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Research article

PREPARATION AND EVALUATION OF KUMKUMADI OIL LOADED TOPICAL MICROEMULSION

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Abstract

The use of chemicals, blends, or physical procedures to lighten skin tone is known as skin whitening. The phrases "bleaching," "brightening," "depigmentation," and "lightening" are also occasionally used. Skin-whitening ingredients are frequently utilized in these kinds of products. The goal of the current study was to prepare and assess a topical microemulsion loaded with Kumkumadi oil for skin whitening. Microemulsions (ME) are transparent (or translucent), isotropic, thermodynamically stable systems consisting of water, oil, and surfactant. Often, a co-surfactant is added, with droplet sizes typically falling between 10 and 100 nm. Kumkumadi oil, turmerone, and surfactant PEG 200 tri isostearate were found to have the best concentrations when the Pseudo Turnery Phase Diagram was created using Chemix® software. The final oil phase preparations included a mixture of 2% v/v and 1% v/v Kumkumadi oil and Turmerone, 30% v/v and 20% IPA v/v PEG 200 tri isostearate, and 47% v/v water for the water phase. A one-month evaluation of the system's stability at room temperature was conducted, along with tests for dilution, dye solubility, zeta potential, globule size determination, FTIR analysis, electric conductivity, pH measurement, percentage transmittance, drug precipitation assessment, microbial limit test, microbial bio-burden, and polydispersity index. The formulation was shown to be stable for a month with the optimized microemulsion having a Zeta potential of 19.24, a percentage transmittance of 99-99.99%, and a PDI of 0.064.

Key words: Microemulsion, Kumkumadi oil, Skin whitening

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Introduction

Cosmetics are skin and hair care products designed to cleanse, enhance, and beautify the qualities of the skin and hair. Skin care isn't a fad these days. Since cosmetics have been used to enhance and protect skin throughout history, we can only conclude that this is an innate desire. The fundamental idea of utilizing cosmetics to increase the characteristics of good health has not changed, despite the fact that cosmetic goods have experienced several alterations in recent decades.

Cosmetics are materials or items that are used to improve or change the way the face, body, or scent appear. A lot of cosmetics are made to be applied to the body, face, and hair. Generally speaking, they are blends of chemical components, some of which are synthetic or artificial and others of which come from natural sources (like coconut oil). Lipstick, mascara, eye shadow, foundation, body lotions and cleansers, shampoo and conditioner, hairstyling products (gel, spray, etc.), perfume, and cologne are examples of common cosmetics.

Makeup or makeup refers to cosmetics applied to the face to improve its appearance. The technique of employing natural and artificial chemicals in the form of soaps, tablets, lotions, and other products to lighten skin tone or produce a balanced skin tone is known as skin whitening. The reasons why different civilizations employ skin-lightening creams differ greatly. Skin whitening is sought after for cosmetic and cultural purposes in many cultures. Whiter skin can convey attributes associated with prosperity, nobility, and beauty in certain cultures.

Kumkumadi Tailam, also known as Kumkumadi Oil, accentuates the skin's inherent, radiant fairness. It has moisturizing properties. All skin types can use it, however dry skin can benefit from it more than others. It prevents dark circles, blemishes, and uneven skin tone while enhancing luster. It is typically a useful ayurvedic treatment for unwelcome blemishes and eruptions. It has safer components that are derived from herbs. It enhances the texture and color of the skin. It reduces wrinkles, dark circles, sun tans, white and black heads, acne, and acne scars. The distilled portion of turmeric oil, known as TEGO®

Turmerone, is taken out of the Curcuma longa root using supercritical carbon dioxide. The environmental impact of this solvent-free extraction method is minimal. Turmeric oil, which is mostly composed of turmerones (about 60%), is produced from Curcuma longa and yields 4-5% of the oil. The second major process, molecular distillation, changes the oil's color from brown to light yellow, enriches the turmerones, gets rid of the unwanted curcumins, and lessens the strong smell without affecting the product's effectiveness. Micro emulsions are isotropic liquid combinations of water, oil, and surfactant that are clear and thermodynamically stable. They are often combined with cosurfactants. A dispersion of one liquid's droplets in another immiscible liquid is called an emulsion. The second liquid, known as the continuous phase, surrounds the dispersed droplets, which constitute the dispersed phase. To stabilize an emulsion and prevent the droplets from coalescing into two separate phases, a surfactant or co-surfactant is introduced. Microemulsions exist in two primary forms based on the phase configuration: water-in-oil (w/o) and oil-in-water (o/w).

Cosmetics are products created for skin and hair care for the purpose of cleansing, beautifying and enhancing the attractive features. Skin care is not a modern trend. In fact, people in every civilization used cosmetics to protect and embellish their skin - which naturally leads us to conclude that this is a primordial need. Although cosmetic products have undergone many changes in modern times, the basic concept of using cosmetics to enhance the features of good health has not changed.

Materials and Methods

Materials

KumKumadi oil was purchased from pure botanical care private limited, Turmerone and PEG 200 Tri Iso Stearate were purchased from Brillare science private limited, Ahmedabad, India. Iso propyl alcohol was purchased from Rakesh chemicals, Ahmedabad, India. Capmul MCM was purchased from Abitec Corporation (OH, USA), Labrasol, and Transcutol P was procured from Gattefosse (Lyon, France).

Methods

Solubility Study

The compatibility of the oil and surfactant mixes was evaluated based on which ones displayed the maximum solubility. The following surfactants were manufactured in addition to the selected oil, which was Kumkumadi oil: Labrafil, IPM, Captex, Transcutol, Arlamol, Capmul, Dow Corning, Lauroglycol 90, Capryol 90, Peceol, Labrasol, PEG 200 Tri isostearate, and Isopropyl alcohol. Using a vortex mixer, the liquids were mixed for five minutes before their physical appearance was assessed.

A. Transparent with good flow
B. Transparent with medium flow
C. Milky with good flow (opaque)
D. Milky with medium flow (Opaque and viscous)

Similarly, Solubility study between the Smix and oil was tested by preparing by mixing oil at 1:1,1:2,1:3,3:1,3:2 respectively. The blends were assessed for as per the above mentioned scale.

Construction of pseudo-ternary phase diagrams

A helpful and significant tool for researching the phase behavior of microemulsions is the pseudo-ternary phase diagram. A triangular phase diagram with three coordinates can be used to depict a pseudo-ternary

phase diagram. Every coordinate denotes a different microemulsion system component, like:

1) Oil phase: Kumkumadi Oil, Turmerone
2) Surfactant: co-surfactant phase (Smix): PEG 200 Tri isostearate & Iso propyl alcohol
3) Aqueous phase

Each point on the coordinate grid also denotes a concentration ranging from 0% to 100% for each phase, incremented by 10%. Pseudo ternary phase diagrams are devised to identify the suitable components and their concentration ranges that yield a substantial microemulsion existence area. Once the appropriate microemulsion components are determined, another pseudo ternary phase diagram is crafted to delineate the extent and characteristics of the microemulsion regions. The size of the microemulsion area on the pseudo ternary phase diagram serves as an indicator of stability within the system; a larger area signifies a more stable system compared to a smaller one. These diagrams were developed using the water titration method to ascertain the components and their concentration range. Changes were made to the surfactant to co-surfactant ratio at 1:2, 3:1, 3:2, and 4:1. A volume ratio of oil to Smix was used to prepare each Smix ratio, oily combination combining oil, surfactant, and co-surfactant, at 0.1:0.9,0.2:0.8,0.3:0.7,0.4:0.6,0.5:0.5,0.6:0.4,0.7:0.3,0.8:0.2,0.9:0,1, respectively. Drop by drop, double-distilled water was added to the mixture at room temperature while being stirred with a magnetic device. The goal of the aqueous titration approach was to obtain a transparent and clear microemulsion. The pseudo ternary phase diagram was plotted using the component concentration, which was determined.

Preliminary trials:

General method for preparation of microemulsion:

Phase diagrams can be used to illustrate microemulsions, which are created using the spontaneous emulsification method (also known as the phase titration method). Phase diagram construction is crucial for understanding the intricate web of interactions that arises from the mixing of various components. Depending on the component concentration, microemulsions and different association structures (gel, oil dispersion, etc.) form. Phase diagrams with pseudoturbulence are frequently created to identify various zones, including microemulsion zones. Depending on whether the area is water- or oil-rich, it might be classified as an o/w or w/o microemulsion.

Trials conducted:

Ratio of 1:1 was taken as for oil: surfactant for primary trials. In this Kumkumadi oil and different types of surfactants were used including Labrafil, IPM, Captex, Transcutol, Arlamol, Capmul, Dow corning, Lauroglycol 90, Capryol 90, Peceol, Labrasol, PEG 200 Tri isostearate to obtain thermodynamically stable transparent system of these mixture.

Preparation of Microemulsion using Novel carrier oil and Surfactant:

Preparation of oil phase:

Mixture of Kumkumadi oil and Turmerone of 2% v/v & 1% v/v concentration was taken in the beaker.

Mixture of PEG 200 Tri isostearate and Iso propyl alcohol of 30% v/v & 20% v/v was added into above mixture.

Preparation of water phase:

Water phase was added drop by drop with the help of syringe into oil phase with constant stirring on magnetic stirrer till clear microemulsion solution is obtained. The end point and total amount of water consumed by the system were noted.

Evaluation of the microemulsion based formulation:

(A) Type of emulsion identification tests

Dilution test

Dilution tests rely on the emulsion's compatibility solely with the liquid forming its continuous phase. Depending on whether the microemulsion is prepared using the oil or the aqueous phase, it is diluted with the respective phase. Thus, in an o/w system, dilution occurs using the aqueous phase, while in a w/o microemulsion, the dilution employs the oil phase being utilized.

Dye solubility test

Another name for it is the strain test. This test shows the continuous phase's nature by sprinkling a dye onto the emulsion's surface. A water-soluble dye is rapidly incorporated into the system in an o/w emulsion, whereas in a w/o emulsion the dye forms clumps that are visible up close. When an oil-soluble dye is added, the opposite occurs. In essence, the continuous phase is determined by this test.

Zeta potential determination

Zeta sizer was used to measure the zeta potential of the samples. Samples were put into single-use, transparent zeta cells, and the outcomes were noted. Cuvettes were cleaned with methanol and rinsed with the sample that was going to be measured before to each experiment, before being filled with fresh material.

IR studies

Diffuse reflectance spectroscopy (DRS)-FTIR employing a KBr disc was employed to capture the infrared spectra of the pharmaceutical compound within the homogeneous blends of excipients (Capmul MCM NF, Acrysol k-150, and Propylene Glycol) using a Shimadzu FTIR-8400S spectrophotometer equipped with an attenuated total reflectance (ATR) accessory. Prior to

spectrum acquisition, all samples underwent vacuum drying to mitigate the influence of any residual moisture. Each spectrum was obtained through eight scans at a resolution of 4 cm-1 across a frequency range of 4000-400 cm-1.

Globule Size Determination

The average droplet size and Polydispersity Index (PDI) of the samples were measured at 25°C using a Malvern zeta sizer. The microemulsion (2–2.5 ml) was transferred to a disposable polystyrene cuvette using a plastic syringe or micropipette. The droplet size of the microemulsion was ascertained by combining laser Doppler velocimetry with phase analysis light scattering (PALS) at an angle of 900 at 250C.

Microbial limit test

To validate microbial counting method, we used following media: Nutrient agar, Peptone water, Water, Soya bean casein digest medium,0.45 micrometer nylon filter, Filtration assembly, Micropipette, Mac Conkey agar, Mac Conkey broth, Cetrimide agar, Mannitol salt agar, RVSE broth (For Salmonella) for micro along with four organisms for reference.

Microbial bio-burden

Membrane filtration method was used for the determination of microbial bio-burden.

Viscosity

Using a tiny sample holder and a Brookfield DV+II Pro Rheometer (Brookfield Engineering Labs, USA) with a spindle DIN-87, the viscosity of the microemulsion was measured in 5 g samples without dilution. Using the same apparatus and the correct spindle, continuous shear studies were conducted to examine the rheological characteristics of the microemulsion. The resulting hear stress (Pa) was measured when the shear rate was increased in increasing order from 0 to 200 D (1/s) (up curve) and subsequently dropped from 200 to 0 D (1/s) (down curve)15. At 25°C, the measurements were taken.

(B) Drug precipitation assessment

Drug precipitation was evaluated by visual inspection of the microemulsion after 24 h. The formulations were then categorized as clear (transparent), non-clear (turbid), stable (no precipitation at the end of 24 h), or unstable (showing precipitation within 24 h).

(C) Percentage transmittance

Percentage transmittance of prepared microemulsion was measured by putting sample which was appropriately diluted with DMSO in the sample holder using UV spectrophotometer (UV 1800, Shimadzu, Japan) at 287 nm.

(D) Electric conductivity

It was measured by conductivity meter (CM-180 ELICO, India).

(E) Measurement of pH

The pH meter was first calibrated with a known pH solution. The pH of optimized ME was determined at 25˚C temperature using pH meter.

Result and Discussion

Solubility Study:

Table 1: Solubility study

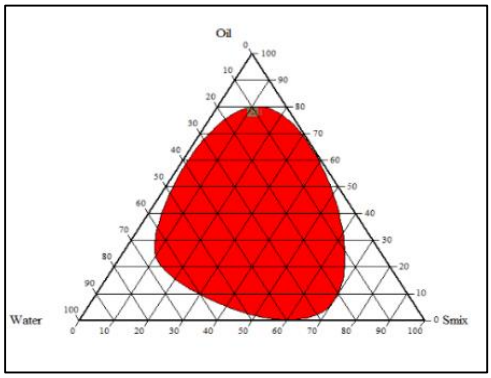
Sr .No.	Smix	Solubility
1	Labrafil	No
2	Isopropyl myristate (IPM)	No
3	Captex	No
4	Transcutol	No
5	Arlamol	No
6	Capmul	No
7	Dow Corning	No
8	Lauroglycol 90	No
9	**Capryol 90**	**Yes**
10	Peceol	No
11	Labrasol	No
12	**PEG 200 Tri isostearate**	**Yes**
13	**Isopropyl alcohol**	**Yes**

Figure 1: Solubility Study

Construction of pseudo-ternary phase diagram:

Pseudo-ternary phase diagrams were utilized to ascertain the concentration and range of components for the current microemulsion range. The ratio of surfactant to co-surfactant (Smix) was adjusted to 3:2,1:1,3:1,1:3,1:2. PEG 200 tri isostearate and isopropyl alcohol (IPA) were the oily mixtures containing Kumkumadi oil, Turmerone, surfactant, and co-surfactant that were used to construct the pseudo-ternary phase diagram at each Smix ratio. These mixtures were made with volume ratios of oil to Smix at 0.1:0.9,0.2:0.8,0.3:0.7,0.4:0.6,0.5:0.5,0.6:0.4,0.7:0.3,0.8:0.2,0.9:0,1, respectively. Drop by drop, room-temperature double-distilled water was added to the oil and Smix mixture while being magnetically agitated. Calculating the component concentrations was necessary in order to plot the pseudo-ternary phase diagram.

Figure 2: Phase behaviour for oil: surfactant 3:2, 1:1, 1:2, 3:1 and 1:3 ratio



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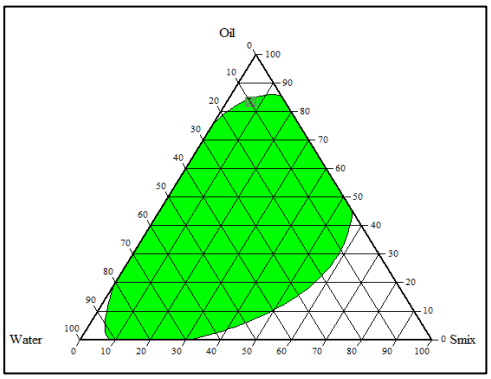

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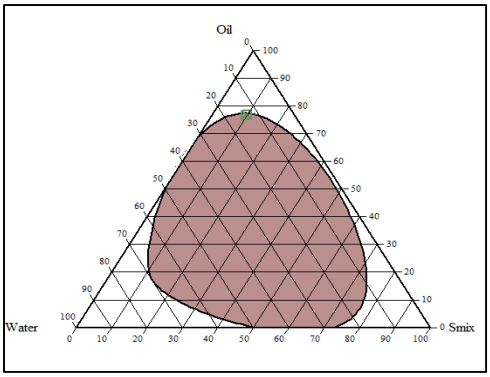

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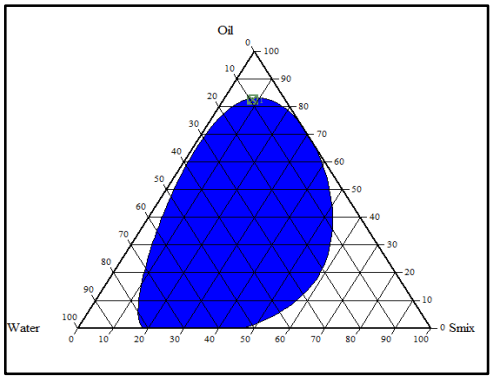

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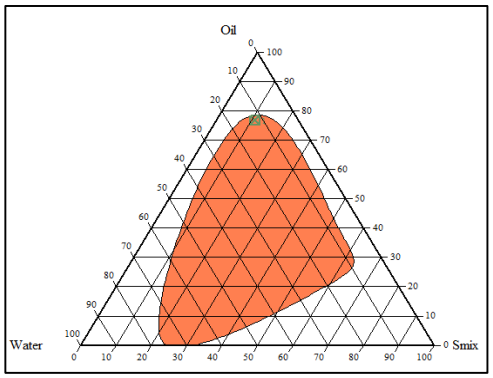


1:3

Trial conducted:
For the primary experiments, a ratio of 2:1 was used for oil and a ratio of 3:2 for Smix. To create a clear solution that is thermodynamically stable, Kumkumadi oil, Turmerone, and surfactants and co-surfactants such PEG 200 Tri isostearate and Isopropyl alcohol (IPA) were added to the mixture.

Table 2: Result of primary trials

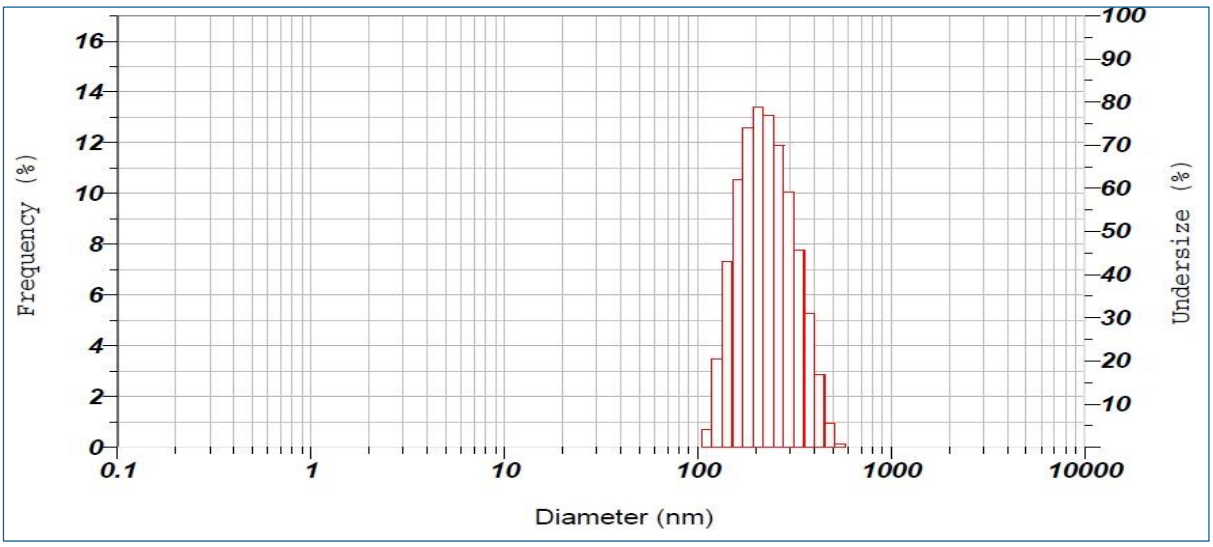
Oil (2:1)	Smix (3:2)	Total amount of Water consumed (ml)	Remark
0.33:0.17	4.44:2.22(40%)	4.4	Milky White Solution
0.33:0.17	5.55:2.77(50%)	5.3	Clear
0.33:0.17	6.66:3.33(60%)	6.1	Clear

Evaluation parameter of Microemulsion:

Table 3: Result of evaluation parameters

Sr. No.	Parameters	Value
1	Dilution Test	O/W
2	Dye solubility Test	O/W
3	Drug Precipitation Assessment	Not found
4	Globule size average	200 nm
5	Percentage Transmittance	99-99.99%
6	Electric Conductivity (1/sec)	17.32
7	Measurement of pH	5.8-6
8	Zeta potential	19.24
9	PDI	0.064
10	Microbial Bio-burden	Bacteria - 136 cfu/gm (Limit: 1000 cfu/gm) Fungus - 13 cfu/gm (Limit : 100 cfu/gm)
11	Microbial Limit test	*Escherichia coli* - Absent in 1 gm sample *Salmonella & Shigella* - Absent in 1 gm sample *Pseudomonas aeruginosa* - Absent in 1 gm sample *Staphylococcus aureus* - Absent in 1 gm sample
12	FTIR	No modification
13	Viscosity	691 cps

Figure 3: Globule size determination



FTIR Study:

Figure 4: Kumkumadi Oil

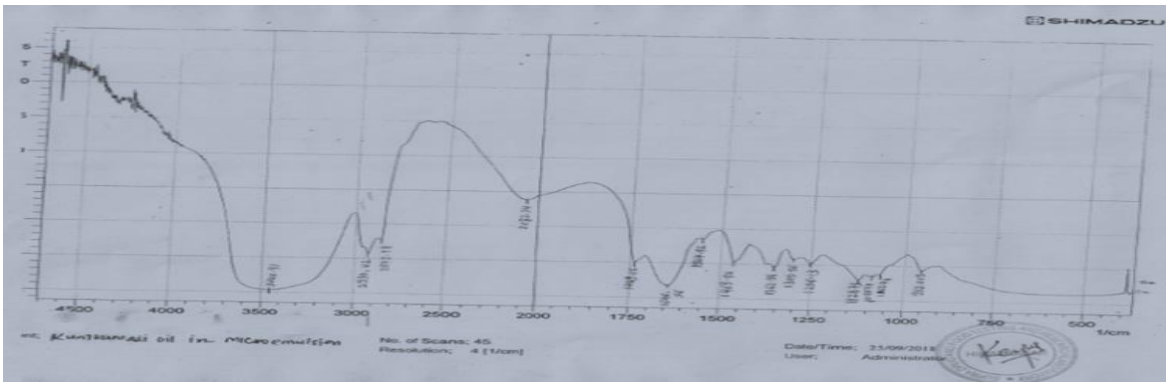
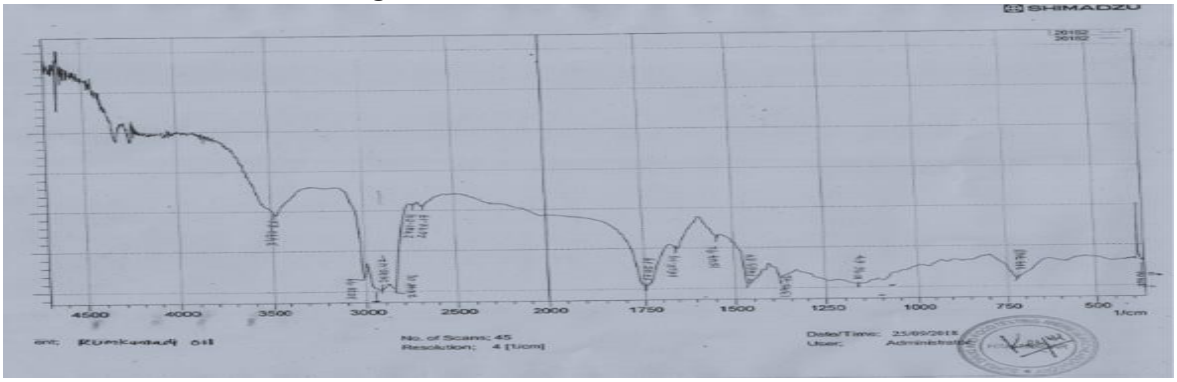


Figure 5: Kumkumadi Oil Microemulsion



Optimization of microemulsion:

Table 4: Result of organoleptic properties

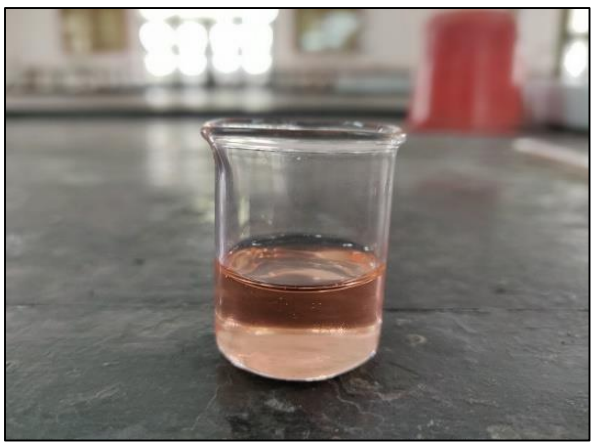
Sr. No.	Parameters	Inference
1	Appearance	Transparent
2	Effect	No skin irritation
3	Odour	characteristic
4	Texture	Thin

Formula for final optimized batch:

Table 5: Final formulation of optimized batch

Excipients	Concentration (v/v)
Kumkumadi oil	2%
Turmerone	1%
PEG 200	30%
IPA	20%
Propyl Paraben	0.2%
BHT	0.2%
Colour	Q.S
Fragrance	Q.S
Water	47%

Figure 6: Microemulsion of Kumkumadi oil



Conclusion

The in vitro study's findings indicate that the produced microemulsion is clear and has smaller globule sizes (200 nm), which may improve turmerone and Kumkumadi oil penetration into the skin. Accelerated stability evaluation of the prepared microemulsion revealed its stability. Therefore, microemulsion may be a useful strategy to enhance skin fairness and penetration.

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