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Formulation and Evaluation of tofacitinib citrate emulsion

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Abstracts.

Emulsion have been widely used in different industrial process. The development and production of good quality emusion depend on the knowledge of emulsion preparation , stability mechanism and rheological studies .
The purpose of the article is to provide information about of emulsion stability mechanism.
Tofacitinib (TFB) is a pioneer JAK (Janus Kinase) inhibitor mainly employed to treat rheumatoid arthritis .
It has been proven efficacy for the treatment of rheumatoid arthritis in the oral dosage form . oral TFB exhibited several toxic effect. Current research aim to develop formulation of TFB to achieve effect treatment without any adverse effects .

Keywords :

Emultion , Emultion type , Rheumatoid arthritis , psoriatic arthritis , ulcerative colitis, polyorticular course juvenile idiopathic arthritis

1.1 Introduction

Certainly! Emulsions are fascinating mixtures with a wide range of applications. Here's a more detailed introduction:

Emulsions are colloidal systems consisting of two immiscible liquids, typically one being dispersed as droplets within the other. The two main components of an emulsion are the continuous phase and the dispersed phase. The continuous phase is the external medium in which the droplets of the dispersed phase are suspended. The dispersed phase consists of the droplets themselves, which are usually smaller in size.

Emulsions are classified based on the nature of the continuous and dispersed phases. For instance, oilin- water (O/W) emulsions have water as the continuous phase and oil droplets dispersed within it, while water-in-oil (W/O) emulsions have oil as the continuous phase and water droplets dispersed within it.

The stability of emulsions is crucial for their functionality. Without proper stabilization, the dispersed phase droplets would coalesce, leading to phase separation. To prevent this, emulsifying agents or surfactants are used. These molecules have hydrophilic (water-attracting) and lipophilic (oil-attracting) parts, which help stabilize the interface between the two immiscible liquids.

Emulsions find widespread use across industries. In the food industry, they are employed in products like mayonnaise, salad dressings, and ice cream to create smooth textures and prevent ingredient separation. In cosmetics, emulsions are used in creams, lotions, and makeup to deliver active ingredients and provide desired textures. They are also utilized in pharmaceuticals for drug delivery systems, where they can enhance bioavailability and stability.

Understanding the principles of emulsion formation and stabilization is essential for optimizing their properties and performance in various applications. Researchers continue to explore novel emulsification techniques and formulations to meet evolving industrial and consumer needs.

1.1 Types of emulsion

Emulsions can be categorized based on the nature of the dispersed phase and the continuous phase. The main types include:

1. Oil-in-water (O/W) emulsions: In these emulsions, oil droplets are dispersed within a continuous phase of water. Examples include milk and most pharmaceutical creams.

2. Water-in-oil (W/O) emulsions: Here, water droplets are dispersed within a continuous phase of oil. Examples include butter and certain types of margarine.

3. Multiple emulsions: These are emulsions within emulsions, such as water-in-oil-in-water (W/O/W) or oil-in-water-in-oil (O/W/O) emulsions. They find applications in cosmetics, pharmaceuticals, and food products.

4. Microemulsions: These are thermodynamically stable, transparent or translucent systems of oil, water, and amphiphilic surfactants. They are used in various industrial applications, including pharmaceuticals, cosmetics, and food.

1.2 Classification of emulsion

Emulsions are classified based on the nature of the dispersed and continuous phases. There are four main types:

1. Oil-in-water (O/W) emulsion: Here, oil droplets are dispersed in a continuous phase of water. Examples include milk and most cosmetic creams.

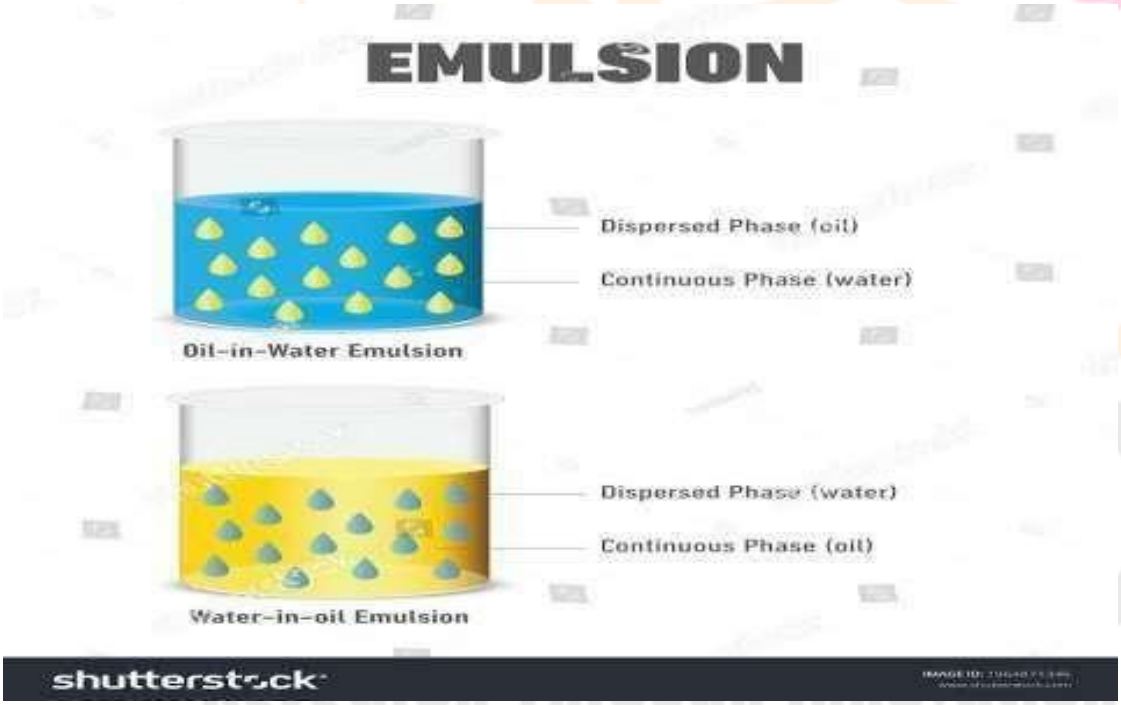


Fig.1 Oil in water emulsion

2. Water-in-oil (W/O) emulsion: In this type, water droplets are dispersed in a continuous phase of oil. Examples include butter and certain types of moisturizing creams.

3. Multiple emulsions: These are emulsions within emulsions. They can be of two types: waterin-oil-in-water (W/O/W) or oil-in-water-in-oil (O/W/O). They find applications in pharmaceuticals and food products.

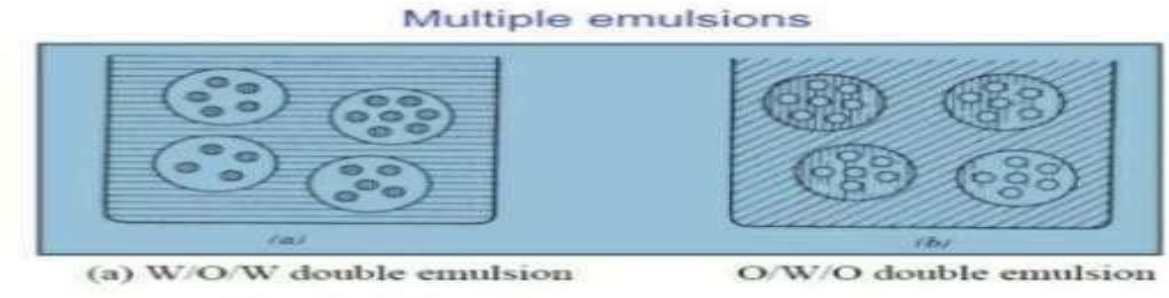


Fig2.Multiple emulsion

4. Microemulsions: These are transparent, thermodynamically stable emulsions of oil and water, usually stabilized by surfactants. They have applications in drug delivery systems and as industrial solvents.

1.3 Formulation of Emulsion:

Emulsion are formulatecd by using following compound:

1. **Surfactant:**surfactant are used as emulsifying agent.
2. **Antioxidant**:used to preventbfrom oxidation.
3. **Preservative**:Prevent the growth of microorganism.ex.methylparaben.

1.4 Mechanism of action emulsion

Emulsions work by stabilizing tiny droplets of one liquid within another liquid that normally wouldn't mix. This is achieved by adding an emulsifying agent, which lowers the surface tension between the two liquids, allowing them to disperse evenly. This can be crucial in various industries, from food to cosmetics to pharmaceuticals, where the even distribution of substances is essential.

1.5 Thearoies of emulsion

Emulsions are mixtures of two or more immiscible liquids, like oil and water, stabilized by an emulsifier. There are several theories explaining how emulsions form and remain stable:

1. **Interfacial Tension Theory**: This theory suggests that emulsions form because an emulsifier lowers the interfacial tension between the immiscible liquids, allowing them to mix.

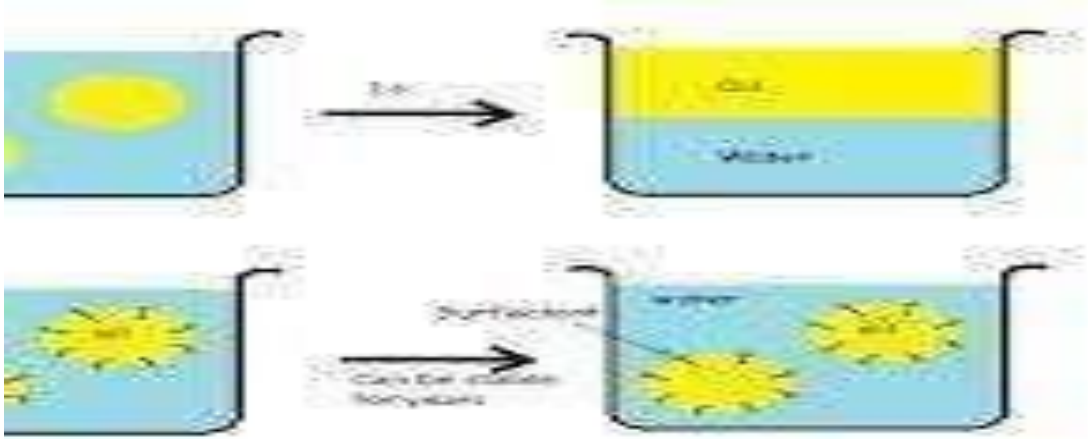
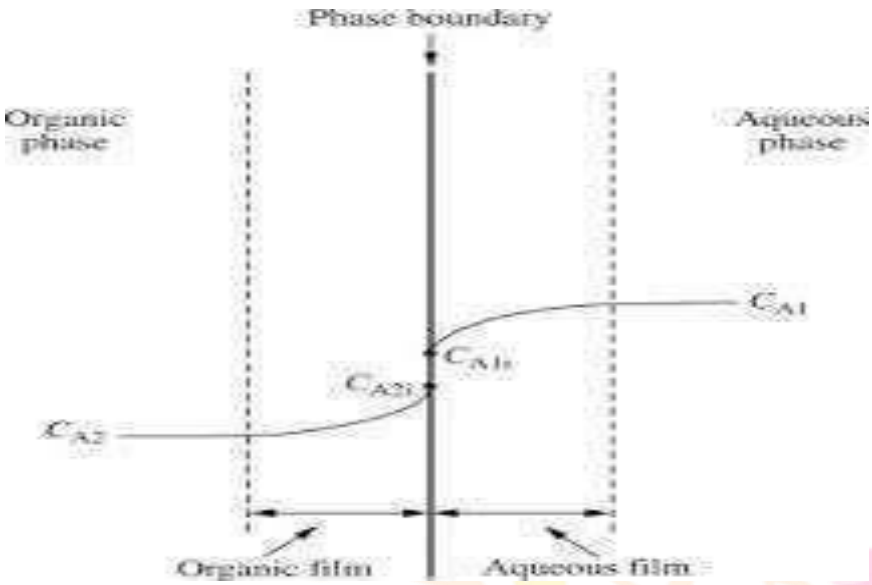


Fig 3.Interfacial tension Diagram

2. **Ostwald's Dilution Theory**: According to this theory, emulsions form because the dispersed phase droplets become more stable as they decrease in size due to continuous dilution.

3. **Film Theory**: Emulsions are thought to form due to the formation of a thin film of emulsifier around the dispersed phase droplets, preventing them from coalescing.



4. **Electrical Double Layer Theory:** This theory explains the stability of emulsions by considering the presence of an electrical double layer around the dispersed phase droplets, which repels them from each other.

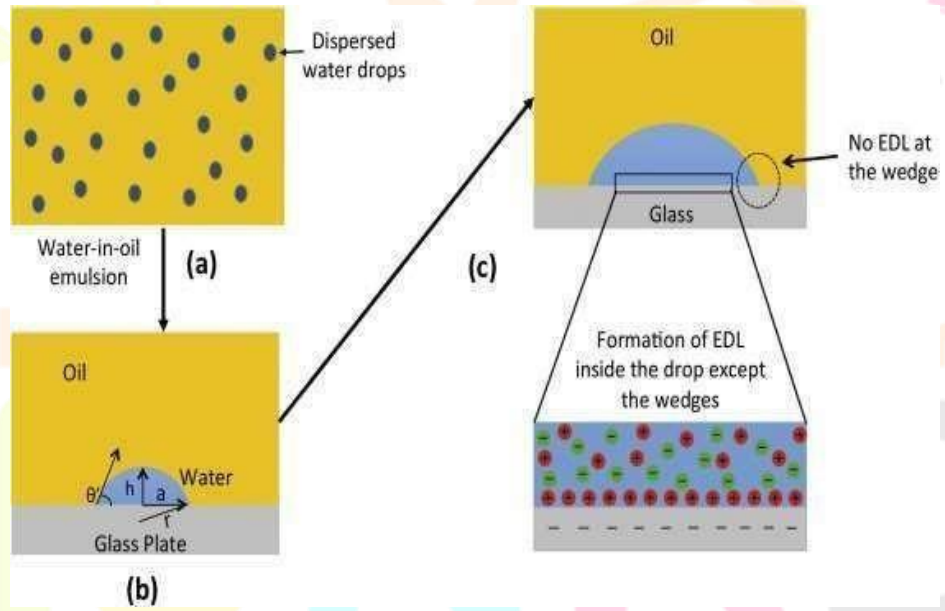


Fig 4.Electrical double Layer Diagram

Prepartion Methods:

1. Dry gum method.

2. Wet gum Method. 3.Homoginizer.

4.Ultra sonifier.

Emulsifying Agent:

1. Acacia

2. Tragacant h 3.Glycerin

4.Sodium Phosphate 5.Sorbitan

1.6 Application of emulsion

Emulsions are widely used in various industries and applications:

1. **Food Industry:** Emulsions are used in food products like mayonnaise, salad dressings, sauces, and ice cream to create smooth textures and prevent separation of ingredients.

2. **Cosmetics and Personal Care:** Emulsions form the base for creams, lotions, and moisturizers, helping to blend water-based and oil-based ingredients for smooth application and hydration.

3. **Pharmaceuticals:** Emulsions are used in drug formulations to improve drug solubility, stability, and bioavailability. They can be found in oral, topical, and injectable medications.

4. **Paints and Coatings:** Emulsions serve as binders in water-based paints and coatings providing adhesion to surfaces and improving durability.

5. **Photography:** Emulsions are used in traditional film photography to capture and develop images on film.

6. **Agriculture**: Emulsions are used in agriculture as pesticide formulations, helping to disperse active ingredients effectively and improve application.

7. **Textile Industry:** Emulsions are used in textile processing for dyeing and finishing fabrics, providing uniform coloration and texture.

8. **Oil and Gas Industry:** Emulsions are used in drilling fluids to carry drilling cuttings to the surface, lubricate the drill bit, and control formation pressures.

These are just a few examples of how emulsions are applied across different industries for various purposes.

1.7 dvantages of emulsion:

- Mask the unpleasant test o/w is convenient means of oral administration of water –insoluble liquid.
- Oil-soluble drugs can be given parentrally in form of oil –in water emulsion (e.g taxol).
- Emulsion can be used for external apllicationin cosmetics and therapeutics. Application because of better and faster absorption.
- Sustained released medication.
- Improve bioavailability.
- Absorption rate increases.
- Nutrition supplement.
- It is economical.
-

1.8 Disadvantages of emulsion:

- Thermodynamic instability.
- increase the risk of inflammatory bowel disease.
- Short shelf life.
- Unstable and liquid phas separate slowly.Improper formulation of emulsion leads to creaming and cracking of emulsion.
- Improper selection of emulsifying agent leads to phase inversion and sometime it may also leads to cracking.
- Being liquid dosage form,these are packed in glass or plastic container.hence,care should be taken in handling and storage.
- A measuring drvice is required for administration.
- Microbial contamination in emulsion may cause cracking.
- If it is not shaken well before used,variation in doseobserve each time.

1.9 Ideal Properties of Emulsion

Ideal characteristics of emulsion in detail

Certainly! Here are the ideal characteristics of an emulsion in detail:

1. **Stability**: The emulsion should maintain its homogeneous state over time, resisting phase separation, coalescence (droplet merging), and creaming (formation of a cream layer on top).

2. **Uniformity**: The droplet size distribution within the emulsion should be consistent, ensuring a smooth texture and appearance.

3. **Particle Size:** Ideally, the droplet size should be small and uniform to enhance stability and minimize sensory perception of oil droplets.

4. **Viscosity**: The emulsion should have appropriate viscosity for its intended use, whether it's a thick cream, a pourable lotion, or a spreadable dressing.

5. **Rheological Properties**: These properties include flow behavior (Newtonian, shear-thinning, etc.) and viscoelasticity, which influence application and product performance.

6. **pH Stability:** The emulsion's pH should be compatible with the intended application and remain stable over time to prevent irritation or degradation of active ingredients.

7. **Texture:** The emulsion should have a pleasing texture, whether it's smooth, creamy, light, or luxurious, depending on the product's purpose and consumer preferences.

8. **Appearance:** It should have an attractive appearance, which may include color, opacity, and absence of visible defects like air bubbles or sedimentation.

9. **Odor and Taste:** If applicable, the emulsion should have a pleasant odor and taste or be odorless and tasteless, depending on the product type.

10. **Compatibility:** The emulsion should be compatible with other ingredients in the formulation to ensure stability and efficacy without causing undesirable interactions.

11. **Microbiological Stability:** The emulsion should be microbiologically stable to prevent microbial growth, contamination, and spoilage during storage and use.

12. **Ease of Application:** It should be easy to dispense, spread, and absorb into the skin or substrate, providing a pleasant user experience.

13. **Longevity:** The emulsion should have a reasonable shelf life, maintaining its quality and performance over time without significant deterioration.

1.10 Identification test for emulsion in detail

Identifying an emulsion involves several steps:

1. **Visual Inspection**: Look for a homogeneous mixture of two or more immiscible liquids, typically one dispersed in the form of small droplets within the other. Emulsions often appear cloudy or milky.

2. **Shake Test:** Agitate the sample vigorously. Emulsions will maintain their homogeneity for some time, while simple mixtures will quickly separate into distinct layers.

3. **Dilution Test**: Add a small amount of water to the sample. If the mixture remains stable, it's likely an emulsion. If it separates into distinct layers, it's not an emulsion.

4. **Microscopic Examination:** Under a microscope, emulsions will reveal small droplets of one liquid dispersed throughout the other. This can help confirm the presence of an emulsion and provide insights into its stability and particle size distribution.

5. **Staining Techniques:** Specialized staining techniques, such as Sudan III for oil droplets or iodine for starch droplets, can help identify specific components within the emulsion.

6. **Physical Properties:** Emulsions often exhibit unique physical properties, such as viscosity, stability, and optical properties, which can be tested using various methods such as viscosity measurements, centrifugation, or optical microscopy.

Adverse effects of emulsion

1. Skin Irritation.
2. Allergic Reactions.
3. Acne and Breakouts.
4. Contact Dermatitis.
5. Eye Irritation.
6. Environmental Impact.Chemical Sensitivity.
7. Inhalation Risks.

Tofacitinib Citrate :

Janus kinases are phosphotransferases, and receptor engagement by cytokines activates their enzymatic function. Janus kinase inhibitors represent a new strategy for the treatment of immune and inflammatory diseases. Tofacitinib is a targeted synthetic small molecule that is an oral inhibitor of Janus kinases (JAKs). It is (JAK) inhibitor FDA-approved in April 2012 and indicated for its use in the management of rheumatoid arthritis (RA), psoriatic arthritis (PA), ulcerative colitis (UC), polyarticular course juvenile idiopathic arthritis (pcJIA).[1] Tofacitinib's action on the nonreceptor tyrosine kinase JAK enzymes is more preferential to the JAK-1 and JAK-3 enzymes.[1]

Tofacitinib's indications in rheumatoid arthritis are for adult patients unresponsive or developed intolerance to one or more disease-modifying rheumatoid drugs (DMARDs) with active moderate to severe disease course.[2] Tofacitinib can be used in sequence with first-line therapy methotrexate (MTX) or conventional DMARDS or can also be used as monotherapy for RA.[2]

Tofacitinib's indication for active psoriatic arthritis received FDA approval following two phase III clinical trials, OPAL Broaden and OPAL Beyond.[3] The trials included subjects with psoriatic arthritis receiving tofacitinib treatment with a 5 mg dosage twice a day in sequence with MTX or other conventional synthetic DMARD therapy. Similar to RA, it is indicated for psoriatic arthritis in adult patients unresponsive or developed interlace to one or more diseasemodifying rheumatoid drugs (DMARDs) with an active moderate to severe psoriatic disease course.Tofacitinib's indication as a treatment for ulcerative colitis (UC) was approved by the FDA following three randomized phase III placebo-controlled clinical trials (OCTAVE Sustain trial, OCTAVE Induction 1, OCTAVE Induction 2), which were conducted following a promising phase 2 trial.[4] The agent is the first medication in the JAK inhibitors class of drugs to be approved in the UC management.[5] Similar to RA and PA, tofacitinib's indication in UC is for adult patients with active moderate or severe disease who have not demonstrated an adequate response to TNF blockers or intolerance to therapy.

Tofacitinib's indication as a treatment for polyarticular course juvenile idiopathic arthritis (pcJIA) is approved for subjects age two and older and available as an oral solution.

2.1 FDA approved use

1) Rheumatoid arthritis 2)Psoriatic arthritis 3)Ulcerative colitis

4) Polyarticular course juvenile idiopathic arthritis.

Administration: -

Tofacitinib is available in tablet form in 5 mg and 10 mg dosages and extended-release (XR) 11 mg dosage for oral consumption for adults. Tofacitinib is also available as a 1 mg/mL oral solution for children 2 years of age or older.

1)Rheumatoid Arthritis

A chronic inflammatory disorder affecting many joints, including those in the hands and feet.

In rheumatoid arthritis, the body's immune system attacks its own tissue, including joints. In severe cases, it attacks internal organs.

The recommended dose of tofacitinib in rheumatoid arthritis treatment is 5 mg twice daily or extended-release (XR) 11 mg once a day.

Subjects with moderate to severe renal impairment or moderate hepatic impairment are recommended 5 mg once daily.

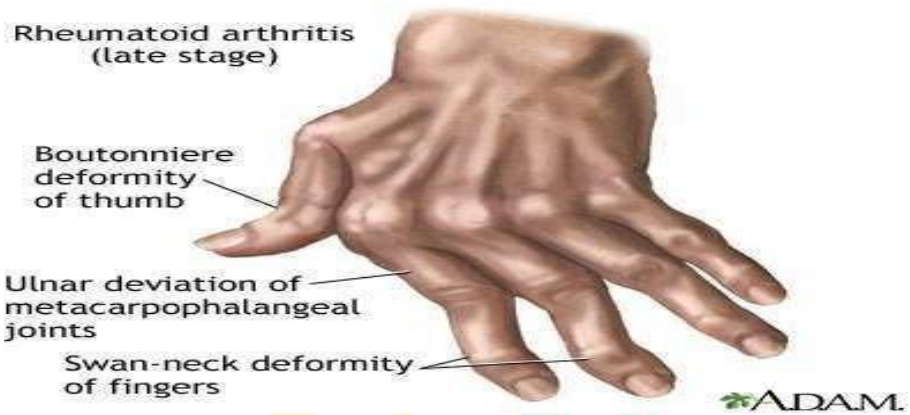


Fig 5 .Rheumatoid Arthritis

Application

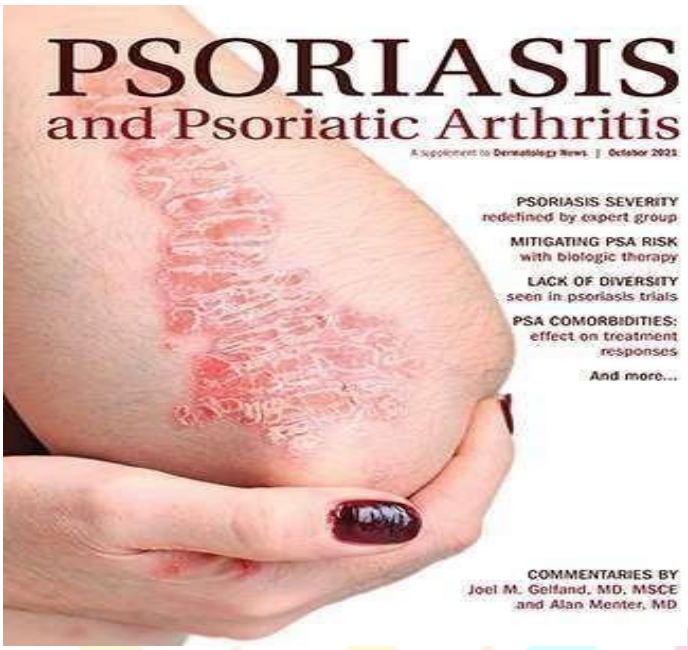
Tofacitinib, an oral Janus kinase (JAK) inhibitor, is a pivotal treatment for rheumatoid arthritis (RA). By selectively targeting JAK enzymes, it disrupts the signaling pathways involved in inflammation, offering relief to patients suffering from joint pain, stiffness, and swelling. Often prescribed when conventional disease-modifying antirheumatic drugs (DMARDs) fail to provide adequate symptom control, tofacitinib provides an alternative for RA patients, potentially delaying disease progression and improving quality of life. Its efficacy and manageable side effect profile make it a valuable addition to the therapeutic armamentarium for rheumatologists combating this chronic autoimmune condition.

2) Psoriatic arthritis

The recommended dose of tofacitinib in the psoriatic arthritis treatment is 5 mg twice daily or extended-release (XR) 11 mg once a day.

Subjects with moderate to severe renal impairment or moderate hepatic impairment are recommended 5 mg once daily.

form of arthritis that affects some people who have the skin condition psoriasis.



Psoriatic arthritis is a type of inflammatory arthritis.

Fig 6. Psoriasis Arthritis Application

Tofacitinib citrate is a medication approved for psoriatic arthritis, an autoimmune condition causing joint pain and skin lesions. By inhibiting certain enzymes involved in the immune response, it helps reduce inflammation and slows joint damage progression. Tofacitinib offers relief from symptoms like joint stiffness and swelling, improving physical function and quality of life for patients. It's often prescribed when other treatments have been ineffective, providing an alternative for those who may not tolerate traditional therapies. Regular monitoring for side effects, such as increased risk of infections, is crucial. Overall, tofacitinib citrate offers a promising option in managing psoriatic arthritis, enhancing patient outcomes.

3. Ulcerative Colitis:

Peripheral arthritis tends to be more common among people who have ulcerative colitis or Crohn's disease of the colon. The level of inflammation in the joints generally mirrors the extent of inflammation in the

colon.

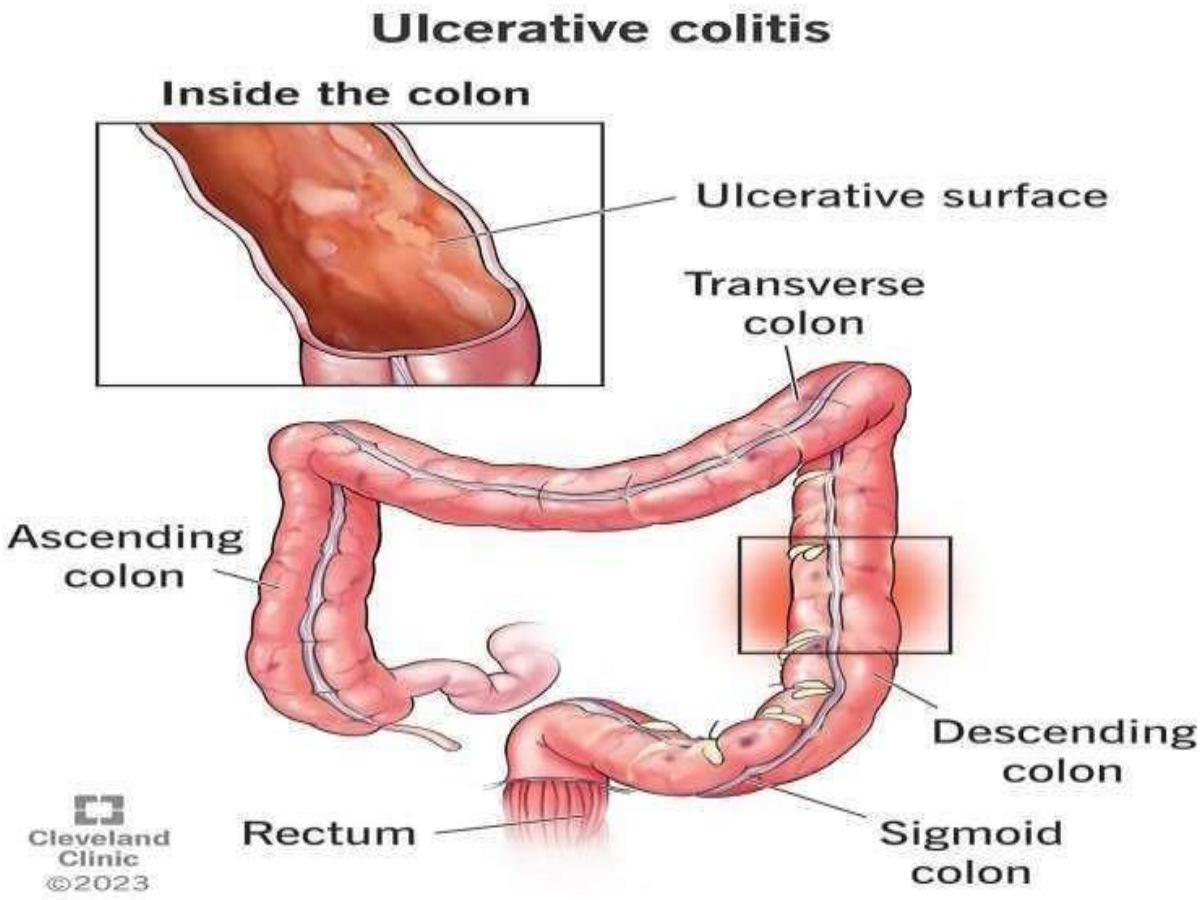


Fig 7. Ulcerative colitis

Recommended dose of tofacitinib in the ulcerative colitis treatment is 10 mg twice daily for a duration of eight weeks initially, then decreased to 5 mg twice a day.

Important to note that tofacitinib 10 mg twice daily is only FDA approved for ulcerative colitis treatment. Tofacitinib treatment should be discontinued if an adequate therapeutic response is not achieved by 16 weeks of therapy at the 10 mg twice a day dosage. Subjects with moderate to severe renal impairment or moderate hepatic impairment are recommended half of the daily dosage of subjects receiving treatment within the normal renal and hepatic function range.

Application

Tofacitinib citrate is used to treat moderate to severe ulcerative colitis (UC) in adults who haven't responded well to other medications. It's a Janus kinase (JAK) inhibitor that helps reduce inflammation in the digestive tract. It's typically prescribed when other treatments like

corticosteroids or immunomodulators haven't been effective or have caused intolerable side effects.

4) Polyarticular course juvenile idiopathic arthritis

The recommended dose of tofacitinib in the polyarticular course juvenile idiopathic arthritis treatment is 5 mg twice daily (oral Solution) or weight-based equivalent twice daily.

Bodyweight greater than or equal to 10 kg and less than 20 kg: 3.2 mg (3.2 mL oral solution) twice daily

Bodyweight greater than or equal to 20 kg and less than 40 kg: 4 mg (4 mL oral solution) twice daily

Bodyweight greater than 40 kg: 5 mg (one 5 mg tablet or 5 mL oral solution) twice daily Subjects with moderate to severe renal impairment or moderate hepatic impairment are

recommended dosing modifications.

Fig.8 Juvenile Idiopathic Arthritis

Application

Tofacitinib citrate is an oral Janus kinase (JAK) inhibitor that has been approved for the treatment of polyarticular course juvenile idiopathic arthritis (pcJIA) in patients aged 2 years and older who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). It works by inhibiting the JAK pathway, which plays a role in inflammation.

2.2 Mechanism of action of Tofacitinib

Tofacitinib exerts its mechanism of action b intracellular cytoplasmic nonreceptor tyrosine kinase JAK enzymes, which are involved in adaptive and innate immune reactions in the process of immune-mediated inflammatory diseases (IMIDs).[6] The Janus kinases are of four tyrosine kinase subtypes(JAK1, JAK2, JAK3, and TYK2).[6] Tofacitinib exhibits its inhibitory effects more selectively to the JAK1 and JAK3 enzymes, further restricting intracellular growth factor and cytokine-mediated signals to be transduced by the JAK-STAT pathway.[6]

The intracellular Janus kinases' natural role is to phosphorylate the signal transducers and activators of transcription (STATs) enzymes which further influence gene expression and impact hematopoiesis and immune cell function.[6] The JAK-STAT signaling pathway plays a major role in the pathogenesis of autoimmune diseases, such as RA. Similar to other JAK inhibitors, tofacitinib blocks the phosphorylation and intracellular activation of signal transducers and activators of transcription, further diminishing their inflammatory effects.

2.3 Adverse effects

1. Gastroenteritis (4%)
2. Nausea (1% to 4%)
3. Headache (4% to 9%)
4. Elevated cholesterol levels (5% to 9%)
5. Increased blood creatine phosphokinase (3% to 7%)
6. Rash (3% to 6%)
7. Hypertension (2% to 9%)
8. Anemia (4%)
9. Herpes zoster (1% to 5)

2.4 Contraindication

1. Severe Infections: Tofacitinib should not be used in patients with active serious infections, including tuberculosis, sepsis, or other opportunistic infections.

2. Chronic or Recurrent Infections: Patients with a history of chronic or recurrent infections should avoid this medication unless benefits outweigh the risks and close monitoring is in place.

3. Severe Hepatic Impairment: It is contraindicated in patients with severe liver impairment due to the potential for increased drug exposure and adverse effects.

3. Literature Review:

1. T. Ichikawa, Electrical demulsification of oil-in-water emulsion, Colloids Surfaces A Physicochem. Eng. Asp. 302 (2007) 581–586. doi:10.1016/j.colsurfa.2007.03.036.

Emulsions have been widely used in different industrial processes. The development and production of good quality emulsions depend on the knowledge of emulsion preparation, stability mechanisms and rheological studies. To form stable emulsions, an emulsifier is required to reduce the droplet sizes of the emulsions and enhance the emulsion stability. The purpose of this review article is to provide information about types of emulsions, stability mechanisms and rheological studies as well as factor affecting the stability of emulsions

2. **R. Pal, Novel shear modulus equations for concentrated emulsions of two immiscible elastic liquids with interfacial tension, 105 (2002) 21–33.**

Starting from the shear modulus equation for a dilute emulsion system of two immiscible liquids with interfacial tension, four new equations have been developed for the shear modulus of concentrated emulsions using a differential scheme. The continuous phase and the dispersed droplets are treated as elastic liquids in the derivation. Out of the four models developed in the paper, two models predict the relative shear modulus (ratio of emulsion modulus to continuous phase modulus) to be a function of three variables: elastocapillary number, modulus ratio (dispersed phase modulus to continuous phase modulus) and volume fraction of dispersed phase. The remaining two models include an additional parameter, i.e. the maximum packing volume fraction of droplets. The proposed models are evaluated using three sets of experimental data on high frequency shear modulus of concentrated polymer-thickened oil-in- water emulsions.

3. **H. Zhu, Z. Guo, Understanding the Separations of Oil / Water Mixtures from Immiscible to Emulsions on Super-wettable Surfaces, J. Bionic Eng. 13 (2016) 1–29. doi:10.1016/S16726529(14)60156-6.**

As the frequent oil spill accidents happens and large quantities of oily wastewater from all kinds of industries are being discharged, the environment has been seriously polluted and our living areas have been horribly threatened. To deal with these issues, attentions have been aroused

on the treatments of the oily wastewater. Recently, numerous superwettable materials have been fabricated. In this

review, we summarize the new development of the materials for the separation of oil/water mixtures, mainly including the immiscible and emulsified mixtures. For the separation of immiscible ones, special materials with fixed wettability are firstly detailed, where three types of materials can be classified based on their wettability, i.e. superhydrophobic and superoleophilic materials, superhydrophilic and underwater superoleophobic materials, and superhydrophilic and superoleophobic materials. Then, the smart materials with switchable wettabilities responsive to external stimulus, for instance, light, solvent, pH, temperature, and electrical potential, are presented. Meanwhile, the single, dual, and multiple stimulus-responsive materials are also described. As for the separation of emulsified oil/water mixtures, the materials for the separation of water-in-oil (W/O), oil-in- water (O/W), and both water-in-oil (W/O) and oil-in-water (O/W) emulsions are sequentially introduced. Finally, some challenges are discussed and the outlook in this filed is proposed.

4. Dhillon S. Tofacitinib: A Review in Rheumatoid Arthritis. Drugs. 2017 Dec;77(18):1987-2001. [PubMed]

Tofacitinib (Xeljanz®) is a potent, selective JAK inhibitor that preferentially inhibits Janus kinase (JAK) 1 and JAK3. In the EU, oral tofacitinib 5 mg twice daily is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant of, one or more DMARDs. Several clinical studies of ≤ 24 months' duration showed that tofacitinib monotherapy (as first- or second-line treatment) and combination therapy with a conventional synthetic DMARD (csDMARD; as second- or third-line treatment) was effective in reducing signs and symptoms of disease and improving health- related quality of life (HR-QOL), with benefits sustained during long-term therapy (≤ 96 months).

Tofacitinib monotherapy inhibited progression of structural damage in methotrexate-naïve patients during ≤ 24 months' treatment, with beneficial effects also seen in patients receiving tofacitinib plus methotrexate as second-line therapy for 12 months. Tofacitinib was generally

well tolerated during ≤ 114 months' treatment, with most adverse events of mild or moderate severity. The tolerability profile of tofacitinib was generally similar to that of biological DMARDs (bDMARDs), with infections and infestations the most common adverse events (AEs) in tofacitinib recipients. However, the incidence of herpes zoster (HZ) was higher with tofacitinib than in the general RA population, although infections were clinically manageable.

Aim and Objective:

Aim:

Formulation and evaluation of Tofacitinib citrate emulsion would likely be to deliver the medication topically, targeting specific areas affected by inflammation ,such as joint pain in arthritis or the gastrointestinal tract. Tofacitinib citrate is typically used to treat rheumatoids arthritis, psoriatic arthritis and ulcerative colitis.

Objective:

1. Identify the mechanism of action of tofacitinib.
2. Describe the potential adverse effects of tofacitinib
3. Review the appropriate monitoring for patients receiving tofacitinib
4. Summarize interprofessional team strategies for improving care coordination and communication to advance tofacitinib use in treating rheumatoid arthritis (RA), psoriatic arthritis (PA), ulcerative colitis (UC), and polyarticular course juvenile idiopathic arthritis (pcJIA) and improve outcome
5. tofacitinib citrate emulsion is to effectively manage the symptoms of autoimmune diseases like RA and improve the patient's quality of life by reducing inflammation, pain, and joint damage. It offers a targeted
6. Tofacitinib citrate emulsion is a medication primarily used to treat moderate to severe rheumatoid

arthritis (RA) in adults who have not responded well to other treatments

7. it should be used under the supervision of a healthcare professional who can monitor its efficacy and safety for each individual patient

8. treatment in ulcerative colitis is to induce and maintain remission, reduce symptoms such as abdominal pain and diarrhea, and improve the quality of life for patients

9. tofacitinib helps to modulate the immune response, thereby reducing inflammation and preventing further damage to the joints.

4. Plan Of Work:

1. Literature Surey.
2. Selection of Drug and polymer.
3. Pre formulation study of drug.

- FTIR
- Drug-Polymer Organoleptic property
- Melting point
- Solubility
- UV spectroscopy
- Copatibility Study

4. Formation of tofacinib citrate emulsion. 5.Evaluation of tofacitinib Citrate Emulsion

- Appearance
- D pH
- II Viscosity
- Intrapment efficiency and loading efficiency
- Drug Content

6.Result and Conclusion

5. Material and Method:

Materials Required:

1. Active Pharmaceutical Ingredient (API): Tofacitinib
2. Oil phase components: e.g., Castor oil
3. Surfactants: e.g., Disodium hydrogen phosphate
4. Co-surfactants: e.g., Propylene glycol, Ethanol
5. Aqueous phase: Purified water
6. Preservatives: e.g., Methylparaben, Propylparaben
7. pH Adjusting agents: e.g Triethanolamine

quipment Required:

1. High-pressure homogenizer or ultrasonicator
2. Magnetic stirrer
3. Beakers
4. pH meter
5. U Shape volumetric mask
6. Special gravity bottle

1. Preparation of Oil Phase

- Measure the required amount of oil.
- Dissolve the tofacitinib citrate in the oil phase if it is oil-soluble. If it is not, it will be incorporated into the aqueous phase.
- Add oil-soluble emulsifiers to the oil phase.
- Heat the oil phase gently to around 40-60°C to ensure all components are dissolved and mixed thoroughly.

2. Preparation of Aqueous Phase

- Measure the required amount of water.
- Dissolve water-soluble emulsifiers and any co-surfactants in the water.
- If tofacitinib citrate is water-soluble, dissolve it in this phase.
- Heat the aqueous phase to the same temperature as the oil phase (40-60°C).

3. Emulsification Process

- Slowly add the oil phase to the aqueous phase while continuously stirring. This can be done using a magnetic stirrer or a mechanical stirrer.
- Once the oil phase is added, switch to a high-shear mixer or homogenizer to create a fine emulsion. The mixing time and speed depend on the equipment and the desired droplet size of the emulsion. Typically, this could be for several minutes to achieve a uniform emulsion.

4. Cooling and Stabilization

- After emulsification, allow the mixture to cool to room temperature while continuing to stir slowly to prevent phase separation.

- Adjust the pH if necessary using suitable acids or bases, ensuring that it is within the acceptable range for tofacitinib citrate's stability and activity.

5. Preservation and Final Adjustment

- Add any preservatives or additional stabilizers as required.

- Perform quality control tests to check for emulsion stability, droplet size distribution, and any other required parameters.

6. Quality control and stability Test

1. **pH Testing:** Ensure the pH remains within the desired range.

2. **Viscosity Measurement:**Use a viscometer to ensure consistency in texture.

3. **Stability Testing**: Subject the emulsion to various conditions (e.g., temperature, light) to ensure it remains stable over time.

7. Evaluation Parameter:

1. **pH Measurement:**Range 6.0- 6.5

2. **Viscosity Testing**: 0.8982cp

3. **Drug Content Analysis**: Assay the content of tofacitinib to ensure uniformity and proper dosing.

Additives:

Sr.no	Ingridients	Property	Quantity
1.	Tofacitinib Citrate	API	0.03gm
2.	Sodium Phosphate	Surfactant	3.5gm
3.	Polyethylene Glycol	Cosurfactant	1.5ml
4.	Methyl paraben	Preservative	1gm

5.	Castor Oil	Oil Phase	1ml
6.	Distilled Water	q.s	44ml

8. Result:

The formulation and evaluation of tofacitinib citrate emulsion involved creating a stable, effective topical delivery system to reduce the side effects associated with oral administration. The optimized emulsion was developed using oleic acid, Disodium hydrogen phosphate and propylene glycol as the oil, surfactant, and co-surfactant, respectively.

Sr.no	Ingridients	Range
1.	pH	6.0-6.5
2.	Viscosity	0.8982cp

9. Conclusion:

The formulation and evaluation of tofacitinib citrate emulsion involved creating a stable, effective topical delivery system to reduce the side effects associated with oral administration. The optimized emulsion was developed using oleic acid, Disodium hydrogen phosphate and propylene glycol as the oil, surfactant, and co-surfactant, respectively.

The introduction of Tofacitinib citrate as an emulsion represents a potentially innovative approach to delivering this medication. Emulsions offer advantages such as improved bioavailability, enhanced stability, and possibly a more convenient route of administration compared to traditional oral formulations. This formulation could be particularly beneficial for patients who have difficulty swallowing pills or who experience gastrointestinal irritation with oral tablets.

Clinical trials and studies evaluating the efficacy and safety of Tofacitinib citrate emulsion would be crucial in determining its effectiveness in treating conditions such as rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. These studies would assess parameters like disease activity scores, inflammatory markers, and adverse events to ensure the emulsion's therapeutic benefits outweigh any potential risks.

Additionally, factors such as patient adherence, cost-effectiveness, and regulatory approvals would play significant roles in the adoption and widespread use of Tofacitinib citrate emulsion in

clinical practice. Collaborative efforts between pharmaceutical companies, researchers, healthcare providers, and regulatory agencies would be essential to streamline the development, approval, and accessibility of this novel formulation.

In conclusion, the introduction of Tofacitinib citrate as an emulsion holds promise as a potentially valuable

therapeutic option for various inflammatory conditions, pending further clinical investigation and regulatory approval. The introduction of Tofacitinib citrate as an emulsion represents a potentially innovative approach to delivering this medication. Emulsions offer advantages such as improved bioavailability, enhanced stability, and possibly a more convenient route of administration compared to traditional oral formulations. This formulation could be particularly beneficial for patients who have difficulty swallowing pills or who experience gastrointestinal irritation with oral tablets.

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