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Pickering Emulsion-Based Approaches for Targeted Herbal Drug Formulations

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Abstract

Pickering emulsions, stabilized by solid particles rather than traditional surfactants, have gained significant attention in pharmaceutical and cosmetic industries for their unique stability and biocompatibility. This emerging technology holds immense promise in enhancing the delivery of herbal drugs, which often face challenges like poor solubility, stability issues, and bioavailability limitations. Herbal drugs, derived from plant sources, contain bioactive compounds that are highly sensitive to environmental factors such as light, temperature, and oxidation. Pickering emulsions provide an innovative approach to overcome these challenges. By using biocompatible solid particles such as silica, starch, or chitosan as stabilizers, these emulsions offer superior physical and chemical stability. Additionally, the absence of surfactants reduces toxicity and irritation, making them suitable for pharmaceutical and dermatological applications. This abstract explores the potential of Pickering emulsion technology in the encapsulation, protection, and controlled release of herbal drugs. It highlights the key advantages, including improved stability of bioactive compounds, targeted delivery, and enhanced therapeutic efficacy. Furthermore, it discusses the application of this technology in formulating herbal-based creams, gels, and oral formulations, emphasizing its role in advancing natural medicine. To fully realize the promise of Pickering emulsions in modern herbal drug delivery systems, the study highlights the importance for more research to optimize particle selection, emulsion stability, and large-scale production.

Keywords: Bioavailability; Biocompatible Particles; Herbal Drugs; Pickering Emulsions

Introduction

Emulsions are thermodynamically unstable systems in which an emulsifying agent, which is superficially active, helps disperse droplets of one immiscible liquid into another liquid. According to the physicochemical properties of the drug, liquid pharmaceuticals often result in faster absorption and higher drug bioavailability. Pickering emulsions, sometimes referred to as molecular-emulsifier-based emulsions and particle-emulsifier-based emulsions, are two categories of emulsion systems based on their emulsifier forms. Surface-active molecules called molecular emulsifiers are absorbed into the oil-water interface, lowering interfacial tension and creating a protective layer. Steric and electrostatic forces generated by the emulsifier molecule layer on the oil-water interface are powerful repellent factors that stop droplet aggregation. This system balances molecular emulsifiers that are absorbed and those that are not. However, in a Pickering emulsion, particles that are partially wetted by both the water and oil phases are permanently integrated into the interface without significantly reducing the interfacial tension. These particles create a mechanical barrier that inhibits droplet coalescence [1] Particle concentration, pH, ionic strength, wettability, oil type and volume fraction, and other factors affect the stability of Pickering emulsions. The wettability of the particles determines the particular type of Pickering emulsion. Particles with a contact angle of $15 \circ < \theta < 90 \circ$ are suitable for o/w emulsions, while particles with a contact angle of $90 \circ < \theta < 165 \circ$ are ideal for w/o emulsions [2].

Pickering emulsions are stabilized by solid particles and do not contain surfactants. An efficient steric barrier is created at the oilwater contact by the almost irreversible adsorption of solid particles, which help to maintain physical stability of emulsion. Compared to surfactant-stabilized emulsions, they have a particularly strong resistance to coalescence [3] and are a novel kind of emulsions where solid particles act as stabilizers. From natural materials like starch, proteins, and their modified derivatives [4,5] to inorganic materials like silica, alumina, and clay [6,7], these stabilizing particles can also extend to synthetic materials like polymers. Carbohydrate polymers are used for developing Pickering emulsions, and cellulose and starch are the two main insoluble biopolymers in this class that are found in large quantities in nature. Other examples are alcohol- soluble prolamines, salt-soluble globulins, water-soluble albumins, acid/alkaline-soluble glutelin, and plant proteins [8].

Pickering (1907) reported that the lifespan of oil droplets and air bubbles in water was extended when a layer of solid particles (proteins or other precipitated colloids) was present [9]. Pickering emulsions generally provide a more stable system than conventional emulsions formed with a surfactant due to their advantages, which include reduced production costs, fewer adverse effects, low toxicity, and superior biocompatibility [10-12].

The stability and consumable qualities of Pickering emulsions with organic biopolymers as emulsifiers are superior to those of synthetic small-molecule surfactants. Pickering emulsions have been the subject of extensive research in recent years due to their many advantages, which include great safety and outstanding stability, particularly for emulsions coated in macroscopic molecules. A barrier that lowers moisture and free fatty acid levels and prolongs food shelf life may be provided by the thick layer of macromolecules covering the Pickering emulsion droplets. In contrast to conventional emulsions stabilized by surfactants, Pickering emulsion provides a substantially stronger protection against destabilization since it irreversibly adsorbs to the surface because of the partial wetting characteristics of solid particles. The wettability of particles affects Pickering emulsion stability in addition to particle size; as a result, environmental conditions, contact angle, and particle-particle interaction at the interface play a significant role in determining the stability of Pickering emulsions.

Formation and stabilization of Pickering emulsions

During the Pickering emulsion production process, it is essential that both phases partially wet the solid particles in order for them to be absorbed at the oil-water interface. By increasing the area of the oil-water contact and reducing energy, solid particles reduce the driving force for particle transmission. The wettability, size, concentration, density, and packing of particles, as well as the pH of the aqueous phase, which serves as a synthesis ingredient, all affect the development of Pickering emulsions [13].

Biomedical applications of Pickering emulsions

Pickering emulsions, stabilized by solid particles rather than traditional surfactants, have emerged as a versatile platform in biomedical applications. Their unique stability, biocompatibility, and tunable properties make them suitable for various healthcare and therapeutic uses. Pickering emulsion structural stability and biocompatibility provide unchangeable Nano cellulose the potential to be used in medication synthesis and delivery. Applications requiring macroscopically homogeneous mixtures or efficient release systems are particularly ensuring for aerospace core-shell nanofibers and hollow nanotubes, as well as for industries such as pharmaceuticals, cosmetics, food, fuel, and models for other materials like porous material, liquid foam, and emulsion films [14]. It is possible to make particle stabilizers for Pickering emulsions and their derivative chemicals to have particular properties such as oxidation resistance, UV protection, environmental responsiveness, and even electromagnetic characteristics. [15].

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The main biomedical uses of Pickering emulsions are listed below

Drug delivery systems

The majority of the pioneering study on Pickering emulsions' applicability in biomedical applications has also been on bio imaging [16], stimulus-responsive materials [17], and drug encapsulation and administration (including topical and oral drug delivery) [18]. The pharmacokinetics of the encapsulated drugs must be determined by bioassays because Pickering emulsions are not widely used for the encapsulation and delivery of bioactive compounds. Therefore, to support the bio-applications of Pickering emulsions stabilized by biocompatible particles, more in vitro and in vivo research is needed. Pickering emulsions improve the stability, solubility, and bioavailability of hydrophilic and hydrophobic medications by acting as efficient carriers. [19]. Applications include:

- **Controlled Release:** Gradual release of drugs, minimizing dosing frequency and side effects.
- **Targeted Delivery:** Functionalization of stabilizing particles allows for site-specific drug delivery
- **Encapsulation of Bioactive:** Efficiently protects sensitive bioactive molecules like peptides, proteins, and herbal extracts from degradation.

Vaccine delivery

As modern medicine has advanced medicines and vaccines are the most effective and direct means for preventing viral outbreaks, adjuvants have become increasingly crucial in vaccine production. Pickering emulsions can be studied as adjuvants, and effective adjuvants can increase vaccine effectiveness [15]. Pickering emulsions have been explored as adjuvants in vaccine formulations. They enhance the immune response by presenting antigens in a stable and controlled manner. Solid particles can also be engineered to mimic pathogen-like structures, stimulating stronger immunogenicity.

Antimicrobial and wound care applications

Pickering emulsions loaded with antimicrobial agents, such as silver nanoparticles or essential oils, are utilized in:

- Antibacterial Coatings: For surgical tools and implant surfaces.
- Wound Dressings: Providing a sustained release of antimicrobials and promoting healing.

Cancer Therapy

- Nanoparticle Delivery: Through the increased permeability and retention (EPR) effect, Pickering emulsions can transport chemotherapeutic drugs and promote their accumulation at tumor locations.
- **Thermal Therapy:** Particles stabilizing the emulsion can be functionalized for photo thermal or magnetic hyperthermia treatments.

Diagnostic imaging

Pickering emulsions can encapsulate contrast agents for imaging techniques like MRI, CT, and ultrasound. Stabilizing particles, such as iron oxide or gold nanoparticles, further enhance imaging contrast and specificity.

Tissue engineering and regenerative medicine

- Hydrogel Formation: Pickering emulsions are used to create hydrogels with tailored porosity and mechanical properties for scaffolds.
- **Delivery of Growth Factors:** Controlled release of bioactive molecules to promote cell proliferation and tissue regeneration.

Cosmetic and dermatological applications

Pickering emulsions can also be used in paintings and cosmetics, for instance. These materials have both favorable mechanical and environmental qualities. Pickering emulsions are extensively used in skin-care formulations for delivering antioxidants, vitamins, and therapeutic agents [13].

They offer:

- Improved Skin Penetration: Stabilized delivery of active ingredients.
- Reduced Irritation: Elimination of surfactants enhances compatibility with sensitive skin.

The stabilization mechanism of Pickering emulsions.

The oil-water interface's high physical barriers and irreversible particle adsorption

Pickering emulsions function differently from biopolymers with two different hydrophilic and hydrophobic zones and emulsions stabilized by traditional surfactants (Figure 1). The most common is that Pickering emulsions are stabilized by important particle adsorption at the interface, removing the need for amphiphilia [20]. Particle wettability is essential for both the ultimate stability of Pickering emulsions and for particles to adsorb at the droplet surface. The strong physical barriers and irreversible adsorption of particles at the oil-water interface must be explained in order to distinguish between them. The partial wettability of some spherical hard solid particles drives the strong adsorption, which results in firm steric hindrance. Thus, by a steric mechanism, it can stop the emulsion droplets from flocculating and coalescing. Both the water and oil phases must partially wet in order for particles to adsorb at the oil-water contact [21]. Additionally, contact angles (θ) can be used to determine wettability. Emulsions are categorized into various categories based on the contact angles (θ) of solid particles. Particles that are readily wetted by water can create O/W emulsions ($\theta < 90 \circ$); otherwise, W/O emulsions ($90 \circ <\theta < 180 \circ$) are produced [22].



Figure 1: Difference between traditional emulsion and Pickering emulsion.

Utilizing equipment to generate pickering emulsions

Pickering emulsions can be made with the same fundamental methods as regular emulsions [23]. In order to produce a Pickering emulsion, solid particles can be added to the mixture utilizing emulsification techniques such as high-speed homogenization with a rotor-stator, high-pressure homogenization and sonication with an ultrasonic processor [24,25].

High-pressure homogenization

The high-pressure homogenization technique is a continuous process for emulsification, primarily utilized for the preparation of Pickering emulsions, which can be achieved using this machinery equipped with a high-pressure valve that allows one liquid to disperse uniformly in small droplets within the other [26]. A highenergy emulsification method called high-pressure homogenization effectively separates water and oil to produce small emulsion droplets. Research has indicated that rotor-stator homogenization results in larger droplets than high-pressure homogenization [27]. In order to produce a lower particle size, turbulence is produced when a pre-emulsion with a dispersion phase containing large droplets travels over an area of high shear. High-pressure pumps and uniform nozzles are features of this apparatus [28].

Via a rotor-stator

Rotor-stator homogenizers operate using a device that features rotating blades, termed the internal rotor, which spins rapidly around its axis within a fixed outer casing, known as the stator. This setup homogenizes samples through mechanical shearing and

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shear forces [29,30]. The liquid sample is pushed toward one side of the mixture by the rotating blades of the mixer, which then eject it through the stator's holes at a high speed. Small droplets form in the Pickering emulsions as a result of the precise speed differential within the rotor-stator gap, which generates substantial hydraulic shear and speeds up homogenization [31].

Stabilizing particles in Pickering emulsions

Pickering conducted an experiment four years after Ramsden's 1903 discovery of the stabilizing impact of solid particles on emulsions [32]. Pickering emulsions are stable because of the adsorption of insoluble solid particles at the oil-water interface, which is made possible by hydration, electrostatic, and steric repulsions. The energy needed for the particles to adsorb and desorb at the interface, which is influenced by the thermal energy from Brownian motion, can be used to explain their higher stability when compared to traditional emulsions. (Equation 1)

E = kBT

Where,

E - Represents thermal energy (Joules);

kB - represents Boltzmann constant (Joules/Kelvin); T- represents absolute temperature (K)

For surfactants used in conventional emulsions, the desorption energy, Δ Gd is less than 10× kBT, which results in a dynamic equilibrium of interface adsorption/desorption that makes the adsorption reversible [33].

In contrast, when particles with "appropriate" contact angles (θ) (far from 0° and 180°) stabilize emulsions, Δ Gd is much greater than kBT, leading to practically irreversible adsorption. The surface characteristics of the adsorbed particles will determine the type of emulsion: more hydrophilic particles will be more appropriate for oil in water (O/W) emulsions, and more hydrophobic particles for W/O emulsions. This is because the adsorbed particles cause the interface to curve towards the phase with lower affinity [34].

A Summary of pickering emulsions' physicochemical properties

Pickering Emulsion Formation

The two phases must fractionally moist the solid particles during the Pickering emulsion generation process in order for them to be absorbed at the oil-water interface. Through the increase of the oil-water interfacial area and the decrease of energy, adsorption of solid particles decreases the driving force for particle transfer [35]. In conclusion, the primary analysis criteria for assessing the stability of this kind of emulsion are the wettability, concentration, size, density, and form of particle packaging, the pH of the aqueous phase, and the presence of additives. These factors basically affect the formation of emulsions stabilized by finely divided particles.

The wettability of the particles used in Pickering emulsions, which is important to their capacity to operate at the oil-water interface, can be measured using the contact angle between the solid particle and the interface. The wettability of the particles in

Herbal Drug Type	Example Actives	Benefits via Pickering Emulsion
Polyphenols	Resveratrol, catechins	Increased stability and bioavailability
Essential oils	Tea tree, eucalyptus	Protection from oxidation, sustained release
Curcuminoids	Curcumin	Enhanced solubility and targeted anti-inflammatory effects.
Flavonoids	Quercetin, rutin	Improved water Dispensability and controlled therapeutic action
Alkaloids	Berberine, capsaicin	Prolonged delivery and enhanced absorption.

Table a: Key Herbal Drug Types Benefiting from Pickering Emulsions.

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the water and oil phases determines whether the emulsion is in an O/W or W/O condition. Since the continuous phase of the emulsion often wets the particle surface the most, the contact angle is an important characteristic [36].

Emulsion stability and the destabilization mechanisms

In different kinds of Emulsion the wettability of particle-stabilized emulsions, is measured by the contact angle, influences the type of emulsion that is chosen. According to the Bancroft rule, hydrophilic particles stabilize O/W emulsions more effectively when their contact angle, as measured via the water phase, is less than 90. On the other hand, particles that are hydrophobic or have a contact angle greater than 90 are more appropriate for stabilizing W/O emulsions. When completely saturated with water or oil, the particles stay scattered in that phase and cannot create an emulsion [37]. While a continuous phase describes a liquid in which droplets are separated from one another, a scattered phase describes a liquid that forms droplets.

Conclusion

Pickering emulsion technology presents a transformative approach to the formulation and delivery of herbal drugs, addressing critical challenges such as stability, solubility, and bioavailability. By utilizing solid particles as stabilizers, this technique eliminates the need for traditional surfactants, offering enhanced biocompatibility and reduced toxicity. The ability to protect sensitive bioactive compounds from degradation and enable controlled release mechanisms positions Pickering emulsions as a valuable platform for advancing herbal drug formulations.

This technology not only improves the therapeutic efficacy of herbal drugs but also broadens their application in pharmaceuticals, cosmetics, and nutraceuticals. Despite its promising potential, further research is essential to optimize emulsion stability, scale-up production, and investigate the long-term safety and efficacy of these systems. With continued advancements, Pickering emulsion technology could significantly contribute to the integration of natural medicine into modern healthcare solutions, fostering the development of innovative, effective, and sustainable herbal drug delivery systems.

Future Directions

While Pickering emulsions have demonstrated significant potential in biomedical fields, challenges like precise particle engineering, long-term stability, and regulatory approval need to be addressed. Ongoing research aims to optimize their properties for widespread clinical and commercial applications, opening new frontiers in personalized medicine and biotherapeutics.

Challenges

- Difficulty in scaling up production.
- Regulatory hurdles for new stabilizing materials.
- Compatibility with diverse herbal actives.

Future prospects

- Development of bio-based nanoparticles tailored for specific herbal drugs.
- Incorporation into advanced drug delivery systems (e.g., microcapsules, hydrogels).
- Broader application in personalized medicine using herbal actives.

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