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Research Progress on Preparation Technology and Application of Coenzyme Q_{10} Delivery System

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Abstract. Coenzyme Q_{10} is a lipid-soluble quinone compound that functions both as a mitochondrial electron transport carrier and as an antioxidant. It is widely used in the fields of cardiovascular disease adjuvant therapy, health products, and cosmetics. However, its poor water solubility, low photothermal stability, and limited bioavailability constrain its practical applications. This paper systematically discusses three delivery systems for coenzyme Q_{10}: nanoemulsions, which enhance water solubility and cellular permeability; nanoparticles, which enable particle size control and high encapsulation efficiency with targeted, sustained-release properties; and gel-based delivery systems, which improve the skin's antioxidant capacity and storage stability. This research offers material design strategies and technological optimization approaches to address the bottlenecks in coenzyme Q_{10} application, providing important academic reference value for improving the bioavailability of lipophilic active substances.

Keywords: Coenzyme Q_{10}, Nano emulsion, Nanoparticles, Gel-based delivery system, Bioavailability.

1. Introduction

Coenzyme Q_{10}, also known as ubiquinone, is a lipid-soluble compound and a safe, vitamin-like substance [1]. As an endogenous vitamin-like compound, it primarily acts in human mitochondria and serves as an essential electron carrier in the respiratory chain. At the same time, it is the only fat-soluble antioxidant that can be synthesized endogenously in the human body, effectively protecting proteins, DNA, and lipids from oxidative damage [2]. It can also inhibit the increase in metalloproteinase levels caused by UV damage in skin fibroblasts, promote cell proliferation, and increase the expression of type IV and VII collagen in fibroblasts [3] . Research has shown that with age, the body's ability to synthesize coenzyme Q_{10} gradually declines, and the level of coenzyme Q_{10} in tissues continues to decrease.

Coenzyme Q_{10} has been recognized as one of the important vitamin-like substances, and many countries have approved its use as a food additive in the fields of food and health products. It plays a valuable auxiliary role in the treatment of cardiovascular diseases, Parkinson's disease, hypertension, and other conditions, and is used as a health supplement to support disease management [4]. However, the molecular structure of coenzyme Q10 contains numerous unsaturated double bonds and hydrophobic groups, resulting in low molecular polarity and poor water solubility.

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It is prone to photodegradation and thermal degradation, and it has a low absorption rate in the human digestive tract, which seriously restricts its widespread application in the fields of health foods and biomedicine [5].

2. Coenzyme Q_{10} emulsion

2.1. Property of coenzyme Q_{10} emulsion

In recent years, emulsion technology has attracted considerable attention in the fields of drug and nutrient delivery due to its advantages in improving the solubility, stability, and bioavailability of hydrophobic substances. Among these systems, nanoemulsions (particle size 1–100 nm) have shown significant potential for delivering lipophilic compounds as thermodynamically stable, low-viscosity colloidal dispersion systems. Nanoemulsions are often used to deliver lipophilic compounds, and nanoemulsions loaded with coenzyme Q_{10} offer many advantages: they can penetrate cell membranes; provide targeted and sustained-release effects; achieve high loading rates; and enhance the physical and chemical stability of coenzyme Q_{10} [6]. Meanwhile, research has found that reducing emulsion particle size can significantly improve the bioavailability of coenzyme Q_{10}. Encapsulation in nanoemulsions significantly improves the storage and light stability of coenzyme Q_{10}, which not only effectively eliminates free radicals but also enhances percutaneous skin absorption [7].

2.2. Preparation method of coenzyme Q_{10} emulsion

Coenzyme Q_{10}, as an important bioactive substance, is widely used in medicine, healthcare, and cosmetics. The main preparation methods for its emulsions include high-pressure homogenization and high-speed shearing, each with distinct technical characteristics and application scenarios.

Huang Juan et al. [8] used the high-pressure homogenization method to prepare a compound flaxseed oil emulsion with gum arabic as the emulsifier to carry coenzyme Q_{10}. The resulting emulsion had an average particle size of 284 nm and a polydispersity index (PDI) of 0.112, showing uniform spherical droplets. Zhou Ben [9] optimized the high-pressure homogenization process and prepared a coenzyme Q_{10} emulsion with a smaller particle size (106.1 nm). The optimal conditions were: coenzyme Q_{10} content 5%; homogenization pressure 750 bar; Tween 80 accounting for 40% of the total emulsifier content; zeta potential -56.32 ± 1.43 mV; PDI 0.200; and encapsulation efficiency 93%, with uniform spherical morphology. FTIR and UV-Vis analyses confirmed good encapsulation, as well as storage and light stability of coenzyme Q_{10}. Yang Yang et al. [10] further optimized the high-pressure homogenization method to prepare a coenzyme Q_{10} nanoemulsion using medium-chain fatty acid as the oil phase, soybean lecithin as the surfactant, and Tween-80 as the cosurfactant. The optimal formulation was 2 g medium-chain fatty acid, 5.4 g soybean phospholipid, and 1 g Tween-80. The nanoemulsion prepared under these conditions had a smaller average particle size (73 nm) and higher encapsulation efficiency (97.6%). Meanwhile, Li Fei [11] used high-pressure homogenization to prepare a coenzyme Q_{10} system using soy protein isolate, whey protein isolate, and sodium caseinate as wall materials, increasing the water solubility of coenzyme Q_{10} by more than 5×10^7 times and achieving good storage stability.

Wednesday Jiu et al. [12] used the high-speed shearing method to construct a coenzyme Q_{10} emulsion system using soluble soybean polysaccharide and pea protein. They found that when the concentration of soluble soybean polysaccharide was 1.0%, the oil droplet size of the emulsion was minimized and stability was optimal. Under varying conditions of pH (6.0), salt ion concentration

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(100/300 mmol/L), and temperature (25–95 °C), the particle size of emulsions containing soluble soybean polysaccharide was significantly smaller than that of the control group without added polysaccharide.

2.3. Application of coenzyme Q_{10} emulsion

Flaxseed oil and coenzyme Q_{10} both have disadvantages such as low water solubility, poor stability, and low bioavailability. These application bottlenecks can be addressed by simultaneously loading flaxseed oil and coenzyme Q_{10} into an emulsion system. When the emulsion prepared by Huang Juan et al. [8]. was digested in simulated small intestinal fluid, the digestion rate and bioavailability of coenzyme Q_{10} in flaxseed oil were significantly higher than those of the suspension, demonstrating a slow-release effect for coenzyme Q_{10}. The emulsion exhibited good dilution and freeze–thaw stability. However, Na^+/Ca^{2+} ions significantly reduced zeta potential, affecting stability. Immobilized coenzyme Q_{10} also provided a protective effect for flaxseed oil.

Chitosan modification can significantly enhance the uptake of coenzyme Q_{10} by human immortalized keratinocytes, improve their resistance to ultraviolet (UVB) radiation damage, and reduce apoptosis induced by UVB exposure. In addition, it promotes the skin penetration of coenzyme Q_{10}. Zhou Ben [9] used a nanoemulsion to deliver coenzyme Q_{10}, achieving superoxide anion and hydroxyl radical scavenging rates of 37.1% and 46.3%, respectively, with low cytotoxicity. This formulation could be absorbed by human immortalized keratinocytes and inhibit UVB-induced damage. The chitosan-modified nanoemulsion had a particle size of 110.9 nm, a zeta potential of 34.5 mV, and an encapsulation efficiency of 86%. It exhibited excellent storage and UV stability, and significantly promoted cellular uptake, anti-UVB apoptosis, and skin penetration.

In order to improve the bioavailability of coenzyme Q_{10}, a coenzyme Q_{10} emulsion system was constructed by using soluble soybean polysaccharide and pea protein. Zhou Sanjiu [12] showed that when the concentration of soluble soybean polysaccharide was 1.0%, the particle size of the coenzyme Q_{10} emulsion was significantly smaller than that of the control group without additive ($p < 0.05$) under conditions of pH 6.0, salt ion concentration (100/300 mmol/L), and temperature (25–95 °C). Soluble soybean polysaccharide, in combination with pea protein, significantly improved the emulsion's multi-environment stress stability. The emulsion prepared by Yang Yang [10], as confirmed by Fourier-transform infrared spectroscopy, achieved complete encapsulation of coenzyme Q_{10}. Transmission electron microscopy showed that the nanoemulsion droplets were spherical and evenly dispersed. It demonstrated good centrifugal, ionic, and storage stability, and its 2,2-bipyridyl-1-pyridyl nitrogen radical, dichloroaniline sulfate, and hydroxyl radical scavenging rates were higher than those of the suspension (79.1%, 93.1%, and 72.2%, respectively). The blood drug concentration in rats (0.77 μg/mL) was 1.4 times that of the oil solution.

Coenzyme Q_{10} mainly binds to three proteins through hydrogen bonding and hydrophobic interactions, increasing its water solubility by more than 5×10^7 times. Li Fei [11] developed a nanoemulsion using soy protein isolate, whey protein isolate, and sodium caseinate as wall materials, which exhibited good storage stability. Different wall materials significantly reduced the crystallinity of coenzyme Q_{10}, and improved its light, heat, digestion stability, and bioavailability. Among them, sodium caseinate microcapsules had the highest encapsulation efficiency (94.7%), loading capacity (898.7 mg/g protein), water solubility (86.67%), and bioavailability (43.35%), with the best resistance to light and heat degradation.

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3. Coenzyme Q_{10} nanoparticles

3.1. Property of coenzyme Q_{10} nanoparticles

Many studies have utilized food-grade materials (proteins, polysaccharides, lipids, etc.) to prepare nanoparticles that improve the water solubility and oral bioavailability of coenzyme Q_{10}. Nanoparticles are considered one of the most promising encapsulation strategies due to their high physical stability at the nanoscale, as well as their ability to effectively encapsulate and protect core materials [13] .

3.2. Preparation method of coenzyme Q_{10} nanoparticles

Preparing coenzyme Q_{10} in nanoparticle form can significantly improve its solubility and bioavailability. Common preparation methods include solvent evaporation, nanoprecipitation, high-pressure homogenization, emulsification–solvent evaporation with low-temperature solidification, and solid dispersion.

Banun V J et al. [14] encapsulated coenzyme Q_{10} in β-lactoglobulin and lactoferrin nanoparticles, both of which formed particles with an average size of approximately 300 nm and exhibited good encapsulation efficiency. Stronger multisite binding demonstrated that, compared to coenzyme Q_{10}–β-lactoglobulin, coenzyme Q_{10}–lactoferrin exhibited significantly higher solubility. Compared with pure coenzyme Q_{10}, the coenzyme Q_{10}–β-lactoglobulin and coenzyme Q_{10}–lactoferrin nanoparticles increased the solubility of coenzyme Q_{10} by 60-fold and 300-fold, respectively, at pH 7.4. In addition, in vitro permeability measurements showed that both types of nanoparticles increased coenzyme Q_{10} permeability across Caco-2 monolayer cells, confirming the enhanced absorption rate. Finally, compared to coenzyme Q_{10} alone, coenzyme Q_{10}–lactoferrin exhibited higher antioxidant properties.

Zhang Xiaoxue et al. [15] synthesized a novel drug-loaded nanosuspension based on a quercetin–xylan copolymer and further encapsulated coenzyme Q_{10} using high-shear homogenization, forming nanoparticles with a smaller average particle size of only 166.7 nm.

3.3. Application of coenzyme Q_{10} nanoparticles

A novel copolymer–loaded coenzyme Q_{10} nanosuspension can increase the water solubility of coenzyme Q_{10} and improve its oral bioavailability. Under optimal process conditions, Zhang Xiaoxue et al. [15] found that the in vitro dissolution rates of the coenzyme Q_{10} nanosuspension were 1.89 and 1.48 times higher than those of pure coenzyme Q_{10} in artificial gastric fluid (SGF) and artificial intestinal fluid (SIF), respectively. In in vivo bioavailability experiments in rats, oral administration (gavage) of the drug-loaded nanosuspension increased bioavailability by 2.64-fold compared to pure coenzyme Q_{10}.

To improve the solubility, permeability, and antioxidant properties of coenzyme Q_{10}, Banun V J et al. [14] developed nanocomposites using milk-derived proteins. The particle sizes of the two types of coenzyme Q_{10} nanoparticles (coenzyme Q_{10}–β-lactoglobulin and coenzyme Q_{10}–lactoferrin) were both in the nanometer range (~250 nm), whereas unencapsulated coenzyme Q_{10} remained in the micrometer range. Both β-lactoglobulin and lactoferrin exhibited excellent encapsulation efficiency (greater than 60%), with no detectable coenzyme Q_{10} crystals in the nanoparticles. Molecular docking studies showed that, due to its higher molecular weight (863 Da) and linear structure, coenzyme Q_{10} binds more strongly to lactoferrin than to β-lactoglobulin. Additionally, in vitro

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antioxidant assays demonstrated that coenzyme Q_{10}–lactoferrin significantly reduced oxidative free radical levels in macrophages by 15–25 μg/mL compared to pre-dissolved coenzyme Q_{10}, which can be harmful to cell viability.

4. Gel-based delivery system of coenzyme Q_{10}

Oil gel is a novel technology involving the structuring of liquid oils. It offers advantages such as edibility, a simple preparation process, and low cost, and presents a promising strategy for reducing saturated fats and eliminating trans fatty acids [16]. Under specific conditions, oil gels can form stable three-dimensional network structures through interactions between vegetable oils and gelling agents [17]. As a lipid-soluble compound, coenzyme Q_{10} can be effectively dissolved and encapsulated within oil gel systems.

4.1. Preparation technology of coenzyme Q_{10} gel

In recent years, oil gels have been widely used in baked goods, meat products, and dairy items, primarily as substitutes or partial replacements for solid fats such as margarine and shortening. The main preparation methods include the direct dispersion method, the emulsion template method, and the foam template method [17].

Zhang et al. [18] prepared a gel using coenzyme Q_{10} as the active component, Carbomer 940 as the gelling matrix, and glycerol and propylene glycol as humectants. When the Carbomer 940 concentration was 0.5%, the humectant concentration was 10%, the mass ratio of glycerol to propylene glycol was 1:1, and triethanolamine was added at 0.4%, the resulting gel was uniform, fine-textured, and stable.

Cheng [19] prepared a composite gel using coenzyme Q_{10} as the embedded compound, Carbomer as the gelling matrix, and varying mass ratios of Sclerotinia sclerotiorum gum. The incorporation of Sclerotinia sclerotiorum gum enhanced the gel performance of the Carbomer-based gel. As the concentration of Sclerotinia sclerotiorum gum increased, both the viscosity and modulus of the composite gel improved significantly. The addition of the humectant glycerin had minimal effect on the overall performance of the gel.

4.2. Application of coenzyme Q_{10} gel

The coenzyme Q_{10} flexible liposome gel prepared by Zhang Yujie et al. [18] can improve skin antioxidant capacity and delay skin aging. Results showed that the in vitro release of coenzyme Q_{10} from flexible liposomes was higher than that from the flexible liposome gel and a commercial coenzyme Q_{10} face cream. The transdermal delivery amount was also higher for the flexible liposomes alone than for the gel, while the skin retention amount was lower than that of the flexible liposome gel. The coenzyme Q_{10} flexible liposome gel increased skin antioxidant activity, enhanced collagen fiber content in the skin, and effectively delayed skin aging. Rheologically, it behaves as a pseudoplastic fluid.

Cheng Rong [19] used an optimized gel matrix formulation (Carbomer/Microzyme gum in a 5:5 ratio with 10% glycerol) to prepare several vesicle-containing gels: coenzyme Q_{10} gel, coenzyme Q_{10} vesicle gel, and polyethylene glycol–coenzyme Q_{10} vesicle gel. It was found that while there may be interactions between the vesicles and the gel matrix, the embedded vesicles did not significantly affect the overall gel performance and existed in the gel in an amorphous form. Storage stability

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tests showed that the retention rate of coenzyme Q_{10} in the vesicle gel remained at 92% after 30 days of storage at 4 °C.

5. Conclusion

Coenzyme Q_{10}, as a fat-soluble antioxidant, has inherent limitations such as poor water solubility, low photothermal stability, and limited gastrointestinal absorption, owing to its molecular structure rich in unsaturated double bonds and hydrophobic groups. These characteristics restrict its application and development in the fields of health food and biomedicine. Currently, delivery systems such as emulsions, nanoparticles, and gels can significantly improve its physicochemical properties and bioavailability through encapsulation, structural modification, and other technological strategies. For example, nanoemulsions can greatly enhance the water dispersibility of coenzyme Q_{10}; nanoparticles constructed from food-grade proteins and polysaccharides offer small particle sizes with targeted and sustained-release effects; and oil gel systems encapsulate coenzyme Q_{10} within a three-dimensional network structure, improving skin permeability and antioxidant capacity. In the future, key directions to overcome the bottlenecks in coenzyme Q_{10} application will include developing multifunctional composite delivery systems, optimizing large-scale production processes, integrating smart responsive materials, and advancing research on mechanisms of action.

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