World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

Check for updates

A review on various plant-derived nanoemulgels and their applications

Warnakulasuriya Thanujee Fernando *, Athuraliya Gamacharige Kasuni Neranja and Samamalee Upekshi Kankanamge

Department of Pharmacy, Faculty of Allied Health Sciences, General Sir John Kotelawala Defence University, Sri Lanka.

World Journal of Advanced Research and Reviews, 2022, 15(03), 214–221

Publication history: Received on 10 August 2022; revised on 15 September 2022; accepted on 17 September 2022

Article DOI: https://doi.org/10.30574/wjarr.2022.15.3.0916

Abstract

Nanoemulgel is an emergent and promising drug delivery system used nowadays in the pharmaceutical industry. As a novel transdermal drug delivery tool, the applications of nanoemulgel have increasingly been used due to their unique characteristic properties and benefits over other oral and topical drug deliveries to avoid poor drug bioavailability and pharmacokinetic variations. These nanoemulgels are principally oil-in-water nanoemulsions gelled with a certain gelling agent in them. Plant extracts provide remarkable therapeutic options to manage different disease conditions due to their various pharmacological activities such as antioxidant, anti-inflammatory, anti-cancer, antibacterial, etc. However, the poor solubility and low bioavailability of lipophilic phytochemicals in plant extracts are two major issues in developing plant-derived formulations. In the past years, pharmaceutical research has focused more on nano-scale delivery systems to overcome the above problems by improving the delivery of herbal extracts and they have also reported nanoemulgel as a good vehicle for lipophilic and poorly soluble drugs. Therefore, the objective of this review is to discuss recent studies and applications of plant-derived nanoemulgels.

Keywords: Nanoemulgel; Plants; Nanotechnology; Therapeutic application

1. Introduction

There is a worldwide trend of moving from synthetic drugs toward herbal treatments due to their extensive use with therapeutic values, and minimal adverse effects over modern medicines. However, herbal medicines are restricted in their use due to poor oral absorption, poor solubility, instability, poor bioavailability, and unpredictable toxicity [01]. To conquer such issues associated with herbal medicines, various pharmaceuticals have been developed using nanotechnology. Herbal drugs are being incorporated into nano-carriers which enrich the effective and valuable effect of drugs [02]. Nanotechnology is accomplished by putting the drug into a carrier system or modifying the drug's structure at the molecular level [03].

The literature reported that nanosized topical formulations enhance the permeability of the active moiety by disrupting the lipid bilayer as evident from the distinct void and empty spaces in the nanoemulsion-treated skin samples [04], extent retention of the drug at the site of action [05] and can be used to overcome the issues faced with the current crystallization processes [06]. As per the studies nanoemulsions exhibit high drug solubilization capacity and their thermodynamic stability offers advantages over emulsions and suspensions [03]. Despite many benefits, low viscosity, and spreadability are the main drawbacks of topical nanoemulsion formulations [07]. However, researchers have overcome the problems associated with nanoemulsion by converting it into a nanoemulgel. Nanoemulgels are nanoemulsions, either of oil-in-water (o/w) or water-in-oil (w/o) type which further converts to nanoemulgel by using a gelling agent [08]. It is considered as one of the appropriate candidates for drug delivery to the skin due to its dual characteristics which are nanoemulsion and gel base. Nanoemulgel consists of particle sizes ranging from 10-100 nm,

* Corresponding author: Warnakulasuriya Thanujee Fernando
Department of Pharmacy, Faculty of Allied Health Sceinces, General Sir John Kotelawala Defence University, Sri Lanka.

through which the drug can penetrate or deliver easily and quickly [03] and the pH of nanoemulgel with essential oil was in the range of 7 to 6, which is safe to be used on the skin [09]. An increasing trend in topical nanoemulgel use in recent years has been noticed because of the better patient compliance due to their noninvasive delivery, avoidance of gastrointestinal side effects, easier applicability and removal, and good therapeutic and safety profile [10]. Their acceptability is further supported by their non-staining, thixotropic, emollient, and non-greasy properties [07].

1.1. Formulation technique of nanoemulgel

Nanoemulgel is composed of nanoemulsion and gel. Both nanoemulsion and gel need to be prepared separately when preparing nanoemulgel. Nanoemulsion can be o/w or w/o type emulsion. The nanoemulsion can be prepared using high-energy or low-energy emulsification methods [11,12]. When using the High-energy emulsification method, external energy will rupture the oil phase to form nanosized droplets in the aqueous phase. It may use ultrasonic emulsification and high-pressure homogenization methods too. As the low-energy emulsification techniques, the solvent displacement method, and phase inversion temperature method can be used [13]. After all, the selected surfactant and co-surfactant are dissolved in either the aqueous phase or in the oil phase as appropriate. Then the active ingredient will be mixed in the suitable phase by applying heat. Then, one phase is gradually added to another with continuous stirring until the complete mixture reaches room temperature to produce the nanoemulsion [14].

Lastly, the nanoemulsion is dispersed in the gel phase and found in the nanoemulgel formulation of any herbal medicine. Usually, nanoemulsion was converted to nanoemulgel by using Carbopol 934, Carbopol 940, and HydroxyPropyl Methyl Cellulose (HPMC) as they increase the thickness of the formulation for better spreadability and they may interact with the surfactant to modify the viscosity of the formulation as needed [15] and the pH was adjusted by triethylamine [16]. Therefore, this composition formulation shows a dual release control system and influences better skin penetration [17]. Gelling phase stabilizes the formulation by reducing the surface and interfacial tension of the emulsion and transport properties.

1.2. Anti-inflammatory activity of *Swietenia macrophylla* nanoemulgel

A study has been conducted on *Swietenia macrophylla* (SM) oil by incorporating nanoemulsion with hydrogel to develop SM oil nanoemulgel to test its effectiveness as an anti-inflammatory agent. Initially, the pre-nanoemulsion was prepared by mixing oil, and glycerol with sucrose ester (Laurate, Oleate, and Palmitate) using the phase inversion technique. Then nanoemulsion was developed using the self-emulsification technique and incorporating it with the hydrogel produced using 0.5% of different grades of Carbopol 934 and 940 to produce the nanoemulgel. It was found that 50% oil with 20% sucrose laurate and 30% of glycerol was able to produce pre-nanoemulsion, and then diluting it with water under gentle agitation produce nanoemulsion with droplets size of 114 nm, the low size distribution of 0.163 and low zeta potential of -43.1 mV. It was found that Carbopol showed no influence on the oil droplets' size in the range from 113 to 117 nm, size distribution from 0.155 to 0.163, and zeta potential range from -43.4 to -44.6 mV. In addition, the produced nanoemulgel was stable at 4°C, 25°C, and 40°C when stored for one year. Furthermore, the study highlights that Carbopol 940 at 0.5% showed priority as a thickening agent over 934 in relation to the nanoemulgel. The anti-inflammatory test uses the carrageenan-induced rat paw edema method for SM oil. It concludes the fact that the anti-inflammatory effect of SM oil is higher in nanoemulgel compared to the oil [18].

1.3. Antimicrobial and anticancer activity of *Coriandrum sativum* oil nanoemulgel

Another study has been performed to develop coriander oil into a nanoemulgel to evaluate antimicrobial and anticancer effects. In this study, Nanoemulsion was produced by using a self-nanoemulsifying technique with Tween 80 and Span 80 while the nanoemulgel was developed using Hydrogel (Carbopol 940) as in the previous study. The nanoemulsion had a polydispersity index (PDI) of 0.188 and a particle size of 165.72 nm. Minimum Inhibitory concentration of *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and methicillin-resistant *Staphylococcus aureus* (MRSA), was 2.3 µg/mL, 3.75 µg/mL, and 6.5 µg/mL, respectively. In addition, the half-maximal inhibitory concentration (IC50) of the nanoemulgel when applying it to human breast cancer cells (MCF-7), hepatocellular carcinoma cells (Hep3B), and human cervical epithelioid carcinoma cells (HeLa) was 28.84 µg/mL, 28.18 µg/mL, and 24.54 µg/mL, respectively, which proves that the nanoemulgel has anticancer effects. The study finally concluded the fact that the development of *Coriandrum sativum* oil into a nanoemulgel by using a self-nanoemulsifying technique showed a bioactive property better than that in crude oil [19].

1.4. Antioxidant, antidiabetic, antibacterial, antifungal, and anticancer activities of safrole oil and safrole (*Sassafras plants*) oil nanoemulgel

A study was done to investigate the antioxidant, antidiabetic, antimicrobial, and anticancer activity of safrole oil and the influence of safrole nanoemulgel on these activities. Safrole oil nanoemulsions were created using a self-emulsifying

process, using safrole oil, Tween® as the surfactant, and Span® as a co-surfactant at different concentrations. As in previous studies, the nanoemulgel has been developed using hydrogel, Carbopol 940. The antimicrobial activity of the safrole oil and safrole nanoemulgel was performed on different microbial species, and cytotoxicity was determined against Hep3B cancer cell lines using the MTS assay. Safrole oil showed moderate antioxidant activity compared with standard Trolox, with IC50 values 50.28 ± 0.44 and 1.55 ± 0.32 µg/mL, respectively. Moreover, it had potent α-amylase inhibitory activity (IC50 11.36 ± 0.67 µg/mL) compared with Acarbose (IC50 value 5.88 ± 0.63). The safrole nanoemulgel had pseudo-plastic behavior, droplet sizes below 200 nm, a polydispersity index (PDI) below 0.3, and a zeta potential of less than - 30 mV. Finally concluding that safrole oil may be applied for the prevention and treatment of oxidative stress, diabetes, different microbial species, and cancer, and these activities could be improved by nano-carriers [20].

1.5. Anticancer, antimicrobial, and antioxidant activities of rosemary (*Rosmarinus officinalis*) oil nanoemulgel

A study has been performed to develop nanoemulgel using *Rosmarinus officinalis* oil by using a self-nanoemulsifying technique with Tween 80 and Span 80 to develop the nanoemulsion while using hydrogel (Carbopol 940) to produce the nano-emulgel. The optimum formulation (50% Tween, 15% Span 80, and 35% *R. officinalis* oil) was used to create the best nanoemulsion, which had a droplet size of 159.23 ±1.22 nm and 0.206 ±0.08 PDI. *R. officinalis* showed strong antioxidant activity, with 22.38 ±0.7 µg/mL when compared to Trolox (2.7 ±0.5 µg/mL). The results obtained for the minimum inhibitory concentration (MIC) with the nanoemulgel against different types of bacteria, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and Methicillin-resistant *Staphylococcus aureus* (MRSA) are as 2.3, 3.75 and 6.5 µg/mL, respectively. In addition, the half-maximal inhibitory concentration (IC50) of the nanoemulgel when applying it to human hepatocellular carcinoma cells (Hep3B) and human cervical epithelioid carcinoma cells (HeLa) was 28.84, 28.18, and 24.54 µg/mL, respectively, which demonstrated that the nanoemulgel has anticancer effects and finally concluded that *R. officinalis* oil nanoemulgel could be used to treat different cancer cell lines and microbial infections [21].

1.6. Oral health management: methylcellulose-based nanoemulgel loaded with *Nigella sativa* oil

Another study has been performed to develop a local dental nanoemulgel formulation of *Nigella sativa* oil (NSO) for the treatment of periodontal diseases. Unlike in other research, in this study, a methylcellulose gel base has been incorporated into the NSO nanoemulsion to develop the nanoemulgel formulation. The developed formulation was optimized using a Box-Behnken statistical design (quadratic model) with 17 runs. The developed formulation had a pH of 7.37, a viscosity of 2343 cp, and a droplet size of 342 ± 36.6 nm. Sustained release of the drug from the gel for up to 8 h was observed, which followed Higuchi release kinetics with non-Fickian diffusion. The developed nanoemulgel formulation showed improved antimicrobial activity compared to the plain NSO. Due to the increasing emergence of periodontal diseases and antimicrobial resistance, an effective formulation based on a natural antibacterial agent would be an advantage in the future. Therefore, the study reveals that not only Carbopol 934 or 940 hydrogels but also methylcellulose gel base would be effective in developing nanoemulgels [14].

1.7. Cumin (*Cuminum cyminum* L.) oil nanoemulgel as skin permeation enhancer

A study has been performed to investigate the transdermal permeation enhancing capability of cumin essential oil in nanoemulgel systems containing diclofenac sodium. 2% and 4% Cumin essential oil nanoemulsion was produced by high-pressure homogenization technique and it has been incorporated into 0.75% Carbopol 940 gel base to develop nanoemulgel. The formulation was optimized by changing HLB (Hydrophilic Lipophilic Balance) values in a range of 9.65-16.7 using Tween 20, Tween 80, and Span 80. Its permeation-enhancing effect was performed through Franz diffusion cells. Anti-nociceptive activities of the formulations were measured in thermal (tail-flick) and chemical (formalin) models of nociception in mice. Characterization exhibited that at an HLB value of 9.65, the smallest particle size (82.20 ± 5.82 nm) was formed. By increasing the essential oil percentage in the nanoemulgel from 1 to 2%, the permeation of diclofenac has increased from 28.39 ± 1.23 to 34.75 ± 1.07 µg/cm2 at 24 h. The value of permeation from the simple gel (21.18 ± 2.51 µg/cm2) and the marketed product (22.97 ± 1.92 µg/cm2) was lower than the formulations containing essential oil. Finally, concluding that the nanoemulgel of diclofenac containing essential oil could be considered as a promising skin enhancer to enhance the therapeutic effect of drugs than simple diclofenac gel formulations available on the market [22].

Curcumin and emu oil derived from the emu bird (*Dromaius novaehollandiae*) has shown promising results against inflammation. Due to low solubility and poor permeation, a study has been performed to evaluate the anti-inflammatory potential of curcumin in combination with emu oil from a nanoemulgel formulation in experimental inflammation and arthritic in vivo models. Nanoemulsion was prepared using emu oil as the oil, Cremophor RH 40 as the surfactant, and Labrafil M2125CS as the co-surfactant. The optimized curcumin-emu oil nanoemulsion was incorporated into Carbopol

gel to produce the nanoemulgel. The anti-inflammatory efficacy was evaluated in carrageenan-induced paw edema and Freund's complete adjuvant (FCA)-induced arthritic rat model. Arthritic scoring, paw volume, biochemical, molecular, radiological, and histological examinations indicated significant improvement in anti-inflammatory activity with formulations containing curcumin in combination with emu oil compared to pure curcumin. Finally demonstrates the potential of formulations containing curcumin and emu oil combination in rheumatoid arthritis [23].

1.8. Antibacterial, antifungal, and analgesic effects against oral microbiota and enhancement of solubility of cinnamon (*Cinnamomum* plants) oil nanoemulgel

A similar study has been performed to develop a cinnamon oil (CO)-loaded nanoemulsion gel (NEG1) to enhance the antibacterial, antifungal, and analgesic actions against oral microbiota. The CO-loaded nanoemulsion (CO-NE) was optimized using a mixture of Pluracare L44 and PlurolOleique CC 497 as the surfactants and Capryol as the co-surfactant and then using hydroxypropyl cellulose as the gelling agent to develop the nanoemulgel. The optimized CO-NE had a globule size of 92 ± 3 nm, a stability index of 95% ± 2%, and a zone of inhibition of 23 ± 1.5 mm. The rheological characterizations revealed that the NEG1 formulation exhibited pseudoplastic behavior. The in vitro release of eugenol, from nanoemulgel, showed an enhanced release compared with that of pure CO. The studies finally revealed that the ex vivo mucosal permeation was found to be highest for nanoemulgel compared to the aqueous dispersion of cinnamon oil nanoemulsion and pure cinnamon oil [24].

1.9. Eucalyptus (*Eucalyptus globulus*) oil nanoemulgel, an innovative carrier for diflunisal topical delivery with profound anti-inflammatory effect: in vitro and in vivo evaluation

A study has been designed to evaluate a nanoemulgel formulation of diflunisal (DIF) and solubility enhanced diflunisal (DIF-IC) for enhanced topical anti-inflammatory activity. Nanoemulsion formulations having a composition of eucalyptus oil (oil phase), Tween 80 (surfactant), and Transcutol-P (co-surfactant) were prepared and characterized successfully. Surfactant and co-surfactant were used in the ratio of 1:2 to examine particle size, in vitro release, and physicochemical properties of DIF and DIF-IC. Nanoemulsion is then converted to nanoemulgel with the use of three different gelling agents, namely carboxymethylcellulose sodium (CMC-Na), sodium alginate (Na-ALG), and xanthan gum (XG). Formulation 2 (NE2) of both DIF and DIF-IC which expressed optimum release and satisfactory physicochemical properties was incorporated with gelling agents to produce final nanoemulgel formulations. The optimized nanoemulgel formulation was subjected to three different in vivo anti-inflammatory models including the carrageenan-induced paw oedema model, histamine-induced paw oedema model, and formalin-induced paw oedema model. DIF-IC-loaded nanoemulgel formulations yielded significantly enhanced in vitro skin permeation than DIF-loaded nanoemulgel. The nanoemulgel formulation of DIF-IC formulated with XG produced improved in vivo anti-inflammatory activity. It was recommended that a DIF-IC-based nanoemulgel formulation prepared with XG could be a better option for the effective topical treatment of inflammatory conditions [07].

1.10. Antimicrobial, antioxidant, sun protection factor, and elastase inhibition of *Eruca sativa* oil nanoemulgel

A study has been conducted using *E. sativa* oil to evaluate its antioxidant, sun protection factor, and elastase inhibition. Then, nanoemulgel formulations were prepared for *E. sativa* oil through the combination of nanoemulsion with hydrogel. *E. sativa* nanoemulsion formulations were prepared with the help of a self-emulsification technique. The optimum formulation was mixed with Carbopol to produce the nanoemulgel. Anti-bacterial and anti-fungal activities were evaluated. Nanoemulsion occurred when the size of the droplets was 195.29 nm with the lowest polydispersibility index of 0.207. The results of antioxidant, anti-elastase, and SPF activities for E. sativa oil were 2.10 µg/ml, 25.1 µg/mL, and an SPF value of 5.57, respectively. In addition, in the anti-bacterial test for *Staphylococcus aureus*, it was found that nanoemulgel has an inhibition zone of 2.1 cm in diameter. According to the MRSA, the inhibition zone was 1.5 cm. Finally, it has been concluded that *E. Sativa* oil in nanoemulgel could be a promising candidate in cosmeceutical and pharmaceutical preparations [25].

1.11. Nanoemulgel mangosteen (*Garcinia mangostana* L.) extract in virgin coconut oil for topical formulation

A study has been conducted to formulate a hydrogel of nanoemulsion system containing mangosteen extract of mangosteen rind was developed and characterized for the purpose of topical formulation to test for its antifungal, antibacterial, antioxidant, antiviral, and antitumor activity. Due to the hydrophobic nature of mangosteen, oil-in-water nanoemulsions were formulated of virgin coconut oil (VCO) as the oil phase and mixed with a surfactant consisting of Tween 80 and Span 80, using the high-speed homogenization method. Nanoemulgel is formed by mixing the nanoemulsion with an aqueous solution of xanthan gum, and phenoxyethanol which has been added as a preservative to form a homogeneous milky white gel. The stability test through accelerated centrifugation and freeze-thaw cycle showed that the nanoemulgel would be stable for at least one year. The nanoemulgel penetrated the skin layer up to

12 μg/cm2 or more than 95% of its total mangosteen content with better skin penetration. The present study revealed that VCO-mangosteen nanoemulgel formulation is a prospective topical formulation [26].

1.12. Wound healing activity of nanoemulgel containing *Artocarpus lakoocha* Roxb. Extract

A study has been performed to evaluate the wound healing ability of nanoemulgel-containing ethanol extract of mobe leaves of *A. lakoocha* Roxb. Artocarpine, one of the secondary metabolites found in mobe leaves, is reported to affect the expression of transforming growth factor-beta (TGF-β) protein, thereby increasing fibroblast cell proliferation, and accelerating the wound healing process. The method used in this study was 96% ethanol, Carbopol 940, PEG 400, Propylene glycol, Methyl Paraben, Propyl Paraben, Triethanolamine, and Aqua Destillata. Mobe leaves which were taken purposively were then formulated in nanoemulgel preparations which were tested for wound healing in male rats.

The nanoemulgel preparation was then evaluated which included homogeneity, emulsion type, pH, viscosity, dispersion, and the stability of nanoemulgel preparation. Tests for the healing effect of burns were carried out on male rats for 14 days. This study showed that wound healing activity of nanoemulgels with concentration variation of mobe leaves is highest in 7% ethanol extract. The percentages of wound diameter reduction and fibroblast cells value were shown to increase significantly different from negative control ($p < 0.05$) in 14 days. Platelet-derived growth factor (PDGF)-BB and TGF-β1 immuno-expression evaluation results showed significantly different results from the Blank group ($p < 0.05$) in 14-day observation. Finally, it has been concluded that nanoemulgel containing mobe leaves extract in 7% ethanol can stimulate more fibroblast cell proliferation by greatly expressing TGF-β1 and PDGF BB in burn wounds [27].

1.13. *Piper betle* oil nanoemulgel formulation for effective droplet size reduction and excellent stability

Piper betle essential oil had been extracted with steam distillation to extract the essential oil. The nanoemulsion has been formed with soybean oil as oil phase, distilled water as aqueous phase, and adding Tween 80 as a surfactant with Glycerol as a co-surfactant. Carbopol 940 is employed as a gelling agent to increase the viscosity of the formulation of the nanoemulgel. Different ratios of the nanoemulsion and nanoemulgel had been formulated and a few characteristics like droplet size, viscosity, pH, and spreadability had been investigated. The droplet size of the nanoemulsion was determined with dynamic light scattering and it has been determined that it was in the range of 35.91 nm to 747.27 nm. The pH was in the range of 5.5 to 6.9, which is nearly neutral. Plant-derived nanoemulgel has been becoming the increasing trend applied in field applications because of their few and so on. Finally, it has been concluded that *P. betle*, being a plant-derived nanoemulgel, will be a promising drug delivery system in the future due to its unique characteristics such as non-toxic, non-greasy, and better spreadability [09].

1.14. Ginger (*Gingiber officinale*) extract-loaded nanoemulgel for the treatment of rheumatoid arthritis

Table 1 Applications of plant-derived nanoemulgels

Name of the plant	Gelling agent used	Biological activities	Route of administration	Reference
Swietenia macrophylla	Carbopol of 934 and 940	Anti-inflammatory	Topical	[18]
Coriandrum sativum	Carbopol 940 hydrogel	Anti-microbial Anti- Cancer	Topical	[19]
Safrole oil from *Sassafras* plants	Carbopol 940 hydrogel	Antioxidant Anti-diabetic Anti-Bacterial Anti-fungal Anti-cancer	Topical	[20]
Rosmarinus officinalis	Carbopol 940 hydrogel	Anti-cancer Anti-microbial Antioxidant	Topical	[21]
Nigella Sativa	Methylcellulose	Anti-bacterial	Oral	[14]
Cuminum cyminum L.	Carbopol 940 hydrogel	Analgesic	Transdermal	[22]

Cuminum cyminum L. and emu oil combination	Carbopol 940 Hydrogel	Anti-inflammatory	Topical	[23]
Cinnamon oil from *Cinnamomum* plant	Hydroxypropyl cellulose	Anti-bacterial Anti-fungal Analgesic	Topical	[24]
Eucalyptus globulus	Carboxymethylcellulose sodium, Sodium alginate and Xanthan gum	Anti-inflammatory	Topical	[07]
Eruca Sativa	Carbopol	Anti-microbial Antioxidant Elastase inhibition	Topical	[25]
Garcinia mangostana L.	Xanthan gum	Skin penetration activity	Topical	[26]
Artocarpus lakoocha Roxb.	Carbopol 940	Wound healing activity	Topical	[27]
Piper betle	Carbopol 940	-	Topical	[09]
Gingiber officinale	Carbopol 934	Analgesic	Transdermal	[28]

According to another study conducted to formulate and evaluate the ginger extract-loaded nanoemulgel for rheumatoid arthritis, the nanoemulsion was first prepared according to the ternary phase diagram, using the water titration method. The S mix (surfactant and co-surfactant) and extract were mixed together and then titrated with water. The S mix was used at the ratio of 1:1, 2:1, and 3:1 (Tween 80: ethanol). The isopropyl myristate as the oil, Tween 80 as the surfactant, and ethanol as the co-surfactant was selected out of the few options available, and water has been used as the aqueous phase. 32 formulations were prepared using different proportions of aforesaid components and 4 formulations (F1, F2, F3, and F4) have been selected accordingly. On the basis of thermodynamic stability, spreadability, and drug release, the nanoemulgel F4 was considered as the best formulation out of the 04 formulations. It consists of 0.33% ginger extract, 10.41% of oil, and 74.46% of surfactant: co-surfactant with 14.89% of water. The particle size was found in the range of 60.32 to 230.8nm, the zeta potential was found between -16.6 to -24.4 and the polydispersibility index was found to be 0.687 to 0.892 for formulations F1 to F4. Nanoemulsion was converted into nanoemulgel by using 0.5% w/v Carbopol 934 as a gelling agent in various concentrations. The pH of the F4 formulation was found to be 5.67 with very good transparency and less viscosity finally concluding that nanoemulgel can be the best dosage form for the transdermal absorption of ginger extract [28].

2. Discussion

To overcome the current issues of low spreadability and viscosity of nanoemulsions researchers are now interested in converting nanoemulsion to a nanoemulgel by simply adding a gelling agent to it. Due to its dual characteristics of nanoemulsion and gel base, nanoemulgel is considered a better candidate for drug delivery to the skin. An increasing trend in using nanoemulgel topical applications has been reported lately due to its non-invasive delivery and better safety profile. Improved pharmacodynamic and pharmacokinetic properties of lipophilic drugs made nanoemulgels even more beneficial compared to available nanoemulsions in the market.

3. Conclusion

This review remarks that combining nanoemulgel and plant-based oils is an excellent method to optimize the formulations through different administration routes and it will create a pathway to meet market demands. The development of a stable nanoemulgel solely depends on its components including gelling agent and oil phase and the methodology that is followed. Researchers have found that nanoemulgel is an effective drug delivery system to deliver drugs to local and systemic sites of action. These plant-derived nanoemulgel formulations possessed many benefits with fewer side effects. Nanoemulgels have also shown their applications in the cosmetic and pharmaceutical industries. Therefore, there is great interest in developing novel drug delivery systems such as nanoemulgel and nanoemulsion using bioactive compounds based on nanotechnology.

Compliance with ethical standards

Acknowledgments

Many thanks to Ms. SU Kankanamge and Ms. AGK Neranja for their continued support and guidance throughout the process of writing this review.

Disclosure of conflict of interest

No conflicts of interests to be declared.

References

[1] Arulanandraj N, Dhivya S, Gopal V. A review on Herbal Nanoparticles. PharmaTutor. 2018, 6(5); 32-37.

[2] Dongare PN, Motule AS, Dubey MR, More MP, Patinge PA, Bakal RL, Manwar JV. Recent development in novel drug delivery systems for delivery of herbal drugs: An updates. GSC Advanced Research and Reviews. 2021, 8(2):008-018.

[3] Gupta S, Gupta J, Anand A, Ojha S. Review on nanogel/emulgel formulations of traditional medicines: This article is a part of Special Issue" Advances in the field of Nanomedicine". Biological Sciences. 2022, 2(3):269-278.

[4] Shakeel F, Baboota S, Ahuja A, Ali J, Shafiq S. Skin permeation mechanism and bioavailability enhancement of celecoxib from transdermally applied nanoemulsion. Journal of nanobiotechnology. 2008, 6(1):1-11.

[5] Weissig V, Lizano C, Torchilin VP. Selective DNA release from DQAsome/DNA complexes at mitochondria-like membranes. Drug delivery. 2000, 7(1):1-5.

[6] Gupta A, Eral HB, Hatton TA, Doyle PS. Nanoemulsions: formation, properties and applications. Soft matter. 2016, 12(11):2826-2841.

[7] Bashir M, Ahmad J, Asif M, Irfan M, Ibrahim AY, Asghar S, Khan IU, Iqbal MS, Haseeb A, Khalid SH, Abourehab MA. Nanoemulgel, an innovative carrier for diflunisal topical delivery with profound anti-inflammatory effect: In vitro and in vivo evaluation. International Journal of Nanomedicine. 2021, 16:1457.

[8] Pund S, Pawar S, Gangurde S, Divate D. Transcutaneous delivery of leflunomide nanoemulgel: Mechanistic investigation into physicomechanical characteristics, in vitro anti-psoriatic and anti-melanoma activity. International journal of pharmaceutics. 2015, 487(1-2):148-156.

[9] Ting TC, Rahim NFA, Zaudin NAC, Abdullah NH, Mohamad M, Shoparwe NF, Ramle SFM, Aimi Z, Hamid ZAA, Yusof AH. December. Development and Characterization of Nanoemulgel Containing *Piper betle* Essential Oil as Active Ingredient. In IOP Conference Series: Earth and Environmental Science. 2020, 596(1):012032).

[10] Sengupta P, Chatterjee B. Potential and future scope of nanoemulgel formulation for topical delivery of lipophilic drugs. International journal of pharmaceutics. 2017, 526(1-2):353-365.

[11] Anton N, Vandamme TF.The universality of low-energy nano-emulsification. International journal of pharmaceutics. 2009, 377(1-2):142-147.

[12] Flanagan J, Kortegaard K, Pinder DN, Rades T, Singh H. Solubilisation of soybean oil in microemulsions using various surfactants. Food hydrocolloids. 2006, 20(2-3):253-260.

[13] Date AA, Desai N, Dixit R, Nagarsenker M. Self-nanoemulsifying drug delivery systems: formulation insights, applications and advances. Nanomedicine. 2010, 5(10):1595-1616.

[14] Sultana N, Akhtar J, Khan MI, Ahmad U, Arif M, Ahmad M, Upadhyay T. Nanoemulgel: For Promising Topical and Systemic Delivery. in J. Akhtar et al. (eds.), Drug Development Life Cycle [Working Title], IntechOpen, London. 2022. 10.5772/intechopen.103878.

[15] Dhawan B, Aggarwal G, Harikumar SL. Enhanced transdermal permeability of piroxicam through novel nanoemulgel formulation. International journal of pharmaceutical investigation. 2014, 4(2):65.

[16] Sampathi S, Mankala SK, Wankar J, Dodoala S. Nanoemulsion based hydrogel of itraconazole for transdermal drug delivery. Journal of Scientific and Industrial Research. 2015, 74:88-92.

[17] Raut BP, Khan SA, Ubhate AA, Ganjiwale RO. A review on herbal nanoemulgel for the treatment of acne vulgaris. World Journal of Pharmaceutical Research. 2021, 10(9):487-497.

[18] Eid AM, El, Enshasy HA, Aziz R, Elmarzugi NA. Preparation, characterization and anti-inflammatory activity of *Swietenia macrophylla* nanoemulgel. J Nanomed Nanotechnol. 2014, 5(2):1-10.

[19] Eid AM, Issa L, Al-Kharouf O, Jaber R, Hreash F. Development of *Coriandrum sativum* Oil Nanoemulgel and Evaluation of Its Antimicrobial and Anticancer Activity. BioMed research international. 2021.

[20] Eid AM, Hawash M. Biological evaluation of Safrole oil and Safrole oil Nanoemulgel as antioxidant, antidiabetic, antibacterial, antifungal and anticancer. BMC Complementary Medicine and Therapies. 2021, 21(1):1-12.

[21] Eid AM, Jaradat N, Issa L, Abu-Hasan A, Salah N, Dalal M, Mousa A, Zarour A. Evaluation of anticancer, antimicrobial and antioxidant activities of Rosemary (*Rosmarinus officinalis*) essential oils and its nanoemulgel. European Journal of Integrative Medicine. 2022, 102175.

[22] Morteza-Semnani K, Saeedi M, Akbari J, Eghbali M, Babaei A, Hashemi SMH, Nokhodchi A. Development of a novel nanoemulgel formulation containing cumin essential oil as skin permeation enhancer. Drug delivery and translational research. 2022, 12(6):1455-1465.

[23] Jeengar MK, Rompicharia SVK, Shrivastava S, Chella N, Shastri NR, Naidu VGM, Sistla R. Emu oil based nanoemulgel for topical delivery of curcumin. International Journal of pharmaceutics. 2016, 506(1-2):222-236.

[24] Hosny KM, Khallaf RA, Asfour HZ, Rizg WY, Alhakamy NA, Sindi AM, Alkhalidi HM, Abualsunun WA, Bakhaidar RB, Almehmady AM, Abdulaal WH. Development and optimization of cinnamon oil nanoemulgel for enhancement of solubility and evaluation of antibacterial, antifungal, and analgesic effects against oral microbiota. Pharmaceutics. 2021, 13(7):1008.

[25] Eid AM, Jaradat NA, Al-Masri M, Issa L, Zubidat F, Asrawi H, Ahmad S. Development and antimicrobial evaluation of *Eruca sativa* oil nanoemulgel with determination of the oil antioxidant, sun protection factor and elastase inhibition. Current Pharmaceutical Biotechnology. 2021, 21(3):244-255.

[26] Mulia K, Ramadhan RM, Krisanti EA. Formulation and characterization of nanoemulgel mangosteen extract in virgin coconut oil for topical formulation. In MATEC Web of Conferences. 2018, 156: 01013.

[27] Tanjung SA, Silalahi J, Reveny J. Wound Healing Activity of Nanoemulgel Containing *Artocarpus lakoocha* Roxb. Extract on Burns Model in Rat. Open Access Macedonian Journal of Medical Sciences. 2022, 10(A):725-733.

[28] Chandra A, Arya RKK, Pal GR, Tewari B. Formulation and evaluation of ginger extract loaded nanoemulgel for the treatment of rheumatoid arthritis. Journal of Drug Delivery and Therapeutics. 2019, 9(4):559-570.

[29] Aithal GC, Narayan R, Nayak UY. Nanoemulgel: A promising phase in drug delivery. Current pharmaceutical design, 2020, 26(2): 279-291.

[30] Anand K, Ray S, Rahman M, Shaharyar A, Bhowmik R, Bera R, Karmakar S. Nano-emulgel: emerging as a smarter topical lipidic emulsion-based nanocarrier for skin healthcare applications. Recent patents on anti-infective drug discovery. 2019, 14(1):16-35.

[31] Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, Chourasia MK. Nanoemulsion: Concepts, development and applications in drug delivery. Journal of controlled release. 2017, 252:28-49.