of 12th Week they were evaluated for physical parameters and integrity of the product.

RESULTS AND DISCUSSION:

Coccinia grandis is widely using vegetable in the daily life. Literature survey revealed that *c. grandis* leaves having good antibacterial effect. Hence, in the present investigation leaves extract of *c. grandis* was formulated as emulgel for treating bacterial infections. The herbal emulgels were formulated, because they are easy to design, stable, non-greasy, non-staining and pleasant appearance.

The fresh leaves of *Coccinia grandis* were collected in and around the Guntur. They were dried by air drying process. The dried leaves of *Coccinia grandis* were extracted by soxhlation process by using ethanol as menstruum. The extract was dried and tested for the phytochemical constituents. The results of the preliminary phytochemical screening revealed the presence of alkaloids, flavonoids, carbohydrates, glycosides, saponins, tannins and steroids. The results were shown in Table 1. For the further studies ethanolic extract was selected do the presence of alkaloids, steroids and tannins. The compatibility of ethanolic extract with the polymers was studied by using IR spectroscopic method. The spectra were shown in Figure 1 and 2. The spectra revealed that formulations having characteristic peaks same as that of the pure extract. It indicated that there is no interaction between drug and exciients.

Table 1: Preliminary screening data of *Coccinia grandis* leaves extract

Bioactive constituents	Ethanolic extract
Alkaloids	+
Flavonoids	+
Carbohydrates	_
Glycosides	+
Saponins	+
Steroids	+
Tannins	+
Triterpinoids	-

Table 2: Formulae of Emulgel

Ingredients	F1	F2	F3	F4	F5	F6
*Cocciniagrandis*Extract	1	1	1	1	1	1
Carbopol 940	1	1	1	-	-	-
Carbopol 934	-	-	-	1	1	1
Liquid paraffin	7.5	-	-	7.5	-	-
Olive oil	-	7.5	-	-	7.5	-
Coconut oil	-	-	7.5	-	-	7.5
Propylene glycol	5	5	5	5	5	5
Methyl Parabene	0.03	0.03	0.03	0.03	0.03	0.03
Propyl Parabene	0.03	0.03	0.03	0.03	0.03	0.03
Water	q.s	q.s	q.s	q.s	q.s	q.s

Table 3: Physicochemical observation data of emulgel formulations

S. No	Formulation code	Colour	Homogeneity	Consistency	p^H
1	F1	Brownish	Excellent	Excellent	6.3±0.01
2	F2	Brownish	Excellent	Excellent	6.3±0.01
3	F3	Brownish	Excellent	Excellent	5.96±0.01
4	F4	Brownish	Excellent	Excellent	6.53±0.05
5	F5	Brownish	Excellent	Excellent	6.08±0.13
6	F6	Brownish	Excellent	Excellent	6.24±0.4

Table 4: Physical evaluation data of herbal Emulgel formulations

S. No	Formulation code	Spreadability	Drug Content	Zone of Inhibition (mm)	Viscosity	Extrudability
1	F1	56.39	89.1±0.03	20	99	++
2	F2	45.5	94.4±0.55	21.5	97	++
3	F3	35.5	95.3±0.01	20.4	94	++
4	F4	71.36	93.6±0.007	20.7	92	+++
5	F5	64	92.9±0.03	20.5	91	++
6	F6	56	93.1±0.01	19.8	90	++

Table 5: Skin irritation study data of emulgel

S.No	Formulation code	Skin Irritation Test
1	F1	A
2	F2	A
3	F3	A
4	F4	A
5	F5	A
6	F6	A

A: No reaction, B: Slight erythema, C: Moderate erythema

Table 6: Kinetics data of the herbal emulgel formulations

Formulation	Regression values (r2)				'n' value
	Zero order	First order	Higuchi	Peppas	
F1	0.825	0.376	0.979	0.971	0.722
F2	0.885	0.386	0.987	0.967	0.694
F3	0.642	.326	0.875	0.951	0.71
F4	0.844	0.372	0.985	0.966	0.731
F4	0.804	0.364	0.965	0.964	0.736
F5	0.807	0.375	0.963	0.969	0.73

Table 7: Stability Study data of herbal emulgel formulation

S.No	Formulation	Days	Appearance	p^H	% Drug Content
1	F1	3months	Brownish	6.3±0.01	89.1±0.03
2	F2	3months	Brownish	6.3±0.01	94.4±0.55
3	F3	3months	Brownish	5.96±0.01	95.3±0.01
4	F4	3months	Brownish	6.53±0.005	93.6±0.007
5	F5	3months	Brownish	6.08±0.13	92.9±0.03
6	F6	3months	Brownish	6.24±0.4	93.1±0.01

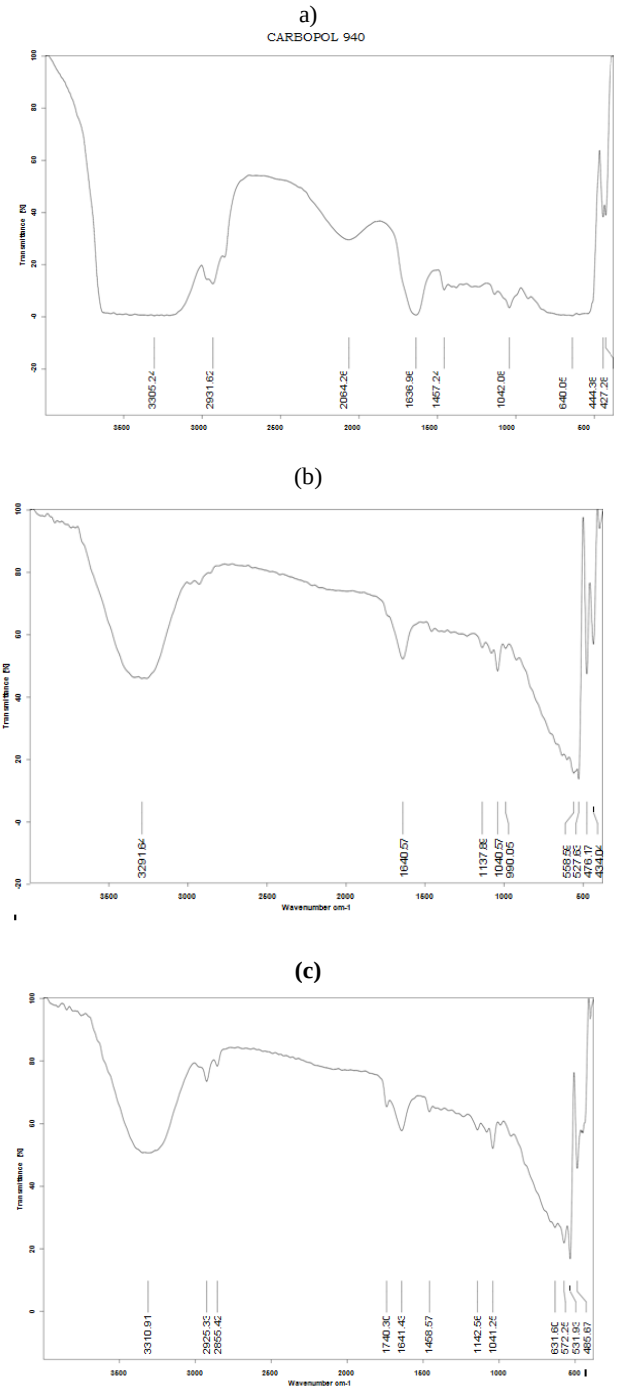

Figure 1: FT-IR Spectra of formulation containing a) Carbopol 936+liquid paraffin b) Carbopol 936+Olive oil c) Carbopol 936+ Coconut oil

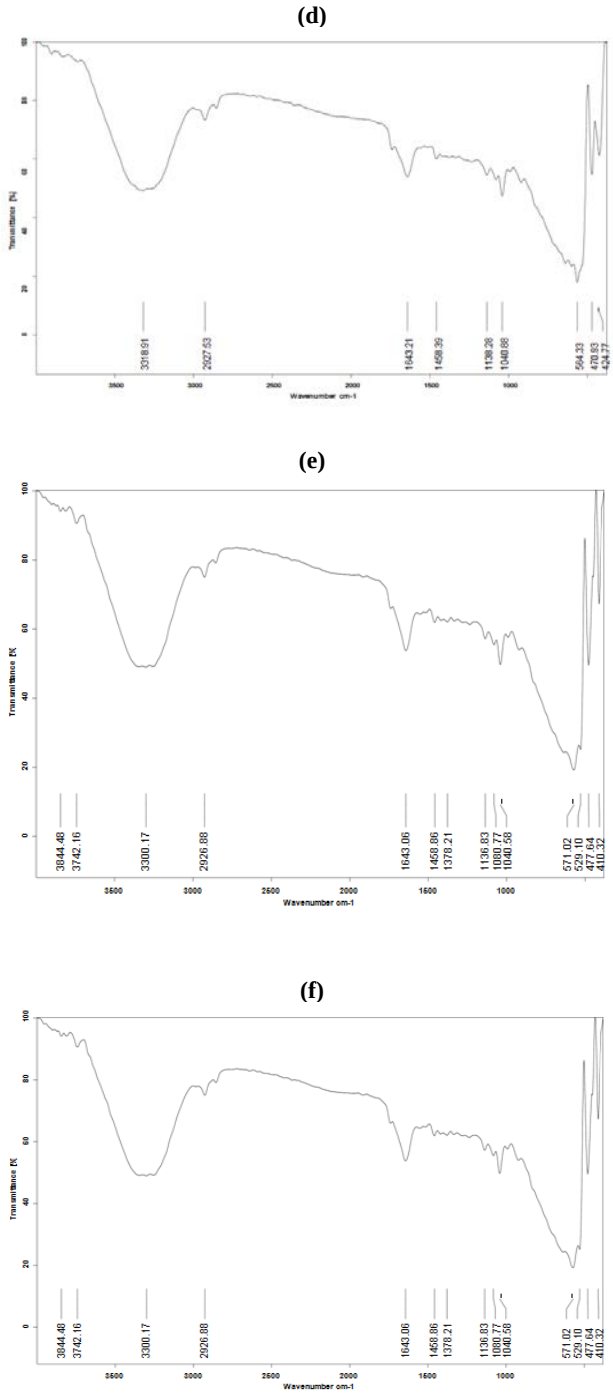

Figure 2: FT-IR Spectra of formulation containing a) Carbopol 940+liquid paraffin b) Carbopol 940+Olive oil c) Carbopol 940 +Coconut oil

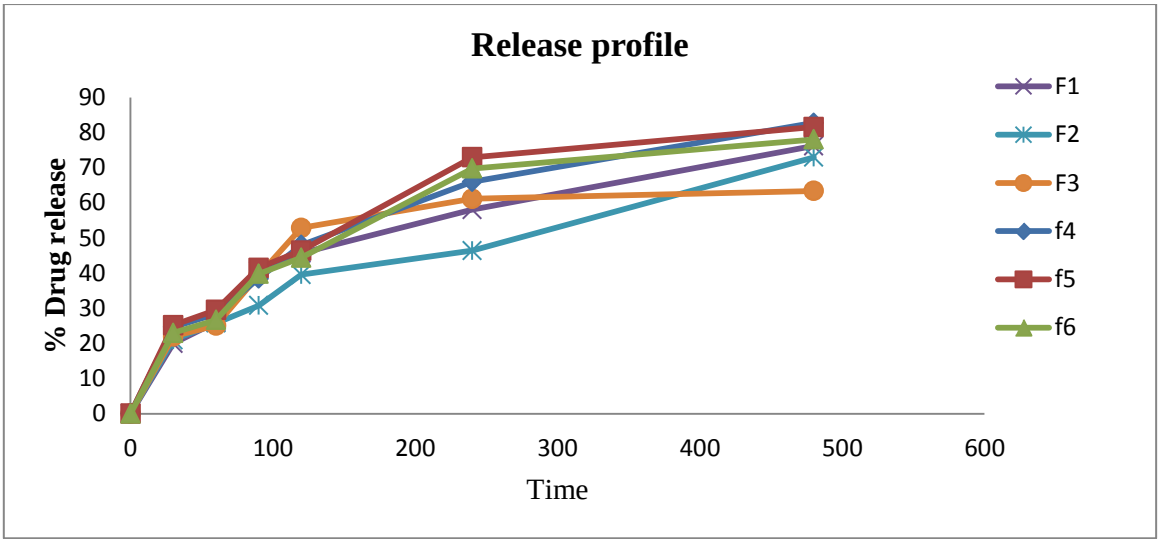

Figure 4: *In vitro* drug release data from the emulgel formulations

Figure 3: Herbal emulgel formulation

The extract was formulated into emulgel by using liquid paraffin, olive oil and coconut oil as oily phase and Carbopol 936 and Carbopol 940 as gelling agents. Fist the emulsion was prepared by using the oil phase, later it was dispersed into the gel base in 1:1 ratio to get the emulgel. The formed herbal emulgel formulations were yellowish white viscous preparations with smooth texture and glossy appearance. The emulgel formulaton was depicted in Figure 3. The pH of the emulgels was measured by pH meter and the values were in the range of 5.96-6.53. The viscosity of all the formulations were determined by using Brookfield Viscometer. The results indicated that all the formulations having uniform consistency and the values were in the range of 90-99 (Cp). The spreadability of all herbal emulgel formulations was measured by parallel glass slide method and the data was found satisfactory, indicated that the emulgels were easily spreadable by application of small amount of shear. The formulations were in the range of 35-71.36 g/cm^2. Extrudability of the emulgels was measured by using suitable tubes and data was given in Table 3. The drug content of prepared herbal emulgel was estimated by using UV-Visible spectrophotometer and the values were in the range of 89.1-95.3%. The medicament in the herbal emulgel was extracted by using phosphate buffer pH 6.8. The sample was estimated after filtration at 215nm. The data was shown in Table 4. The herbal emulgel was tested for the skin irritability test. After application of sample for specific period, the surface of the skin was examined with naked eye. The surface of the skin of the rabbit was free from inflammation, redness and irritation. The data indicated that formulation was passed the test and the data was given in Table 5. It indicated that the formulations are not skin sensitive. The *in vitro* drug release from the emulgels was carried by using Franz diffusion cell for a period of 8h. An aliquot of sample was collected from the cell and replaced with fresh diffusion medium to maintain the sink conditions. The amount of drug release was calculated by measuring the absorbance of the sample by spectroscopic method at 215nm. The process was carried out in triplicate. The release kinetics data was calculated from the calibration curve. The data revealed that the release of herbal extract from the emulgels was following zero order kinetics and by diffusion mechanism. The 'n' value of the Korsmeyer - Peppas equation was in the range of 0.694-0.736. It indicated that the release was by non-Fickian diffusion mechanism, which means diffusion and erosion-controlled release. The release kinetics data was given in Table 6 and the release was depicted in Figure 4.
The herbal emulgel formulations were studied for stability. All the formulations were found to be stable upon storage for a period of 3 months. There was no change in colour, physical appearance, pH, drug content, rheological properties and drug release parameters.

CONCLUSION:

In the future topical drug delivery systems plays an important role to impart patient compliance. Out of various topical formulations emulgels are widespread due to enhanced spreadability, low viscosity, non-greasy and glossy appearance. In the present study, topical herbal

emulgel of *Coccinia grandis* herbal extract was formulated by using various oily phases and gelling agents. The formulated emulgels were subjected to physicochemical studies viz., rheological studies, pH, spreadability, extrudability and *in vitro* drug release studies. From the studies, the formulation F4 showed good release, spreadability and rheological characteristics. The emulgel was tested for antibacterial activity and the results indicated that, they exhibited good antibacterial activity. The stability studies revealed that the formulations were stable without change in physical appearance and release pattern.

Hence, *Coccinia grandis* herbal extract can be formulated as emulgel to treat dermatological complications.

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