## Formulation and Evaluation of Polyherbal Cream-Gel for Treatment of Rosacea

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## Shubham Somnath Dange

Department of Pharmaceutical Chemistry, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: dange9341@gmail.com Contact no: +91 9545182456, 9175548490

## **Revan S. Karodi**

Department of Pharmacognosy, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: revankarodi@gmail.com Contact no: +9860196088

## Sonam J. Bendre

Department of Pharmaceutical Chemistry, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: sonambendre30011999@gmail.com Contact no: +919545127779

## Sakshi S. Kohakade

Department of Pharmaceutical Chemistry, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: sakshikohakade98@gmail.com Contact no: +917057474003

## Shital S. Rajad

Department of Pharmaceutical Chemistry, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: shitalrajad2016@gmail.com Contact no: +919527822411

## \*Corresponding author: Shubham Somnath Dange,

Department of Pharmaceutical Chemistry, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, Maharashtra, India. E-mail address: dange9341@gmail.com Contact no: +919545182456/ 9175548490

## Key Words:

Rosacea, Polyherbal, Cream-gel, Antifungal, Anti-inflammatory

## Abstract:

Rosacea is a widespread, recurrent inflammatory skin disorder that impacts a large number of people globally. Rosacea is a prevalent, persistent, inflammatory skin condition whose cause is unknown. Cream-gel is the combination of cream and gel. Cream-gel products are pleasantly light and aid in the delivery of hydration, emolliency, and active ingredients. As their name implies, they are a cream in a moisturising gel form, therefore there is no need for any conventional emulsifiers. The primary goal of the research is to create a polyherbal cream-gel utilising several herbs, and the effectiveness of the created cream-gel is assessed. The herbs used in the preparation of cream-gel are dried green tea leaves, curcumin, calendula oil. Phenolic acid, flavonoids, terpenoids, glycosides, and saponins are all present in the green tea leaf extract, curcumin and calendula oil which has antibacterial, antifungal, anti-inflammatory properties. The cream-gel was prepared by using fusion method. The main excipient used in preparation of cream-gel was Sepiplus 400 which is a combination of polyacrylate-13, polyisobutene, polysorbate-20. The Sepiplus 400 is used as film forming polymer, polymer, and non-ionic surfactant. The formulation of cream-gel was further evaluated for the various parameters like pH, viscosity, phase separation, spreadability, extrudability, compatibility etc. The results show that all formulations gave satisfied result. In order to treat effectively Rosacea, the present study of green tea leaves, curcumin, calendula oil boost drug penetration from the affected area, which may result in the treatment exhibiting antiinflammation, antifungal and antibacterial activities. The created herbal formulation was more successful at treating Rosacea symptoms than synthetic formulations because it was more stable, safe, and effective.

## 1. Introduction

Rosacea is a long-term disorder, which usually affect facial skin. The typical signs of this condition include flushing, persistent facial redness, visible blood vessels, papules and pustules, thicker skin, sensitive skin, burning, itching, stinging, and pain, as well as dry, rough skin. Up to 10% of people worldwide suffer with rosacea, a chronic, recurrent, and progressive immunemediated illness of the facial skin.<sup>[1,2]</sup> Rosacea is a very diverse condition with an unidentified epidemiology and pathogenesis. Etiopathogenesis and physiology are unclear due to the lack of a laboratory benchmark test. According to several experts, further problems include the emergence of persistent lymphedema, thickening of the afflicted skin, and rhinophyma. [3] Vascular changes, particularly flushing, are the initial and enduring feature, followed by inflammatory changes like papules and pustules. Depending on symptoms rosacea is categorized into four types [4,5]

#### • Erythematotelangiectatic Rosacea

The form most people are familiar with is erythematotelangiectatic rosacea, also known as ETR. Usually affecting the cheeks, nose, and forehead, it causes facial redness and flushing. However, individuals may also see redness on their chin, neck, and scalp, particularly if their rosacea is poorly controlled.<sup>[6,7]</sup>

#### • Papulopustular Rosacea

Papulopustular rosacea, also known as acne rosacea, causes facial redness and irritation as well as the noticeable spider veins that are present in many rosacea patients. But there are also breakouts that resemble acne associated with this kind of rosacea.<sup>[8]</sup>

#### • Phymatous Rosacea

Phymatous rosacea patients experience thickening of the skin, which may begin as tiny plaque-filled patches, similar to the thickened plaques seen with papulopustular rosacea. The skin may sag and develop bumps with time. People compare this texture to scar tissue when describing it. Rhinophyma, a similar disorder, is frequently developed by people with phymatous rosacea. As disorders affecting the nose are referred to as "rhino" in medicine, it is not surprising that the most typical side effect of rhinophyma is a bulbous nose. <sup>[9]</sup>

#### Ocular Rosacea

Eye problems are caused by ocular rosacea. The eyelids and skin surrounding the eyes become red and swollen, just like with other types of rosacea. Bloodshot eyes, eyelid lumps that mimic styes, and swollen eyelids are a few symptoms that people may experience. Watery, burning, and irritated eyes are common in people with ocular rosacea. People say it feels very much like having dirt or dust in their eyes.<sup>[10]</sup>





Phymatous Rosacea



Papulopustular Rosacea



Ocular Rosacea

Figure 1: Types of Rosacea

#### Curcuma longa

The main curcuminoid in turmeric, a well-known Indian spice that belongs to the ginger family (Zingiberaceae), is called curcumin. Desmethoxycurcumin and bis-desmethoxycurcumin are the other two forms of the curcumin molecule. The Turmeric's bright yellow colour is due to the polyphenol curcuminoids. Keto and enol are the two tautomeric forms of curcumin that are known to exist. In both the solid phase and solution, the enol form is more energetically stable. When combined with boric acid, it combines to produce rosocyanine, a red-colored chemical. The vibrant yellow colour of curcumin makes it suitable for use as food colouring. Its E100 food additive code represents it. Curcumin possesses anti-inflammatory, antiviral, antifungal, and antioxidant properties. Studies have demonstrated that curcumin is not hazardous to people. By inhibiting a variety of compounds that are crucial to inflammation, curcumin exhibits anti-inflammatory effect. [11,12]

#### Camellia sinensis

Everywhere in the world, the leaves of the shrub Camellia sinensis are drunk as a beverage and are said to offer a number of therapeutic benefits. Green tea catechins (GTCs) have been linked to the biological and pharmacological effects of green tea leaf extract, including its anti-inflammatory, anti-microbial, antitumor, and anti-oxidative properties. <sup>[13,14]</sup>

#### Calendula Officinalis

More than 35 qualities have been assigned to tinctures and decoctions made from Calendula officinalis flowers, which have been used in folk therapy for a very long period. The principal applications include treating burns (including sunburns), bruising, and inflammatory cutaneous and interior disorders with various causes. The suggested doses depend on the kind and severity of the ailment that needs to be treated as well as the unique circumstances of each patient. In order to minimise UV radiation-induced oxidative stress in skin, the current study looked into the potential usage of Calendula officinalis extract. <sup>[15,16]</sup>

#### Cream-gel

Polyherbal cream-gel is a combination of cream and gel. The main purpose of the formulation is to provide hydration to skin. As the name says it is a cream in a hydrating gel form. There is no etiology for the disease so the curing of disease is to target symptoms of the disease. The cream-gel helps to provide moisturizer along with medication. The gel helps to keep skin hydrated which reduce burning sensation and dryness which occur during rosacea. <sup>[17,18]</sup>

#### 2. Material and Methods

Sr. no	Materials	Suppliers			
1	Curcumin	Herbo Nutra extract Pvt. Ltd., Pune			
2	Green tea extraxt	Herbo Nutra extract Pvt. Ltd., Pune			
3	Calendula oil	Deve Herbs			
4	Sepiplus 400	Seppic			
5	Methyl paraben	Research Lab Fine Chem Mumbai			
6	Glycerine	Research Lab Fine Chem Mumbai			

 Table 1: Materials

#### Sepiplus 400

A new class of thickening emulsifiers called "Hydro Swelling Droplet" (HSD) emulsifiers includes Sepiplus 400. In the presence of electrolytes (NaCl, mineral water), as well as solvents (ethanol, glycerin, and glycols), Sepiplus 400 thickens extremely well. It maintains stability throughout a large pH range (pH 2.5–11). Without additional emulsifiers and regardless of the oil's composition or viscosity, Sepiplus 400 emulsifies and stabilises up to 50% of the oil phase. Sepiplus 400 contains Polyacrylate-13 (and) Polyisobutene (and) Polysorbate 20

#### **Cream-gel Formulation**

For the formulation of cream-gel fusion method was used. The API *Curcuma longa, Camellia sinensis,* and *Calendula Officinalis* were weighed separately. Sepiplus 400 was used as polymer, surfactant and stabilizer. Liquid paraffin was taken as oil phase. Methylparaben and propyl paraben were taken as preservative. For preparation of cream-gel three phases were taken in phase 1 camellia sinensis was dissolved in water. In phase 2 the curcuma longa was dissolved in ethanol as it is not soluble in water. In phase 3 liquid paraffin, Sepiplus 400 were mixed together. Phase 1 and phase 2 were mixed together with the help of magnetic stirrer. This mixture was added to oil phase and mixer with magnetic sterrier until the homogenous mixture was formed. pH was adjusted.

Ingredients	Category	F1	F2	F3	F4	F5	F6	F7	F8	F9
ingreutents	Cutegory	11	12	15	1 7	15	10	17	10	17
Curcumin	A.P.I	200	200	200	200	200	200	200	200	200
		mg								
Green tea	A.P.I	200	200	200	200	200	200	200	200	200
Extract		mg								
Calendula oil	A.P.I	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
		ml								
Liquid paraffin	Base	1	2	2	0.5	3.14	3	2	3	1
Sepiplus 400	Polymer+Surfactant+Stabilizer	3.5	5.2	4.2	3.5	4.1	3.7	0.6	0.3	0.3
Glycerin	Moisturizer	1ml	2ml	2ml	3ml	1ml	1.ml	2ml	2ml	3ml
Methylparaben	preservative	0.2g								
Purified water	Vehicle	Q.S								

#### FTIR

Drug-excipient interactions play an important role with respect to biological performance and formulation stability. FT-IR spectroscopy was done to analyse the physical and chemical interactions between drug and excipients. The characteristic absorption peaks obtained for the drug alone and in the presence of polymer were detected. <sup>[18]</sup>

A quantity of EGCG standard powder (10

mg) was dissolved in 30 ml of distilled

water contained in 100 ml volumetric flask and was made up to mark with the same solvent to produce a 100 µg/ml solution. Determination of wavelength of maximum absorption 1 ml was withdrawn from the stock solution

into a 10 ml volumetric flask and made up to

mark with distilled water to produce 10  $\mu$ g/ml solution. This was then scanned in the spectrophotometer through range wavelengths (240 - 400 nm) so as to obtain

the wavelength of maximum absorption

#### **HPTLC** Analysis of extract

HPTLC analysis for plant extracts include quantification of marker compounds from the extract, checking the quality of extracts, and detection of the class of compounds from a particular extract, by fingerprint analysis.

Weighed 100 mg of extract sample, dissolved in 10 ml of MeOH, sonicated for 30 mins, centrifuged at 10000 rpm for 15 mins and supernatant was filtered and used for spotting.<sup>[19]</sup>

#### **Organoleptic evaluation**

The organoleptic properties of cream-gel were evaluated. The colour, odour and state were checked. By grading the roughness and colour of the cream-gel, the look was determined.

#### Stability research

Drug product stability testing starts with drug discovery and lasts until the chemical or commercial product is destroyed. Stability studies were carried out in accordance with ICH recommendations to evaluate the stability of the medication and formulation. According to ICH requirements, the stability investigations were completed. For two months, the cream-gel was placed in a bottle and stored in a humidification chamber at 30 2 °C and 65 5% relative humidity and 40 2 °C and 75 5%. Samples physical characteristics and viscosity were examined at the conclusion of the studies.

### pH of Cream-gel

Using buffer solution, the pH metre was calibrated. The pH of the cream-gel was determined after it was

weighed, dissolved in 50.0 ml of distilled water, and weighed again.

#### Spreadability Test

The formulation was placed on one of the fixed slides. Over it was positioned the second movable slide, which had one end fastened to a string to which weight could be imparted using just a pan and a basic pulley. The amount of time it took for the upper slide to move 5.0 cm and separate from the lower slide under the influence of a 30g weight was measured after the weight was placed on the pan.

## Viscosity

The Brookfield Viscometer was used to measure the formulation's viscosity. The Brookfield DV-II + viscometer with an LV-4 spindle was used to measure viscosity. The created formulation was added to the adaptor of the viscometer, and the angular velocity steadily increased from 0.5 to 20 rpm.

#### Homogeneity

By looking at them and feeling them, the formulations were examined for homogeneity. After feel Test

Checks were made on the amount of residue left after applying a specific amount of cream-gel, as well as emolliency and slipperiness.

#### **Cleaning Test**

By rinsing the applied section with tap water, it was possible to determine how easily the cream-gel could be removed.

#### Irritancy test

Mark a square of one cm2 on the left. Applying the cream-gel to the designated area and timing the process. Irritability, erythema, and edoema were monitored and reported if present at regular intervals for up to 24 hours.

## 3. Result and Discussion

- A. FTIR
- a) Curcuma longa



Figure 2: FT-IR of Curcuma longa

#### b) Camellia Sinensis



Figure 3: FT-IR of Camellia sinensis

## **B. HPTLC**

#### a) Curcuma longa

**Sample Preparation:** Weighed 100 mg of extract sample, dissolved in 10 ml of MeOH, sonicated for 30

mins, centrifuged at 10000 rpm for 15 mins and supernatant was filtered and used for spotting. ACN:H20 (5:5 v/v) as mobile phase, Silica Gel 60 F254 (Merck) as stationary phase, saturation time was 20 min



Figure 4: Hptlc analysis of Curcuma longa

### b) Camellia Sinensis

**Sample Preparation:** Weighed 100 mg of extract sample, dissolved in 10 ml of MeOH, sonicated for 30 mins, centrifuged at 10000 rpm for 15 mins and supernatant was filtered and

used for spotting. a) Tol:Ace:FA (7.8:2.2:0.15 v/v/v) b) Tol:EA:FA (8.5:1.5:0.1 v/v/v) c) Tol:Ace:FA (9:9:2 v/v/v) mobile phase, Silica Gel 60  $F_{254}$  (Merck) as stationary phase, 20 min saturation time



Figure 5: Hptlc analysis of *Camellia Sinensis* 

Batch	pН	Spreadability	Viscosity	%Drug	%Drug	
		g.cm/sec	mPa.s	Release of Curcumin	Release of Green tea	
F1	5.7	16.81	14162	54.225	48.24	
F2	5.6	15.45	15285	58.022	46.12	
F3	5.5	20.96	15865	91.365	77.14	
F4	6.3	13.24	14000	29.531	55.17	
F5	6.6	17.67	14051	45.235	56.54	
F6	6.2	16.45	15971	72.975	93.6	
F7	6.5	12.13	16112	45.235	60.64	
F8	6.2	14.79	15125	72.946	65.96	
F9	5.3	16.74	15617	64.658	76.13	

Table 3: Evaluation Parameter of Cream-gel

## C. pH of the Cream-gel

The cream-gel's pH was discovered to be between 5.5 and 6.5, which is good for the skin's pH. Each creamgel composition was demonstrated to need a pH that is closer to skin. The viscosity of the formulation affects spreadability. The Model F-value of 13.99 implies the model is significant. There is only a 2.73% chance that an F-value this large could occur due to noise. Spreadability estimates for all runs performed experimentally ranged from 12.17 to 20.97 Gm.cm/Sec.

## D. Spreadability



Figure 6: 3D Plot for Spreadability

#### D. Viscosity

The cream-gel's viscosity was within a range, which means that it can be easily distributed with



Figure 7: 3D Plot for Viscosity

#### E. Drug Release

#### a) % Drug Release of Curcumin



Figure 8: % Drug Release of Curcumin

only a little shear. Compared to other formulations, F6 exhibits good spreadability.



#### b) % Drug Release of Green tea



#### F. Drug Content

The drug composition of each formulation was tested in accordance with industry standards. The table revealed that the drug content was present.

## a) Drug Content of Curcuma longa



Figure 10: % Drug Content of Curcuma longa

## % Drug Content of Camellia Sinensis





## H.

## **Stability Study**

After 2 month there were no change in the stability of formulation. The pH, viscosity and colour of the formulation was checked and the formulation is stable.

## I. Homogeneity

In cream-gel, all formulations result in a consistent distribution of extracts. Both touch and outward look provided proof of this.

## J. After feel

Emolliency, slipperiness, and how much residue remained after using a particular amount of cream-gel were all judged to be positive attributes.

## K. Removal

Washing with tap water made it simple to remove the skin-care product that had been applied.

## L. Skin irritation test (patch test):

There were no allergy signs, such as swelling, redness, or irritation, during 24 hours.

## G. Appearance

It was discovered that the cream-gel's hue did not alter after a prolonged storage period.

## 4. Conclusion

The major goal of the research work is to formulate a cream-gel. The main purpose of formulation is to provide hydration and relief to the symptoms of disease. An effective selection of medicinal plant and their extract in the right concentration, and flawless formulation can have positive impact on body and also boost the potency of medication. As there is no cure for the disease the main goal is to target symptoms. The formulation provides long lasting hydration to skin and also give relief from skin irritation. The F6 batch was considered as optimized batch among all the batches as it shows high drug release as compare to other batches. The spreadability, viscosity, drug release, drug content, and other factors were taken into consideration when evaluating all 9 batches. Among these 9 batches the F6 batch shows high drug release and other parameters were also within the range. The created herbal

formulation was safer, more effective at treating Rosacea, and more stable than synthetic formulations. We can conclude that industrial manufacturing of the cream-gel formulation of the curcumin, green tea and calendula oil can be taken up after conducting clinical trials on human volunteers.

## **Conflict of interest:**

The authors have no conflicts of interest regarding this investigation.

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