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Microemulsions and Natural Products

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Microemulsions are stable single-phase liquid-in-liquid systems that have a droplet size between 10 and 100 nm, are thermodynamically stable, and have a spontaneous formation in which the phenomenon of Ostwald ripening rarely occurs. These systems are made of a mixture of surfactant, co-surfactant, and water and have the ability to dissolve both types of water and lipophilic substances. The low viscosity of these systems has led to improving patient acceptance and increasing their use as drug carriers for drug delivery. The transdermal permeability mechanism of microemulsions is similar to that of nanoemulsions, and in short, they include high solubility potential for hydrophilic drugs, increased absorption of microemulsion constituents, and increased thermodynamic activity of drugs in carriers (1).

Natural oils are very complex mixtures, some of which have physiological or therapeutic activities and are used in pharmaceutical, agricultural, food, health, and cosmetic industries. The increasing use of these oils is due to their great potential to prevent and treat many human diseases (2).

Natural products have long played a vital role in providing healthcare in many societies. Currently, about 50% of the drugs in the market are derived from natural products. The low absorption and distribution of some of these biologically active compounds decrease their bioavailability and efficiency and hinder their use in the hospital. One of the approaches to overcome these obstacles is using new drug delivery systems, particularly microemulsions (3).

Babassu oil microemulsions, a natural product, can be an alternative for future immunotherapy strategies and vaccine drug delivery, particularly for infectious diseases (4).

Myrcia bella is used in Brazil as a medicinal plant to treat diabetes, bleeding, and high blood pressure. The positive antifungal effect of *M. bella* microemulsion against *Candida* spp., which contains polyoxyethylene 20 cetyl ether and soybean phosphatidylcholine, grape seed oil, cholesterol, and purified water, emphasizes the importance of using microemulsions of natural products as a strategy to control infections caused by this fungus (5).

Antibiotic resistance is a global threat, so moving toward eliminating the use of these drugs and finding alternatives is a vital step toward solving this problem. Thyme microemulsion (10% oil/water) has an anti-salmon effect similar to cotrimoxazole antibiotic in the poultry industry while reducing the toxicity caused by drug use. Therefore, the microemulsion of this substance can be an alternative economic choice for the treatment of multidrug resistance of *Salmonella* Enteritidis in poultry farms (6).

The use of microemulsions for drug carriers of natural substances such as injectable squalene for the treatment of coronavirus disease 2019 (COVID-19) improved the need for oxygen therapy for two days without fever, reduced cough, and improved high-resolution computed tomography. This study suggests that squalene-containing microemulsion can be considered a potential treatment for COVID-19 (7).

The natural product Tanshinone IIA (TanIIA) improves differentiation in hepatocellular carcinoma (HCC) cells while inducing apoptosis, but its clinical use is limited due to its low solubility in water and providing a suitable

drug delivery system. Microemulsions containing this natural substance as a drug delivery system can increase the antitumor effects of TanIIA (8).

The anti-cancer, anti-inflammatory, and antioxidant effects of a natural flavonoid called quercetin, which has low toxicity, have received much attention. Considering its low solubility in water and improving the penetration of the cornea into the eye, the related microemulsion could increase the transcorneal penetration (9).

Numerous uses of microemulsions with natural substances (both as active pharmaceutical ingredients and as pharmaceutical carriers) have been mentioned in the research. Increasing the oral bioavailability of berberine (10), improving the anti-cancer function of tanshinone (11), increasing the liver-protective effect of silymarin (12), increasing the immune system function caused by propolis (13), etc., are some of these uses. It seems that further study on this part of knowledge is necessary, while the use of microemulsions in the market can also improve the use of natural products and their effectiveness.

Footnotes

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