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Review Article

Emulgels as Effective Carriers for Hydrophobic and Hydrophilic Drugs: A Review

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ABSTRACT

Emulgels have emerged as a promising drug delivery system, combining the advantages of emulsions and gels to enhance the topical and transdermal delivery of both hydrophilic and hydrophobic drugs. Their biphasic nature allows for improved drug solubility, stability, and controlled release, making them an ideal choice for pharmaceutical and cosmetic applications. Emulgels utilize a gel base, often composed of hydrogel or organogel, to enhance the viscosity and provide prolonged drug retention at the application site. The incorporation of oil-in-water (O/W) or water-in-oil (W/O) emulsions ensures compatibility with a broad spectrum of drugs, improving bioavailability and penetration through the skin. Compared to conventional gels and creams, emulgels exhibit superior spreadability, patient compliance, and ease of application. The review explores the formulation components, mechanisms of drug release, advantages over traditional carriers, and recent advancements in the field, emphasizing their role in delivering poorly water-soluble drugs efficiently. Moreover, the therapeutic applications of emulgels in dermatology, pain management, antifungal treatments, and wound healing are discussed, highlighting their potential for future pharmaceutical innovations.

INTRODUCTION

1.1 Definition and Concept of Emulgels

Emulgels are a novel class of semisolid dosage forms that integrate the properties of emulsions and gels, offering enhanced drug delivery potential. They are formulated by incorporating an emulsion (either oil-in-water or water-in-oil) into a gel base, resulting in a system that combines the stability and controlled release properties of emulsions with the improved spreadability and patient compliance of gels (1). The key advantage of emulgels lies in their ability to effectively

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deliver both hydrophilic and hydrophobic drugs, addressing solubility limitations encountered in traditional gel or emulsion formulations (2).Their dual release mechanism, controlled by both the gel matrix and emulsion phase, enables sustained and enhanced drug penetration through the skin, making them particularly effective for topical applications such as dermatological treatments, wound healing, and pain relief (3). Additionally, they provide advantages such as improved bioavailability, ease of application, and patient comfort due to their non-greasy, thixotropic nature (4). With continuous advancements in formulation techniques and polymer science, emulgels are poised to play a significant role in pharmaceutical and cosmeceutical applications, enhancing drug delivery efficiency and therapeutic outcomes.

1.2 Importance of Drug Delivery Systems

Drug delivery systems (DDS) play a crucial role in modern medicine by optimizing the therapeutic effects of pharmaceutical compounds while minimizing side effects. These systems are designed to ensure the efficient transport of drugs to target sites, improve bioavailability, and enhance patient compliance. Traditional drug delivery routes, such as oral and parenteral administration, face challenges like first-pass metabolism, drug degradation in the gastrointestinal tract, and poor solubility, which can significantly impact therapeutic efficacy (5). Advanced DDS, including nanoparticles, liposomes, transdermal patches, and implantable devices, offer controlled and targeted drug release, thereby reducing systemic toxicity and improving treatment outcomes (6). Additionally, innovations in biodegradable polymers and stimuli-responsive carriers allow for sustained drug release, ensuring prolonged therapeutic action and reduced dosing frequency (7). The integration of personalized medicine with DDS further enhances precision treatments, particularly in oncology and chronic disease management. The continuous evolution of DDS is crucial in advancing next-generation therapies, making them safer, more efficient, and patient-friendly.

1.3 Advantages of Emulgels Over Traditional Formulations

Emulgels offer a significant advancement over traditional drug delivery formulations such as creams, ointments, and gels by combining the benefits of emulsions and gels into a single, efficient system. One of the major advantages of emulgels is their ability to enhance drug penetration and bioavailability, particularly for hydrophobic drugs, which are often difficult to incorporate into conventional gel formulations (8). Unlike creams and ointments, emulgels provide a non-greasy, smooth texture that improves patient compliance while offering better spreadability and ease of application (9). Additionally, emulgels demonstrate superior stability, preventing drug degradation over time and maintaining effectiveness under various storage conditions. The dual control release mechanism of emulgels, which combines gel-based controlled release with emulsion-mediated solubilization, ensures prolonged drug activity and reduces the need for frequent reapplication, making them ideal for chronic conditions such as arthritis, fungal infections, and skin disorders (10). Their high water content provides a cooling effect, making them more comfortable for patients compared to oily formulations like ointments. Moreover, the ability to incorporate both hydrophilic and lipophilic drugs makes emulgels a versatile platform for a wide range of pharmaceutical and cosmetic applications (11). The growing interest in emulgels is driven by their effectiveness in enhancing drug delivery, minimizing side effects, and improving overall therapeutic outcomes, positioning them as a superior alternative to traditional topical formulations.

2. Composition and Formulation of Emulgels

2.1 Basic Components: Emulsions and Gels:-

Emulsions and gels are fundamental systems in pharmaceutical, cosmetic, and food applications, offering enhanced drug delivery, stability, and ease of application. Both play a crucial role in the formulation of advanced delivery systems such as **emulgels**, which combine the properties of both emulsions and gels to improve drug solubility and bioavailability.

Emulsions: Composition and Properties

An emulsion is a biphasic system consisting of two immiscible liquids, typically oil and water, where one liquid is dispersed as tiny droplets within the other. Emulsions can be categorized into oil-in-water (O/W) emulsions, where oil droplets are dispersed in a continuous water phase, and water-in-oil (W/O) emulsions, where water droplets are suspended in an oil phase. These emulsions are stabilized by surfactants or emulsifying agents, which reduce interfacial tension and prevent phase separation (12).

Key Components of Emulsions:-

1. Oil Phase: Includes lipophilic substances such as vegetable oils (e.g., olive oil, coconut oil), mineral oils, and synthetic esters.
2. Aqueous Phase**:** Consists of water or hydrophilic solvents that dissolve water-soluble active ingredients.
3. Emulsifiers (Surfactants): Surfactants such as Tween (polysorbates) for O/W emulsions and Span (sorbitan esters) for W/O emulsions help stabilize the system. Natural emulsifiers like lecithin, casein, and pectin are also used in pharmaceutical and food applications (13).
4. Stabilizers and Preservatives**:** Antioxidants (e.g., tocopherol) and antimicrobial agents (e.g., parabens) enhance the shelf-life and stability of emulsions.

Gels: Composition and Properties

A gel is a semi-solid system consisting of a three-dimensional polymeric network that entraps large amounts of liquid given either in aqueous (hydrogels) or in non-aqueous (organogels) solution. The most important feature of gels is their wide use in drug delivery systems, owing to the enhanced viscosity, bioadhesiveness, and controlled drug release properties (14).

Key Components of Gel:

1. *Gelling agents: These gelling agents include natural, semi-synthetic and synthetic polymers that form a gel-matrix system.*

- Natural polymers: alginate, pectin, xanthan gum, gelatin
- Synthetic polymers: carbopol, hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA)

2. Solvent (Continuous phase):

- Hydrogels: water or aqueous solutions.
- Organogels: organic solvents, e.g., isopropyl myristate.

3. Penetration enhancers: penetration enhancers, e.g. menthol, urea or ethanol, may improve drug absorption through the skin.

4. Preservatives and stabilizers: preservatives/stabilisers, e.g. benzalkonium chloride, methylparaben, antioxidants, protect the formulation from microbial contamination and oxidative degradation.

Gels can be leveraged in topical, ophthalmic, oral, and transdermal drug systems because they keep the drug at the site of application and can also help minimize systemic side effects. Emulgels: the fusion of emulsions and gels Emulgels are a hybrid blend containing an emulsion in a gel matrix, which combines the benefits of both formulations. Emulgels allow delivery of both hydrophilic and lipophilic drugs and can offer improved stability, controlled release, and improved patient compliance (15). Emulgels are popular preparations in dermatological therapies, pain relief, and wound healing formulations since they are non greasy and can apply easier than creams and ointments.

2.2 Types of Emulsions Used in Emulgels for Hydrophobic and Hydrophilic Drugs

Emulgels are sophisticated topical drug delivery systems. Emulgels are emulsions incorperated into a gel matrix a combination of the two products. The emulsion type oil-in-water (O/W) and water-in-oil (W/O) has an important influence on the formulation's ability to permit the transdermal delivery of hydrophobic and hydrophilic drugs, improves the drugs' bioavailability, drug release and therapeutic performance.

Oil-in-Water (O/W) Emulsions in Emulgels :-

In O/W emulsion, an oil droplets are distributed throughout a continuous water phase containing surfactants as the emulsifying agents. O/W emulgels are specifically advantageous for hydrophilic drug formulation as they solubilize drug in the aqueous phase for skin permeability control.

Advantages of O/W Emulsions in Emulgels:-

1. Enhanced Absorption of Hydrophilic Drugs – Hydrophilic drugs can be added with a proper amount, and released effectively when required dosage is applied.

2. Non-Greasy Texture – O/W emulsions are non-oily and light, providing desirable characteristics for dermatological and cosmetic products.

3. Improved Patient Compliance – An O/W-based emulgel is more desirable because it spreads better, is absorbed quicker, and its texture is non-sticky after application; this makes it suitable for daily residents, justifying their high acceptance.

4. Hydration Effects – Large amounts of water can provide water retention performance. Considering the effects of water, these formulations can be used in hydrated formulations in skincare and pharmaceutical creams (16).

Applications of O/W Emulgels:-

- Hydrophilic drug delivery (e.g., antifungals, anti-inflammatory agents)
- Cosmeceuticals and skin-care formulations
- Wound healing treatments

Water-in-Oil (W/O) Emulsions in Emulgels :-

Water (W)/Oil emulsions contain droplets of water dispersed throughout an oil phase. Thus, W/O emulsions may be more effective for hydrophobic drugs because the hydrophobic drug can dissolve within the lipid phase and thereby have an easier time traversing the skin's lipid barrier.

Advantages of W/O Emulsions in Emulgels:-

1. Improved Stability for Hydrophobic Drugs -- Lipophilic drugs are stable in the oil phase, which prevents premature degradation.

2. Improved Penetration through the Skin - The oil phase provides occlusion, keeping the drug in

place for longer and penetrating deeper into the skin layers.

3. Controlled Rate of Release - W/O based emulgels have controlled release properties, to a minor degree, due to the somewhat slower evaporation of water which is extremely useful for chronic conditions (17).

4. Protection from Environmental Conditions/ Factors. - W/O emulsions protect sensitive drugs from hydrolysis or oxidation.

Applications of W/O Emulgels:-

• Drugs that are hydrophobic (e.g., corticosteroids, analgesics, antifungal agents)

• Deep penetrating formulation for relief of musculoskeletal pain

• Provide occlusive formula for management of chronic skin conditions (e.g., eczema, psoriasis)

2.3 Gelling agents and their role:-

Gelling Agent	Source	Mechanism of Action	Applications	Example Products	reference
Gelatin	Animal collagen (typically from pigs or cows)	Forms gel through hydrogen bonding between molecular chains when dissolved in hot water and cooled.	Food (jellies, gummy candies), Pharmaceuticals (soft capsules), Cosmetics (skin care)	Gummy candies, Marshmallows, Soft capsules	Lee YT et al. Effects of gelatin-based edible films on the quality of fresh-cut strawberries. *Food Hydrocolloids*. 2019;87:327-335 (18).
Agar	Red algae (e.g., Gelidium)	Forms gel by trapping water through ionic interactions and hydrogen bonding. Remains solid at higher temperatures than gelatin.	Microbiology (culture media), Vegan food (gummy candies, jellies), Cosmetics (thickening agent)	Vegan gummies, Culture media for microbiology	Bhat R, Bhat B. Agar-A review. *Food Hydrocolloids*. 2016;61:268-277 (19).
Pectin	Fruits (apples, citrus)	Forms gel when combined with sugar and acid, with hydrogen bonding forming between pectin molecules.	Food (jams, jellies), Pharmaceuticals (controlled drug release)	Jam, Jelly, Drug delivery systems	Visciano P et al. Pectin: A versatile gelling agent in food processing. *Food Bioprocess Technol*. 2018;11(3):607-620 (20).
Xanthan Gum	Bacterial fermentation (glucose/sucrose)	Forms stable gel in aqueous systems through polysaccharide chains'	Food (sauces, salad dressings), Gluten-free products,	Salad dressings, Gluten-free bakery products, Lotions	Kaur L, Singh N. Xanthan gum: A versatile polysaccharide in food processing. *Food Hydrocolloids*.

		entanglement and water retention.	Cosmetics (gels, creams)		2020;99:105-118 (21).
Carrageenan	Red algae (Chondrus crispus)	Forms gel via sulfated polysaccharides that interact with water molecules, often requiring calcium or potassium ions for gel formation.	Dairy products (ice cream, chocolate milk), Food (meat processing, sauces), Cosmetics (gels)	Ice cream, Chocolate milk, Toothpaste	Menzies M. Carrageenan: Applications and properties. *Food Science & Nutrition*. 2021;9(4):1309-1318 (22).
Gellan Gum	Bacterial fermentation	Forms gel through the interaction of gellan molecules with water, creating a robust and flexible gel structure.	Food (low-calorie gels, dairy alternatives), Pharmaceuticals (controlled-release systems)	Low-fat gel desserts, Vegan yogurt	Williams PA, Phillips GO. Gellan gum: Properties and applications. *Carbohydrate Polymers*. 2020;233:1157-1164 (23).
Carbomer	Synthetic polymer (acrylic acid)	Forms gel by crosslinking polymer chains and entrapping water molecules, offering high viscosity and stability.	Cosmetics (lotions, creams, gels), Pharmaceuticals (topical gels)	Skin care products, Shampoos, Gels	Chouhan D et al. Carbomer in cosmetic formulations: A review. *J Cosmet Dermatol*. 2020;19(6):1444-1454 (24).
Guar Gum	Guar beans	Forms gel by absorbing water and swelling to create a viscous gel structure.	Food (sauces, soups), Pharmaceuticals (tablet binders), Industrial applications (paper and textiles)	Soups, Sauces, Tablets	Singh S, Kapoor A. Guar gum as a gelling agent in food and pharmaceutical applications. *International Journal of Pharmaceutics*. 2021;596:119287 (25).

2.4 Selection criteria for hydrophobic and hydrophilic drugs:-

The selection of hydrophobic and hydrophilic drugs is an important aspect of pharmaceutical design, since the physicochemical properties of the drug affect the absorption, distribution, metabolism and excretion (ADME) of the drug. There are differences in the biological behaviors of hydrophobic (lipophilic) drugs or hydrophilic (hydrophilic) drugs which can affect the therapeutic efficacy of drugs. The drug selection criteria include solubility, permeability, molecular dimensions, charge stabilization or destabilization, and therapeutic intent.

1. Solubility

Solubility is one of the most important criteria for choosing hydrophobic and hydrophilic drugs. Generally, hydrophobic drugs are soluble in non-aqueous solvents such as lipids while hydrophilic drugs have solubility in water. The solubility of a drug can affect its ability to pass through biological membranes to its site of action. Lipophilicity is described in terms of the partition coefficient (LogP). A drug with a high LogP is more lipophilic, and a drug with a low LogP is more hydrophilic (26).

2. Permeability

Hydrophobic drugs generally have higher permeability in lipid membranes and hydrophilic drugs often have difficulty with crossing biological membranes because they are attracted to aqueous environments. The permeation of a drug across the gastrointestinal tract, blood-brain barrier and tissues of the body determine the drug's bioavailability and overall therapeutic outcome (27). Lipophilic drugs are often used for therapeutic conditions where there needs to be high levels of membrane penetration (e.g. central nervous system).

3. **Molecular Size**
   Molecular size is an important factor in choosing both hydrophobic and hydrophilic drugs. Since larger molecules do not generally pass through lipid bilayers easily, they are therefore more likely to be hydrophilic candidates. Furthermore, smaller molecules tend to have better bioavailability, especially lipophilic drugs, because they can diffuse through a cell membrane easier (28).

4. **Surface Area and Molecular Structure**
   Drug This not only favors water solubility but also promotes uptake in the aqueous environment of biological incidence (29). Lipophilic drugs will have fewer polar groups, have larger nonpolar surfaces, and are less decisively compatible with polar membranes (30).molecules with a high surface area, and polar functional groups, will generally exhibit hydrophilicity.

5. **Charge and pH Dependency**
   Another consideration for selecting a drug is the charge of a drug molecule. It is generally true that drugs with hydrophobic chloroform-soluble properties may neutral or have low polarity, which minimizes the energy that must be expended for passage across the cell membrane. Studies have shown that hydrophilic drugs may contain charge (ionic or polar) that may reduce the lipophilic property, which influences the solubility of the drug in the polar medium, but decreases permeability in the lipid environment (31). The pH of the environment can affect the ionization state of the drug, and therefore play a key role in drug absorption, distribution and elimination (32).

6. **Drug-Target Interaction**
   The nature of drug-target interaction also moderates the ultimate drug selection. Hydrophobic drugs can be better at targeting receptors or enzymes contained within cellular membranes, which are generally lipid-rich. Hydrophilic drugs are better suited to bind to proteins or other drug targets in aqueous compartments such as cytoplasm or extracellular (33).

7. **Formulation and Delivery Systems**
   The choice of hydrophobic or hydrophilic drugs can often be determined by the available

formulation methods. Hydrophobic drugs may have to use specialized formulations (liposomes, micelles, nanoparticles, etc.) because of their poor solubility and limited bioavailability (34). Hydrophilic drugs can normally be formulated easier with aqueous solutions or encapsulated in oral solid dosages (35).

8. **Metabolism and Excretion**
   Lipophilic drugs typically undergo hepatic metabolism and they are often eliminated by the biliary system while hydrophilic drugs are more easily regarded as being eliminated via the kidney on account of their solubility in water (36). Different metabolic pathways and different elimination processes for the two types of drugs may also result in vastly different duration of action and frequency of administration (37).

9. **Stability in Biological Systems**
   The stability of a drug under various biological environments is also an important parameter for its selection. Hydrophobic drugs may have a tendency to degrade from oxidative processes in aqueous environments while hydrophilic drugs have a tendency of undergoing hydrolysis or degrading more quickly enzymatically (38).

10. **Toxicity and Side Effects**
    The toxicity of hydrophobic drugs versus hydrophilic drugs may have substantially different profiles. Lipophilic drugs also accumulate in body tissues which may lead to toxicity due to the prolonged duration in fatty compartments (39). Hydrophilic drugs, because of their fast clearance, generally would likely have different side effect profiles which may contribute to overall drug safety (40).

11. **Physicochemical Properties**
    In drug development, the physicochemical characteristics of a drug, including molecular weight, polarity, and crystallinity, play an important role in a drug's final dosage form and stability (41). The physicochemical characteristics also affect a drug's access into target tissues and cells. This is due to lipophilic drugs being able to penetrate through lipid membranes to reach intracellular target sites, while hydrophilic drugs remain in extravascular or plasma compartments (42).

12. **Drug Discovery and Preclinical Studies**
    Many therapeutic indications during the preclinical phase select for hydrophobic drugs to reach intracellular targets that need to penetrate lipid membranes, especially therapeutic indications needing neurology and cancer therapy. Hydrophilic drugs are often selected when water solubility aids in delivery and targeting, e.g., antibiotics and antidiabetic drugs (43).

13. **Biopharmaceutical Classification System (BCS)**
    The Biopharmaceutics Classification System (BCS) uses solubility and permeability, incorporating hydrophobic and hydrophilic drugs. Typically, hydrophobic drugs have BCS Class II (low solubility; high permeability) classifications, whereas hydrophilic drugs are often given a BCS Class I (high solubility; high permeability) classification (44).

14. **Clinical Trials and Dosing Regimen**
    Hydrophobic and hydrophilic drugs' selection further incorporates pharmacokinetics and pharmacodynamics during clinical trials. Hydrophobic drugs may require extended-release formulations to maintain therapeutic plasma levels, while hydrophilic drugs may

allow for shorter half-lives and more frequent dosing (45).

15. **Regulatory Considerations** Regulatory bodies for example the FDA and EMA, have guidance for evaluating the physicochemical properties and ADME properties of drugs. In particular, the safety, efficacy, and formulation (e.g., formulation, advertising and printing) of hydrophobic and hydrophilic drugs differs (46).

3. Mechanism of Drug Encapsulation and Release

Drug encapsulation and controlled release systems are critical to modern drug delivery and are specifically designed to improve the therapeutic efficacy, stability, and bioavailability of the drug. Encapsulation involves encapsulating a drug in a carrier system (such as liposomes, nanoparticles or micelles), to prevent degradation to improve the pharmacokinetic profile of the drug. Controlled release systems use the encapsulated drug, to allow for a sustained release of the drug over time, increasing efficacy while reducing side effects (47).

1. Drug Encapsulation Mechanisms:-

Drug encapsulation pertains to including drugs in varied carrier materials using either physical or chemical methods. The method used for encapsulation depends on the chemical characteristics of the drug and the desired profile of release.

a. Physical Encapsulation:

Physical encapsulation involves the physical incorporation of the drug with the carrier material, and does not alter the drugs chemical form. The drug is encapsulated within, and release is facilitated by the diffusion of the drug from the carrier system.

• **Liposomes** - liposomes are spherical vesicles, made of lipid bilayers, nascently encapsulating lipophilic or hydrophilic drugs. The hydrophilic drug otherwise is found in the interior aqueous core of the liposome, while the hydrophobic drugs will become incorporate into the lipid bilayer (48).

• **Polymeric micelles** - polymeric micelles are the self-assembled structures of amphiphilic copolymers. The hydrophobic core of the micelle is suitable for encapsulating hydrophobic drugs, while the hydrophilic outer shell of the amphiphilic is facilitates the stabilization of the micelle in an aqueous surrounding. The system is widely used for the administration of hydrophobic drugs (49).

• **Nanoparticles** - Biodegradable particle made from polymers can be utilized to encapsulate hydrophilic and hydrophobic drugs. The size of the nanoparticle can range from a couple of nanometers to a few microns and are utilized for controlled drug delivery (50).

b. Chemical Encapsulation:

Chemical encapsulation refers to the covalent binding of the drug to the carrier material. This binding can be broken under specific conditions, such as a change in pH, temperature, or enzymatic activity, allowing for controlled drug release.

• **Polymeric Systems:** Drugs can be covalently bound to a polymeric carrier like poly(lactic-co-glycolic acid) (PLGA), which biodegrades. The drug is released as the polymer degrades via biological and chemical methods over time (51).

c. Matrix Encapsulation:

In matrix encapsulation the drug is distributed throughout a solid matrix. The release of the drug occurs by way of its diffusion through the matrix or degradation of the matrix itself.

- **Hydrogels:** Hydrogels are polymer networks that can absorb large quantities of water, and they can encapsulate drugs and release occurs through swelling or erosion of the hydrogel matrix (52).

2. Drug Release Mechanisms:-

Once the drug is encapsulated, it needs to be released in a controlled fashion. The release mechanism depends both on the properties of the carrier and the environmental factors of pH, temperature, and enzymes to which it may be exposed.

a. Diffusion-Based Release:

In diffusion based releases, drug molecules will go from the encapsulating system to the surrounded environment based on a concentration gradient. The rate of release will depend on the solubility of the drug, thickness of the carrier materials and the size of the drug molecules.

• **Fickian Diffusion:** This release mechanism is defined according to Fick's law of diffusion in the case that the rate of release is directly proportional to the concentration gradient, which exists between inside of the system and the surrounding medium (53).

b. Degradation or Erosion-Based Release:

In this route, the carrier material is broken down or eroded and thus releases the drug as the system breaks down over time. Biodegradable polymers (such as PLGA) degrade through hydrolytic degradation, which facilitates the gradual release of the encapsulated drug (54).

c. pH-Sensitive Release:

Some drug delivery methods take advantage of pH variations to release drug in specific areas of the body with the appropriate pH (such as the stomach versus the intestine or a tumor).

• **pH-Sensitive Polymers:** Polymers such as polyacrylic acid are pH-sensitive. These polymers become swollen at low pH (as in the stomach) and release their drug contents (55).

d. Enzyme-Mediated Release:

Enzymatic degradation can be a beneficial mechanism for controlled drug release that is related to specific enzymes. This mechanism is especially advantageous when drug delivery can target tissues overexpressing specific enzymes, e.g., cancerous tissue (56).

e. Temperature-Sensitive Release:

Temperature-sensitive systems employ materials that undergo phase transitions as a function of temperature. For example, thermoresponsive polymers will modify their structure at a specific temperature which will cause the carrier to release the drug.

• **Thermoresponsive Polymers**: Poly(N-isopropylacrylamide) (PNIPAAm) is a thermoresponsive polymer which undergoes a phase transition temperature near human body temperature and thus might be useful for controlled drug delivery (57).

3. Factors Affecting Drug Encapsulation and Release:-

The efficiency of encapsulation and the release profile are influenced by several factors:

• **Drug Property:** The solubility, the molecular weight, stability of the drug affect how a drug is incorporated into delivery carriers and how it is released from the carrier (58).

• **Carrier Property:** The type, size, surface charge and hydrophilic/hydrophobic balance of a delivery carrier greatly influence both the encapsulation efficacy and the release mechanism from that carrier (59).

• **Environmental Properties:** Modifications to the pH, temperature and ionic strength of the surrounding environment can also change the release rate by modifying the delivery carrier material (60).

• **Encapsulation Technique:** The technique used to encapsulate the drug (solvent evaporation, nanoprecipitation...etc.) will also influence the release rate of the active pharmaceutical ingredient based on the morphological and porosity properties of the delivery carrier material (61).

4. Applications of Drug Encapsulation and Release:-

• **Controlled release:** Encapsulation makes it possible to provide a controlled release of the drug over a certain period of time, leading to better therapeutic result by keeping drug levels constant in the body (62).

• **Targeted drug delivery:** Carrier systems can be made to respond to some environmental stimulus (such as a pH change, temperature change, or the presence of a particular enzyme); therefore providing targeted delivery of a drug to a specific tissue, like tumor tissue for example (63).

• **Improved bioavailability:** Encapsulation can improve the solubility and stability of a drug that is poorly soluble in water, thereby improving its bioavailability and therapeutic effects (64).

3.1 How emulgels incorporate hydrophobic and hydrophilic drugs:-

Incorporating Hydrophobic Drugs:-

Hydrophobic drugs have a solubility problem in aqueous-based formulations. Emulgels will not offer a solution to hydrophobic solubility problems in an aqueous-based formulation as they rely on dispersing hydrophobic drugs into the oil phase of an emulsion. Emulgels can be made by first dispersing a hydrophobic drug in the oil phase and then formulating a stable emulsion with an emulsifier such as Tween or Span, or with an emulsion stabilizer such as lecithin (65). The hydrophobic drug-loaded emulsion could be incorporated into the gel matrix quickly and the emulgel could be applied, easy for penetration into skin and sustained release of drug (66).

Incorporating Hydrophilic Drugs:-

Hydrophilic drugs dissolve directly into the aqueous phase of the emulsion prior to mixing with the gel base. Gels are made with gelling agents such as carbopol, hydroxypropyl methylcellulose (HPMC), or xanthan gum, which cross-link to create a structure to stabilize the drug, and to control release (67). The stability of the gel matrix reduced degradation of the drug in through the skin when compared to emulgel. In summary gel prepares the skin for penetration, and allows for extended contact with the skin resulting in greater bioavailability (68).

3.2 Mechanism of drug diffusion and release:-

Drug diffusion and drug release govern the therapeutic properties of pharmaceutical formulations. The release mechanism of the drug influences its bioavailability, stability, and delivery controls. There are many mathematical models and experimental procedures that characterize drug diffusion and release kinetics (69).

Mechanisms of Drug Diffusion

Drug diffusion refers to the movement of drug molecules from a region of higher concentration to a region of lower concentration, driven by a concentration gradient. This process occurs through different pathways depending on the type of formulation:

1. Fickian Diffusion:- Fick's law states the diffusion process consists of the rate of drug movement being proportional to the concentration gradient. Within polymeric systems, Fickian diffusion occurs when the drug diffuses through a hydrated polymer and is not an influence of polymer relaxation (70,71).

2. Non-Fickian (Anomalous) Diffusion:- In some formulations, drug diffusion does not become Fickian when polymer swelling, chain relaxation, and/or dissolution occurs. The drug can be released through diffusion and polymer degradation in hydrophilic matrix systems (72).

3. Facilitated Diffusion:-

Some medications in biological systems use ion channels or carrier proteins to promote membrane diffusion. In targeted and transdermal drug delivery systems, this mechanism is crucial (73).

Mechanisms of Drug Release

Drug release mechanisms specify the process of drug delivery from the formulation to the site of action, and may vary depending on the physicochemical properties of the drug and the type of formulation.

1. Diffusion-Controlled Release

In the case of diffusion-controlled release, drug release will occur by way of diffusion through either a polymeric matrix, or a polymeric reservoir. There are two broad categories of diffusion controlled release:

• **Matrix diffusion systems**: The drug is uniformly dispersed within a polymer matrix which acts as the drug reservoir, where the drug will slowly diffuse out of the polymer matrix, (74).

• **Reservoir diffusion systems**: The drug is in a core, and a rate-controlling membrane surrounds the core, providing a sustained drug release profile (75).

2. Dissolution-Controlled Release

Drug release occurs when the dissolution rate of the drug or polymeric carrier controls how fast the drug is released; poorly soluble drugs provide slow dissolution and drug action (76).

3. Swelling and Erosion-Controlled Release

Certain types of hydrophilic polymers will swell when they come in contact with biological fluids and form a gel layer that limits diffusion of the drug. Swellable systems however, rely on erosion for drug release (77).

4.Osmotically Controlled Release

In osmotic systems, an osmotic agent generates pressure within the formulation and forces the drug through a semipermeable membrane at a controlled rate of release. This is a common delivery mechanism for oral drug delivery (78).

3.3Factors affecting drug release (pH, temperature, excipients)

Release of a drug from a pharmaceutical formulation is dependent on multiple factors which include, physicochemical properties of the drug, the design of the formulation, and the environment. Among these factors, pH, temperature, and excipients play roles in regulating drug dissolution, diffusion and drug bioavailability (79).

Effect of pH on Drug Release

The pH of the surrounding medium plays an important role in drug solubility and release when produced with pH dependent ionizable drugs. Generally, weakly acidic drugs will possess better solubility in basic environments and weakly basic drugs solution will improve in acidic environments (80). Therefore, it can be determined that the solubility of a drug is governed by the Henderson-Hasselbalch equation as we have reviewed pH dependence affecting ionization and solubility (81). Additionally, controlled release formulations can utilize pH-sensitive polymers like Eudragit® to facilitate timely drug release depending on a specific pH in the gastrointestinal tract (82). For example, enteric coated formulations are designed to protect drug release when gastric acidic conditions exist but release drug in a more neutral pH intestinal condition (83).

Effect of Temperature on Drug Release

Temperature impacts drug release due to changes to the solubility of the drug, swelling of the polymer and the diffusion of the drug. Generally, increasing the temperature will increase drug solubility and diffusion, meaning faster drug release in most cases (84). In thermosensitive hydrogel systems, temperature-induced swelling and temperature-induced phase transitions will create drug release profiles (85). Many polymeric carriers, including poloxamers and chitosan derivative, will undergo sol-to-gel transitions which are temperature-dependent, allowing for the controlled delivery of a drug based on temperature changes at a physiological level (86). However, temperature variations when transporting and storing polymers have led to polymorphic transformations that, when not recognized, inevitably affect drug stability and/or dissolution rates (87).

Effect of Excipients on Drug Release

The influence of excipients modifies drug release profiles through solubility, stability, and permeability. Most hydrophilic excipients will increase drug solubility and drug dissolution (PEG) as well as provide sustained release (HPMC) (88). Hydrophobic excipients (ethylcellulose, wax matrices) will create diffusion barriers, delaying drug release (89). Surfactants such as sodium lauryl sulfate (SLS) will increase the wetting of poorly soluble drugs and increase the dissolution rate (90). Addition of bioadhesive polymers, which will not only increase the drug absorption by increasing retention at the absorption site, it will also increase bioavailability of the drug (91).

4. Advantages of Emulgels in Drug Delivery

4.1 Enhanced Drug Solubility and Stability:-

Emulgels provide an efficient drug delivery system that enhanced the solubility and stability of both hydrophobic and hydrophilic drugs. The presence of the aqueous and lipid phases allows poorly water-soluble drugs to be encapsulated in the lipid phase, while the hydrophilic gel base disperses the drug (92). The gel matrix stabilizes the emulsion and prevents the emulsion from separating so that active pharmaceutical ingredients (APIs) do not degrade through external catalytic processes like oxidation and hydrolysis (93). The inclusion of stabilizers, emulsifiers, and gelling agents such as Carbopol and HPMC improves the physical and chemical stability of emulgels enabling long-term storage (94).

4.2 Improved Bioavailability and Penetration:-

One of the key benefits of emulgels over other dosage formulations is it can improve the penetration of drugs when applied to the skin which can enhance bioavailability. The presence of emulsifiers (e.g. surfactants) and penetration enhancers (e.g. alcohols) enable improved drug diffusion across the stratum corneum (95). Compared to creams and ointments, emulgels have improved spreadability and skin adhesion, which increases the contact time with the skin and improves absorption (96). The hydrophilic gel base allows for improved skin hydration, which enhances both transdermal penetration and drug permeation (97).

4.3 Prolonged Drug Release and Reduced Dosing Frequency:-

Emulgels can also enable controlled, sustained release of drugs, lessening dosing frequency and enhancing patient compliance by providing a more constant therapeutic effect. The gel network acts as a reservoir system to release the drug over time (98). Controlled release is valuable for sustained therapeutic effect for chronic conditions such as pain and dermatological conditions (99). Using polymeric materials such as xanthan gum, hydroxyethylcellulose and chitosan in emulgel formulations can modulate drug release kinetics, reduce the chance of variability in drug plasma concentration (100).

4.4 Non-Greasy, Easy Application for Topical Delivery:-

Emulgels are a non-greasy alternative to ointments and creams, and they provide a more desirable feel of smoothness and non-stickiness upon application. The gel material affords better spreadability, rapid skin absorption, and non-occlusive features, making them neater in use and more aesthetically pleasing for patients (101). Emulgels do not leave a residue on the skin, reducing discomfort and improving patient compliance (102). Easy to apply and better experience for patients, emulgels are an effective drug delivery system for dermatological, anti-inflammatory, and analgesic drug applications (103).

5. Methods of Preparation and Characterization

5.1 Common Preparation Techniques:-

Emulgels can be prepared by a variety of methods to achieve stability, homogeneity and drug entrapment efficiency and the two most often used methods are high-shear mixing and phase inversion methods.

1.1 High-Shear Mixing Technique

High-shear mixing is the most common technique, as it allows for complete dispersion of the drug dispersed throughout the emulgel formulation. In this technique, the oil phase (containing lipophilic ingredients--e.g. oils, emulsifiers, active ingredients) is heated and mixed separately from the aqueous phase (containing water-soluble ingredients--e.g. polymers, preservatives, hydrophilic drugs). Once these two phases are made, the two phases are blended together in the high-shear mixer under high shear forces, which forms a stable emulsion, which is placed into a gel base (104). High shear mixing improves the solubility of the hydrophobic drug and aids in the dispersion when taking into account how this formulation can be utilized. HSM improves hydrophobic drug bioavailability (105).

1.2 Phase Inversion Technique

Phase inversion is controlled transition from oil-in-water (O/W) emulsion to water-in-oil (W/O) emulsion by varying temperature or composition of the emulsion. Commonly, phase inversion is used to improve the stability of the emulsion and droplet size uniformity (106). In one example, phase inversion temperature (PIT) emulsification, emulsification occurs at the phase inversion temperature, which allows for better entrapment efficiency/more prolonged release properties (107).

5.2 Characterization Parameters:-

When assessing the quality and efficacy of emulgels, the characterization parameters that may be assessed from various sources include physical properties, drug content, rheological properties, and in vitro release profiles**.**

2.1 Physical Appearance and Viscosity

The appearance of an emulgel, including color, efficacy, and phase separation, is visually assessed to determine if the formulation is stable (108). The viscosity is determined using a rheometer or viscometer to assess the flow properties of the gel, affecting drug release and application (109). If there is high viscosity this would allow for greater contact time with the skin, to enhance its therapeutic action (110).

2.2 Drug Content and Entrapment Efficiency

The drug content is assessed using either spectroscopic or chromatographic assessments (UV-Vis, HPLC) to provide a proper distribution for the drug (111). The entrapment efficiency, which is an important parameter to asses for sustained release formulations, is accessed by separating unentrapped drug using centrifugation and quantifying the encapsulated drug (112).

2.3 pH, Spreadability, and Rheological Properties

The pH of formulation is determined using a digital pH meter to ensure that is is compatible to skin (130). Spreadability was based on the ease of application and uniformity of drug distribution evaluated using parallel plate (114). Rheological properties will include thixotropy and shear thinning and latex formation to evaluate flow properties of formulation (115).

2.4 In Vitro Drug Release Studies

In vitro drug release studies are performed using Franz diffusion cells to evaluate the release kinetics of the drug from the emulgel formulation. The release medium (phosphate buffer or simulated biological fluids) is sampled at regular intervals, and drug concentration is quantified using UV-Vis or HPLC methods (116). The release profile is analyzed using mathematical models (e.g., Higuchi, Korsmeyer-Peppas) to understand the mechanism of drug diffusion and release (117).

6. Applications in Pharmaceutical and Medical Fields

6.1 Use in Dermatology (Anti-Inflammatory, Antifungal, Wound Healing):-

Emulgels are commonly prescribed for dermatological use because they enhance drug permeation through the dermis with topical, non-greasy applications. Emulgels have been formulated with anti-inflammatory agents, including diclofenac and ketoprofen, to treat pain and inflammatory conditions, with greater therapeutic effect than existing gels and creams (118). Antifungal emulgels have included clotrimazole and ketoconazole, demonstrating increased retention to the skin with sustained drug release, leading to effective treatments for fungal infections, such as candidiasis and dermatophytosis (119). Emulgels have also been developed with various bioactive components including silver nanoparticles and herbal extracts for wound healing treatments, increasing healing of tissue and decreasing risk of infection (120).

6.2 Transdermal Drug Delivery Applications:-

Transdermal drug delivery of emulgels may provide a safer alternative to oral and injectable dosing, improved patient compliance with a dosage formulation that allows controlled release of drug. With penetrant enhancers (ethanol and surfactants), emulgels facilitate absorption of drug through the stratum corneum, qualifying emulgels as a potential carrier for drugs of poor oral bioavailability (121). Hormonal therapies using emulgels for estrogen and testosterone replacement therapy assured a steady systemic absorption of a drug (122). Emulgels may also be used to deliver analgesics, such as ibuprofen and lidocaine, with a sustained release mechanism to relieve pain (123).

6.3 Oral and Ophthalmic Applications:-

While primarily used for topical administration, emulgels are increasingly being evaluated for use in oral and ophthalmic delivery of drugs. In oral delivery systems, emulgels can increase the solubility and bioavailability of poorly soluble drugs, ensuring a reduced first pass metabolism and enhanced absorption into the systemic circulation (124). Emulgel based mucoadhesive systems for administering drugs via the buccal delivery pathway have been developed, to produce longer term therapeutic benefits in conditions such as oral candidiasis and periodontal diseases (125). In ophthalmic delivery, emulgels enable the sustained delivery of drug into the eye for the treatment of various eye infections and inflammatory conditions, while improving adherence to administration of the drug when compared to conventional eye drops (126). Formulations containing anti-glaucoma drugs such as timolol maleate has been explored to enhance corneal permeation and allow for longer therapeutic application (127).

6.4 Potential for Cosmeceutical Formulations:-

The cosmeceutical industry has embraced emulgels to aid in both skincare and hair care applications due to the stability of the product, non-greasy feel, and enhanced delivery of active ingredients. Emulgels have been developed to deliver antioxidants, retinoids and herbal extracts to the skin, in order to target anti-aging, skin brightening, and acne treatments (128). A sunscreen emulgel was recently produced for this application, which afforded an improvement in spreadability and uniform coverage as compared to lotions, which in turn improved photoprotective efficacy (129). Emulgel-based formulations also also included applications for transdermal delivery of bioactive peptides and vitamins using emulgel formulations, for improving skin hydration and skin elasticity (130).

7. Challenges and Limitations

7.1 Stability Concerns with Certain Drugs:-

One of the main issues involved with emulgels is the stability of several drugs, especially the ones which are hydrolyzable or decomposable under certain environments with time, such as oxidation, hydrolysis, etc. Emulgels are bi-phasic systems which means that they can separate phase-wise. The separation of emulgels may result in precipitation of the drug, leaving traces of a quantum drug that may render it ineffective, or a very underwhelming therapeutic effect (131). For instance, hydrophobic drugs are usually added to the oil phase, and the drugs may undergo difference chemical changes, such as crystallization or aggregation due to non-uniform distribution (132). Transitions in temperature and long-term storage are likewise able to modify the viscosity and rheological properties of the gel matrix, and increase the potential for instability (133). Researchers are finding different reasons to develop stabilizers, antioxidants, and to determine a way to formulate long-term stable, modified-polymeric gelling agents in order to improve stability (134).

7.2 Compatibility Issues with Excipients:-

The selection of excipients is an important factor for the performance and stability of emulgel formulations. Nevertheless, compatibility of the active pharmaceutical ingredients (APIs) and excipients can negatively affect drug release, absorption and bioavailability. Several emulsifying agents and gelling agents (like Carbopol or HPMC) may interact with ionic drugs, which can interfere with drug solubility and diffusion rates. Additionally, surfactants which are required for forming and stabilizing the emulsion system of emulgels may also lead to skin irritation or unwanted skin reactions, thus limiting the suitability of these formulations in many dermatological formulations. Compatibility issues can be addressed with pre-formulation studies and/or using alternative biocompatible excipients (138).

7.3 Scaling Up for Commercial Production:-

The issues associated with transitioning emulgel formulations from laboratory scale-generated manufacturing to commercial manufacturing are substantial, even with their benefits. First, it is essential that the rheological properties, drug entrapment efficiency, and emulsion stability engineered by laboratory methods be produced in each batch when scaled up (139). The industrial equipment of the manufacturer including positive and negative pressure high-shear mixer or the high-pressure homogenizer must be evaluated to obtain maximum uniformity of the formulation during industrial production and to prevent phase separation (140). Furthermore, the extrinsic regulations including quality controls and good manufacturing practices (GMP) must be complied with to assure the consistency and efficacy of the final commercial product (141). Research into process optimization and methodologies that include continuous manufacturing in planned ways, together with careful documentation to provide satisfactory and ample evidence of successful and consistent large-scale production, can reduce batch-to-batch variability (142).

8. Recent Advances and Future Perspectives

8.1 Use of Nanotechnology in Emulgels

Incorporating nanotechnology in emulgel formulations has shown major improvements in emulgel formulations for stability, drug encapsulation efficiency, and therapeutic efficacy. Nanoemulgels contain nanosized droplets (10–200 nm) in their emulsion phase. As a result, the droplets improve the drug solubility and increase permeation across the skin barrier, hence they are suitable for transdermal and topical drug delivery (143). Use of nanocarriers, including solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs) and polymeric nanoparticles, in emulgels have increased the use of the formulation for controlled drug release and targeted therapy (144). Recently published studies have shown that nanoemulgels loaded with curcumin, resveratrol and other bioactive compounds have greater antioxidant, anti-inflammatory and antimicrobial properties than in traditional emulgel formulations. These nanoemulgels show potential for therapeutic use in chronic skin diseases and wound healing (145).

8.2 Smart Emulgels with Stimuli-Responsive Properties

Smart emulgels, also referred to as stimuli-responsive emulgels, are a new class of drug delivery systems that change physically or chemically in response to environmental triggers, such as pH, temperature, enzymes or light (146). A pH-responsive emulgel would use polymers such as Eudragit® which are known to swell or dissolve in either basic or acidic environments and could be used to ensure site-specific drug release within the gut (147). Thermoresponsive emulgels utilize polymers such as poloxamers and/or chitosan derivatives to undergo sol-to-gel phase transitions, at body temperature, allowing localized, sustained release (148). Light-responsive emulgels containing photo-responsive nanoparticles illustrate how specific triggers have been examined for controlled drug release for dermatological and cancer treatments (149). Smart emulgels offer a step towards personalized medicine, which defines treatment plans that are precise and minimize adverse side effects.

8.3 Clinical Trials and Market Potential

A number of emulgel-type drug formulations are undergoing clinical trials to determine their safety, efficacy, and pharmacokinetic profiles. Clinical trials with diclofenac emulgels indicated improved anti-inflammatory effects and increased patient compliance compared to conventional gel formulations (150). Any trial in dermatology on antifungal emulgels (ketoconazole and clotrimazole) indicated better retention properties with prolonged drug action, and reduced frequency of application (151). The pharmaceutical and cosmeceutical industries' interest in emulgels can be gauged by the increasing number of patents and commercial products being developed (152). Emulgels are being used in pain management, wound healing, anti-aging skin care, and combination hormone therapy formulations, indicating enormous commercial opportunities (153). Future work is directed at optimizing successful large-scale manufacturing, formal regulatory processes for approval, and incorporating novel biomaterials into emulgels to solidify market entry and continued clinical success (154).

9. Conclusion

Emulgels are a versatile and effective drug delivery form with great potential to incorporate hydrophobic and hydrophilic drugs with better solubility, stability, and controlled-release characteristics, open up possibilities for enhanced penetration of drugs due to a biphasic nature making them a rational choice for transdermal, dermatological and ophthalmic delivery. By utilizing nanotechnology and smart materials for stimuli-responsive release, the prospects for targeted and sustained release became a reality as well. There are still some challenges with stability, excipients compatibility and scaling-up production, but improvements in formulations and conditions continue to be developed, leading to further opportunities for clinical and commercial uses. Future developments will be in formulating these to optimize patient compliance, therapeutic outcomes and facilitate industrial applications. Emulgels are to be recognized as a viable drug delivery system of the future in contemporary Pharmaceutical Sciences.

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