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Research Article

FORMULATION, DEVELOPMENT AND EVALUATION OF EUGENOL OIL NANOEMULSION GEL FOR TOPICAL DELIVERY

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ABSTRACT

The aim of the present work was to formulate and characterized the nanoemulsion based gel for poorly water soluble eugenol oil in order to overcome the side-effects associated with its oral delivery. Pseudo-ternary phase diagrams were constructed using titration method. Various components of nanoemulsion were selected on the basis of compatibility study, solubility study and emulsification ability. Nanoemulsion was formulated by ultra-sonication method and characterized for droplet size, poldispersity index, zeta potential, rheological study and in-vitro skin permeation study. The optimized nanoemulsion (FA6) is then converted into nanoemulsion gel using 1% carbapol 934. Drug loaded nanoemulsion gels were evaluated for rheology study, pH, swelling index, uniformity of drug content and permeation study. Transdermal permeation of eugenol oil from nanoemulsion gel was determined by using Franz diffusion cell across excised rat skin. Nanoemulsion gel containing 5% eugenol oil as oil, 30% tween 80, 15% propylene glycol as surfactant and co-surfactant respectively, 60% water and 1% carbapol 934 was concluded as optimized formulation. Formulated nanoemulsion gel was compared with conventional gel formulation for in-vitro permeability. Nanoemulsion gel showed three-fold higher cumulative amount of drug permeation and flux (38.66±0.20) than conventional gel formulation (13.18±0.27). Anti-microbial activity of nanoemulsion gel was done by cup and plate method which shows the high anti-microbial activity than conventional gel and plain drug. Release kinetic study done by using number of release kinetic models for nanoemulsion gel formulation. First order kinetic release model which fit best for the nanoemulsion gel formulation shows the higher linearity of plot was achieved (R^2 – 0.995). Nanoemulsion gel release profile could be best explained by higuchi models. Regression line achieved higher R^2 value (R^2 - 0.991). This indicates slow diffusion of nanoemulsion gel and follows non-fickian transport mechanism as indicated by the n value of 0.860 when fitted to Kors-peppas model. Hence, it can be concluded that nanoemulsion gel formulation will treat microbial growth more effectively than conventional gel formulation.

KEYWORD: *Eugenol oil, Nanoemulsion, Nanoemulsion gel, Anti-bacterial activity.*

INTRODUCTION

Acne is common dermatological diseases that affect the skins oil gland and hair follicle the small hole in your skin which connect to oil gland that make an oily substance called sebum. This is good medium for growth of propionibacterium acnes which will exacerbate the acne condition [1]. It develops the blackheads, whiteheads and pimple on body. The most affected area of the skin having the population of sebaceous follicle is the face; the upper part of chest and the back [2]. There are some topical and systemic drug therapies available for treatment of acne including antibiotics and antifungal topical formulation like gel, cream, lotion and some hormonal therapy [3].

Essential oils have an antibacterial activity, which is indicated by several reports. Examining against the propionibacterium acne microorganism involved in acne inflammation by Essential oils from medicinal plants which have been traditionally used as antibacterial agents [4]. Gram-negative organisms are believed to be slightly less sensitive to essential oils than Gram-positive bacteria. The readily available aroma therapeutic literature has reported over 90 commercial essential oils that may be used for treating dermatological conditions [5]. Essential oils are volatile natural mixtures extracted from different plant parts and are composed of terpenoid structures with broad activities. Essential oils show better beneficial effects than a chemically synthesized pure compound [6].

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Plant extracts from herbs and spices are rich in phenolics, of which some were proven to show anti-microbial activity [6]. Eugenol (C10H12O2) is a phenolic aromatic substance with a pleasant odor and taste. It is usually found in the form of a yellowish oily liquid. Eugenol is a hydroxyphenyl propene. Eugenol oils are naturally occurring in the several plants belonging to the Lamiaceae, Lauraceae, Myrtaceae, and Myristicaceae families. It is one of the major constituents of clove oil. It is largely used in both foods and cosmetics as a flavoring agent. Clove is an important medicinal plant widely used in folk medicine in several countries due to its wide range of pharmacological effects. In fact, clove oil is used to treat many diseases including acne, asthma, rheumatoid arthritis, scarring, warts, and various allergies; also used as analgesic, antispasmodic and general antiseptic in medical dental practice. Traditional medicine that eugenol exerts beneficial effects on human health mainly associated with antioxidant and anti-inflammatory activities claim by a large body of recent scientific evidence. Eugenol has also shown excellent antimicrobial activity in studies, being active against fungi and a wide range of gram-negative and gram-positive bacteria. The antimicrobial activity of essential oils (EOs) is general dependent on their chemical composition and the quantities of each active component. Clove essential oil contain major bioactive component eugenol which show the high antimicrobial activity [7, 8]. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders like acne the main goal of this delivery is intent of confining the pharmacological effect of the drug to the surface of the skin or within the skin [9].

Nanoemulsions is one of the growing technologies especially in food, cosmetic and pharmaceutical industries as a novel delivery system for drugs and lipophilic materials such as essential oils, flavors, colors, fatty acids etc. Nanoemulsions contain of fine oil-in-water dispersion, which having droplet size range in 100-600nm.Nanoemulsion shows great promise for the future of cosmetics, diagnostics, drug therapies and biotechnologies. Nanoemulsions are the colloidal particulate system in the submicron size range acting as carriers of drug molecules. These carriers are solid spheres and having amorphous and lipophilic surface with a negative charge. As a drug delivery system they improve therapeutic efficacy of the drug and minimize adverse effect and toxic reactions. It is thermodynamically unstable system which can be stabilizing by the presence of an emulsifying agent. The dispersed phase is also known as internal phase or the discontinuous phase while the outer phase is caller dispersion medium, external phase and continuous phase. The modification related the incorporation of nanoemulsions and gels it is term as nanoemulgels. With the gelling system, it's enhancing the viscosity of the aqueous for better administration topically and shows the better stability of nanoemulsion by reducing the surface and interfacial tension. They have a high patient acceptability since they possess the previously mentioned advantage of both nanoemulsions and gels. Therefore, they have been recently used as vehicles to deliver various drugs to skin [10].

The present work describes effective use of nanoemulsion gel for topical delivery of eugenol oil using nonirritating, pharmaceutically acceptable ingredients without using penetration enhancers. The objective of the research work was to investigate the potential of eugenol oil loaded nanoemulsion gel for topical delivery, this alternative route will help to achieve the fast effect and avoid the oral side effect of the drug.

MATERIAL AND METHODS

Material:

Eugenol oil, Surfactant Tween 80, Co-surfactant Propylene glycol, Gelling agent Carbapol 934 purchased from loba chemical's Mumbai. pH adjacent Triethanolamine, and Preservative Methyl paraben and Propyle paraben. All the chemicals and solvent used in this study were of analytical reagent grade. Double distilled Water was used for all the experiments throughout the study.

Method:

Preformulation study:

Compatibility study:

Fourier transforms infrared spectroscopy (FT-IR): The IR spectra of eugenol oil and excipients were recorded by shimadzu S 8400 FTIR spectrophotometer. Sample was prepared by KBr disc method and examed in the transmission mode. Spectrum was measured over frequency range of 4000-400 cm^{-1}. The peaks obtained in the spectra were then compared with the corresponding functional groups in structure of eugenol oil [11].

Differential Scanning Calorimetry: Thermogram of eugenol oil, eugenol oil and carbapol 394 and formulation was recorded on TA WS Thermal analysis (shimadzu). The samples were hermetically sealed in aluminum pans and heated at a constant rate of 10°c/min over temperature range of 40 to 300°c. purging nitrogen gas at flow rate of 50 ml/min which was maintain inert atmosphere [11].

Pseudo-ternary phase diagram study: The preliminary study was conducted in advance to obtain a nanoemulsion formulation with clear appearance (transparent), physical homogeneity and easy flowability using the aqueous titration method. Drug was selected as the oil phase. Tween 80 and Propylene glycol were selected as surfactant and co-surfactant as per their emulsification capability for the system. Distilled water was used as an aqueous phase for the construction of phase diagram for the determination of existence zone of nanoemulsion. Using aqueous titration method were constructed Pseudo ternary phase diagrams. To construct pseudo ternary phase diagrams for the oil phase was mix with surfactant:cosurfactant used for titrations are 1:0,1:1,1:2,1:3,1:4,2:1,3:1,4:1. The mixture was titrated with distilled water, drop wise using micro syringe until the onset of turbidity or phase separation the mixtures were stirred vigorously for a sufficient length of time for homogenization, and the end point was visually monitored against a dark background. From the end point, compositions of the titrated samples were calculated and plotted on the pseudo ternary phase diagrams were constructed by using chemix software [12].

Preparation of nanoemulsion formulation:

Different formulations of nanoemulsion were prepared by using the varying amount of emulsifier by sonication method. Oil-in-water nanoemulsion was formulated using eugenol oil, surfactant Tween 80, Co-surfactant Propylene glycol and water. Coarse emulsion was prepared by Adding the water to organic phase containing oil, surfactant and co-surfactant in different ratio using a magnetic stirrer at 400rpm.The coarse emulsion was then subjected to ultrasonic emulsification using a 50 kHz sonicator [13].

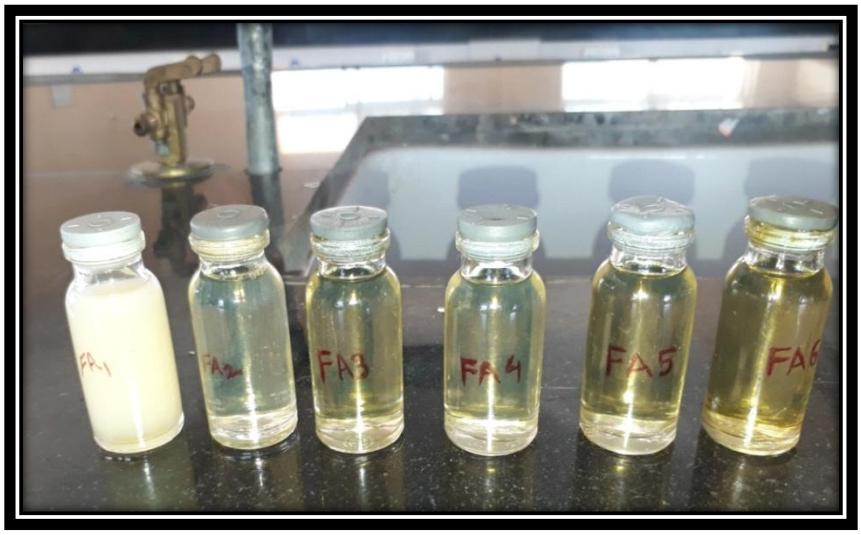

Fig. 1: Nanoemulsion formulations of eugenol oil

Preparation of nanoemulsion gel:

Carbapol gels were prepared by incorporating different concentration, 1%, 1.5% W/V of carbapol in 1% W/V triethanolamine in double distilled water. Weighted amount of carbapol was taken and dispersed over in distilled water for 2 hours till all the carbapol is socked. After socking add triethanolamine and Homogenization for 2hr at 600 rpm. After homogenization carbapol gel was subjected for two cycles of sonication for 15 min to expel out the entrapped air bubbles from the prepared gel [14]. Selected formulation of nanoemulsion FA6 was incorporated in prepared gel base with constant stirring to form a nanoemulsion gel.

Manufacturing formula for nanoemulsion formulations:

Table No. 1: Manufacturing formula for nanoemulsion formulations

Code	% Drug	% S mix Tween 80: Propylene glycol	% Water
F-A1	5	35% (1:1)	60
F-A2	5	40% (1:1)	55
F-A3	5	45% (1:1)	50
F-A4	5	35% (2:1)	60
F-A5	5	40% (2:1)	55
F-A6	5	45% (2:1)	60

Manufacturing formula for nanoemulsion gel:

Table No. 2: Manufacturing formula for gel formulation

Formulation	Carbapol 934 (%)	Triethanolamine (%)	Methyl paraben (%)	Propyl Paraben (%)
Nanoemulsion gel	1	1	0.2	0.2
Conventional gel	1	1	0.2	0.2

Characterization of nanoemulsion:

Physical appearance:

The prepared formulations for their color were inspected visually.

Polydispersity index (PDI), zeta potential and droplet size analysis:

Polydispersity, zeta potential and droplet size distribution of nanoemulsion are determined using zetasizer. Samples were diluted 200 times with purified water. Diluted samples were directly placed into the module and measurements were made in triplicate after 2-min stirring. Droplet size was calculated from the volume size distribution [15].

Rheology study:

The viscosity of nanoemulsion formulations was determined by using Brookfield viscometer using spindle number 61 at 100 rpm [16].

In-vitro permeation study:

The in vitro skin permeation study was carried out using a Franz diffusion cell. Nanoemulsion formulation were taken from each formulation (FA1-FA6) was applied the surface of rat skin which was placed between the donor and receptor compartment of the FD cell. Phosphate buffer pH 7.4 was used as dissolution media. The temperature of dissolution cell was maintained at 37^{o}c by circulating water jacket. This whole assembly was kept on a magnetic stirrer and the solution was

stirred continuously using a magnetic bead. Sample (2ml) was withdrawn at suitable time intervals and dilute up to 10 ml with the same solvent and replace with equal amounts of fresh dissolution media. Samples were analyzed spectrophotometrically at 281 nm and the cumulative drug permeation was calculated. Optimized formulation was selected to incorporate with a gelling agent for further study [17].

Characterization of gel:

pH determination:

pH determination of prepared formulations was done by using digital pH meter. The procedure was carried out by taking gel in 250 ml beaker immersing pH meter into the formulation and readings of pH meter were recorded. Same process repeated two more time with the same formulation. Similar procedure was used for the determination of the pH of all the prepared formulation thrice [18].

Rheology study of gel:

The viscosity of carbapol 934 of different formulations was measured by Brook-field type rotary viscometer with spindle 64 at 0 rpm.

Characterization of nanoemulsion gel:

Physical appearance:

The prepared nanoemulsion gel formulations inspected visually for their color, homogeneity, consistency, grittiness and phase separation.

pH determination:

Nanoemulsion gel is a topical formulation hence pH of the formulation should be suitable to the pH of the skin. It should not cause any skin irritation. pH determination of prepared formulations was done by using digital pH meter. The procedure was carried out by taking nanoemulsion gel 250 ml beaker immersing pH meter into the formulation and readings of pH meter were recorded. Same process was repeated two more time with the same formulation.

Rheology study:

The viscosity of nanoemulsion gel of different formulations was measure by Brook-field type rotary viscometer with spindle 63 at 10 rpm.

Swelling index:

To determine the swelling index of prepared nanoemulsion gel 1 gm of gel was taken on porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaoH. Then sample were removed from beakers at different time intervals and put it on dry place for some time after it reweighed. Swelling index was calculated as follows [19].

$$\text{Swelling index (SW) \%} = [(Wt\text{-}Wo) / Wo] \times 100$$

Where, (SW) % = Equilibrium percent swelling. Wt = Weight of swelling emulgel after time t. Wo = at zero time Original weight of emulgel.

Drug content determination:

1 gm of nanoemulsion gel was taken dissolve using 100ml of methanol. Sonicated for the period of 15 min filter it by whatman filter paper. A further dilution was made by using methanol prepared concentration with in Beer's range. The absorbance was measured at 281 nm by UV-Visible spectrophotometer and drug content was determined [19].

In-vitro permeation studies as compare to conventional gel formulation:

The in vitro skin permeation study were carried out using a Franz diffusion cell for prediction of drug transport across to skin and to compare with a conventional gel formulation for observing effective permeation of nanoemulsion gel.

Antibacterial activity:

Bactericidal activity of the nanoemulsion gel of eugenol oil, plain drug and surfactant was investigated using cup plate method studies. This study based on the diffusion of an antibiotic form a vertical cylinder or a cavity through the solidified agar layer of a Petri-dish or plate used for study. Growth of inoculated microorganism is inhibited in circle area zone around cylinder or a cavity containing a solution of the antibiotics.

Prepare the microbial inoculums with the required quantity or suspension of E.coli organism. Add prepared microbial suspension in the media and mix it and transfer into petri-dish. Prepare the nanoemulsion gel formulation of eugenol oil, plan drug and surfactant to be examined. Apply the nanoemulsion gel formulation, plan drug and surfactant to the surface of the solid media in sterile cylinder and in cavities prepared in agar plate. Leave the plate for one to four hours at room temperature. Incubate the plate at 20-30^{0}C for 18 hours [20].

Kinetic release study:

The release kinetics determines by linear regression analysis of the in-vitro release curves in four models: zero order (cumulative amount (%) of the released with time), first order (log cumulative amount (%) of drug released with time), higuchi (log cumulative amount (%) of drug released with square root of time) and korsemeyer-peppas (log cumulative amount (%) of drug released with log time) The mathematical model that best expressed the kinetic release profile selected based on the highest coefficient of determination (R^2) [21].

RESULT AND DISCUSSION

Compatibility studies:

Drug-drug and drug-excipients compatibility were studied by FTIR and DSC. Drugs and excipients do not show any interaction.

Pseudo-ternary phase diagram study:

Three different ratios of tween 80 and propylene glycol (1:1, 1:2 and 2:1) were prepared and plotted with pseudo ternary phase diagram, the ratio 2:1 give best or more region of as compare to the other two ratios, so 2:1 ratio of surfactant was selected for the preparation of the nanoemulsion gel.

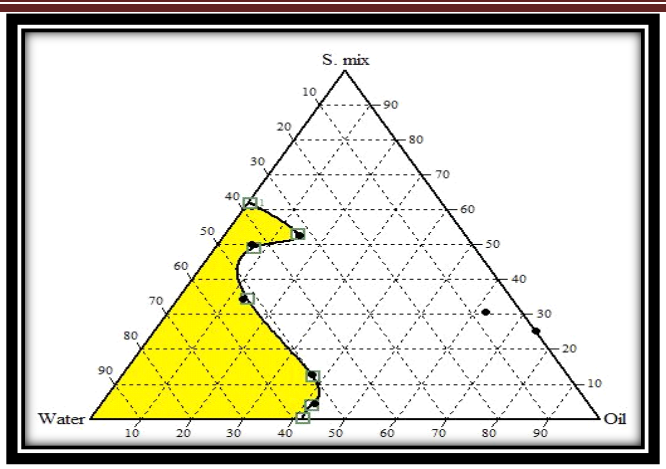

Fig. 2: Ternary phase diagram of 1:1 ratio

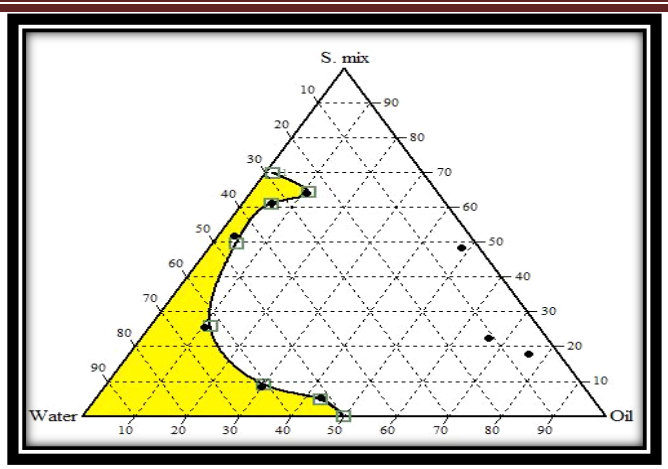

Fig. 3: Ternary phase diagram of 1:2 ratio

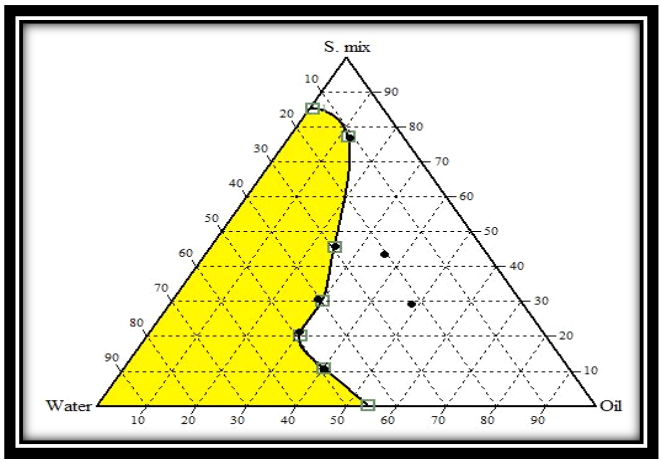

Fig. 4: Ternary phase diagram of 2:1 Ratio

Characterization of nanoemulsion:

Physical appearance:

Formulation was examed for appearance which shows transparent formulation. They do not show any turbidity.

Droplet size measurement, polydispersity index, zeta potential analysis and rheology study of the prepared nanoemulsion:

Polydispersity index 0.3 and below is consider being acceptable and indicating homogeneous population. Although the polydispersity values of all formulations is between 0.247±0.34 to 0.117±0.32. It indicating uniformity of droplet size within each formulation, the polydispersity of formulation FA6 was lowest (0.117±0.32).

A droplet size of all nanoemulsion formulations was found in range of 751±0.44 to 219±0.36 nm. FA6 formulation shows lower droplet size 219±0.36 nm.

Zeta potential for all the formulation is in the range of -18.5±0.22 to -20.4±0.37 (FA1 to FA6). Negative zeta potential shows the greater stability. Zeta potential of FA6 shows lowest value -20.4±0.37 hence it shows good stability.

Viscosity of nanoemulsion was determined by Brookfield viscometer using spindle number 61. It was observe that increase in concentration of surfactant and co-surfactant leads to increase the viscosity while lowering the amount of surfactant and co-surfactant leads to decrease the viscosity. From above results (table no: 3) it was found that FA6 is the best formulation among all formulations.

Table No 3: Characterization of nanoemulsion formulations

Sr. No.	Formulation Code	Droplet Size	Polydispersity Index	Zeta Potential	Viscosity (cp)	Flux (µg/cm²/hr)
1.	FA1	751±0.44	0.247±0.34	-18.5±0.22	42400±16	13.74±027
2.	FA2	476±0.39	0.182±0.49	-19.3±0.48	44200±10	65.35±0.32
3.	FA3	607±0.27	-1.754±0.27	-20.3±0.36	48800±25	36.70±0.10
4.	FA4	350±0.45	0.276±0.36	-19.9±0.47	67400±15	69.48±0.13
5.	FA5	515±0.48	0.321±0.47	-8.92±0.25	79500±30	52.80±0.42
6.	FA6	219±0.36	0.117±0.32	-20.4±0.37	72300±12	83.79±0.10
7.	Drug Solution					7.037±0.15

Values are expressed in mean ± SD, where n=3

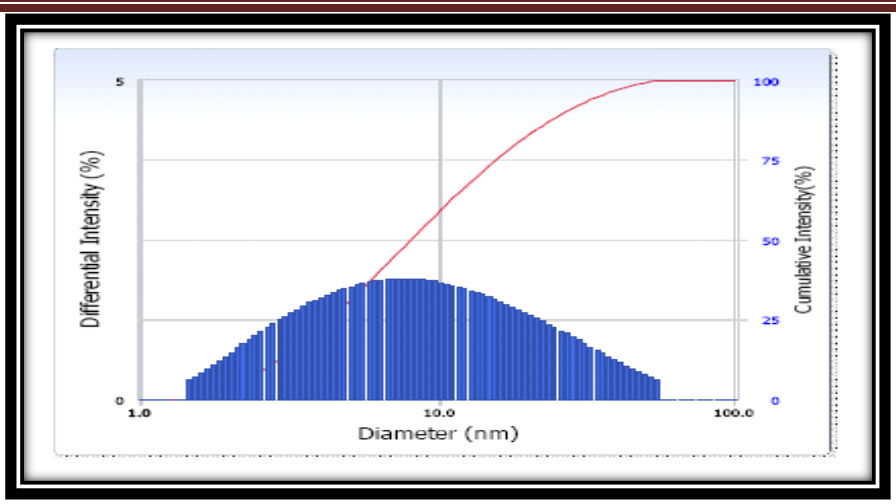

Fig. 5: Droplet size analysis of FA6 formulation

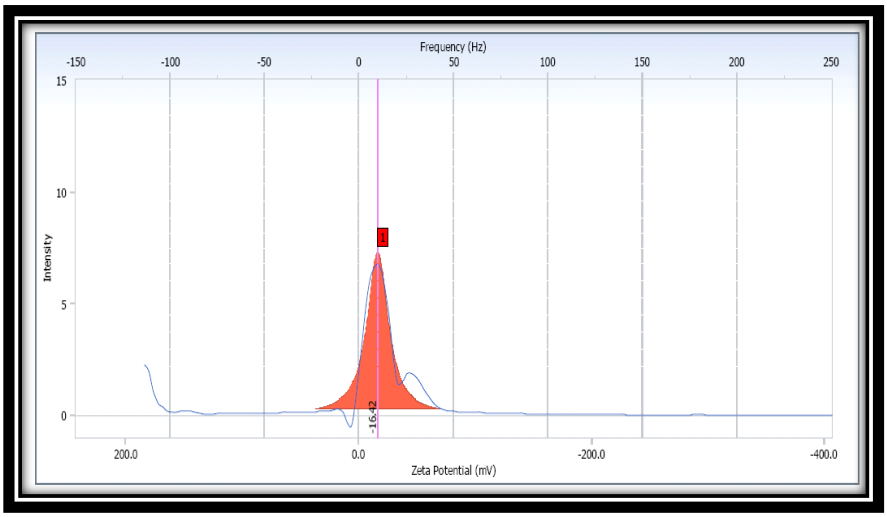

Fig. 6: Zeta potential distribution of FA6 formulation

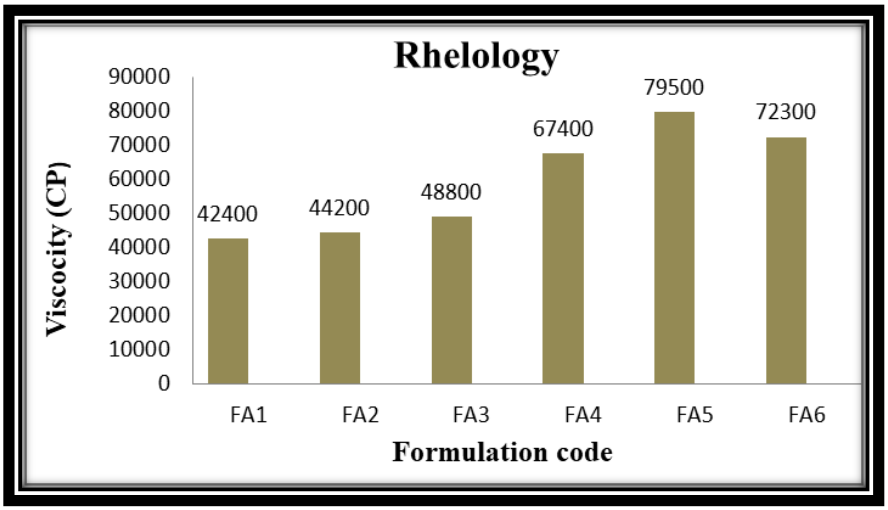

Fig. 7: Rheology study of nanoemulsion formulations

In-vitro skin permeation studies:

In-vitro skin permeation study of nanoemulsion formulations through the rat skin is shown in fig no: 14. Studied were carried out to confirm and to compare the permeation potential of Nanoemulsion formulations (FA1-FA6), the cumulative amount of drug permeated, flux were calculated for each formulation. Nanoemulsion formulations show transdermal flux form 13.74±027 to 83.79±0.10.

Statistical evaluation of flux throughout the 6 hr. of the study showed that among all the formulations, nanoemulsion FA6 exhibited maximum permeation at the end 6 hr. and show highest transdermal flux (83.79±0.10). It may be depend on small and uniformity droplet size distribution in FA6 formulation (Fig. 8).

Evaluation of gel:

pH determination:

The pH of plain gel in between 6 to 6.5 which shows in between normal pH range of skin which does not produce any skin irritation (Table 4).

Rheology study of gel:

Viscosity of plain gel was determined by Brookfield viscometer using spindle number 64. Viscosity of gel depends on the concentration of carbapol 934 GF1 formulation contain 1% carbapol and GF2 formulation contain 1.5% carbapol. 1% carbapol 934 selected for nanoemulsion gel preparation (Table 5).

Comparative study of nanoemulsion gel and conventional gel:

The pH value of nanoemulsion gel was found to be 6.13±0.01, suitable for use for skin. The performance of topical formulation monitored by its rheological behavior. Viscosity of nanoemulsion gel was found to be 36400±25. Swelling index of nanoemulsion gel formulation was found to be 12±0.02. Drug content of nanoemulsion gel formulation was 94.55±0.25. The result showed that the drug was uniformly distributed all over the formulation and drug loss minimum while formulated in nanoemulsion gel formulation (Table 7).

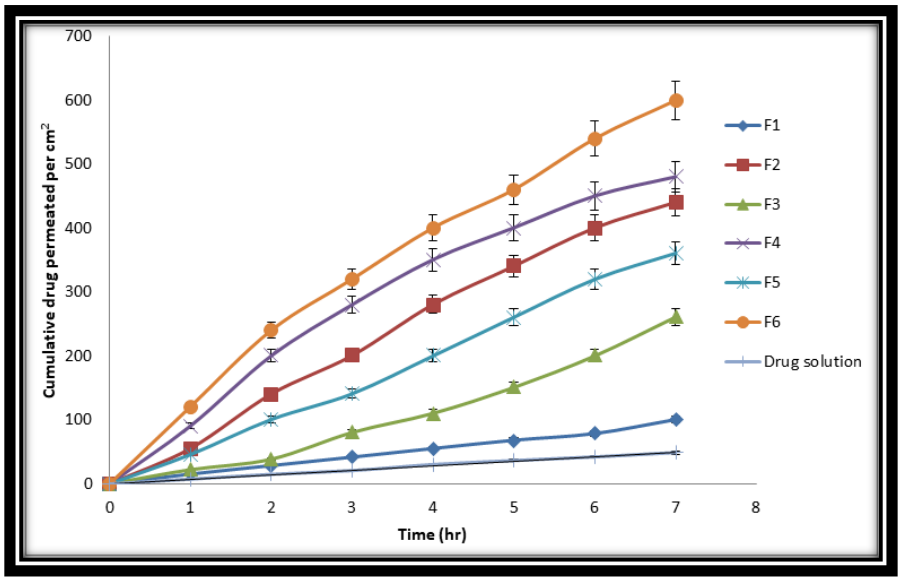

Fig. 8: In vitro release of nanoemulsion formulation

Table No. 4: pH of gel formulations

Sr. No	Formulation Code	pH
1.	GF1	6.45±0.08
2.	GF2	6.47±0.02

Values are expressed in mean ± SD, where n=3

Table No. 5: Rheology study of gel formulation

Sr. No	Formulation Code	Viscosity
1.	GF1	49400±15
2.	GF2	54700±10

Values are expressed in mean ± SD, where n=3

Evaluation of nanoemulsion gel:

Physical appearance:

Table No. 6: Physical appearance of nanemulsion gel formulation

Sr. No	Formulation Code	Color and appearance	Phase separation	Grittiness	Homogeneity
1.	Nanoemulsion gel	Transparent yellow	None	None	Homogeneous
2.	Conventional gel	Transparent yellow	None	None	Homogeneous

Table No. 7: Characterization of nanoemulsion gel and conventional gel

Sr. No	Formulation	pH	Viscosity (cp)	Swelling index (%)	Drug content (%)	Flux (µg/cm²/hr)
1.	Nanoemulsion gel	6.13±0.01	36400±25	12±0.02	94.55±0.25	38.66±0.20
2.	Conventional gel	6.54±0.01	43700±0.8	16±0.06	88.94±0.10	13.18±0.27

Values are expressed in mean ± SD, where n=3

In-vitro release study of nanoemulsion gel:

In-vitro skin permeation study was carried out to compare and confirm the permeation potential of nanoemulsion gel formulation. Nanoemulsion gel formulation showed the maximum permeation flux (38.66±0.20) as compare to conventional gel formulation (13.18±0.27). Nanoemulsion gel shows three times more permeation as compare to conventional gel (Fig. 9).

Anti-microbial activity:

Nanoemulsion gel formulation inhibits the E.coli growth (fig no.10). Equal amount eugenol oil along inhibited bacterial growth to a lesser extent than nanoemulsion gel formulation of eugenol oil. Conventional gel along (same concentration as in nanoemulsion gel) didn't inhibit the bacterial growth. Hence, it can conclude that nanoemulsion gel inhibited bacterial growth due to its reduced droplet diameter and maximum permeation.

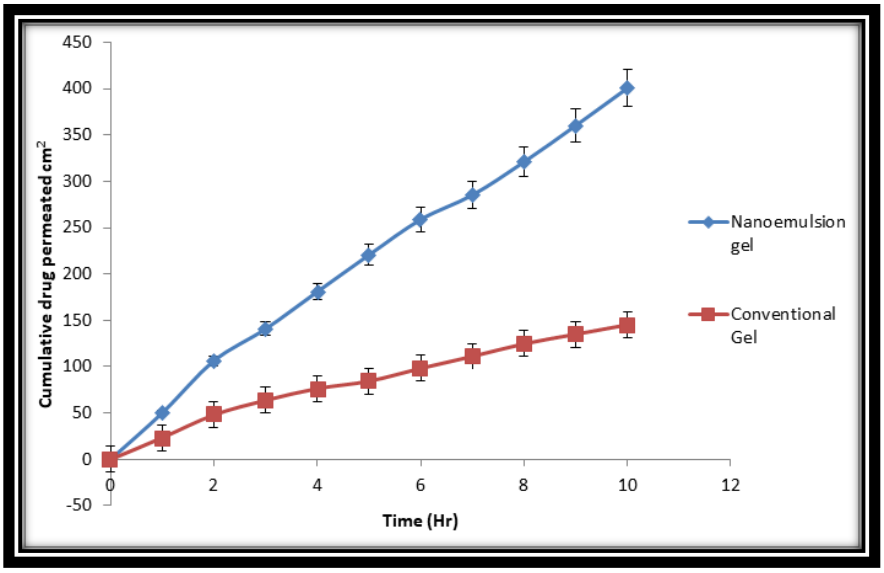

Fig. 9: In-vitro skin permeation study of nanoemulsion gel and conventional gel

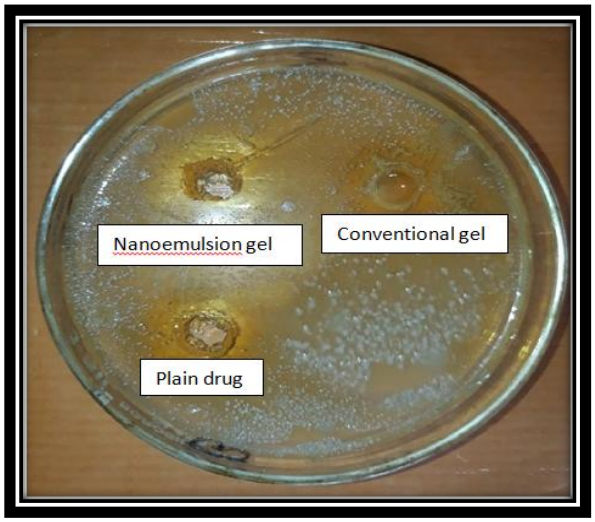

Fig. 10: Anti-microbial activity of components

Kinetic release study:

For better understanding the efficiency of the nanoemulsion gel, study of their release kinetics are important. The selection of a suitable kinetic model for fitting the nanoemulsion gel release data helps determine the release characteristics. There are number of kinetic models, which describe the overall release of nanoemulsion gel formulation. The most common mathematical model used is: zero order model, first order model, higuchi model, and korsmeyer-Pappas.

According to data the profile of nanoemulsion gel, it best fit to first order kinetic model. High linearity of the plots was achieved (R^2 – 0.995). It means that the nanoemulsion gel is released fast, with the constant rate, dependent of the initial drug concentration in the nanoemulsion gel.

Nanoemulsion gel release profile could be best explained by higuchi models. Regression line is characterized by higher R^2 value (R^2 - 0.991). This indicates slow diffusion of nanoemulsion gel and follows non-fickian transport mechanism as indicated by the n value of 0.860 when fitted to Kors-peppas model.

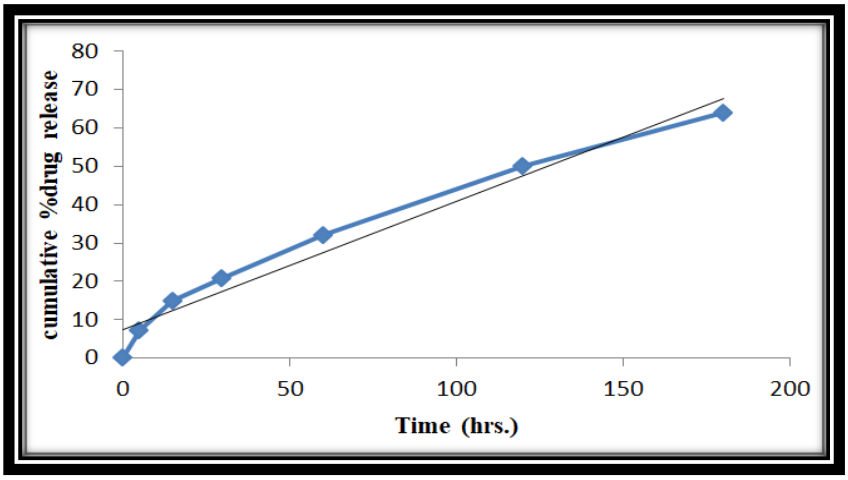

Fig. 11: Zero order kinetic release

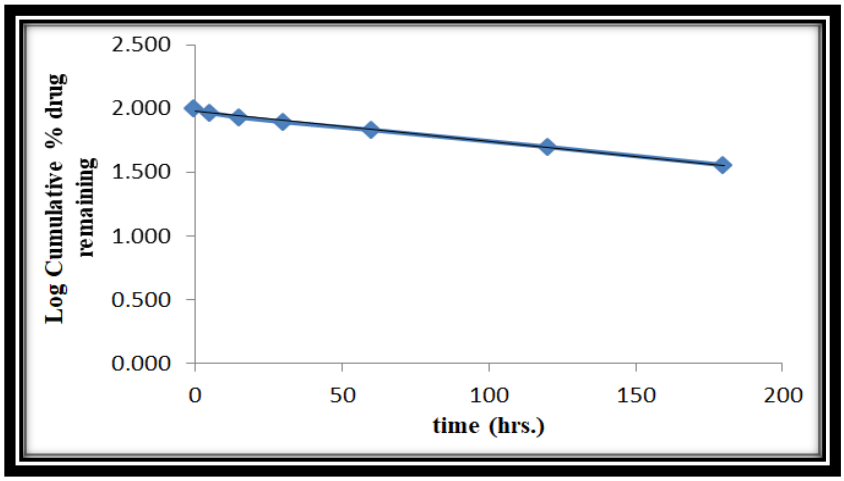

Fig. 12: first order release kinetic

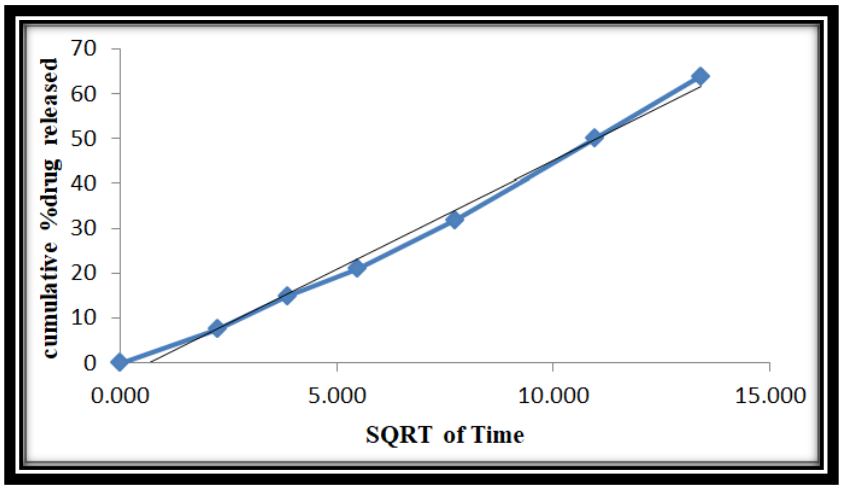

Fig. 13: Higuchi kinetic release

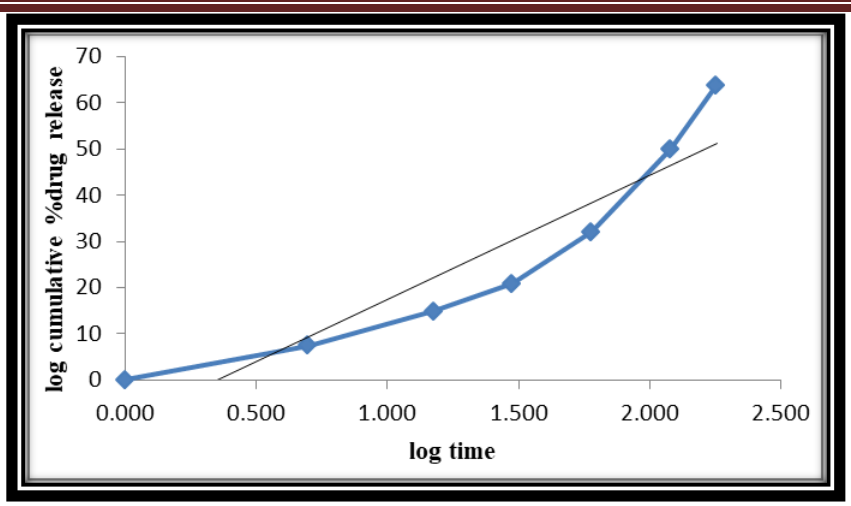

Fig. 14: Kors-peppas kinetic release

CONCLUSION

In present work, nanoemulsion of eugenol oil was formulated by sonication method and characterized for vesicle size, polydispersity index, zeta potential and ex-vivo permeability across excised rat skin. FA6 formulation showed smallest droplet size (219±0.36 nm), PI (0.117±0.32). Ex-vivo permeation study result for FA6 formulation shows significant higher transdermal flux 83.79±0.10 µg/cm^2/hr across excised rat skin due to their small droplet size as compared to other formulation. The optimized nanoemulsion formulation i.e. FA6 was formulated into nanoemulsion gel formulation by incorporated it into 1% w/w carbapol 394 gel. The transdermal flux of nanoemulsion gel formulation was calculated and compare with conventional gel formulation. The transdermal flux of nanoemulsion gel was found 38.66±0.20 µg/cm^2/hr. The result showed that nanoemulsion gel formulation shows significant higher permeability as compared to conventional gel formulation. Finally, it can be concluded that formulated nanoemulsion gel formulation loaded with eugenol oil can be prepared with appropriate size, maximum drug content and enhanced transdermal flux as compared to conventional gel formulation. Anti-microbial activity of nanoemulsion gel was done by cup and plate method which shows the high anti-microbial activity than conventional gel and plain drug. Release kinetic study done by using number of release kinetic models for nanoemulsion gel formulation. First order kinetic release model which fit best for the nanoemulsion gel formulation shows the higher linearity of plot was achieved (R^2 – 0.995). Nanoemulsion gel release profile could be best explained by higuchi models. Regression line achieved higher R^2 value (R^2 - 0.991). This indicates slow diffusion of nanoemulsion gel and follows non-fickian transport mechanism as indicated by the n value of 0.860 when fitted to Kors-peppas model. It can be concluded that nanoemulsion gel formulation is potential and effective transdermal drug delivery system for eugenol oil.

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