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FORMULATION AND EVALUATION OF HERBAL NANOEMULGEL OF TERMINALIA CHEBULA

[1]Mr. Chaudhari Sagar Rajendra ,[2]Dr. Mrs. Samiksha Prashant Warke
[3] Ms.Rajashri.V.Patil,[4]Dr.P.D.Warke
[1]Research student,[2]Associate Professor,[3]Assistant Professor,[4]Principal
Department of Pharmaceutics,
KYDSCT's College of Pharmacy, Sakegaon (Bhusawal) Dist. Jalgaon, Maharashtra, India.

Abstarct :-

The aim of this study is to formulate and evaluate Terminalia Chebula nanoemulgel followed by its incorporation into topical gel.The objectives of present study are,Formulation and characterization of Nanoemulsion, Formulation, Formulation and evaluation of nanoemulgel. Terminalia chebula may grow in a variety of soils like clayey or shady, in areas with 100 to 150 cm annual rainfall and 0-17 °C temperature, up to 2000 m height from the sea level. It is about 25 to 30 m in height; leaves are 10 to 30 cm in length and have toothed edges. The flowers are white or yellow in colour, and possess a strong smell. The fruits of Terminalia chebula are green in colour, they become yellowish brown on ripening. Terminalia chebula is useful in treatment of obesity as it detoxifies the colon and relieves digestive problems.Formulation development involves Solubility studies Screening of oil, surfactant and co surfactant, Construction of pseudo ternary phase diagram,Preparation of various batches of formulation from pseudo ternary phase diagram Characterization of optimized nanoemulsion formulation involves Particle size analysis,Zeta potential,Polydispersity index,pH and viscosity,Thermodynamic stability,% Drug Content.Characterization of optimized nanoemulgel involves Appearance,pH,Viscosity,Drug content,Spreadability,In vitro drug diffusion,Antimicrobial study.Eucalyptus oil,Tween 80,Propylene glycol, Triethanolamine, Methanol, Carbopol 934,Methyl paraben, Propyl paraben it is used as raw material for experimental work.

Keywords :- Terminalia Chebula,inflammation,Nanoemulgel

Introduction :-

Acne is caused by the effects of hormones on the pilosebaceous unit, consisting of a hair follicle, sebaceous gland, and a hair. Propionibacterium acnes, causes destruction of the lining of the follicle. This process allows follicular material to enter the dermis, causing an inflammatory response.Skin consist of epidermis,dermis and subcutaneous layer. Terminalia chebula is used as herbal medicine in Ayurveda, Unani, Siddha and Homeopathy systems of medicine. Terminalia chebula is widely used for its broad spectrum activity. Terminalia chebula, a member of family Combretaceae.

Phytochemical composition of T.chebula [16,17]

Terminalia chebula fruits are widely known for their high content of phenolic compounds, which include tannins, flavonoids, and phenolic acid. Terminalia chebula is the rich source of tannins and has major compounds of tannins such as chebulic acid, corilagin, gallic acid, chebulagic acid, ellagic acid, etc.

Terminalia chebula contains 33% of hydrolysable tannins, varies from 20-50% due to geographical variation as reported by forestry research in India. Recently, researchers have discovered 14 new compounds of hydrolysable tannins.

Terminalia chebula consists of nutrients like protein amino acids minerals and Vitamin C. It also consists of fructose, chebumeinin, succinic acid, casuarinin, pentagalloyl glucose, resin, glycoside, triterpenoids, coumarin conjugate with gallic acid which is called as chebulin.

Emulgel :-

Emulgel is prepared both in oil- in- water and water- in-oil type emulsion mixed with gel. Oil- in- water type is used for lipophilic drugs and water- in- oil type is used for hydrophobic drugs' delivery. The emulgel have many advantages like thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, bio-friendly, pleasing appearance, transparent and cosmetically acceptable, which also have a good skin penetration and long shelf- life. But the gels show some limitations as hydrophobic drug delivery. This limitation is overcoming by emulgel. By the use of gelling agent classical emulsion can be converted in to emulgel.

2. Experimental

1. Procurement of drug sample

The powdered drug sample was purchased from MPREX Helthcare Pvt Ltd, Pune

2. Characterization of Terminalia chebula

2.1. Organoleptic properties

About 500 mg of the drugs powders was evenly spread on a petriplate with the help of a spatula and observed for appearance, colour, and odour and taste by manually.

2.2. Ash value of powdered drug

1. Total Ash

3 gm of drug was weighed and incinerated in a China dish at a temperature not exceeding 450oC until free from carbon, cooled and weighed, until a constant weight was obtained for three successive readings. Percentage of ash was calculated with reference to air dried drug.

Total Ash = (Wt. of ash / Wt. of drug)*100

2. Acid-Insoluble Ash

The total ash was obtained by boiling for 5 min with 25 ml of dilute hydrochloric acid; the insoluble matter was collected in a Gooch crucible, the insoluble matter was washed with hot water and ignited to constant weight. The percentage of acid insoluble ash with reference to the air dried drug was calculated.

Acid insoluble Ash =100*(Initial wt of ash – Final wt of ash)/ Initial wt of ash.

2.3 Spectroscopic characteristics:

2.3.1 Infrared spectroscopy of Terminalia chebula

FTIR absorption spectrum of Terminalia chebula was recorded by potassium bromide dispersion technique in which dry samples and potassium bromide were placed in sample holder and infrared spectrum was recorded using FTIR Spectrophotometer.

2.3.2 UV – Visible spectrophotometry [64]

a) Determination of λ_{max} of Terminalia chebula:

Accurately weighed quantity (100 mg) of terminalia chebula was dissolved in 100 ml of water placed in100 ml volumetric flask , the solution was sonicated and the volume was made with water. This stock solution (1000 µg/ml) was further diluted to get concentration of 50 µg/ ml. The solution was scanned in the range of 200 and 400 nm using water as a blank and λmax was reported. The same procedure was carried out to determine the λmax of terminalia chebula in phosphate buffer (pH 7.4) and methanol.

b) Calibration curve of Terminalia chebula:

The stock solution of Terminalia chebula (1000 µg/ml) in water was prepared as mentioned above. This stock solution was further diluted to get concentration of 50,100,150,200,250 and 300µg/mL. The stock solutions and dilutions of terminalia chebula were also prepared in phosphate buffer pH 7.4 and methanol. The UV absorbance of these solutions were recorded.

2.4. Solubility Study

The solubility of Terminalia chebula was determined in various oils, surfactants and co-surfactants. An excess amount of Terminalia chebula was added in 5 ml of each of the selected oils, surfactants and co-surfactants taken in 5-ml stoppered vials separately, and mixed by vortexing. The vials were then kept at 37±1 °C in an orbital shaker for 72 hrs to reach equilibrium. The equilibrated samples were removed from shaker and centrifuged at 5000 rpm for 15 min. The supernatants were filtered through Whatman filter paper. The absorbance of these solutions were noted using UV- spectrophotometer and the concentration of Terminalia chebula was calculated in respective oils, surfactants and co-surfactants.

2.5. Preliminary Screening of oil, surfactant and cosurfactant

The oils, surfactant and co surfactant are further screened for their miscibility in each other for that 1 ml of oil is added to 1 ml of surfactant and co surfactant and observed for miscibility.The resulting mixtures were observed visually for the relative turbidity.

2.6. Construction of Pseudo Ternary Phase Diagram

Various pseudo-ternary phase diagrams were constructed by titrating mixtures of oil and Smix (mixture of surfactant and co-solvent) with water at room temperature. For this, the selected surfactant & co-solvent were blended together in different ratios like, 1:1, 2:1, 3:1 and 4:1. Every mixture was mixed with selected oil phase to give weight ratio of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9 (w/w) by using magnetic stirrer. These mixtures were titrated slowly with distilled water taking care for proper stirring of liquid phases to achieve equilibrium. After being equilibrated, the mixtures were assessed visually for transparency and further titrated over the entire phase region. The pseudo ternary phase diagram was constructed for each system by plotting concentration of oil, surfactant and co-solvent on different ordinates. The influence of various co-solvents and the influence of ratio of surfactant to co-solvent on one phase region in a pseudo-ternary phase diagram. Based on results of above studies and solubility of drug in a co-surfactant/co-solvent, a proper co-solvent/co-surfactant was selected for the further studies.

2.7.Selection of Formulation from Pseudo ternary Phase Diagram

From the results of above studies, pseudo ternary phase diagrams constructed using Eucalyptus oil as oil phase, Tween 80 as surfactant and Propylene Glycol as co-solvent was selected for further study. Various compositions of oil and Smix were selected for nanoemulsion formulations on the basis of following criteria:

- ☐ The oil concentration should be enough to solubilise the drug equivalent effective concentration considering the solubility of the drug in the selected oil (mg/ml).
- ☐ The optimum quantity of Smix should be used so as to efficiently emulsify the selected quantity of oil.
- ☐ For a particular percentage of oil selected, that formula was taken from the phase diagram, which used minimum concentration of Smix for the formation of nanoemulsion

2.8. Preparation of Nanoemulsion

The Terminalia chebula nanoemulsions were prepared through the high-energy emulsification technique by uniformly mixing optimized oil and Smix phases with a help of mechanical stirrer, using the optimum ratio of components obtained from the phase diagrams. After uniform miscibility of the oil and Smix phases, purified water was added dropwise as an aqueous phase and stirred continuously to form coarse emulsion. Further, the coarse emulsion is converted into desired nanosized emulsion droplets with the help of a sonicator probe. The

sonicator probe creates high sonication sound waves of more than 20 KHz. The high intensity of sound waves breaks the coarse emulsion into fine droplets of nanosize (5-500nm). Various kinds of probes with various dimensions are available for the size reduction up to desirable limits. Along with the kinds of the probe, the input power and time for sonication decide the size of the droplet. Various batches of nanoemulsions were prepared by (table 8.1)varying the quantity of oil, surfactant and cosurfactant to check its effect on particle size, PDI, zeta potential and stability of nanoemulsion.These thermodynamically stable formulations of NE were then characterized for droplet size, polydispersity index (PDI), zeta potential, and percentage of contained Terminalia chebula.

. **Table 2.1. Different batches of nanoemulsions**

Batch No.	Oil (%)	S_{mix} (%)	Water (%)
F1	10	10	80
F2	10	15	75
F3	10	20	70
F4	12.5	12.5	75
F5	12.5	18.75	68.75
F6	12.5	25	62.5
F7	15	15	70
F8	15	22.5	62.5
F9	15	30	55

2.9.Characterization of nanoemulsion

2.9.1. Droplet Size, PDI Analysis and Zeta Potential Determination

The droplet size distributions and PDIs of the optimized NE systems were investigated in triplicate by dynamic light scattering using a Particle Size Analyzer (Horiba). Each sample was diluted with distilled water at a ratio of 1:100 before the analysis. The zeta potentials of the optimized NE systems were assessed through laser Doppleranemometry using a Zetasizer (Horiba). Each sample (100 µl)was diluted with distilled water at a ratio of 1:100 before the analysis.

2.9.2. pH and viscosity determination

The digital pH meter was used for the determination of the pH of nanoemulsion. 2g of Nanoemulsion was weighed and dispersed in purified water (20 ml). The samples were repeated in the triplicate manner and mean were calculated

The viscosities of nanoemulsion samples were measured by using a Brookfield viscometer. The 2 number spindle was used in viscometer and dipped in nanoemulsion then rotated at 5, 10, 20, 50 and 100 rpm at room temperature .At every speed, readings were noted on viscometer.

2.9.3. Thermodynamic Stability Study

The Terminalia chebula NEs were subjected to centrifugation test. The NEs were monitored for any physical instabilities during stress testing (indicated by phase separations, drug precipitations, or color changes), to exclude those NEs from further investigation and characterization. The prepared formulations were centrifuged (REMI International, Mumbai, India) at 5000 rpm for 30 minute and observed for phase separation, creaming or cracking.

2.10 Preparation of nanoemulgel

Nanoemulgel containing the optimized NE systems were prepared using Carbopol 934 (0.5 to 2.5% w/w) for topical administration. Accurately weighed amounts of Carbopol were dispersed in distilled water and keep overnight to achieve uniform swelling. Propylene glycol as humectant was incorporated into the dispersion system in order to provide a smooth and soothing effect. Triethanolamine was added into the dispersion system drop-by-drop to neutralize the pH to 6.5, resulting in instant conversion to a hydrogel system. The different batches of gels were prepared (Table 2.2).

Table 2.2 Different batches of gel formulations

Formula	A1	A2	A3	A4	A5
Carbopol 934(%)	0.5	1	1.5	2	2.5
Propylene glycol	5	5	5	5	5
Triethanolamine	q.s	q.s.	q.s,	q.s.	q.s.
Methyl paraben	0.2	0.2	0.2	0.2	0.2
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Distilled water	q.s.	q.s.	q.s.	q.s.	q.s.

Finally, the optimized NE systems were homogeneously incorporated into the gel in 1:1 ratio to obtain Terminalia chebula nanoemulgel. The pH, rheology, spreadability, extrudability, and drug content uniformity of the various Terminalia chebula Nanoemulgel were evaluated as follows:

2.11. Characterization of nanoemulgel

2.11.1. Drug Content

The weighed samples were dissolved in methanol and stirred by vortex mixer. The solutions were filtered, using Whatman filter paper and were estimated by UV visible spectroscopy method.

2.11.2. pH

The pH was determined by using digital pH meter.0.5 g of Nanoemulgel was dissolved in the 50 mL of distilled water and stored at 25ºC.

2.11.3. Viscosity

The viscosities of the optimized Terminalia chebula Nanoemulgel systems were determined using Brookfield viscometer at room temperature

2.11.4. Spreadability study

It consists of wooden block, which was provided by a pulley at one end. By this method spreadability was measured on the basis of "slip" and "drag" characteristics of gels. To determine the spreadability of nanoemulgel, 1 g of gel is placed within circle of 1 cm diameter pre-marked on a glass slide, over which second slide is placed. A weight of 100 mg is allowed to rest on the upper glass plate for 5 min. The increase in diameter is observed due to nanostructured lipid carrier based gel, the spreading is noted. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from nanostructured lipid carrier based gel. It is calculated by using the formula.

S=ML/T

Where,

M = weight tied to upper slide

L = length of glass slides

T= time taken to separate the slides.

2.11.5. In Vitro diffusion study:

The study was performed using Franz diffusion cells by using dialysis membrane. I gm of Terminalia chebula nanoemulgel was placed in the donor compartment and the receptor compartment was filled with mixture of phosphate buffer (pH 7.4) maintained at 37°C and stirred by using magnetic stirrer bars (300 rpm). For in-vitro release studies, artificial dialysis membrane was soaked in the same buffer solution for 24 hr before mounting on the diffusion cells. Samples were removed after every hour up to 8 hours and sink condition was maintained by replacing same volume of liquid kept at same temperature. The samples were analyzed for the content of Terminalia chebula by UV-spectroscopy at Lambda max 274 nm.

2.12. Antibacterial activity

In- vitro determination of the antibacterial activity of Terminalia chebula gel and Terminalia chebula nanoemulgel in same concentration were measured by using the agar diffusion method (cup plate method). S. aureus and E. coli bacteria were used in the study. The culture media for antibacterial assay were nutrient agar media and MacConkey agar for S. aureus and E. coli respectively. Sterilized molten nutrient agar and MacConkey agar were poured into sterilized petri dishes separately and allowed to solidify. The plates were swabbed with the100 µL culture of the microorganisms. Uniform sized cups of 6 mm diameter were aseptically punched into the seeded agar medium using a sterilized well bore at equidistant position. The prepared gel samples were filled into the cylinder cup and incubated at 37°± 0.5°C for 48 h. The diameter (mm) of the zone of growth inhibition was measured as the diameter (mm). All the tests were carried out in triplicate (n=3).

3.Result And Discussion

3.1. Characterization of Terminalia chebula:

The characterization of drug was carried out by various physicochemical tests organoleptic properties, ash value determination, spectral analysis such as UV spectrum, IR spectrum and solubility analysis.

3.1.1. Organoleptic Properties:

1. Appearance: Amorphous powder.
2. Colour: Brown.
3. Odour: Odourless.
4. Taste: Astringent.

3.1.2 Ash value:

The total ash value and the percent acid insoluble ash value were found to be 4.3 % and 3.3 % respectively. The standard value reported is less than 5% for both total ash and percent acid insoluble ash.

Table 3.1 Ash value of Terminalia chebula.

Parameter	Standard values	Drug sample value
Total ash	NMT 5%	4.3%
Acid insoluble ash	NMT 5%	3.3%

3.1.3. Spectroscopic characteristics:

3.1.3.1. Infrared spectroscopy of Terminalia chebula

Major functional groups present in Terminalia chebula are amide, OH stretch, carboxylic stretch, aromatic stretch .IR spectrum of Terminalia chebula is shown in figure and the interpretation of IR spectrum is shown in table 3.2.

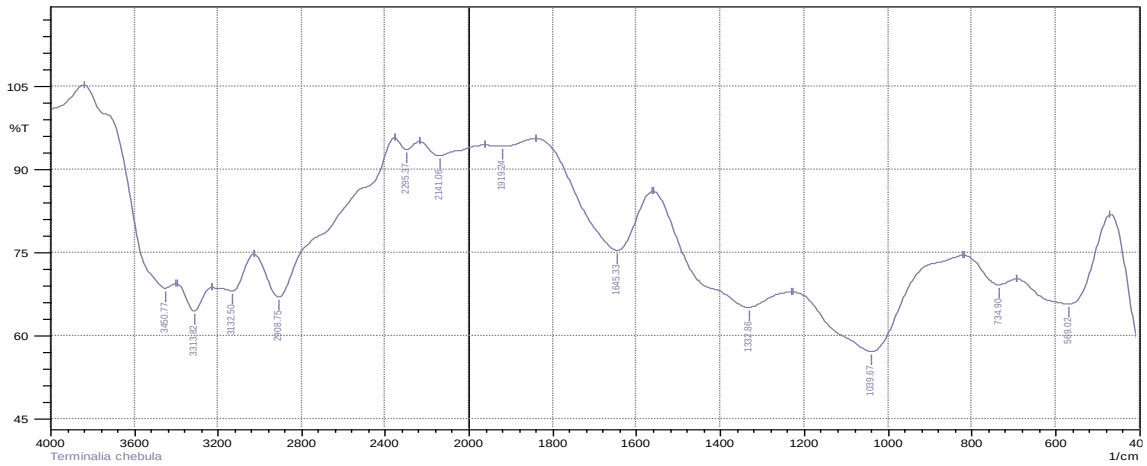

Fig. 3.1 IR spectrum of Terminalia chebula

Table 3.2. Characteristic ferquencies in IR spectrum of Terminalia chebula

Functional group	Wave number (cm^{-1})
OH	3313.82
CH	2908.75
C=O	1645.33
C=C	1322.86
-C-O	1039.67

The major peaks in the IR spectrum are identical to functional group of Terminalia chebula; the sample was confirmed as Terminalia chebula

3.1.3.2 UV – Visible spectrophotometry:

a) λmax value:

The wavelength of maximum absorbance (λ max) was found to be 274 nm which is same as reported.

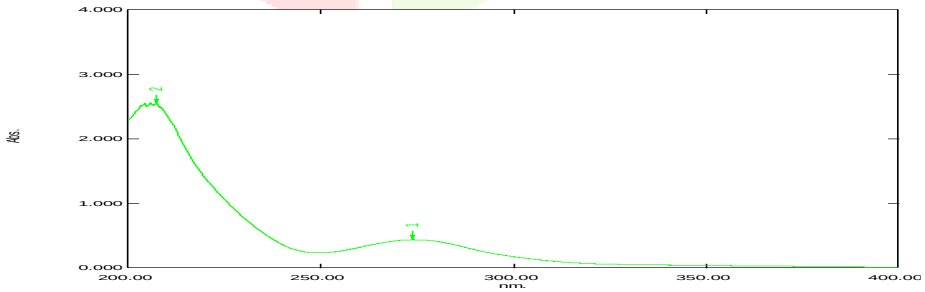

Fig. 3.2 U.V absorbance of Terminalia chebula in water

b) Calibration curves of Terminalia chebula :

The data for the calibration curve of drug in distilled water, methanol, phosphate buffer pH 7.4 is shown in Table 3.3 and 3.4 respectively. Calibration curves of Terminalia chebula in distilled water, methanol and phosphate buffer are shown in figure. Bear-Lambert law was followed in concentration range 50-250 µg/ml

Sr. No.	Concentration (µg/ml)	In Distilled Water	In Methanol	In Phosphate buffer pH 7.4
1.	50	0.2	0.245	0.213
2.	100	0.388	0.459	0.412
3.	150	0.562	0.675	0.581
4.	200	0.76	0.901	0.785
5.	250	0.95	1.12	0.98

Table 3.3 Data for calibration curve of Terminalia chebula in different solvents.

Media	Regression coefficient	R^2
Distilled water	y = 0.0038x + 0.005	0.9997
Methanol	y = 0.0044x + 0.0107	0.9997
Phosphate buffer pH 7.4	y = 0.0039x + 0.0105	0.9992

Table 3.4 Linear regression analysis data

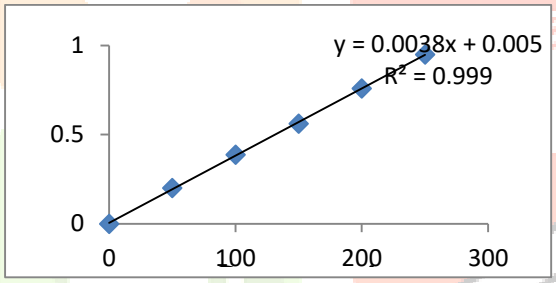

Fig. 3.3 Calibration curve of Terminalia chebula in Distilled Water

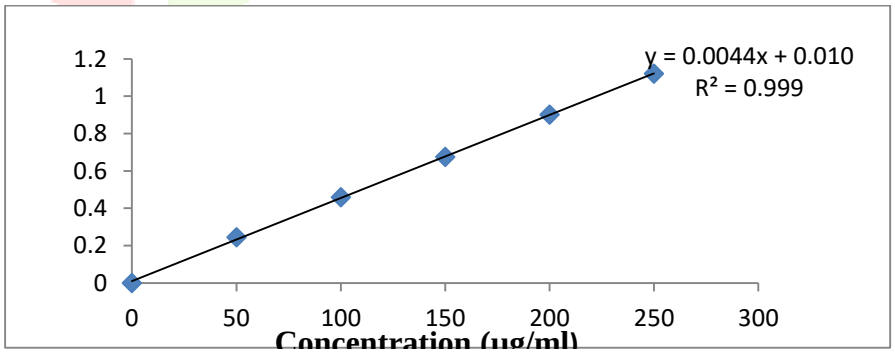

Fig. 3.4 Calibration curve of Terminalia chebula in methanol

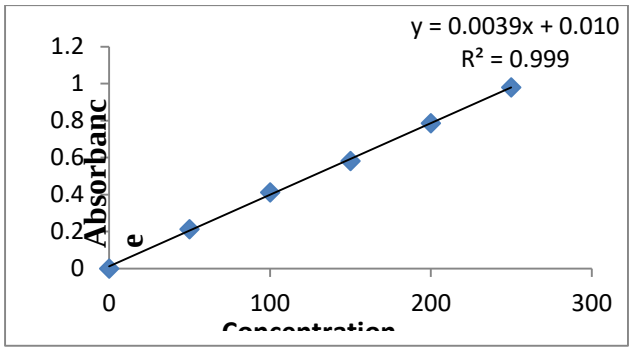

Fig. 3.5 Calibration curve of Terminalia chebula in Phosphate buffer pH 7.4

3.2. Solubility Study

The most important criterion for the screening of components is the solubility of poorly soluble drug in oil. The higher solubility of the drug in the oil phase is important for the nanoemulsion to maintain the drug in the solubilised form. Different type of oils were used for the design of nanoemulsions. Since the drug showed highest solubility in eucalyptus oil, it was selected as the oil phase for the development of nanoemulsion. Surfactant and cosurfactant having higher solubility screened for misciblity in eucalyptus oil. The solubility of drug in water was found to be 36.86 mg/ml.

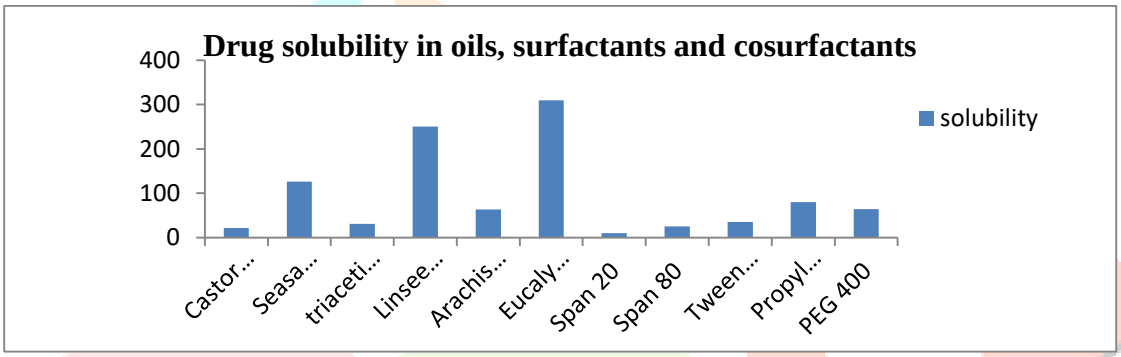

Fig. 3.6 Solubility studies for screening of suitable oil, surfactant & cosurfactant.

3.3. Preliminary Screening of oil, surfactant and cosurfactant

The surfactant Tween 80 and cosurfactant Propylene glycol were miscible with eucalyptus oil when taken in 1:1 ratio. Therefore Tween 80 was selected as surfactant and Propylene glycol was selected as cosurfactant.

9.4. Construction of Pseudo Ternary Phase Diagram

Pseudo ternary phase diagrams were constructed with the help of ternaryplot.com for each Smix ratio. On the basis of solubility studies, eucalyptus oil was used as the oil phase for the development of nanoemulsions. Tween 80, Propylene glycol and distilled water were used as surfactant, cosurfactant and aqueous phase respectively.

It was found that as the ratio of surfactant in Smix was increased the area of nanoemulsion region changed slightly. In the ternary phase diagrams, the existence of small or large nanoemulsion region depends on the capability of the particular Smix to solubilise the oil phase.

In the Smix ratio 1:1 had a low nanoemulsion area and at ratio of 2:1 produced more nanoemulsion area than 1:1. Thus, it was observed that increasing the proportion of Tween 80 in the Smix increases the nanoemulsion region. The nanoemulsion region was found to increase till Smix ratio of 4:1 and thereafter a decrease in area was observed. When Smix ratio 5:1 was studied, nanoemulsion region was not increased as compared to Smix 4:1 which might be due to insufficient amount of cosurfactant for emulsification and required HLB value was not obtained. The Smix ratio of 4:1 was selected as it provided the widest nanoemulsion region.

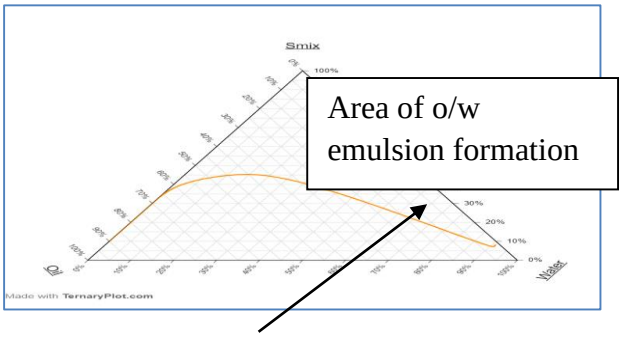

Fig. 3.7. Ternary phase diagram of T80 and PG (1:1)

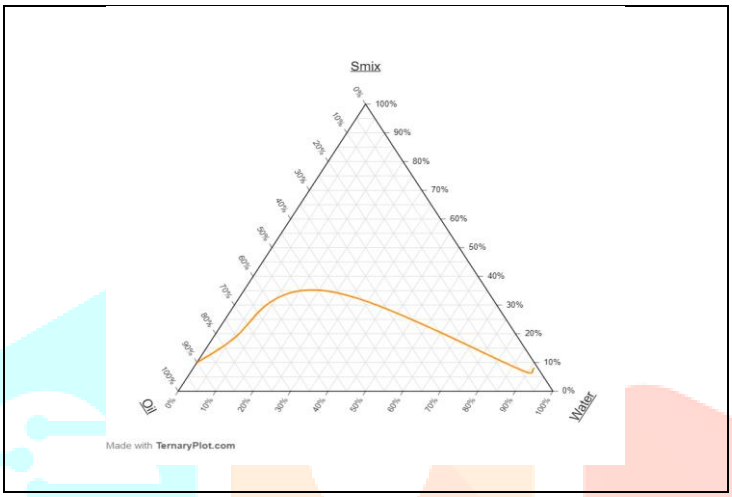

Fig. 3.8. Ternary phase diagram of T80 and PG (2:1)

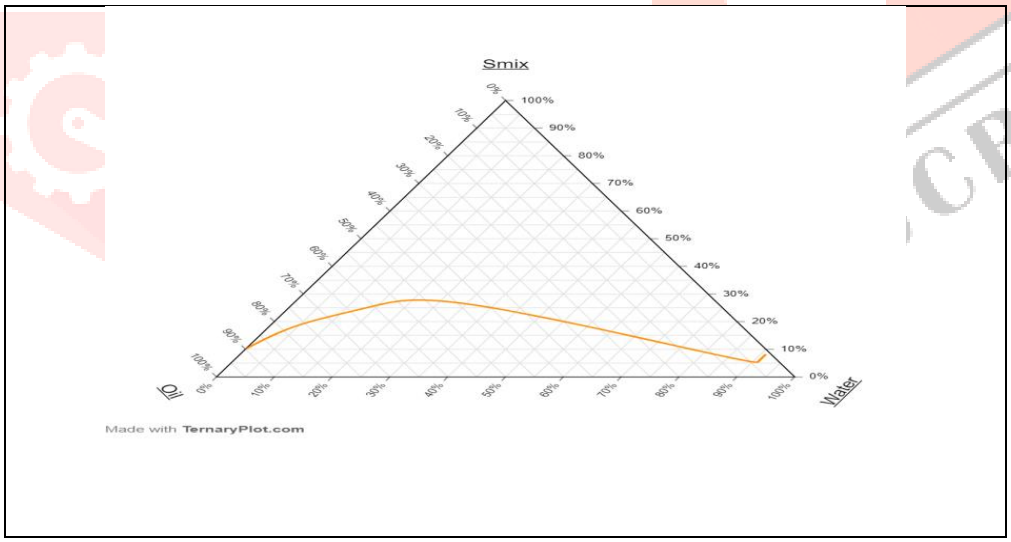

Fig.3.9 Ternary phase diagram of T80 and PG (3:1)

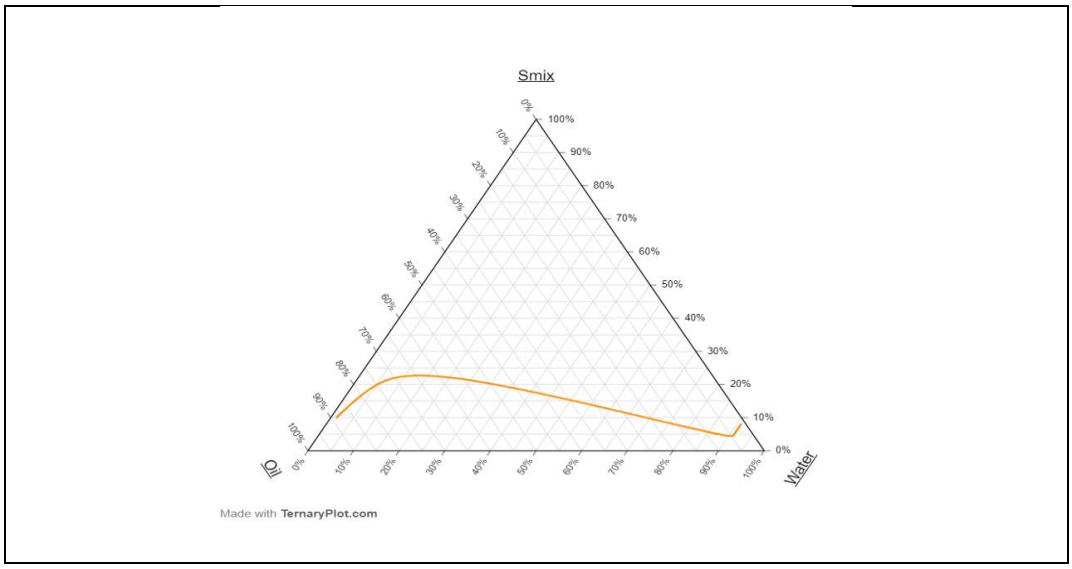

Fig. 3.10 Ternary phase diagram of T80 and PG (4:1)

3.5. Selection of formulation from Pseudo Ternary Phase diagrams:

From the pseudo ternary phase diagrams, different ratios of formulation were prepared. For each percentage of oil selected, only those formulation were taken from the phase diagram which needed minimum concentration of Smix. There was no sign of change in the phase behavior and microemulsion area of phase diagram. Terminalia chebula (2%) was incorporated in the formulations, which indicated that the formulation and stability of microemulsions consisting of nonionic components, was not affected by ionic strength.

3.6. Formulation of Nanoemulsion

With the help of ternary phase diagram different batches of nanoemulsions were formulated by using eucalyptus oil as oil phase and tween 80 and propylene glycol as surfactant and cosurfactant respectively. Varying the concentration of oil phase and Smix and their effect on particle size, PDI and zeta potential were recorded.

3.7. Characterization of nanoemulsion formulation

Table 3.5.Characterization of nanoemulsion formulation

Batch. No.	Oil (%)	S_{mix} (%)	Water (%)	Particle size (nm)	PDI	Zeta Potential (mV)
F1	10	10	80	65.4±2.5	0.377±0.012	-17±0.21
F2	10	15	75	50.4±2.6	0.399±0.063	-19±0.17
F3	10	20	70	29.6±1.23	0.220±0.026	-23±0.12
F4	12.5	12.5	75	70.3±5.12	0.412±0.035	-18.5±0.25
F5	12.5	18.75	68.75	55.8±2.23	0.322±0.040	-20±0.18
F6	12.5	25	62.5	30.6±3.21	0.388±0.054	-24±0.24
F7	15	15	70	65.8±4.12	0.342±0.081	-18.2±0.31
F8	15	22.5	62.5	57.6±3.56	0.413±0.062	-22±0.26
F9	15	30	55	32.4±2.6	0.431±0.034	-23.5±0.21

(All values are expressed as mean ± S.D)

3.7.1. Effect of oil and Smix concentration on

1. Particle size

Droplet size is a key parameter for assessing the nanoemulsions. It was found that the increased concentration of Smix decreased the particle size of nanoemulsion. There were no significant effect of oil and water concentration seen on particle size.

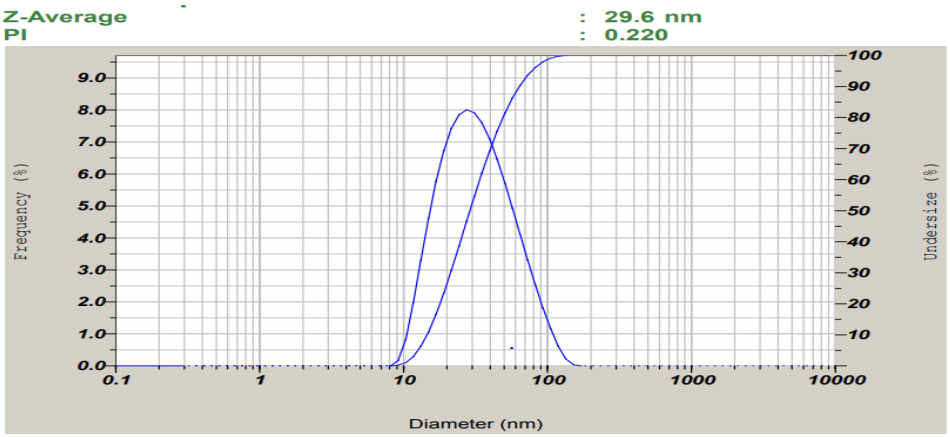

Fig. 3.11 Particle size analysis graph of optimized batch F3

2. PDI and Zeta potential

The PDI is a ratio that gives information about the homogeneity of the particle size distribution in a nanoemulsion system. It was found that the Increased the concentration of Smix decreased the PDI of nanoemulsions at certain level then further increased in concentration of Smix, PDI increased, where as increased the oil concentration, increased the PDI but less changes as compare to Smix.

The optimized nanoemulsion was in the desired nano size range 29.6 nm with low PDI and zeta potential value -23±0.12 to prevent aggregation. The stability of nanoemulsion significantly depends on the value of zeta potential. It showed that increased concentration of surfactant decreased the zeta potential.

3.7. Percent Drug Content

The results of percent drug content are expressed in Table. All the formulations showed percent drug content in the range of 98 % to 100 %. Since the drug content of dispersed formulation is not decreased below the permissible limit. This indicates that the components selected for the prepration of nanoemulsion were in optimum concentration so as to keep drug in dissolved state after dilution in water.

3.8. Thermodynamic Stability Study

The results of thermodynamic stability study showed that all batches of nanoemulsion were showing no change in the integrity of nanoemulsions So all the batches were found thermodynamically stable.

3.9. Formulation of Terminalia chebula nanoemulgel

In order to provide physical stability to nanoemulsion formulation and ease of application, optimized nanoemulsion formulation (B3) was fabricate into gel using carbopol 934. Terminalia chebula nanoemulgel (1% carbopol) showed good spreadability and extrudability as compared to higher carbopol concentration (1.5 to 2.5%). Hence, 1% w/w carbopol concentration was selected.

3.10. Characterization of nanoemulgel:

3.10.1 Appearance, clarity

The nanoemulgel formulation was brownish and translucent

3.10.2. Drug content and pH

The Terminalia chebula nanoemulgel formulations with different concentration of carbopol 934 were provided a wide range of consistency. It was found that drug content of all the formulations (A1 to A5) were nearly same in the range between 97.12 ± 0.55% to 100.14 ± 0.44%. The pH values of all nanoemulgels were found nearly to neutral pH range of 6.5 ± 0.004 to 6.75 ± 0.006 which indicated the suitability of topical drug delivery without irritation

Table 3.6 pH and drug content value of different formulation batches.

Formulation	pH	% Drug content
A1	6.67±0.045	98.43±0.45
A2	6.56±0.056	97.12±0.55
A3	6.58±0.075	99.91±0.72
A4	6.70±0.065	100.14±0.44

(All values are expressed as mean ± S.D.)

3.10.3. Viscosity

The viscosity of gel is consider to be the most critical factor for topical application. The viscosity of gel offers slower dissolution and diffusion of drug and hence, prolonged duration of action is achieved. As the shear rates of the gel sample were increased, there was decrease in viscosity of gel.The viscosity of nanoemulgel was found to be less as compared to plain gel due to incorporation of nanoemulsion.

Table 3.7 Viscosity of plain gel formulation

RPM	Viscosity in cp	% Torque
5	22000	7.02
10	16000	8.25
20	8000	9.87
50	3500	12.12
100	2200	14.56

Table 3.8 Viscosity of nanoemulgel formulation (A2)

RPM	Viscosity in cp	% Torque
5	16000	6.66
10	9100	7.92
20	4500	8.16
50	2400	11.12
100	1650	12.65

3.11. Spreadability

Spreadability is a characteristic of the semisolid formulations and it is responsible for correct dosage transfer to the target site, ease of application on the topical area. The efficacy of local or topical therapy depends on the spreading properties of the formulation on the application surface. Table 3.9 represents the spreadability of gel. The Spreadability of nanoemulgel was found to br more as compared to plain gel formulation

Table 3.9 Spreadability study

Sr.no	S1	S2	S3	Spreadability (gcm/sec)
Nanoemulgel	10.12	10.50	10.62	10.41±0.26
Plain Gel	8.75	7.70	8.75	8.4±0.49

(All values are expressed as mean ± S.D.)

3.12. In vitro drug diffusion study

The in vitro release profile of Terminalia chebula from gel and nanoemulgel formulation is shown in Table 3.10 and in fig. 3.11. The in vitro release of Terminalia chebula from the nanoemulgel follows initial burst effect followed by gradual release. The nanoemulgel formulation shows 82.63% release,
whereas the gel releases up to 48.93% of Terminalia chebula within 8 hrs, which shows that nanoemulgel has better release.

Table 3.10 Drug release through dialysis membrane

Time (hrs)	% drug release (gel)	% drug release (nanoemulgel)
0	0	0
1	22.599±0.054	29.437±1.20
2	27.056±0.176	36.539±0.580
3	31.797±0.578	43.321±0.761
4	36.333±0.403	52.989±0.707
5	40.593±0.380	67.388±1.025
6	43.505±0.485	78.644±0.1677
7	47.333±0.865	82.109±1.58
8	48.935±0.218	82.636±0.706

(All values are expressed as mean ± S.D.)

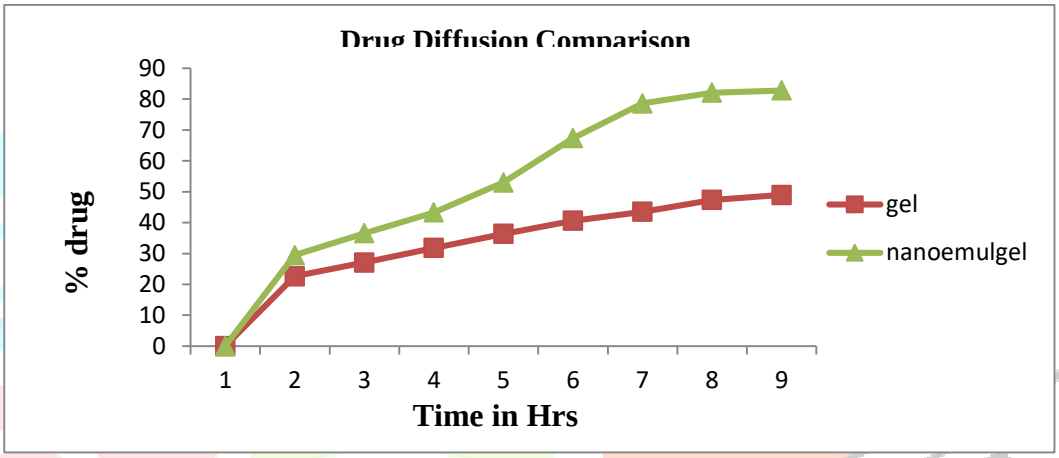

Fig 3.12 Drug release comparison between gel and emulgel.

3.13. Antimicrobial study

The Terminalia chebula nanoemulgel showed significant antibacterial effect on microbes S. aureus and E. coli having the zone of growth inhibition 15.5 ± 0.25 mm and 18.6 ± 0.23 mm respectively. The zone of growth inhibition of S. aureus and E. coli by Terminalia chebula gels were found 5.7 ± 0.18 mm and 6.4 ± 0.21 mm respectively.

The result indicate that nanoemulgel formulation has better antimicrobial effect as compared to gel due to good penetration and better release.

Table 3.12 Zone of inhibition shown by Terminalia chebula gel and nanoemulgel

Sr. No.	Formulation	Zone of inhibition (mm)	
		S. aureus	E. coli
1.	T. chebula gel	5.7 ± 0.18	6.4 ± 0.21
2.	T. chebula nanoemulgel	15.5 ± 0.25	18.6 ± 0.23

(All values are expressed as mean ± S.D.)

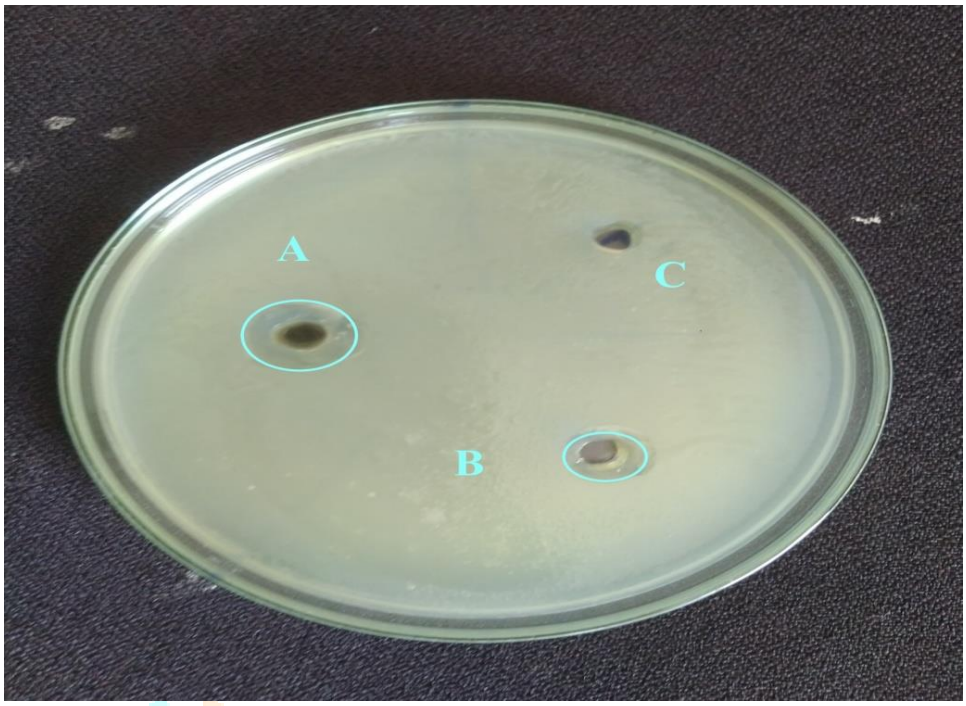

Fig. 3.13 Zone of inhibition shown by A. Nanoemulgel B. Gel C. control for S. aureus

Fig. 3.14 Zone of inhibition shown by A. Nanoemulgel, B. Gel, C. Control for E. coli

4. Conclusion :-

The percent drug release from nanoemulgel formulation was found to be more as compared to gel formulation. The Terminalia chebula nanoemulgel showed significant antibacterial effect of microbes S. aureus and E. coli having the zone of growth inhibition as compared to gel.This present study confirms that the nanoemulgel of Terminalia chebula could be a possible alternative to conventional topical formulation for the treatment of acne.

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