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Review Article

Herbal Nanoemulgel-: A Comprehensive Review On Formulation, Mechanism, Characterization And Method Of Preparation

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ABSTRACT

Herbal nanoemulgel technology has emerged as an advanced topical delivery system that combines the advantages of nano emulsions and hydrogels to enhance the effectiveness of herbal hair dyes. This review highlights the formulation, mechanism of action, characterization, therapeutic potential, and applications of herbal nanoemulgel-based hair dye systems. The incorporation of herbal ingredients such as Lawsonia inermis (henna), Indigofera tinctoria (indigo), Phyllanthus emblica (amla), Eclipta prostrata (Bhringraj), Juglans regia (walnut), Coffea arabica (coffee), Tagetes erecta (marigold), Aloe barbadensis (aloe vera), and Hibiscus rosa-sinensis provides natural pigmentation along with antioxidant, conditioning, and scalp-protective properties. The nanoemulgel system enhances dye penetration into the hair shaft through nanosized droplets, improves colour retention, offers controlled release of bioactive compounds, and minimizes dripping and scalp irritation compared with conventional hair dyes. This review also discusses formulation components, preparation methods, characterization parameters, advantages, limitations, and various types of Nanoemulgel, while comparing herbal nanoemulgel formulations with conventional and synthetic hair dyes. Overall, herbal nanoemulgel-based hair dyes represent a safe, eco-friendly, and biocompatible alternative for effective hair coloring with additional hair and scalp health benefits. However, further optimization, standardization, and clinical studies are required to establish their long-term safety, efficacy, and commercial applicability.

INTRODUCTION

Nano-emulsions are heterogeneous colloidal mixtures of oil and water, with one component as a dispersed phase and the other as a continuous phase. A surfactant known as an emulsifier is adsorbed at the interface between the dispersed and continuous phases, lowering the surface tension and thus stabilizing the system. These

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systems possess high thermodynamic stability leading to longer shelf life compared to simple emulsions, micelles or suspensions, etc. Despite having various advantages, nano-emulsions are limited by their low viscosity leading to low retention time and spread ability.[1]

These problems can be resolved by modifying nano -emulsion into a nano- emulgel by using a suitable gelling agent.[2]

Emulgels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, long shelf-life surfactant [3]

Natural dyes have been used since ancient times, when they were used not only for hair coloration, but also for medicinal, decoration and religious purposes.[4,5,6] In the early days, hair dyes were obtained from metallic compounds, plant extracts, dried plants or their mixtures.[7] Before the invention of first synthetic aniline dye, mauve, in 1856, different plant extracts and herbal preparations such as mullein, birch bark, turmeric, and saffron have been used for hair dyeing.

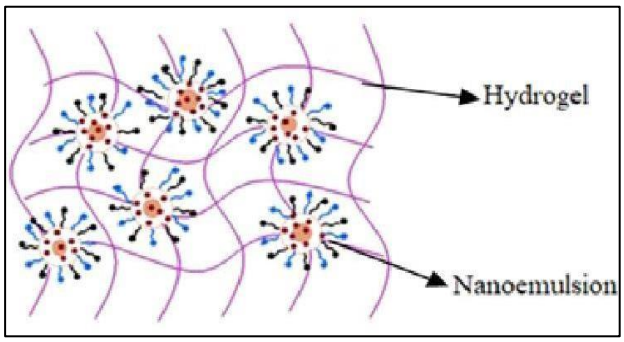

Figure 1: Structure of nanoemulgel.[8]

Types of Emulgel[9,10,11]

1. Microemulsion-Based Emulgel:

Microemulsions are isotropic, thermodynamically stable mixtures of oil and water stabilized with surfactants and cosurfactants, typically forming oil-in-water (O/W) systems. The droplet size ranges from 10 to 100 nm, and the droplets remain dispersed without coalescence. Microemulsions are characterized by extremely low interfacial tension, a broad interfacial region, and the ability to solubilize both hydrophilic and lipophilic compounds.

These properties enhance drug permeation by reducing the diffusion barrier of the stratum corneum. However, their low viscosity limits skin retention and topical application. To overcome this, gelling agents such as HPMC K100M, Carbopol 940, or guar gum are incorporated to form microemulsion-based gels, which increase viscosity and improve topical retention while maintaining the permeation advantages of microemulsions.

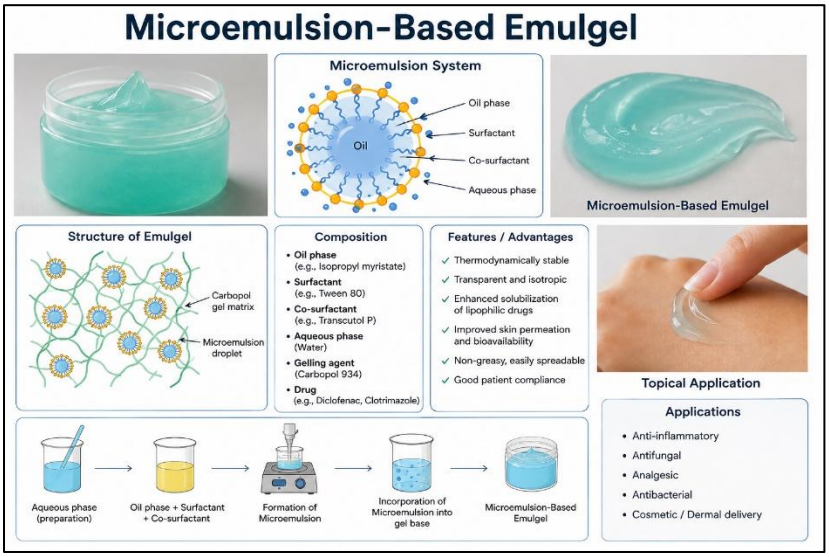

Fig.2. Microemulsion-Based Emulgel

2. Nanoemulgel:

Nanoemulsion are thermodynamically stable, translucent or transparent oil-in-water dispersions with droplet sizes typically ranging from 1 to 100 nm. When these nanoemulsion are incorporated into a gel base, the resulting formulation is termed a nanoemulgel. Due to their small droplet size and high surface area, nanoemulgel exhibit enhanced transdermal and dermal drug delivery compared to conventional emulsions or gels. They offer high drug loading capacity, improved skin penetration, and faster onset of therapeutic action.

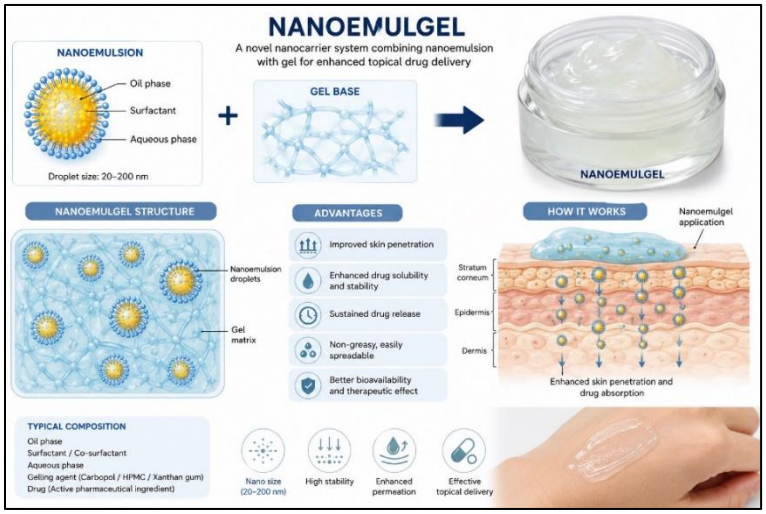

Fig.3. Nanoemulgel

3. Macroemulsion-Based Emulgel:

Macroemulsions contain larger droplets, typically greater than 400 nm in size. While the emulsion appears uniform to the naked eye, individual droplets can be visualized under a microscope. Macroemulsions are thermodynamically unstable, but their stability can be enhanced using surfactants and emulsifying agents. Macroemulsion-based gels combine the advantages of emulsion and gel formulations but

generally have lower transdermal permeation compared to micro- and nanoemulgel.

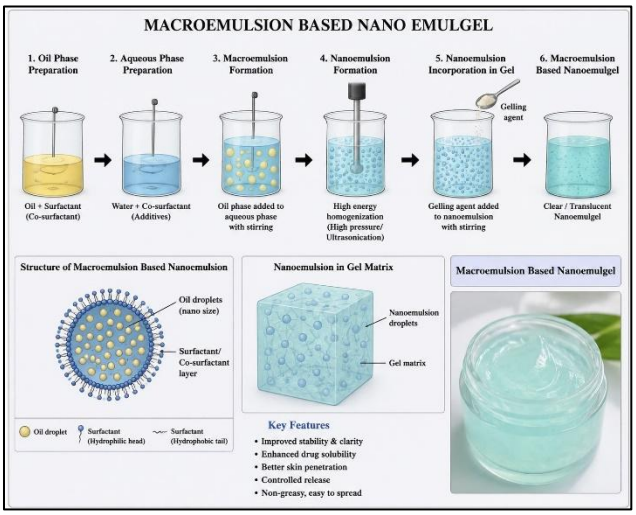

Fig.4. Macroemulsion based nano emulgel

Important Component of Nano emulgel: -

a. Oils: Oils used in Nanoemulsion are generally mineral oils used as the vehicle for drugs[12] E.g. castor oils and various fixed oils (cottonseed oil, maize oils, arachis oil) Olive Oil, Coconut Oil, eucalyptus oil, rose oil, clove oil etc.[13]

b. Aqueous Phase: Commonly distilled water is used as an aqueous phase for the preparation of Nanoemulsion and hydrogel.[14]

c. Surfactant and Co-Surfactant: surfactants are used both to give emulsification at the time of formulation and control day to day stability during shelf life of prepared Nanoemulsion. General selection of surfactant depends on the type of emulsion.[15] (O/W or W/O) E.g. Span 80 (Sorbitan monooleate), Acrysol K 140, Polyethyleneglycol-40-stearate, Acrysol, Labrasol, Stearic acid, PlurolOleique, Tween 80 (Polyoxymethylene- sorbitan monooleate), Labrafil, Sodium stearate, where agents like Transcutol, Captex, Cammul, Migyol, etc. can be use as cosurfactant or co-solvents.[16]

d. Gelling Agent: Polymers essential to give the structural network for the preparation of gels are known as gelling agents E.g. Natural - Agar, Tragacanth, Guar gum, Xanthan Gum, Semisynthetic and Synthetic Carbopol, Poloxamer, HPMC (cellulose derivatives)

e. Permeation Enhancers: They interact with different skin constituents to produce a reversible temporary increase in permeability. They can act by one or more mechanisms like,

i. Disrupting the highly compact structure of SC.

ii. Improving partition of drug[17] or solvent or co-enhancer into the SC.

iii. Interacting intercellular protein. Causing conformational changes in protein or solvent swelling is the key for alternating polar path. Some enhancers improve the fluidity of protein in SC, where some act on both pathways by disrupting multilaminate pathway. They can increase the diffusion of drug through skin proteins. Type of enhancer has a significant impact product designing[18]

E.g. Eucalyptus oil, Linoleic acid, Lecithin, Oleic acid, Chenopodium oil, Isopropyl myristate, Urea.

Characterization of nanoemulgel Visual examination:

It could be visually examined to determine its colour, appearance, and homogeneity.[19]

pH evaluation:

It is determined by using a digital pH meter.[20]

Determination of viscosity:

The viscosity of the gel is essential for efficient skin application. Viscosity is the measure of a fluid's resistance to flowing and a higher viscosity indicates a greater flow resistance. Viscosity is measured by using Brookfield's Viscometer.

Spreadability measurement:

The spreadability of nanoemulgels is assessed using their "Slip" and "Drag" properties. Measurement of droplet size and polydispersity index: To determine droplet size, the dynamic light scattering (DLS) method is used. According to the light scattering theory, the polydispersity index (PDI) measurement indicates droplet diameter and size distribution and is determined by scattered light intensity.[21]

Zeta potential:

Nanoemulgels containing gelling agents and nano emulsions that exhibit an electrical charge due to the presence of different types of surface-active agents may affect the stability of the formulation, as measured by Malvern Zetas Izer® nano-ZS ZEN 3600, ZeeCom-2000, etc. Drug content: The total quantity of drug present in the formulations is determined by various analytical methods.[22]

Accelerated stability study:

According to International Council for Harmonization (ICH) guidelines, the formulations are maintained for three months in an oven at 37 ± 2°C, 45 ± 2°C, and 60 ± 2°C. Every two weeks, the drug content is determined.

Skin irritation test:

The preparation is applied to the well-shaved skin of a rat, and any negative effects, such as irritation, colour change in the skin, or morphology, should be observed for up to 24 h. The test is considered successful if no irritation occurs [23]

Method Of Preparation for Nanoemulgel:

1. **High-pressure homogenization method:**

This method involves the use of a high-pressure homogenizer to break down the oil phase into nanosized droplets that can be easily dispersed in a hydrophilic gel matrix. The homogenization process generates high shear forces that help to reduce the droplet size and create a stable Nanoemulgel.

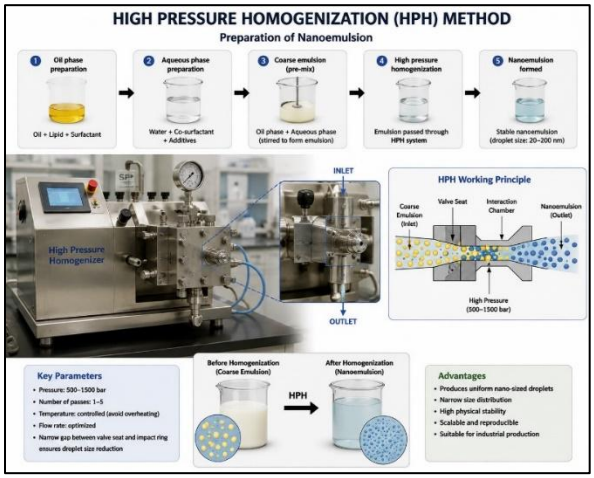

Fig.5. High pressure homogenization (HPH) method

2. **Ultrasonication method:**

In this method, ultrasonic waves are used to create Nanoemulgel. The oil phase and the hydrophilic matrix are mixed together, and the mixture is subjected to high-frequency ultrasound waves. The ultrasonic energy breaks down the oil phase into nanosized droplets, which are dispersed uniformly in the gel matrix.

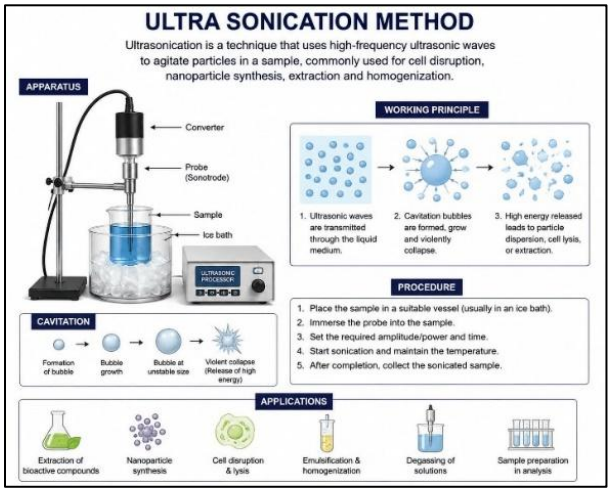

Fig.6. Ultra sonication Method

3. **Solvent evaporation method:**

This method involves the use of a water-miscible solvent to dissolve the oil phase and the hydrophilic matrix. The solvent is then evaporated under reduced pressure, leaving behind a Nanoemulgel with nanosized droplets of oil dispersed throughout the gel matrix.

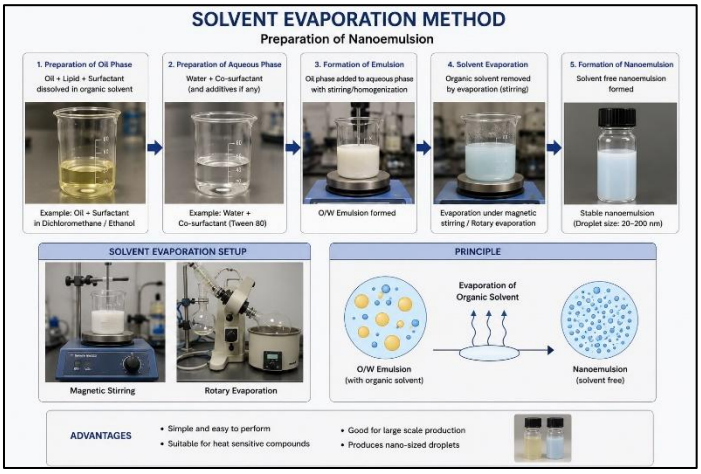

Fig.7. Solvent Evaporation method

4. **Micro fluidization method:**

In this method, the oil phase and the hydrophilic matrix are passed through a microfluidizer to create Nanoemulgel. The microfluidizer generates high shear forces that break down the oil phase into nanosized droplets, which are dispersed in the gel matrix.

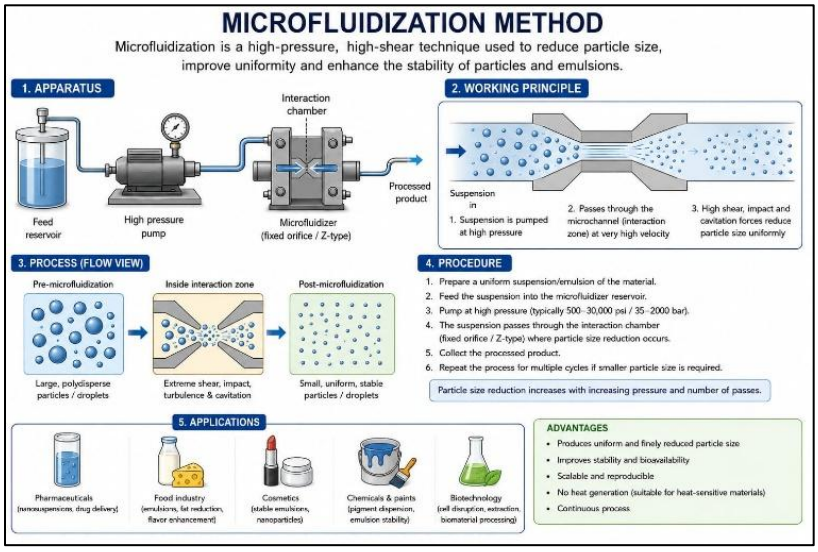

Fig.8. Micro fluidization Method

5. **Self-emulsifying gel method:**

This method involves the use of a self-emulsifying drug delivery system (SEDDS)that can create Nanoemulgel in situ. The SEDDS is a mixture of oil, surfactants, and co-solvents that can spontaneously emulsify when in contact with water. When the SEDDS is mixed with a hydrophilic gel matrix, a nanoemulgel is formed.

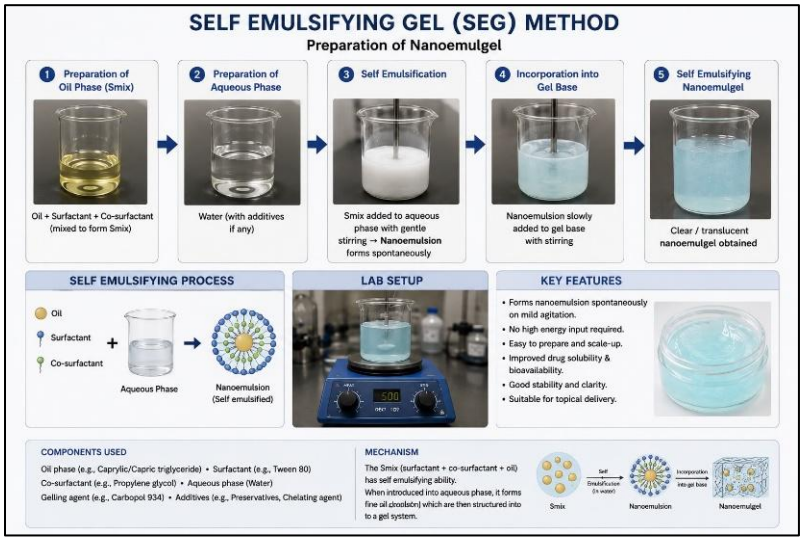

Fig.9.Self emulsifying gel (SEG) method

6. **High-energy emulsification method**:

This method involves the use of high-energy input to create small droplets of the dispersed phase (oil) in the continuous phase (water). This can be achieved through various methods such as sonication, high-pressure homogenization, or micro fluidization. The resulting emulsion can then be transformed into a gel by adding a gelling agent such as a polymer or a surfactant.

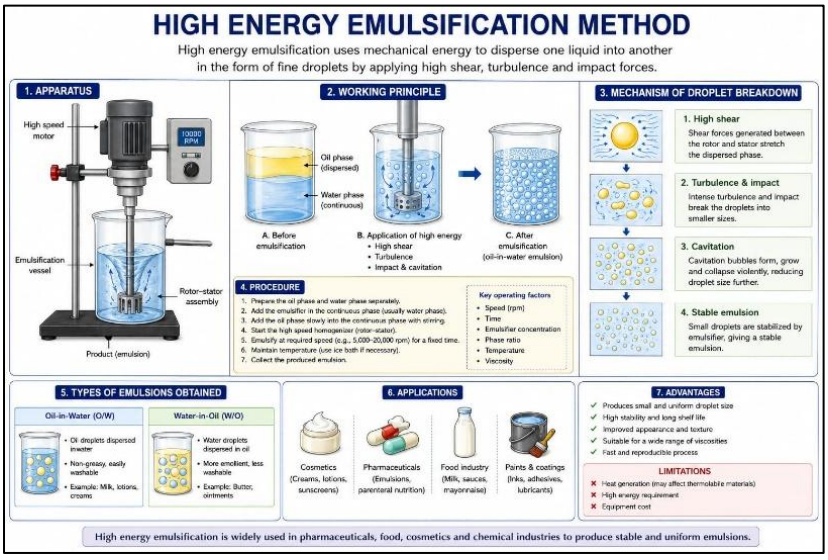

Fig.10. High energy emulsification method

7. **Phase inversion temperature (PIT) method:**

This method involves the use of a thermosensitive surfactant that undergoes a phase transition from a water-soluble to a water-insoluble state at a certain temperature. By adjusting the temperature of the system, the surfactant can be induced to form a gel-like structure that entraps the dispersed phase.

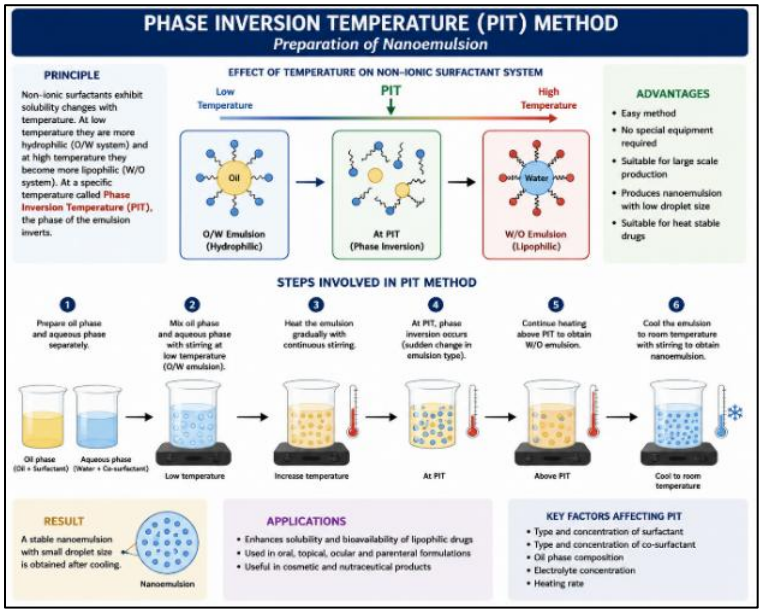

Fig.11. Phase inversion temperature (PIT) method

8. **Sol-gel transition method:**

This method involves the use of a sol-gel transition system, where a gel is formed by the aggregation of a network of particles or polymers in a solvent. This can be achieved by adding a crosslinking agent or a thermosensitive polymer to the emulsion, which triggers the formation of a gel-like structure at a certain temperature or under certain conditions.

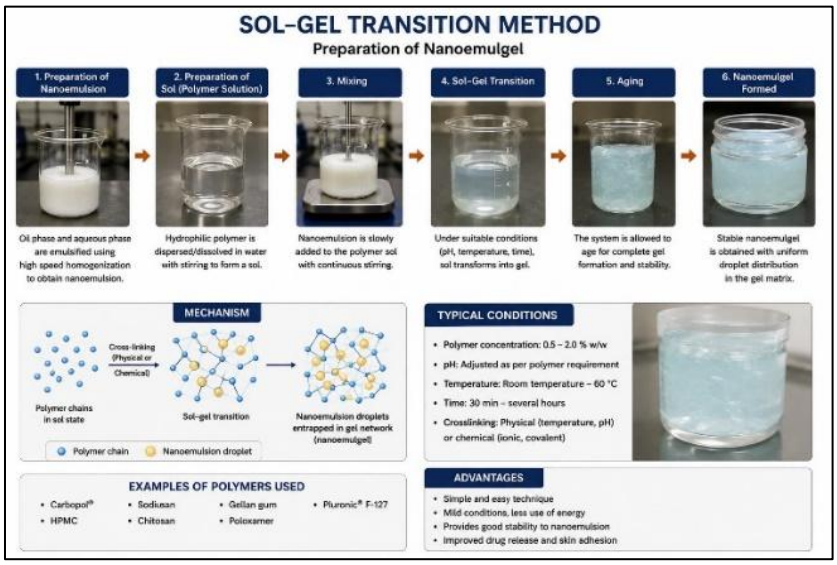

Fig.12. Sol-Gel transition method

9. **Electrostatic complexation method:**

This method involves the use of oppositely charged polymers or surfactants to create a stable emulsion, which can then be transformed into a gel by adding a crosslinking agent or a gelling agent.

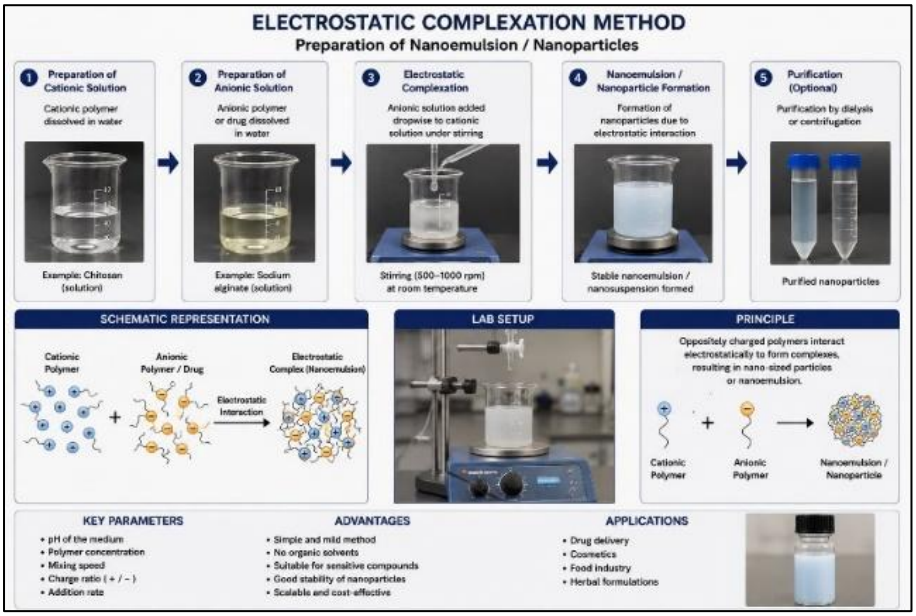

Fig.13. Electrostatic complexation method

10. **Coacervation method:**

This method involves the use of two or more polymers that undergo phase separation in the presence of an electrolyte or a pH change, resulting in the formation of a gel-like structure. The dispersed phase can then be incorporated into the gel by high-energy emulsification or other methods.[24]

Steps Involved in Method of Formulation of Nanoemulgel:

a) Screening of components
b) Preparation of Nanoemulsion
c) Preparation of Nano emulgel
d) Preparation of Gelling Agent
e) Incorporation of Gelling Agent

- **Screening of compound:** Drug solubility was determined in different oils by adding more than drugs in different ingredients, then stirring continuously for 72 h to reach equilibrium. Then, samples were centrifuged and the supernatant was collected and the solubility was determined using appropriate analytical methods. Thereafter, excipients from each class with the highest drug solubility were selected for additional studies.

- **Preparation of Nanoemulsion:** The drug is then solubilized in oil and oil is added to Nmix, this mixture is diluted with water to form of Nanoemulsion of the given drug.

- **Preparation of Nanoemulgel:** Gel base is ready mistreatment 1g of the Carbopol in a very needed amount of water. When the Carbopol solution has fully swelled and dispersed over a twenty-four-hour period, the ready nanoemulsion is progressively added to the mixture while stirring continues. The addition of Triethanolamine offers homogenized gel dispersion. Finally needed remaining half is adjusted with H2O.[25]

- **Preparation of Gelling Agent:** In fabrication of a nanoemulgel, the purpose of using a gelling agent is to change the physical form from liquid to semi-solid which has many advantages in terms of patient compliances. Various categories of the gel

base for the purpose of gelling can be prepared by adding the polymer in purified water and stirred continuously with a glass rod or any other suitable mechanical device until desired texture achieved and then pH should be adjusted. In various experimental works, the preparation of the gelling agent is carried out by adding the polymer in purified water by a cold method. In cold method, the components are added in purified water at 20o C followed by the addition of gelling polymer and cooling the water up to 4o C.

- **Incorporation of Gelling Agent:** After the preparation of nanoemulsion as well as the gelling agent, both are mixed and a nanoemulgel is prepared. Here a liquefied form of water in oil (w/o) or oil in water (o/w) nanoemulsion is converted into a thick and semisolid nanoemulgel with the help of various polymeric gelling agents. This gel form can change again into a solution form after applying a mechanical force such as rubbing. This property of the material is known as thixotropy where gel to sol and sol to gel transformation occurs on the application of shear stress and reversal of the same respectively without a change in volume. Innumerable polymers have been used as gelling agents such as Carbomer 940, Carbopol 943, Chitosan, Carbopol 934, Carbopol 940, Poloxamer 407, Methyl cellulose etc. for the preparation of nanoemulgel of desired characteristics for various applications.[26]

Applications of nanoemulgel formulations

Nanoemulgel is an innovative topical delivery system with a variety of pharmacological actions. These impacts can be categorized as follows:

- Nanoemulgel is a promising alternative to other topicals for the treatment of pain and inflammation that have improved pharmacokinetic and pharmacodynamic action.
- For the treatment of psoriasis
- It produces antifungal activity for Candida infection in several folds when compared to other commercial emulgels.

Biocompatible polymers containing nanoemulgel produce a better therapeutic effect than traditional ophthalmic preparations for the treatment of ocular diseases.[22]

Advantages of nanoemulgel

- Nanoemulgel is non-irritating and non-toxic.
- Increased drug solubility, deposition, and skin permeability

Additionally, a strong concentration gradient produced by good skin adherence, spreadability, stability, and high solubilizing power increases drug penetration as it moves downward.

- Drug loading is better in comparison to other formulations.
- Drugs with a shorter half-life can be released under controlled conditions and produce a prolonged therapeutic effect.[27]

Mechanism involved to enhance permeability and bioavailability from nanoemulgel preparations (Table 1)

The skin permeability as well as bioavailability of nanoemulgel may be enhanced by various mechanisms. Some of the studied mechanisms with types of nanoemulgel are listed in **Table 1**

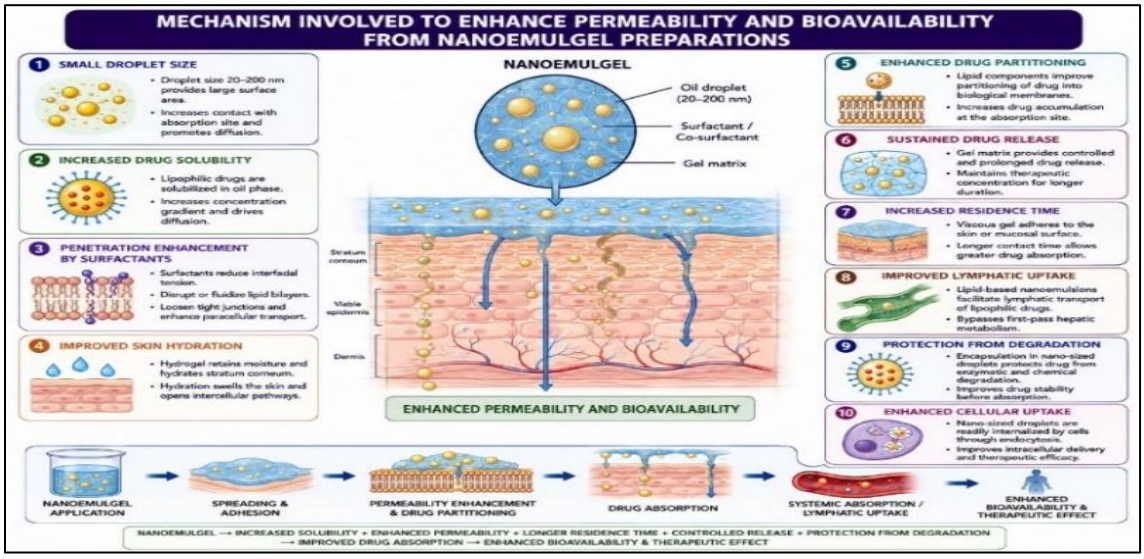

Fig.14. Mechanism involved to enhance permeability and bioavailability from nanoemulgel preparations

Table 1: Mechanism involved to enhance permeability and bioavailability from nanoemulgel preparations

Types of nanoemulgel	Mechanism of permeability/bioavailability	References
Conjugate of curcumin	Induced apoptosis in cancer cells, suppressing the expression of NF-κB, TNF-α, and COX-2 cellular targets	[28]
Clove essential oil	Dispersion of the nanoemulsion in the polymeric matrices of the prepared nanoemulgel.	[29]
Snakehead fish (pphiocephalus striatus)	Ex vivo transdermal permeation value	[30]
Methotrexate	Change in temperature experienced by the nanogel	[31]
Terbinafine	Ex vivo drug permeation and in vivo antifungal activity	[32]
Paclitaxel	Nanogel exerts high cytotoxicity to cancer cells and reverses multidrug resistant effectively.	[33]
Diphenhydramine	First-order kinetics and Fickian diffusion	[34]

Raloxifene hydrochloride	Ex vivo permeation, histopathology, SEM, DSC, and CLSM studies.	[35]
Desonide	DES, Franz diffusion cell system, CLSM	[36]
Ketoconazole	Ex vivo permeation	[37]
Telmisartan	Ex vivo permeation, first-order reaction, and Higuchi model with non- Fickian diffusion.	[38]
Ibuprofen	Drug diffusion, however, drug partition, and matrix erosion	[39]
Piroxicam	Franz diffusion cell	[40]

Table 2: List Of Drugs Used In Nanoemulgel Hair Dye

Fig.15. List of plant materials used in nanoemulgel hair dye

Difference between normal hair dye and nanoemulgel hair dye.

Parameter	Normal hair dye	Nano emulgel hair dye
Formulation	Conventional liquid, cream, or powder formulation	Nano emulsion incorporated into a gel base
Particle size	Micron-sized particles	Nanometer-sized droplets (20–

		200 nm)
Penetration into hair	Limited penetration	Improved penetration due to nanosized droplets
Colour retention	Moderate; fades relatively quickly	Better colour retention and prolonged effect
Application	May drip and spread unevenly	Easy to apply, non-dripping gel
Stability	Moderate physical stability	Enhanced physical and chemical stability
Release of Dye	Immediate release	Controlled and sustained release
Safety	Synthetic dyes may cause scalp irritation or allergic reactions	Herbal nano emulgels may reduce irritation and improve biocompatibility
Delivery of Herbal extracts	Less efficient	Enhanced delivery and bioavailability of herbal actives

Benefits:

Normal Hair Dye:

- Provides quick and effective hair coloring.
- Covers Gray hair effectively.
- Available in a wide range of shades and formulations.
- Easy to manufacture and widely available.
- Cost-effective compared to advanced formulations.
- Suitable for home and salon use.

Nano Emulgel Hair Dye:

- Enhances penetration of dye int the hair shaft due to nan-sized droplets.
- Produces more uniform and consistent hair coloring.
- Offers longer-lasting colour with improved colour retention.
- Provides controlled and sustained release of herbal colorants.
- Non-dripping gel improves ease of application and user convenience.
- Improves physical and chemical stability of the formulation.
- Enhances delivery and effectiveness of herbal extracts such as henna and hibiscus.

CONCLUSION

Nanoemulgel technology has emerged as a promising and advanced topical drug delivery system by combining the advantages of nano emulsions and hydrogels. It offers enhanced drug solubility, improved skin penetration, controlled and sustained release, better stability, and increased patient compliance compared with conventional topical formulations.

The incorporation of nanosized droplets into a gel matrix improves spreadability, prolongs retention time, and enhances the bioavailability of both

hydrophilic and lipophilic active compounds. Nanoemulgels have demonstrated significant potential in pharmaceutical and cosmetic applications, particularly in the delivery of herbal formulations for skin and hair care. Despite these advantages, challenges such as formulation optimization, long-term stability, large-scale manufacturing, and regulatory approval remain. Further research and clinical evaluation are essential to establish the safety, efficacy, and commercial feasibility of nanoemulgel formulations. Overall, nanoemulgels represent an innovative and effective platform for topical drug delivery with broad future applications in healthcare and cosmetic sciences.

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