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Open Access REVIEW

Preparation methods and applications of Thiocolchicoside Nanoemulsion: An Updated Review

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ABSTRACT

Unlike the milky-white color associated with coarse dispersion, nanoemulsions, sometimes called nanometric-sized emulsions, are fine water-in-oil (w/o) and oil-in-water (o/w) dispersions of two immiscible fluids. The present review was based on the preparation methods and applications of thiocolchicoside nanoemulsion. Nanoemulsion is easier to move since it has a larger surface area and free energy. Nanoemulsions don't exhibit process-inherent phenomena like creaming, flocculation, coalescence, and sedimentation. In cell cultures, it enhances the uptake of hydrophilic molecules and can be substituted for liposomes, vesicles, and lamellar liquid crystalline phases. High energy technologies have been used by researchers to improve the distribution of bioactive food ingredients and the administration of medications. High energy approaches are more advantageous for delivering nanoemulsions containing bioactive food components since they require less surfactant. It was determined that nanoemulsion-based drug delivery devices effectively tackle the problem of limited bioavailability caused by hydrophobic and highly first-pass metabolic drug and food ingredients. Further research is required to properly investigate the possibilities of phase inversion emulsification methods for effective medicate on loading and distribution.

Keywords: thiocolchicoside, nanoemulsion, preparation methods, advantages, emulsion.

INTRODUCTION

Unlike the milky-white color associated with coarse dispersion, nanoemulsions, sometimes called nanometric-sized emulsions, are fine water-in-oil (w/o) and oil-in-water (o/w) dispersions of two immiscible fluids [1]. By adding the proper amphiphilic emulsifiers or emulsifiers, these 20-200 nm droplets are stabilized. Thus, mini-emulsions are another name for nanoemulsions [2]. Unlike microemulsions (ME), nanoemulsions (NE) are stable on heterogeneous systems because of kinetic stability. Nanoemulsions, often referred to as "potential thermodynamic stability" and distinguished by their prolonged physical consistency, do not seem to agglomerate or flocculate. Researchers originally started working with colloidal systems in the early 20th century, which is when the history of nanoemulsions began [3].

Although early research concentrated on macroemulsions and microemulsions, it set the stage for the creation of nanoemulsions. In the 1990s, nanoemulsions as a separate class of emulsions attracted a lot of interest. Their exceptionally tiny droplet sizes, which usually range from 20 to 200 nanometers, prompted researchers to investigate their special qualities [4]. Understanding the possible uses of nanoemulsions, especially in the food and pharmaceutical sectors, became more important during this time [5].

Salient features of Nanoemulsion [6][7]

1. Compared to ME, which requires a high concentration (20%), nanoemulsion may be made with lower emulsifier concentrations (3-10%).
2. Because of its enormous surface area, nanoemulsion promotes penetration in the emulsion system and facilitates the efficient transportation of active chemicals over a semipermeable membrane.
3. The tiny globule size of nanoemulsions not only prevents droplet flocculation but also prevents bigger droplet flocculation. As a result, the system may endure in isolation without being split.
4. The decrease in Brownian motion and gravitational forces in a nanoemulsion is caused by tiny droplets or globules. As a result, neither creaming nor sedimentation occurs during the product's storage.
5. Making nanoemulsions is easy and requires little energy. It is claimed that nanoemulsion formulations increase the bioavailability and repeatability of the plasma concentration profile.
6. Because they include both hydrophilic and lipophilic medications, nanoemulsions are super solvents.
7. The medication is shielded from environmental factors including pH hydrolysis and oxidation when the active ingredient is contained within a nanoemulsion formulation.
8. Among other dosage forms, nanoemulsions can be made into gels, creams, foams, aerosols, and sprays. They can also be administered orally, topically, intravenously, intrapulmonary, intranasally, and intramuscularly. Nanoemulsions are more thermo-kinetically stable and have a greater solubilization capability than micelle dispersion.
9. Because it is an oil/lipid-based drug delivery method, it helps escape hepatic first-pass metabolism.
10. Additionally, nanoemulsion can successfully cover up the bitter and metallic tastes of drugs that may cause unpleasant side effects including nausea and vomiting.
11. Nanoemulsions can occasionally be constructed to create lamellar liquid crystalline surrounding globules, and they can be a helpful substitute for liposomes and vesicles (which have poor stability).

Advantages [8]

- Nanoemulsion is easier to move since it has a larger surface area and free energy.
- They don't exhibit process-inherent phenomena like creaming, flocculation, coalescence, and sedimentation.
- They do not cause irritation or poisoning.
- It can be ingested if it contains biocompatible surfactants.
- It is superior for usage with humans and animals.
- In cell cultures, it enhances the uptake of hydrophilic molecules and can be substituted for liposomes, vesicles, and lamellar liquid crystalline phases.

Disadvantages [9]

- Temperature and pH affect stability
- High concentrations of surfactants.
- Instability may result from the Oswald ripening effect.

Preparation methods

Producing nanoemulsions requires a greater amount of energy than producing macroemulsions. The surface tensions between water and oil are lessened with the use of surfactants. Small molecules, such as non-ionic surfactants, reduce surface tension more than polymeric surfactants, such as poly (vinyl alcohol). Another important function of the surfactant is its effect on the interfacial dilatational modulus. Emulsification produces an increase in the interfacial area and a decrease in surface excess. The equilibrium is restored by the surfactant's adsorption from the bulk, but this process takes time [10].

➢ High-pressure homogenization

High-pressure homogenizers produce the lowest particle sizes by providing uniform flow and high energy. As a result, the most popular method for creating nanoemulsions is using high-pressure homogenizers. To manufacture nanoemulsions with incredibly small particle sizes (up to 1 nm), high-pressure homogenizers are employed to generate highly disruptive forces [11].

The content of the sample, the kind of homogenizer, and the homogenizer's operational parameters such as temperature, time, and energy intensity- all affect the size of the nanoemulsions that high-pressure homogenizers create. The size of the nanoemulsion droplets decreases as homogenization intensity increases. Intense homogenization may occasionally result in an increase in the final nanoemulsion's particle size, such as when biopolymers are utilised as an emulsifier. Because small-molecule surfactants are more efficient than biopolymers at creating nanoemulsions, they ought to be utilised as emulsifiers in high-pressure homogenizers [12].

➢ Microfluidization

A tool known as a microfluidizer is used in the microfluidization process, which is a mixing technique at the microscale level. Fluids are pushed through the microchannels at high pressure (500–20,000 psi) during the microfludization process. Microchannels are typically microsize channels that permit mixing at the micro size level [13]. The water and oil phases of the macroemulsion are combined and then run through a microfluidizer. Under intense pressure, the macroemulsion is directed towards the interaction chamber via the microchannels. Two fast-moving streams of macroemulsions collide inside the interaction chamber. Shearing, cavitation, and impact forces created by this collision result in stable nanoemulsions [14].

Compared to homogenizers, microfluidizers yield smaller and narrower nanoemulsion particle size distributions. Moreover, stable nanoemulsions are produced by microfluidizers at low surfactant concentrations. Nanoemulsions of food ingredients have been made via microfluidization techniques [15]. Food-grade nanoemulsions with consistent droplet size distributions and increased stabilities are created via microfluidization processes.

➢ Ultrasonication

When it comes to cleaning and operation, ultrasonication performs better than other high energy techniques. Ultrasonic waves create cavitation forces during ultrasonic emulsifications, which split the macroemulsion into nanoemulsions. This technique makes use of ultrasonicators, which are probes that produce ultrasonic waves. The nanoemulsion can be stabilised and the particle size can be adjusted by adjusting the time and ultrasonic energy input. The mechanism of acoustic cavitation is the primary source of physical shear in ultrasonic emulsification. The process of microbubble production, growth, and collapse known as cavitation is brought on by variations in the sonic wave's pressure. Nanosized droplets occur as a result of the extreme turbulence caused by the collapse of microbubbles [16].

➢ Phase inversion emulsification method

Phase transition in this method is caused by the surfactant's spontaneous curvature during the emulsification process. Variations in temperature, composition, etc., can cause changes in the surfactant's spontaneous curvature. Variations in temperature and composition might cause variations in the surfactant's spontaneous curvature or affinity, which can lead to transitional phase inversion. Nevertheless, CPI happens when a dispersed phase is constantly introduced until the drops of the dispersed phase combine to form bi-continuous or lamellar structural phases. A catastrophe is an abrupt shift in a system's behaviour brought on by shifting circumstances. Quick phase inversion necessitates a high rate of coalescence, which is mostly caused by the surfactant being present in the dispersed phase, for catastrophic phase inversion to occur. While spontaneous curvature or surfactant affinity is altered during transitional phase inversion, they remain unchanged during catastrophic phase inversion [17].

➢ Self-nanoemulsification method

The self-emulsification technique creates nanoemulsions without altering the surfactant's spontaneous curvature. Nano-sized emulsion droplets are produced when surfactant and/or co-solvent molecules quickly migrate from the dispersed phase to the continuous phase. Another name for the self-emulsification technique is the spontaneous emulsification technique. Based on the self-emulsification phenomena, SNEDDS have a reduced lipid content and a higher concentration of hydrophilic surfactants, also known as co-surfactants or co-solvents. An isotropic combination of an oil, surfactant, co-surfactant, and medication is known as SNEDDS. With the help of the stomach and intestine's mildly agitating digestive motility, this mixture forms a thin and optically transparent O/W nanoemulsion when diluted by aqueous fluids in-vivo [18].

Nanoemulsion applications in Medicine

1. Passive tumor targeting with nanocarriers

Using passive targeting of nanocarriers delivering therapeutic chemicals to cancer tissues and abnormal physiology of tumours. parenterally administered medications using nanotherapeutics, which make use of nanoparticle technology. In a pioneering study, Matsumura and Maeda showed that proteins with molecular weights between 15,000 and 70,000 g/mol may aggregate effectively in solid tumours. More slowly than larger particles, particles less than 400 nm are removed from the bloodstream. For instance, polymeric micelles are unstable in blood and fully release after 15 minutes [19].

2. Nanoparticles in gene delivery

Targeted delivery-which uses active targeting of nanocarriers to bind with receptors on cancer cell surfaces and deliver drugs to the appropriate tissue region-has been studied. The interaction between the receptor and ligand facilitates absorption by endocytosis when an active chemical-containing nanocarrier enters the cancer site through systemic circulation. Because it can lessen adverse effects, active targeting is helpful in oncology, particularly for the treatment of cancers. Traditional instant release (red) and extended-release formulations' pharmacokinetic properties are examined (blue). Red arrows denote the regular dosage time and blue arrows denote the sustained release formulation dose time. Interfacial diffusion restrictions in nanoparticle formulations during active release.

3. Nanocarriers in parenteral drug delivery

Parenteral nanoparticle preparations have garnered a lot of interest due to the potential for improved therapeutic targeting to cancer locations as well as higher solubility/partition in the circulating blood without the necessity of several excipients. For parenteral drug administration, nanocarrier systems have been investigated in contrast to their free-drug counterparts. The use of nanotechnology in parenteral delivery of several substances has been extensively studied. Some of these substances must be administered locally utilising nanoparticles because of their hazardous non-target effects or uncontrolled systemic dispersion. For instance, the use of doxorubicin, a potent anticancer drug, is restricted due to serious side effects like cardiotoxicity [20].

4. Nanoparticles as drug carrier vehicle

It helps to reduce toxicity, enhance release, and provide better formulation alternatives in addition to improving drug solubility and bioavailability.

It has numerous advantages as follows:

- Better solubility
- More surface area
- A faster rate of dissolution
- Better oral absorption
- A quicker onset of medication effects
- A lower dose needed
- Less fed/fasted fluctuations
- Less variability in patient care

5. In delivery of proteins & peptides

The study conducted in this field indicates that they can be engineered to hold hydrophobic or hydrophilic proteins under the right circumstances, and they seem to fulfil the requirements for the perfect particle carrier system. Benefits of nanoemulsion formulation include enhanced protein stability, defence against proteolytic cleavage, and continual release of the integrated molecules. Important peptides including cyclosporine A, insulin, calcitonin, and somatostatin that have been incorporated into solid lipid particles are presently the subject of research [21]. After oral nanoemulsion administration, a significantly higher concentration of paclitaxel was discovered in the systemic circulation as compared to the control water solution.

6. In parasitic diseases

Among the most common parasite diseases that still affect people today are tryanosomiasis, leishmaniasis, and malaria. Since successful vaccination may not be possible, antiparasitic chemotherapy is the main treatment option for many parasite illnesses. Furthermore, nanoemulsion exhibits great promise in the treatment of parasitic diseases because of their intrinsic structure and particle nature.

Even though we live in a period of incredible technology and ingenuity, infectious diseases like malaria still represent one of the largest global health concerns. The primary issues with traditional chemotherapy for malaria are the rise of drug resistance to multiple drugs. Numerous nanoscale delivery techniques have previously shown promise in treating and preventing malaria in animal models.

7. In tuberculosis

Compared to polymeric nanoparticles, the production of SLN requires significantly less organic solvent and produces encapsulated particles that are more stable and efficient than liposomes. In experimental tuberculosis, anti-tubercular medications have been effectively encapsulated using nanoemulsion. ATD were co-incorporated into SLN in order to evaluate their potential for usage in oral TB chemotherapy. The study's findings demonstrated the great potential of SLN in providing ATD by reducing dosage frequency and improving patient adherence to tuberculosis therapy [22].

8. In preparations of cosmetics and dermatological

Topical applications with SLN technology have a fast time to market and a lot of promise, including pharmaceutical and cosmetic compositions. Nanoemulsion are thought to be the next generation of delivery methods, following liposomes. Since topical therapies for skin conditions are less likely to have negative systemic consequences, they seem desirable; yet, healthy skin is shielded from xenobiotic penetration by the stratum corneum. Particulate transporter-based systems may offer a means of improving cutaneous penetration. Since lipid carriers that stick to the skin's surface, known as epidermal lipids, are present in substantial levels in the penetration barrier [23].

Nenemulsions have been utilised for cleaning and disinfection. A nontoxic disinfection cleaner for use in travel, healthcare, food preservation, and military applications has been developed through in vitro systems. In just five to ten minutes, they have been demonstrated to eradicate a variety of viruses, bacteria, fungi, and tuberculosis without offering any of the hazards connected to other disinfectant types.

9. In agriculture

The essential oil of Artemisia arboreseens was able to reduce the rate of evaporation when applied to SLN. As pesticide transporters, these systems have been used in agriculture.

10. Transfection agent

For gene transfer, cationic nanoemulsion are made from the same cationic lipid. Studies were conducted to examine the differences in structure and function between liposomes and nanoemulsion. While PCS showed that the created nanoemulsion had smaller diameters than the equivalent liposomes, AFM confirmed the expected structural changes. There were very minor differences in DNA binding. The in vitro transfection performance is determined more by the composition of cationic lipids than by the colloidal structure in which it is built. Consequently, cationic nanoemulsion expands the pool of incredibly potent non-viral transfection agents by introducing a novel agent with desirable and distinctive technological properties. To increase transfection efficiency one hundred times, cationic SLN and the nuclear localization signal TAT2 were combined [24].

11. In treatment of lung diseases

The development of colloidal delivery techniques including liposomes, micelles, and nanoparticles has improved drug delivery. Nanoparticles are advantageous over conventional delivery systems due to their distinctive characteristics, which include their small particle size, high surface area, and ability to modify their surface properties. Targeted delivery of nanoparticles to the lungs is a growing field of research [25].

CONCLUSION

In nanoemulsion drug delivery systems, high energy techniques provide more compositional flexibility and control over particle size dispersion. High energy technologies have been used by researchers to improve the

distribution of bioactive food ingredients and the administration of medications. High energy approaches are more advantageous for delivering nanoemulsions containing bioactive food components since they require less surfactant. It was determined that nanoemulsion-based drug delivery devices effectively tackle the problem of limited bioavailability caused by hydrophobic and highly first-pass metabolic drug and food ingredients. Further research is required to properly investigate the possibilities of phase inversion emulsification methods for effective medication loading and distribution.

CONFLICT OF INTEREST

Authors declare for none conflict of interest.

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