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Principles and Applications of Interfacial Rheology in (Pre)Formulation Development of Pharmaceutical Preparations

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Abstract

Rheology is a science that deals with the movement and deformation of materials, while interfacial rheology is a branch of rheology that focuses on the study of the mechanical properties of fluid interfaces, such as liquid-liquid and liquid-gas interfaces. The behavior of fluid interfaces differs significantly from that of bulk materials, and standard rheological measurements of bulk materials cannot adequately describe their properties. Interfacial rheology is a specialized approach to the study of viscoelasticity and interfacial tension at liquid interfaces and provides valuable insight into intermolecular interactions and surface forces. This knowledge is particularly important for the development of advanced formulations and systems with tailored properties and functionalities. Interfacial rheology is a rapidly growing research field with diverse applications in science and industry. It plays a pivotal role in the development and optimization of pharmaceutical formulations and design of innovative drug delivery carriers with improved stability, enhanced drug release profiles, and targeted delivery capabilities. This review article aims to provide a comprehensive overview of interfacial rheology, its principles, measurement techniques, and applications in various industries. By exploring recent advancements and emerging trends in the field, we aim to highlight the significance of interfacial rheology in optimizing formulations, enhancing product performance, and driving innovations, particularly in pharmaceutical science.

Key words: interfacial rheology, viscoelasticity, emulsion, foam, preformulation

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Introduction

A large number of pharmaceutical formulations used for drug delivery are dispersed systems. Some of the most popular pharmaceutical dispersions are emulsions and foams. Emulsions have the ability to incorporate several active pharmaceutical ingredients in both aqueous and oily phases. In addition, they can mask the unpleasant taste or smell of the active ingredients, reduce the toxicity of the drug, increase the possibility of penetration into the skin, etc. One of the most important characteristics of emulsions is that they can provide the encapsulation of active pharmaceutical components that are in the dispersed phase and thus protect them from the influence of the external environment and, at the same time, ensure their controlled release (1). On the other hand, foams are most often used for topical application due to the possibility of incorporating active substances and often show better properties than traditional formulations such as oils, creams, lotions, and gels. The advantage of the foams lies in the fact that, due to their low viscosity, they are easily spread over the skin without causing irritation. Moreover, due to their low specific density and ability to become carriers for modified forms of drugs, foams are used for oral (e.g. as gastroretentive formulations) and parenteral administration (e.g. as implants that serve simultaneously as drug carriers and scaffolds for regenerating the tissue) (2-4).

Both types of dispersion systems, emulsions and foams, are made of two or more immiscible fluids. Emulsions consist of two immiscible liquid phases (water and oil), where one liquid (the dispersed phase) is dispersed in the other (the continuous phase), while foams are produced as dispersions of a high concentration of gas bubbles in a small amount of a continuous liquid phase. They are thermodynamically unstable systems and their pronounced instability originates from the physicochemical nature of the phases. Therefore, they always contain a third component, which is called an emulsifier (for emulsions) or foaming agent (for foams), and it is most often a surfactant (5, 6). The dispersion process is non-spontaneous, due to the fact that energy is required for the production of the smaller particles from the larger ones. In this process, such as emulsification or foaming, droplets or bubbles are suspended in another substance producing an emulsion (liquid/liquid) or foam (liquid/gas), most often by applying mechanical energy. During the process of dispersion, a large amount of interface area created between immiscible fluids in combination with a high value of interfacial or surface tension produces a surface-free energy i.e., potential energy, which leads to the instability of the system. Emulsions and foams are, therefore, thermodynamically unstable systems in which, after the emulsification or foaming is completed, different processes occur over time that aim to reduce the amount of free surface energy. In emulsions, destabilization may occur as a result of gravitational separation (creaming or sedimentation), droplet aggregation (flocculation, coalescence, and partial coalescence), and Ostwald ripening (7, 8). In foams, physicochemical processes such as liquid drainage, Ostwald ripening and bubble coalescence influence their stability (2-4). These physicochemical processes are highly dependent on the characteristics of the type of

surfactant used in the formulation, as well as on the properties of the formed layer at the interface.

For example, the coalescence of droplets or bubbles is a phenomenon that occurs in emulsions and foams and leads to a decrease of potential energy, which is the result of a high amount of specific surface area. It is accelerated by the gravitational force that enables the interaction of the particles of the dispersed phase. In the case of pure fluids, which do not contain an added stabilizing agent, coalescence occurs fast and the system returns to its initial state in a short time after the mechanical energy used in the dispersing process ceases (2, 7). Therefore, it is necessary to include different types of stabilizing agents in the formulation of emulsions and foams, such as surfactants and stabilizers (which act as texture modifiers, thickeners, etc.), in order to ensure the long-term stability of the formulation (6, 8).

Surface-active agents (also known as surfactants) are amphiphilic molecules consisting of two parts, polar and non-polar. This molecular structure sets this group of compounds apart from the others, due to the fact that it makes surfactants both hydrophilic and hydrophobic at the same time. The presence of both parts in the compound gives surfactants specific properties, such as adsorption on different interfaces and the formation of aggregates in solutions, known as micelles (9-12). Surfactants are essential for the process of formation of emulsions and foams, as well as their stabilization. Therefore, the selection of an adequate surfactant is crucial for the production and obtaining of a stable emulsion or foam (8, 13). In addition to low molecular weight surfactants, some synthetic macromolecules or biopolymers are frequently used to obtain and stabilize these systems. The surfactants included in the formulation of emulsion or foam can slow down the destabilization processes or even, in certain circumstances, completely stabilize them.

Interfacial properties and rheology of interfacial layers

The interface can be described as a dividing line between two immiscible phases of a certain thickness, with properties that are different from the properties of the individual phases. The interfacial tension that occurs is a consequence of the difference in the cohesive forces on molecules of a liquid at the interface compared to the molecules in bulk (7, 14).

The roles of the surfactant during the emulsification or foaming are to enable their production and ensure its stability for a certain period of time. In order to successfully carry out this task, the surfactant must fulfill the following requirements: to be adsorbed in a short time on the surface of the droplets of the dispersed liquid or bubbles formed in the production process, it must significantly reduce the interfacial or surface tension between the phases and form a protective layer (film) on the surface of the dispersed droplets or bubbles and protect them from aggregation or coalescence (13, 15, 16) (Figure 1). Surfactants, amphiphilic molecules, at liquid–liquid or liquid–gas interface influence interfacial or surface tension, but those values alone cannot fully describe the phenomena that occur after external perturbations and the response of surfactants monolayers on

them. In addition, surface activity or interfacial tension gradients cannot be considered as dominant factors in emulsion or foam stability. It is necessary to consider adsorption kinetics, surface coverage, surface charge, packing, and thickness of the emulsifier or foaming agent in order to achieve emulsion or foam long-term stability. It is also well known that thin liquid films that represent a barrier to the coalescence of droplets or bubbles are in some correlation with the rheology characteristics of adsorbed surfactant monolayers at the interface (8, 17). The adsorption rate of emulsifiers at the oil–water interface and the rate of formation of the interfacial layer should exceed the collision rate between freshly formed droplets during the emulsions formation process. There are differences in the stabilization mechanism of emulsions between low-molecular weight surfactants and surface-active macromolecules. Small-molecule surfactants can quickly and easily be adsorbed onto freshly formed oil droplets' surfaces, reducing interfacial tension and stabilizing the emulsion. Surface active macromolecules (proteins and hydrocolloids) are sometimes slower than low-molecular weight surfactants in adsorption rate, but they can form a viscoelastic interfacial layer on surface of droplets and provide long-term emulsion stability during further processing. For example, the thickness of interfaces formed by adsorbing polysorbate molecules is about 1 nm, which is not enough to provide long-term stability for emulsions. Therefore, polysorbates are often combined with macromolecular surfactants (proteins and polysaccharides) to improve the rheological properties of the interfacial layer and thereby ensure better stability of the system in the long term (8). In addition to the interfacial tension in the examination of the interface, it is necessary to include the rheological characteristics as well. Optimizing

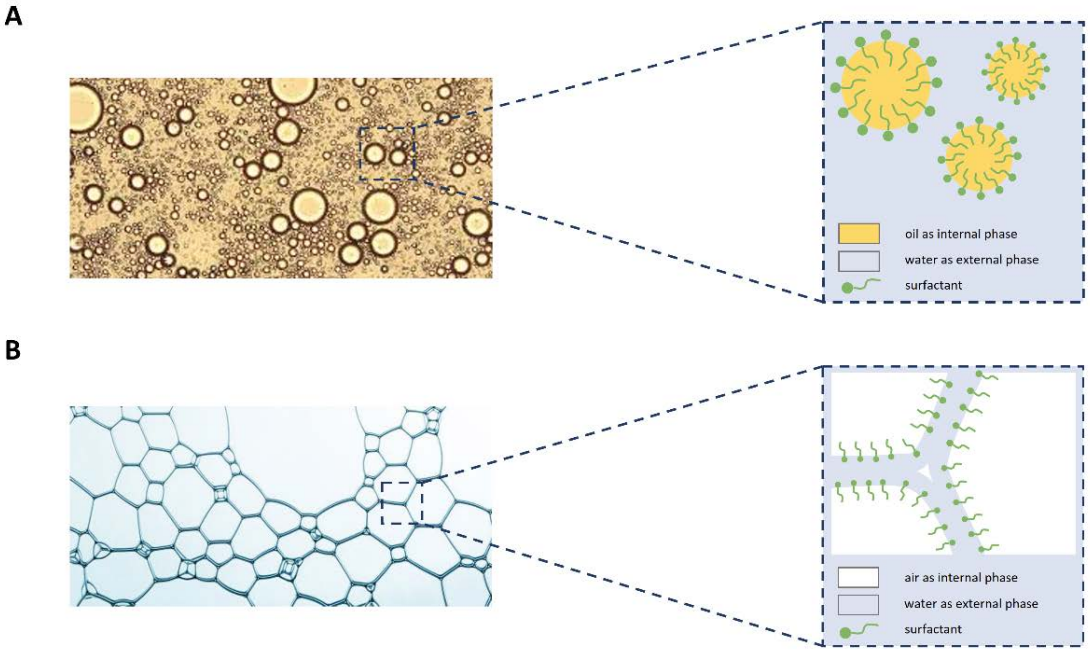

Figure 1. Internal structure of (A) emulsions and (B) foams
Slika 1. Unutrašnja struktura (A) emulzija i (B) pena

interfacial rheological properties is vital to prevent phase separation and improve the long-term stability of formulations. Those properties, which express the viscoelasticity of the monolayer, are very important for numerous processes and applications such as emulsification, foaming, wetting and dewetting, foam and emulsion stability, etc (18, 19).

Rheology is a science that studies the movement and deformation of materials (fluid and solid). It describes how certain materials respond to the force (20). Consequently, the main subject of interfacial rheology is the response of the mobile interface to deformation. For bulk material, three different types of deformation can be distinguished: shear, dilation, and extension (Figure 2). The rheological characteristics of the system are independent of the plane of determination, and therefore rheology can be treated as a three-dimensional characteristic. Much like bulk materials, interfaces can also be deformed in a different way. But unlike rheology for bulk materials, interfacial rheology can be defined only for two types of deformation: shear and dilation. Interfacial rheology is used to study how different emulsifiers interact with the interface and affect dispersion stability. Therefore, interfacial rheology can be defined as the rheology of a thin layer of surfactants that forms between the interface of two liquid phases or the surface of liquid and gas phases. Unlike bulk rheology, interfacial rheology is limited only to the interfacial layer, so it can be called two-dimensional rheology (21). If there is a non-uniform distribution of the concentration of surfactants at the phase boundary, a gradient of interfacial tension arises and it depends on the surface area of the interface. Sometimes this gradient is also defined by Gibbs elasticity:

$$\varepsilon = \frac{d\gamma}{d\ln A} \quad (1)$$

where γ is interfacial tension, and A is the surface area of interface, which induces volumetric liquid motion, which is the basis of the so-called “Marangoni effect” (11). The Marangoni effect is a crucial phenomenon in interfacial rheology, which occurs due to differences in surface tension across the interface. When the surface tension gradient is present, it generates surface flow, known as the Marangoni flow, which can, together with Van der Waals forces, destabilize the final remaining film of surfactants at the interface. If the drainage of the film of surfactant occurs, a surfactant concentration gradient arises that causes a Marangoni stress, which acts in the direction opposing the drainage flow. This stress tends to immobilize the interface and inhibits film drainage and thus coalescence. Marangoni effect is particularly significant in emulsions and foams stabilization (22). Many films made by low molecular weight or macromolecular surfactants exhibit non-Newtonian interfacial behavior. In interfacial rheology the same techniques are used as in bulk rheology in order to investigate the viscose response of interface, which is under applied stress or strain. Different types of deformation (shear and dilation) should be considered in order to define conditions for the stability of dispersed systems. Since interfacial rheology examines the rheological properties of interfaces, which is the basis for the stability of the dispersed system, it can be considered that interfacial rheology describes the factors that contribute to the stability of the

dispersed system better than bulk rheology (21). In shear rheology, if the interface is in thermodynamic equilibrium with the bulk solution, the data of the change in the shape of the interface at a constant surface area can be obtained. On the contrary, dilatational rheology explains the changes in surface area while keeping the shape constant. These are two complementary methods that deal with different aspects of the interfacial layer. The changes in the rheological parameters of the interfacial layer during shearing can contribute to the long-term stabilization of dispersed systems, while dilatational rheology affects the stabilization in the short term (23). In addition, bulk and interfacial shear rheology can be used to explain the effect of external factors such as temperature, ion strength, pH, and solvent on the functional properties of proteins. Bulk rheology studies the response of a system (protein solution or gel) to external mechanical deformation, while surface rheology provides data on the kinetics of adsorption to the oil/water or air/water interface during emulsification or foaming of proteins or other surfactants and the stability of the formed film on the surface over time (24, 25).

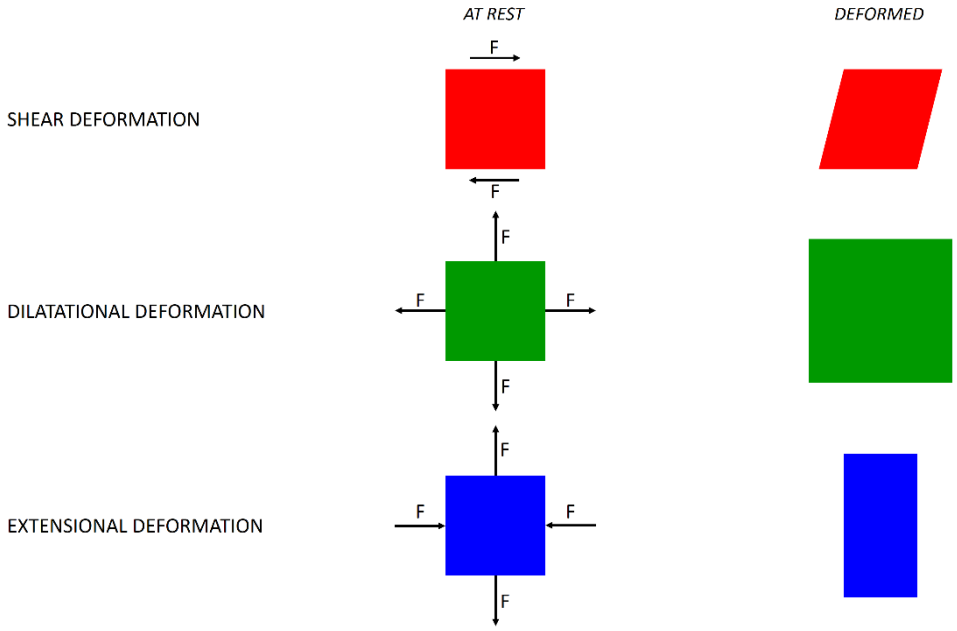

Figure 2. Types of material deformation: shear, dilatational and extensional
Slika 2. Tipovi deformacije materije: smicanjem, dilataciona i ekstenziona

Adsorption dynamics shows that with increase in surface aging time, the concentration of surfactants at the interface becomes higher, which leads to a decrease in interfacial tension. Interfacial or surface tension decreases with increasing numbers of surfactant molecules at the interface before adsorption equilibrium. At the same time, an increased number of surfactant molecules in the interface leads to thicker adsorbed surfactant layers and their higher packing density exhibiting higher values of surface viscosity and viscoelastic moduli due to an increase in interactions between them (26, 27). Finally, it can be concluded that while interfacial tension decreases, surface viscosity

and viscoelastic moduli increase with the increase in surfactant adsorption (Figure 3). After the adsorption is completed, both the interfacial tension and surface viscosity and viscoelastic moduli reach equilibrium values.

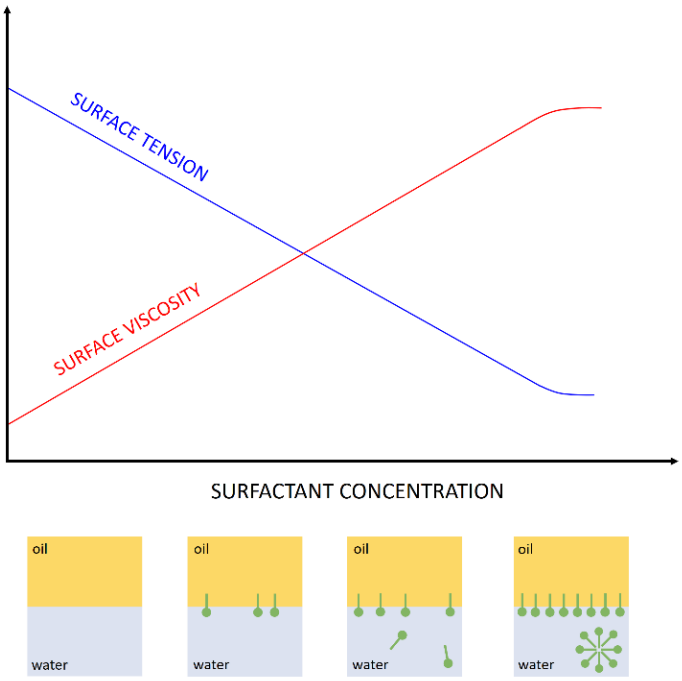

Figure 3. Influence of surfactant concentration on surface tension and surface viscosity

Slika 3. Uticaj koncentracije surfaktanta na površinski napon i površinski viskozitet

Measurement techniques of interfacial rheology

There are a number of different methods that can be used to measure the rheological properties of interfaces (Figure 4), each with its own advantages and disadvantages. The choice of method depends on the specific application.

Interfacial rheology measurements are typically divided into shear and dilatation methods. Interfacial shear rheology techniques measure the shear stress required to deform an interface. In interfacial shear rheology, the area of the interface stays constant, but instead the shape of the interface is deformed. Interfacial dilatational rheology techniques measure the stress required to increase or decrease the area of an interface, and the response to the change is typically detected by measuring the surface tension or surface pressure change. Besides, there are measuring techniques that determine interfacial viscoelasticity. These techniques measure the storage (G′) and loss (G″) moduli of the interfacial layer. The storage modulus is a measure of the elastic response of the interface, while the loss modulus is a measure of its viscous response (19, 28).

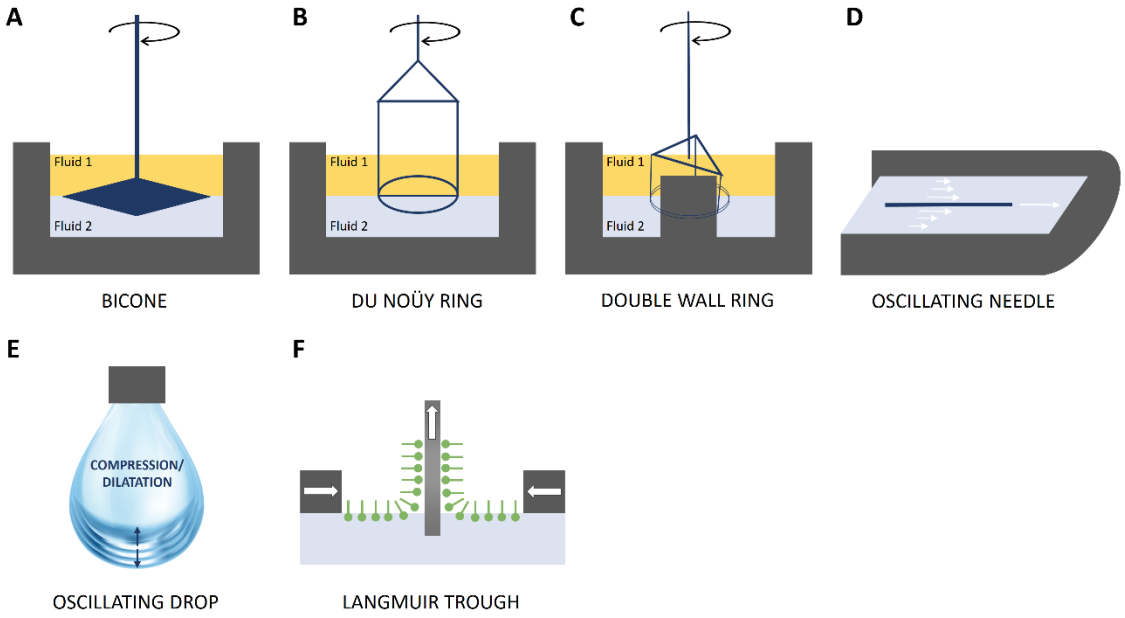

Figure 4. **Measurement techniques for interfacial rheology: (A) bicone system, (B) Du Noüy ring, (C) double-wall ring, (D) oscillating needle, (E) oscillating drop, (F) Langmuir-Blodgett method**

Slika 4. **Tehnike merenja međufazne reologije: (A) bikonusni sistem, (B) Du Noüy prsten, (C) prsten dvostrukog zida, (D) oscilatorna igla, (E) oscilatorna kap, (F) Langmir-Blodžet metod**

The bicone system (Figure 4A) is a type of interfacial shear rheometer that is used to measure the shear stress required to deform a liquid interface. The bicone is a cone-shaped object that is placed at the liquid-liquid or air-liquid interface. The bicone is then rotated and the shear stress at the interface is measured as a function of the shear rate. The bicone system is a relatively simple and inexpensive way to measure the shear stress at an interface. However, it has a limitation of being sensitive only to relatively large shear stresses, and the method is thus mainly suitable for stiff interfaces. Besides, the bicone system can only be used to measure the shear stress at a single point in the interface and the positioning of the plate at the interface can be sometimes challenging. Due to the large size of the probe, the contribution of bulk fluids to total torque needs to be taken into account (21, 29, 30).

With the bicone interfacial rheology configuration, both rotational and oscillatory experiments can be conducted. Firstly, in order to determine the interface position, an axial ramp experiment needs to be performed for finding the correct interfacial position of the bicone rotor. When plotting the normal force as a function of the gap, the point where the normal force goes from negative to positive numbers indicates the ideal position of the bicone rotor at the interfacial layer. The zero-crossing point can be determined precisely by applying a quadratic fit in the software. Before the viscosity or viscoelastic parameters of an interfacial layer can be tested, the individual upper and

lower liquids need to be tested separately. The individual contributions from the two bulk fluids to the total resistance acting on the bicone rotor need to be subtracted from the total results (19, 29).

The interfacial viscosity can thus be calculated using the equation:

$$\eta_i(\dot{\gamma}) = \eta_{total}(\dot{\gamma}) - \frac{\eta_A(\dot{\gamma})}{2} - \frac{\eta_B(\dot{\gamma})}{2} \quad (2)$$

where $\eta_i(\dot{\gamma})$ represents interfacial viscosity as a function of the applied shear rate, $\eta_{total}(\dot{\gamma})$ total viscosity signal from the measurement with the two liquids, while $\eta_A(\dot{\gamma})$ and $\eta_B(\dot{\gamma})$ represent viscosity signals from the bulk fluids A and B, respectively. For oscillatory experiments, a similar approach can be applied using interfacial and total storage (G') and loss (G") moduli, along with storage and loss moduli of bulk fluids.

The Du Noüy ring method (Figure 4B) was firstly used to measure the surface tension of a liquid, but it can be used for interfacial rheological measurements as well. A horizontal ring is placed at the interface (or on the surface) and rotates around its axis. Compared to the bicone method, it is a light and fragile geometry with a small moment of inertia, but the inner area of the ring is not considered, which may be an issue when the film is formed both inside and outside of the ring. Due to low inertia, this geometry is good for oscillatory measurements, but it is not suitable for very strong interfaces. Besides, it is more difficult to place the ring at the interface due to the round cross-section (19, 31).

The double-wall ring (Figure 4C) combines the advantages of the bicone (bigger contact area) and those of Du Noüy ring (lightweight and low inertia). Moreover, the cross-section of the ring is diamond-shaped, which enables to place the probe at the interface more easily (21, 32).

The oscillating needle (Figure 4D) is the most sensitive interfacial shear rheology measurement method. A floating magnetized needle oscillates longitudinally at the air-liquid or liquid-liquid interface by the use of a mobile magnetic trap. This needle is aligned along with the flow cell and the sheared interface is the horizontal surface between the needle and the edge of the cell. The needle position and movement are recorded with a high-resolution camera and the viscoelastic properties of the film can be calculated. Since the needle is floating at the interface, there are no positioning problems, as in the previously described methods (33, 34).

The oscillating drop (Figure 4E) and oscillating bubble methods are dynamic techniques employed to study dilatational surface rheology, i.e. interfacial viscoelasticity. In the oscillating drop method, the volume of a pendant drop is oscillated using compression and dilatation with ultrafine control, while in the oscillating bubble method, a bubble is formed at the end of a capillary submerged in the liquid phase and is periodically expanded and contracted at the interface. The resulting frequency and amplitude response provide valuable insights into the viscoelastic properties of the fluid interface, especially in complex systems like surfactant-based formulations (35). To study interfacial viscoelasticity, the software analyses the sinusioidally increasing and shrinking

drop area, as well as the interfacial tension, and their phase shift determines the viscoelastic parameters of the studied system. These methods provide valuable information for designing drug delivery systems with tailored release kinetics and enhanced stability (36, 37).

Similarly, drop shape analysis is a non-invasive technique used to measure dynamic interfacial tension in pharmaceutical systems. Drop shape analysis, often using optical techniques, enables the determination of surface tension and dynamic interfacial properties. In this method, a droplet of a dispersed phase is formed at the tip of a needle and placed in contact with the continuous phase. The shape of the droplet is recorded over time, and interfacial tension is calculated based on the droplet deformation. This technique is particularly valuable in optimizing self-emulsifying drug delivery systems (SEDDS) and assessing the stability of pharmaceutical emulsions during storage and administration (38, 39). Axisymmetric drop shape analysis - profile (ADSA-P) is an extension of the drop shape analysis method that provides high-precision measurements of surface tension and interfacial viscoelasticity. By analyzing the profile of a pendant drop or sessile drop, ADSA-P allows for the investigation of time-dependent interfacial properties, including relaxation times and surface dilatational moduli (40, 41).

The Langmuir-Blodgett method or Langmuir trough (Figure 4F) is one of the most widely used techniques for dilatational rheology measurements, mainly for studying interfacial film properties. The Langmuir trough is a versatile apparatus fitted with a contact probe (Wilhelmy plate) and two symmetric barriers that allow the precise control of the surface area. A thin film of liquid is spread on a solid surface, and the surface is then subjected to a variety of deformations. The vertical transference of a film from the air-liquid interface to a solid substrate is assessed following the Langmuir-Blodgett method. By compressing or expanding the interface at a constant rate, surface pressure-area isotherms are obtained, which reveal valuable information about the surface elasticity and interactions between molecules at the interface. The Langmuir trough method has applications in studying surfactant monolayers, biomembranes, and interfacial interactions in colloidal systems. Langmuir trough experiments may also aid in the design of lipid-based drug delivery systems, where the mechanical properties of interfacial films are crucial for drug encapsulation and controlled release (42, 43).

There are some other emerging measurement techniques for interfacial rheology in pharmaceutical systems. Brewster angle microscopy (BAM) is a powerful imaging technique employed in pharmaceutical science to visualize monolayers and drug-lipid interactions at fluid interfaces. BAM exploits the changes in polarized light reflection to reveal structural information about the interfacial films formed by lipids and surfactants. This technique offers real-time visualization of surface processes and is particularly valuable for studying drug-lipid interactions and membrane-related phenomena, contributing to the development of liposomal and vesicular drug delivery systems (44, 45). Furthermore, microfluidics and droplet-based systems offer versatile platforms for studying interfacial properties at small length scales. These systems enable researchers to manipulate fluid interfaces and perform high-throughput experiments. In pharmaceutical

research, microfluidics is used to study the behavior of drug carriers at biological interfaces, providing insights into targeted drug delivery (46, 47). Recent advancements in surface rheology have led to the development of novel measurement techniques, such as optical surface stress sensors and micro-interferometry (48, 49). These emerging techniques offer higher sensitivity and improved spatial resolution, paving the way for deeper insights into interfacial mechanics and enabling new applications in materials science, biotechnology, and nanotechnology.

Applications of interfacial rheology

Interfacial rheology is a relatively new field of research, but it has gained increasing importance in recent years due to its potential applications in a wide range of industries, including pharmaceuticals and food. Interfacial rheology is also used in a number of other fields, such as cosmetics, paints, and textiles. It is a powerful tool for studying the rheological properties of interfaces, and for developing new materials with specific rheological properties. As the field of interfacial rheology continues to develop, it is likely to find even more applications in a wide range of industries.

Interfacial rheology in the development and optimization of conventional formulations

Interfacial rheology techniques play a critical role in the formulation optimization of pharmaceutical products, cosmetics, and various industrial formulations. By investigating the mechanical behavior of fluid interfaces, surface rheology provides valuable insights into the stability, performance, and processing of formulations. Besides, interfacial rheology can be used to characterize the surface properties of new surfactants and polymers, and to study their interactions with other molecules (28, 50).

As previously explained, interfacial rheology can be used to study the stability of emulsions and foams, and to optimize their formulation. Emulsions and foams are ubiquitous in numerous products, from food and beverages to pharmaceuticals and personal care items. Surface rheology plays a pivotal role in understanding and optimizing the stability of these dispersed systems. By tailoring the interfacial properties, such as surface tension and viscoelasticity, through surface pressure control and surfactant engineering, interfacial rheology allows for the design of stable emulsions and foams with desirable texture, shelf-life, and sensory attributes (51, 52).

Interfacial rheology is also widely used in the development of cosmetics and personal care formulations. From creams and lotions to shampoos and conditioners, the interfacial properties significantly influence the sensory attributes and application characteristics of these products. Interfacial rheology measurements help in designing formulations with desired spreadability, texture, and skin feel (53).

Additionally, interfacial rheology is integral in understanding the mechanics of thin liquid films, such as those found in coatings and coating processes (54, 55). In coating and printing applications, controlling the properties of thin liquid films is crucial for achieving uniform and precise deposition. Interfacial rheology provides valuable insights

into the dynamics of liquid film formation and flow behavior on solid surfaces. By investigating the mechanical properties of paint films and coatings at the air-substrate interface, formulations for better adhesion, leveling, and film formation can be optimized (56-58).

Interfacial rheology in the development and optimization of drug delivery systems

Interfacial rheology plays a central role in the field of drug delivery systems, where understanding the behavior of fluid interfaces is essential for designing efficient drug carriers and optimizing drug release profiles. By characterizing drug-lipid interactions and the mechanical properties of drug carriers at fluid interfaces, interfacial rheology provides valuable insights into the design and performance of drug delivery systems. Besides, by investigating dynamic interfacial tension, viscoelasticity, and phase transitions at fluid interfaces, drug carriers with enhanced drug encapsulation, targeted delivery, and controlled release can be designed (59, 60).

For example, biodegradable lignin-based nanoparticles were developed as drug delivery systems, but lignin derivatives were also shown to stabilize oil-in-water emulsions. The dilational complex moduli E* of the lignin- and protein-based emulsion systems were determined by varying deformation between 5 and 10 %, at constant frequency of 0.1 Hz, and lignins were shown to form a denser and more elastic interfacial layer than whey protein isolate. The highest complex dilational modulus of the lignin systems was suggested to be a consequence of strong hydrophobic interactions among the emulsifier molecules (61).

Nanoparticles, such as polymeric nanoparticles and lipid nanoparticles, have gained significant attention in drug delivery due to their ability to target specific tissues and cells. Interfacial rheology plays a critical role in characterizing the viscoelastic behavior of nanoparticle interfaces, and the interfacial viscoelasticity is the main driver in design of nanoparticles with controlled drug release profiles and improved cellular uptake (62). Interfacial rheology also helps in characterizing the interactions between lipids and drug molecules, which aids in formulating liposomal drug delivery systems with improved stability, prolonged circulation time, and enhanced drug bioavailability (63). Microemulsions and self-emulsifying systems are versatile drug delivery platforms for both oral and topical administration. By optimizing the surfactant composition and interfacial viscoelasticity, researchers can design microemulsions with enhanced drug solubilization and bioavailability (64).

Interfacial rheology may contribute to the development of drug carriers with targeted and controlled drug delivery. Targeted drug delivery aims to deliver drugs specifically to disease sites, reducing systemic side effects and improving treatment outcomes. By understanding the mechanical behavior of lipid-based carriers at biological interfaces, drug delivery systems with improved cell penetration and targeted drug delivery can be designed (65). Controlled drug delivery systems are designed to release drugs in a sustained and controlled manner, enhancing therapeutic efficacy and

minimizing side effects. Interfacial rheology measurements provide valuable information about the mechanical behavior of drug-loaded carriers at fluid interfaces, influencing the design of systems with tunable release rates. By optimizing interfacial properties, researchers can develop drug delivery systems with controlled and predictable drug release profiles (66, 67). Interfacial rheology is also used to study the mechanical behavior of stimuli-responsive interfaces, guiding the design of smart drug carriers with controlled drug release mechanisms. By understanding the interfacial viscoelasticity under different stimuli, such as pH, temperature, or enzymes, researchers can tailor drug release profiles for targeted therapies (68, 69).

Interfacial rheology in the development of new and advanced materials

Interfacial rheology can be used to develop new materials with specific rheological properties, such as new surfactants and polymers in surfactant-based formulations. Interfacial rheology plays a pivotal role in the development of advanced materials, offering valuable insights into the mechanical behavior of fluid interfaces and influencing the properties and functionalities of complex materials. Some of those advanced materials include self-assembled monolayers (SAMs), thin films, nanostructured materials and biomaterials. SAMs are organized layers of molecules spontaneously formed at fluid interfaces. Interfacial rheology is a powerful tool for characterizing SAMs and understanding their mechanical properties, such as surface elasticity and viscoelasticity. Interfacial rheology has applications in developing SAMs for surface modification, lubrication, and as model systems to study biological interfaces (70, 71). Interfacial rheology plays a crucial role in studying nanostructured materials, including nanocomposites and nanoscale emulsions, as well as in the development of biomaterials, where understanding the mechanical behavior of biointerfaces is crucial. By investigating the interactions between biomolecules and fluid interfaces, interfacial rheology guides the design of functional biomaterials for tissue engineering, regenerative medicine, and drug delivery applications (72, 73).

Interfacial rheology in biointerface characterization

Biological membranes play a vital role in cellular functions and interactions. Interfacial rheology has emerged as a powerful tool for investigating membrane mechanics and biophysical processes at the cell membrane interface. By probing the mechanical properties of lipid bilayers and exploring interactions with biomolecules, interfacial rheology contributes to a deeper understanding of cell adhesion, signaling, and drug delivery (74).

Interfacial rheology techniques offer valuable insights into the mechanical behavior of drug carriers and nanoparticles at the cell membrane interface. By investigating the viscoelastic properties of drug-loaded carriers at the cell surface, researchers can understand how carriers interact with cell membranes, which further guides the design of drug delivery systems with optimized cell penetration and enhanced drug uptake, ensuring efficient drug delivery to target cells (75, 76).

In oral and mucosal drug delivery, the mucoadhesive properties of drug formulations significantly impact drug retention and absorption. Interfacial rheology provides critical information about the adhesive interactions between drug carriers and mucus layers. By characterizing the interfacial viscoelasticity and surface tension, drug delivery systems with improved mucoadhesion, prolonging drug residence time and enhancing drug absorption can be tailored (77, 78).

Interfacial rheology enables the investigation of biomolecular interactions at fluid interfaces, such as protein-lipid interactions. By understanding the mechanical behavior of biological interfaces, researchers can design drug carriers with reduced immunogenicity and improved biocompatibility (79, 80). Eventually, in biomaterial engineering, understanding the mechanical behavior of biological interfaces is vital for designing functional and biocompatible materials (81).

Future perspectives and emerging trends in interfacial rheology in pharmaceutical science

Interfacial rheology in pharmaceutical science continues to evolve, driven by advancements in experimental techniques, computational modeling, and interdisciplinary collaborations. The field holds immense potential for designing innovative drug delivery systems, understanding drug-membrane interactions, and optimizing formulation performance. Some of the future perspectives and emerging trends in interfacial rheology research in the pharmaceutical field involve advanced characterization techniques, the integration of computational modeling, bioinspired interfacial engineering, and the development of sustainable formulations and personalized drug delivery systems.

Emerging advanced characterization techniques, such as neutron reflectometry and atomic force microscopy, offer non-invasive ways to probe interfacial structures and mechanical properties. These techniques provide complementary information to traditional interfacial rheology methods, facilitating a more comprehensive understanding of drug carriers' behavior at fluid interfaces (82).

The integration of computational modeling with interfacial rheology experiments enhances the ability to predict drug-membrane interactions and optimize drug delivery systems. Molecular dynamics simulations and coarse-grained models are becoming increasingly valuable in understanding the interactions between drug carriers and cell membranes, providing insights into membrane penetration and drug release mechanisms (83).

Bioinspired approaches draw inspiration from nature to design functional materials and interfaces. Future perspectives in interfacial rheology involve exploring biomimetic surfactants and lipids that mimic the behavior of biological molecules at fluid interfaces. Such bioinspired interfacial engineering could lead to the development of more biocompatible and targeted drug delivery carriers (84, 85).

With a growing emphasis on sustainability, future trends in interfacial rheology research include the development of green and sustainable drug delivery formulations.

Researchers are exploring environmentally friendly surfactants and stabilizers that reduce the environmental impact without compromising performance. Interfacial rheology plays a crucial role in understanding the behavior of sustainable interfaces and optimizing green formulations (86, 87).

Eventually, the future of drug delivery lies in personalized medicine, where therapies are tailored to individual patient needs. Interfacial rheology can contribute to this paradigm shift by enabling the design of drug carriers specific to patient characteristics and diseases (88, 89).

Conclusion

Interfacial rheology is a rapidly growing field of research with diverse applications across scientific and industrial fields. Interfacial rheology plays a pivotal role in the development and optimization of pharmaceutical formulations. By characterizing the mechanical properties of fluid interfaces in nanoparticle systems, researchers can design innovative drug delivery carriers with improved stability, enhanced drug release profiles, and targeted delivery capabilities. Furthermore, interfacial rheology research in pharmaceutical science is continuously evolving to address current challenges and cater to emerging needs. By embracing advanced characterization techniques, computational modeling, and sustainable approaches, researchers can unlock the full potential of interfacial rheology in optimizing drug delivery systems. In addition to the applications mentioned above, interfacial rheology is also used in a number of other fields, such as cosmetics, paints, and textiles. As the field of interfacial rheology continues to develop, it is likely to find even more applications in a wide range of industries.

References

1. Beladjine M, Albert C, Sintès M, Mekhloufi G, Gueutin C, Nicolas V, et al. Pickering emulsions stabilized with biodegradable nanoparticles for the co-encapsulation of two active pharmaceutical ingredients. Int J Pharm. 2023;637:122870.
2. Arzhavitina A, Steckel H. Foams for pharmaceutical and cosmetic application. Int J Pharm. 2010;394(1-2):1-7.
3. Farkas D, Kállai-Szabó N, Antal I. Foams as carrier systems for pharmaceuticals and cosmetics. Acta Pharm Hung. 2019;89:5-15.
4. Hoc D, Haznar-Garbacz D. Foams as unique drug delivery systems. Eur J Pharm Biopharm. 2021;167:73-82.
5. McClements DJ. Food Emulsions: Principles, Practices, and Technique. 3rd ed. Boca Raton: CRC Press; 2015.
6. Parsa M, Trybala A, Malik DJ, Starov V. Foam in pharmaceutical and medical applications. Curr Opin Colloid Interface Sci. 2019;44:153-167.

7. Simonsen G, Kjølaas J, Leinan PR, Schümann H. Literature review on surface-active components in emulsions and foams: Theory and modelling efforts. Geoenergy Sci Eng. 2023;230:21215
8. Cai Z, Wei Y, Shi A, Zhong J, Rao P, Wang Q, Zhang H. Correlation between interfacial layer properties and physical stability of food emulsions: Current trends, challenges, strategies, and further perspectives. Adv Colloid Interface Sci. 2023;313:102863.
9. Đaković Lj. Koloidna hemija. 4th ed. Beograd: Zavod za udžbenike i nastavna sredstva; 2006.
10. Dokić P. Emulzije, pene, aerosoli. Novi Sad: WUS Austria; 2005.
11. Tadros TF. Applied surfactants. Principles and applications. Weinheim: Wiley – VCH; 2005.
12. Rosen MJ. Surfactants and interfacial phenomena. Hoboken (NJ): John Wiley & Sons; 2004.
13. Zhao Y, Brown MB, Jones SA. Pharmaceutical foams: are they the answer to the dilemma of topical nanoparticles? Nanomedicine: Nanotech Biol Med. 2010;6(2):227-36.
14. Tadros T. Encyclopedia of Colloid and Interface Science. Heidelberg: Springer Berlin; 2013.
15. Friberg SE. A few common sense observations on emulsion stability. In: Proceedings of 2nd World Congress on Emulsions. Bordeaux, France; 1997; p. 43-64.
16. Walstra P, Smulders P. Formation of emulsions. In: Proceedings of 2nd World Congress on Emulsion. Bordeaux, France; 1997; p. 67-74.
17. Santini E, Ravera F, Ferrari M, Stubenrauch C, Makievski A, Krägel J. A surface rheological study of non-ionic surfactants at the water–air interface and the stability of the corresponding thin foam films. Colloids Surf A: Physicochem Eng Asp. 2007;298(1-2):12-21.
18. Langevin D, Monroy F. Interfacial rheology of polyelectrolytes and polymer monolayers at the air–water interface. Curr Opin Colloid Interface Sci. 2010;15(4):283-93.
19. El Omari Y, Yousfi M, Duchet-Rumeau J, Maazouz A. Recent Advances in the Interfacial Shear and Dilational Rheology of Polymer Systems: From Fundamentals to Applications. Polymers. 2022;14(14):2844.
20. Wilson DI. What is rheology? Eye. 2018;32(2):179-83.
21. Pelipenko J, Kristl J, Rošic R, Baumgartner S, Kocbek P. Interfacial rheology: an overview of measuring techniques and its role in dispersions and electrospinning. Acta Pharm. 2012;62(2):123-40.
22. Martin JD, Marhefka JN, Migler KB, Hudson SD. Interfacial rheology through microfluidics. Adv Mater. 2011;23:426-432.
23. Maldonado-Valderrama J, Patino JM. Interfacial rheology of protein–surfactant mixtures. Curr Opin Colloid Interface Sci. 2010;15(4):271-82.
24. Gul O, Gul LB, Baskıncı T, Parlak ME, Saricaoglu FT. Influence of pH and ionic strength on the bulk and interfacial rheology and technofunctional properties of hazelnut meal protein isolate. Food Res Int. 2023;169:112906.
25. Madadlou A, Famelart MH, Pezennec S, Rousseau F, Floury J, Dupont D. Interfacial and (emulsion) gel rheology of hydrophobised whey proteins. Int Dairy J. 2020;100:104556.
26. Cao C, Zhang L, Zhang XX, Du FP. Effect of gum arabic on the surface tension and surface dilational rheology of trisiloxane surfactant. Food Hydrocoll. 2013;30(1):456-62.
27. Qiao X, Miller R, Schneck E, Sun K. Foaming properties and the dynamics of adsorption and surface rheology of silk fibroin at the air/water interface. Colloids Surf A: Physicochem Eng Asp. 2020;591:124553.

28. Murray BS. Interfacial rheology of food emulsifiers and proteins. Curr Opin Colloid Interface Sci. 2002;7(5-6):426-31.
29. Golemanov K, Tcholakova S, Denkov N, Pelan E, Stoyanov SD. Surface shear rheology of saponin adsorption layers. Langmuir. 2012;28(33):12071-84.
30. Miller R, Ferri JK, Javadi A, Krägel J, Mucic N, Wüstneck R. Rheology of interfacial layers. Colloid Polym Sci. 2010;288:937-50.
31. El Omari Y, Yousfi M, Duchet-Rumeau J, Maazouz A. Interfacial rheology testing of molten polymer systems: Effect of molecular weight and temperature on the interfacial properties. Polym Test. 2021;101:107280.
32. Renggli D, Alicke A, Ewoldt RH, Vermant J. Operating windows for oscillatory interfacial shear rheology. J Rheol. 2020;64(1):141-60.
33. Dan A, Gochev G, Krägel J, Aksenenko EV, Fainerman VB, Miller R. Interfacial rheology of mixed layers of food proteins and surfactants. Curr Opin Colloid Interface Sci. 2013;18(4):302-10.
34. Carrera C, Felix M, López-Castejón ML, Pizones VM. Understanding Interfacial Rheology in Food Emulsions. In: Lai WF, editor. Materials Science and Engineering in Food Product Development. Hoboken: John Wiley & Sons; 2023; pp. 57-72.
35. Ravera F, Loglio G, Kovalchuk VI. Interfacial dilational rheology by oscillating bubble/drop methods. Curr Opin Colloid Interface Sci. 2010;15(4):217-28.
36. Zamora JM, Marquez R, Forgiarini AM, Langevin D, Salager JL. Interfacial rheology of low interfacial tension systems using a new oscillating spinning drop method. J Colloid Interface Sci. 2018;519:27-37.
37. Fainerman VB, Kovalchuk VI, Aksenenko EV, Miller R. Dilational viscoelasticity of adsorption layers measured by drop and bubble profile analysis: reason for different results. Langmuir. 2016;32(22):5500-9.
38. Drelich J, Fang C, White CL. Measurement of interfacial tension in fluid-fluid systems. Encycl Surf Colloid Sci. 2002;3:3158-63.
39. Alexandrov NA, Marinova KG, Gurkov TD, Danov KD, Kralchevsky PA, Stoyanov SD, et al. Interfacial layers from the protein HFBII hydrophobin: Dynamic surface tension, dilatational elasticity and relaxation times. J Colloid Interface Sci. 2012;376(1):296-306.
40. Saad SM, Neumann AW. Axisymmetric drop shape analysis (ADSA): an outline. Adv Colloid Interface Sci. 2016;238:62-87.
41. Bagalkot N, Hamouda AA, Isdahl OM. Dynamic interfacial tension measurement method using axisymmetric drop shape analysis. MethodsX. 2018;5:676-83.
42. Kale SK, Cope AJ, Goggin DM, Samaniuk JR. A miniaturized radial Langmuir trough for simultaneous dilatational deformation and interfacial microscopy. J Colloid Interface Sci. 2021;582:1085-98.
43. Ciutara CO, Barman S, Iasella S, Huang B, Zasadzinski JA. Dilatational and shear rheology of soluble and insoluble monolayers with a Langmuir trough. J Colloid Interface Sci. 2023;629:125-35.
44. Daear W, Mahadeo M, Prenner EJ. Applications of Brewster angle microscopy from biological materials to biological systems. Biochim Biophys Acta Biomembr. 2017;1859(10):1749-66.
45. Vollhardt D. Brewster angle microscopy: A preferential method for mesoscopic characterization of monolayers at the air/water interface. Curr Opin Colloid Interface Sci. 2014;19(3):183-97.

46. Martin JD, Marhefka JN, Migler KB, Hudson SD. Interfacial rheology through microfluidics. Adv Mater. 2011;23(3):426-32.
47. Tregouët C, Salez T, Monteux C, Reyssat M. Microfluidic probing of the complex interfacial rheology of multilayer capsules. Soft Matter. 2019;15(13):2782-90.
48. Yasuda T, Shimokasa K. Improved system for measuring rheological properties of thickened liquid using an inclined parallel plate and optical sensor. J Texture Stud. 2023;54(4):510-20.
49. Malara P, Zullo R, Filippone G, Verdolotti L, Lavorgna M, Giorgini A, et al. Rheology of complex fluids with vibrating fiber-optic sensors. Sens Actuator A Phys. 2017;264:219-23.
50. Karbaschi M, Lotfi M, Krägel J, Javadi A, Bastani D, Miller R. Rheology of interfacial layers. Curr Opin Colloid Interface Sci. 2014;19:514-9.
51. Kokini J, van Aken G. Discussion session on food emulsions and foams. Food Hydrocoll. 2006;20(4):438-45.
52. Tóth M, Kaszab T, Meretei A. Texture profile analysis and sensory evaluation of commercially available gluten-free bread samples. Eur Food Res Technol. 2022;248(6):1447-55.
53. Gillece T, Mcmullen RL, Fares H, Senak L, Ozkan S, Foltis L. Probing the textures of composite skin care formulations using large amplitude oscillatory shear. J Cosmet Sci. 2016;67(2):121-59.
54. Luengo GS, Fameau AL, Leonforte F, Greaves AJ. Surface science of cosmetic substrates, cleansing actives and formulations. Adv Colloid Interface Sci. 2021;290:102383.
55. Masschaele K, Vandebril S, Vermant J, Madivala B. Interfacial rheology. Rheology-Volume I. 2010.
56. Jaensson N, Vermant J. Tensiometry and rheology of complex interfaces. Curr Opin Colloid Interface Sci. 2018;37:136-50.
57. Gilleo KB. Rheology and surface chemistry. In: Tracton AA, editor. Coatings Technology Handbook, 3rd edition. Boca Raton (FL): CRC Press; 2006; p. 13-7.
58. Freer EM, Svitova T, Radke CJ. The role of interfacial rheology in reservoir mixed wettability. J Pet Sci Eng. 2003;39(1-2):137-58.
59. Li H, Van der Meeren P. Sequential adsorption of whey proteins and low methoxy pectin at the oil-water interface: An interfacial rheology study. Food Hydrocoll. 2022;128:107570.
60. Beltramo PJ, Gupta M, Alicke A, Liascukiene I, Gunes DZ, Baroud CN, Vermant J. Arresting dissolution by interfacial rheology design. Proc Natl Acad Sci. 2017;114(39):10373-8.
61. Czaikoski A, Gomes A, Kaufmann KC, Liszbinski RB, de Jesus MB, da Cunha RL. Lignin derivatives stabilizing oil-in-water emulsions: Technological aspects, interfacial rheology and cytotoxicity. Ind Crops Prod. 2020;154:112762.
62. Xie K, De Loubens C, Dubreuil F, Gunes DZ, Jaeger M, Léonetti M. Interfacial rheological properties of self-assembling biopolymer microcapsules. Soft Matter. 2017;13(36):6208-17.
63. Paul S, Nahire R, Mallik S, Sarkar K. Encapsulated microbubbles and echogenic liposomes for contrast ultrasound imaging and targeted drug delivery. Comput Mech. 2014;53:413-35.
64. Shahzadi I, Dizdarević A, Efiana NA, Matuszczak B, Bernkop-Schnürch A. Trypsin decorated self-emulsifying drug delivery systems (SEDDS): Key to enhanced mucus permeation. J Colloid Interface Sci. 2018;531:253-60.
65. Bertsch P, Bergfreund J, Windhab EJ, Fischer P. Physiological fluid interfaces: Functional microenvironments, drug delivery targets, and first line of defense. Acta Biomater. 2021;130:32-53.

66. Petrova VA, Elokhovskiy VY, Raik SV, Poshina DN, Romanov DP, Skorik YA. Alginate gel reinforcement with chitin nanowhiskers modulates rheological properties and drug release profile. Biomolecules. 2019;9(7):291.
67. Marapureddy SG, Thareja P. Structure and rheology of hydrogels: applications in drug delivery. In: Chandra P, Pandey LM, editors. Biointerface Engineering: Prospects in Medical Diagnostics and Drug Delivery. Springer Nature eBook; 2020; pp. 75-99.
68. Dieng SM, Anton N, Bouriat P, Thioune O, Sy PM, Massaddeq N, et al. Pickering nano-emulsions stabilized by solid lipid nanoparticles as a temperature sensitive drug delivery system. Soft Matter. 2019;15(40):8164-74.
69. Pasquino R, Di Domenico M, Izzo F, Gaudino D, Vanzanella V, Grizzuti N, de Gennaro B. Rheology-sensitive response of zeolite-supported anti-inflammatory drug systems. Colloids Surf B. 2016;146:938-44.
70. Yoshimoto M, Honda K, Kurosawa S, Tanaka M. Rheology of self-assembled monolayers on solid-liquid interface oscillating at MHz frequency. Chin J Phys. 2017;55(1):16-21.
71. Knobler CM, Schwartz DK. Langmuir and self-assembled monolayers. Curr Opin Colloid Interface Sci. 1999;4(1):46-51.
72. Mohammadinejad R, Kumar A, Ranjbar-Mohammadi M, Ashrafizadeh M, Han SS, Khang G, Roveimiab Z. Recent advances in natural gum-based biomaterials for tissue engineering and regenerative medicine: A review. Polymers. 2020;12(1):176.
73. Gudapati H, Parisi D, Colby RH, Ozbolat IT. Rheological investigation of collagen, fibrinogen, and thrombin solutions for drop-on-demand 3D bioprinting. Soft Matter. 2020;16(46):10506-17.
74. Skrzypiec M, Prochaska K. Detailed characterization of POSS-poly (ethylene glycol) interaction with model phospholipid membrane at the air/water interface. Colloids Surf B. 2018;171:167-75.
75. de Andrade Escobar B, Valerio GL, Caseli L. Biological activity of pectic polysaccharides investigated through biomembrane models formed at the air-water interface. Colloids Surf B. 2022;216:112530.
76. Zhang X, Kirby SM, Chen Y, Anna SL, Walker LM, Hung FR, Russo PS. Formation and elasticity of membranes of the class II hydrophobin Cerato-ulmin at oil-water interfaces. Colloids Surf B. 2018;164:98-106.
77. Çelebioğlu HY, Kmiecik-Palczewska J, Lee S, Chronakis IS. Interfacial shear rheology of β-lactoglobulin—Bovine submaxillary mucin layers adsorbed at air/water interface. Int J Biol Macromol. 2017;102:857-67.
78. Bayer IS. Recent advances in mucoadhesive interface materials, mucoadhesion characterization, and technologies. Adv Mater Interfaces. 2022;9(18):2200211.
79. Goldberg M, Langer R, Jia X. Nanostructured materials for applications in drug delivery and tissue engineering. J Biomater Sci Polym Ed. 2007;18(3):241-68.
80. Li J, Krause ME, Chen X, Cheng Y, Dai W, Hill JJ, et al. Interfacial stress in the development of biologics: fundamental understanding, current practice, and future perspective. AAPS J. 2019;21:1-7.
81. Schöne AC, Roch T, Schulz B, Lendlein A. Evaluating polymeric biomaterial–environment interfaces by Langmuir monolayer techniques. J R Soc Interface. 2017;14(130):20161028.

82. Collada A, Maestro A, Mertens J, Batllori-Badia E, Galindo A, Perez-Gil J, Cruz A. Pulmonary surfactant structure as solved by neutron reflectometry and atomic force microscopy. Biophys J. 2023;122(3):86a.
83. Jaensson NO, Anderson PD, Vermant J. Computational interfacial rheology. J Non-Newton Fluid Mech. 2021;290:104507.
84. Kondej D, Sosnowski TR. Interfacial rheology for the assessment of potential health effects of inhaled carbon nanomaterials at variable breathing conditions. Sci Rep. 2020;10(1):14044.
85. Li MC, Wu Q, Moon RJ, Hubbe MA, Bortner MJ. Rheological aspects of cellulose nanomaterials: Governing factors and emerging applications. Adv Mater. 2021;33(21):2006052.
86. Trujillo-Cayado LA, Santos J, Ramírez P, Alfaro MC, Muñoz J. Strategy for the development and characterization of environmental friendly emulsions by microfluidization technique. J Clean Prod. 2018;178:723-30.
87. Tatini D, Raudino M, Ambrosi M, Carretti E, Davidovich I, Talmon Y, et al. Physicochemical characterization of green sodium oleate-based formulations. Part 1. Structure and rheology. J Colloid Interface Sci. 2021;590:238-48.
88. Shopova D, Yaneva A, Bakova D, Mihaylova A, Kasnakova P, Hristozova M, et al. (Bio)printing in Personalized Medicine—Opportunities and Potential Benefits. Bioeng. 2023;10(3):287.
89. Garbin V, Crocker JC, Stebe KJ. Nanoparticles at fluid interfaces: Exploiting capping ligands to control adsorption, stability and dynamics. J Colloid Interface Sci. 2012;387(1):1-11.

Principi i primena međufazne reologije u (pre)formulacionom razvoju farmaceutskih preparata

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Kratak sadržaj

Reologija je nauka koja proučava proticanje i deformacije materije, dok je međufazna reologija grana reologije čiji je fokus na proučavanju mehaničkih svojstava granice faza, pre svega tečnost-tečnost i tečnost-gas. Ponašanje granice faza fluida se značajno razlikuje od ponašanja unutrašnjosti materijala, te standardna reološka merenja često ne opisuju adekvatno svojstva na granici faza. Međufazna reologija pruža specijalizovan pristup za proučavanje viskoelastičnosti i međupovršinskog napona na granicama faza, pri čemu se stiče uvid u delovanje sila na granicama faza, kao i u međumolekulske interakcije. Ovo je posebno značajno za dizajniranje naprednih formulacija i terapijskih sistema sa željenim karakteristikama. Međufazna reologija je naučna oblast koja se brzo razvija i pronalazi primenu u različitim naučnim oblastima i industrijama. Međufazna reologija igra ključnu ulogu u razvoju i optimizaciji farmaceutskih formulacija i dizajnu inovativnih nosača za isporuku lekova sa poboljšanom stabilnošću, poboljšanim profilima oslobađanja leka i mogućnostima ciljane isporuke. Ovaj rad ima za cilj da pruži sveobuhvatan pregled međufazne reologije, njenih principa, tehnika merenja i primene u različitim oblastima. Analizirajući skorašnja dostignuća i nove trendove u ovoj oblasti, cilj rada je da se istakne značaj međufazne reologije u optimizaciji formulacija, poboljšanju karakteristika proizvoda i pronalaženju inovativnih rešenja, posebno u farmaceutskoj nauci.

Ključne reči: međufazna reologija, viskoelastičnost, emulzija, pena, preformulacija