MICROSUSPENSION: SYNTHESIS EVALUATION AND THEIR APPLICATION

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Abstract

Pharmaceutical micro-suspensions are a type of drug formulation designed to improve how well poorly soluble drugs work in the body. In these formulations, tiny particles of the drug, usually between 1 and 10 micrometres in size, are mixed into a liquid to make them easier to absorb. This helps increase the drug's effectiveness, ensure steady release, and improve its stability. These suspensions are made up of the drug itself, agents that keep the particles from clumping together, and stabilizers that help the particles stay evenly mixed.

Several methods, such as grinding the drug into smaller particles or using high pressure, are used to create micro-suspensions. These drug formulations can be used in different ways, including oral medicines, injections, skin treatments, and eye drops. However, keeping the particle size stable and preventing the particles from settling out of the liquid over time can be challenging.

Looking ahead, researchers are exploring new technologies, such as Nano suspensions (with even smaller particles), to further enhance drug delivery. Micro-suspensions are becoming increasingly important for delivering drugs that don't dissolve well in water, making them more effective and easier for the body to use.

Pharmaceutical micro-suspensions are a special way to deliver drugs that don't dissolve well in water. In these, the drug is broken down into tiny particles and mixed into a liquid to help it absorb better in the body, making it more effective.

These suspensions are made up of the drug itself, plus extra ingredients that stop the particles from clumping or settling at the bottom. The goal is to keep the particles evenly spread out so the drug works as it should.

There are several methods to create micro-suspensions, such as grinding the drug into smaller particles or using pressure to break them apart. These mixtures can be used in different ways, like oral medicines, injections, creams, and eye drops.

A challenge with micro-suspensions is keeping the particles stable over time, so they don't settle or change size. In the future, scientists are looking at ways to make even smaller particles to improve drug delivery even more.

In short, micro-suspensions help drugs that don't dissolve easily to work better in the body and offer a useful solution for making medications more effective.

Key points:

Definition: Micro-suspensions consist of tiny drug particles (1-10 micrometres) dispersed in a liquid medium to improve drug absorption and effectiveness.

Purpose: Designed to enhance the bioavailability of poorly water-soluble drugs by increasing their surface area for dissolution.

Composition : Active Drug: Poorly soluble drug particles.

Suspending Agents: To keep particles dispersed.

Surfactants and Stabilizers: To prevent clumping and maintain stability.

Preservatives: To avoid microbial growth.

Advantages: Improved drug absorption. Controlled or sustained drug release .Enhanced stability of drugs in liquid form.

Preparation Methods: Wet Milling. High-Pressure Homogenization. Precipitation.

Sonication. Applications: Used in oral, injectable, topical, and ophthalmic formulations.

Challenges: Maintaining particle size stability. Preventing sedimentation. Managing viscosity for ease of administration.

Future Trends: Increasing interest in nanotechnology to further improve drug delivery.

Introduction

A pharmaceutical micro suspension is a system in which micron-sized particles of a drug are dispersed in a liquid medium, typically water or another suitable solvent. These suspensions are used to improve the solubility, stability, and bioavailability of drugs that are poorly soluble in water. The small particle size increases the surface area available for dissolution, which can enhance the drug's absorption when administered.

Key Characteristics:

Particle Size: The particles in a micro suspension usually range between 1 to 10 micrometres.

Stability: The suspension must be stabilized to prevent the particles from agglomerating or settling over time. Stabilizers like surfactants or polymers are often added to achieve this.

Solubility: Micro suspensions are particularly beneficial for drugs that have poor water solubility (Biopharmaceutics Classification System class II or IV drugs).

Bioavailability: By reducing particle size, the drug's surface area is increased, potentially enhancing dissolution rates and improving bioavailability.

Route of Administration: Micro suspensions can be used in various drug delivery systems, including oral, injectable, and topical formulations.

Applications:

Oral Drug Delivery: Enhances the dissolution of poorly soluble drugs for better absorption in the gastrointestinal tract.

Injectable Formulations: Used when a drug has poor solubility in water but requires parenteral administration.

Topical Delivery: Can improve the penetration of drugs through the skin or mucous membranes.

In the pharmaceutical industry, micro suspensions are a valuable formulation strategy to overcome challenges associated with drugs that have poor water solubility and require enhanced delivery to ensure therapeutic efficacy.

Micro suspensions are used for several reasons:

1.Enhanced bioavailability

2.Controlled release

3.Stability

Methods of Preparation:

1.Top-down techniques: Particle size is reduced through mechanical processes like high-pressure homogenization or milling.

2.Bottom-up techniques: Precipitation methods where drug particles are formed directly at the desired size through controlled crystallization.

3.Advantages: Enhanced bioavailability for poorly soluble drugs. Potential for improved pharmacokinetics and reduced dose variability. Suitable for oral, parenteral, or topical delivery systems.

4.Regulatory Considerations: Like other pharmaceutical formulations, micro-suspensions must meet strict guidelines for particle size distribution, stability, and sterility, depending on the route of administration.

Advantages of micro suspension:

1.Enhanced Bioavailability: Micro suspensions increase the surface area of the drug particles, leading to faster dissolution and improved bioavailability for poorly water-soluble drugs.

2.Controlled Release: Micro suspensions can be designed for sustained or controlled release, providing longer therapeutic effects and reducing the frequency of dosing.

3.Improved Stability: Drugs that are unstable in solution form can be formulated as micro suspensions, which may enhance their chemical and physical stability.

4.Reduced Irritation: For drugs that cause irritation when administered in solution, micro suspensions can mitigate this by controlling the release rate and reducing direct contact with tissues.

5.Flexibility in Administration Routes: Micro suspensions can be administered via multiple routes, including oral, injectable, ophthalmic, and topical, making them versatile for different medical needs.

6.Higher Drug Loading: Compared to solutions, micro suspensions allow for higher concentrations of the drug without solubility limitations.

7.Masking Taste: In oral formulations, micro suspensions can help in masking the unpleasant taste of drugs, improving patient compliance.

8.Customization for Targeted Therapy: The particle size and distribution in micro suspensions can be optimized to target specific tissues or organs, improving drug efficacy and reducing side effects.

9.Reduced Dose Variability: Micro suspensions allow for uniform particle size distribution, which leads to more consistent drug dosing and better control over therapeutic outcomes.

10.Minimal Use of Organic Solvents: Since micro suspensions often rely on water or other biocompatible liquids as the dispersing medium, they reduce or eliminate the need for potentially toxic organic solvents used in other drug formulations.

11.Improved Patient Compliance: In cases where patients have difficulty swallowing tablets or capsules, micro suspensions (especially oral and injectable forms) offer a more easily administrable alternative.

12.Improved Delivery in Biological Environments: Due to their small particle size, micro suspensions can better penetrate biological barriers, such as mucous membranes, enhancing drug absorption and efficacy for local and systemic treatment.

Disadvantages of micro suspension:

1.Physical Instability: Micro suspensions can suffer from issues like sedimentation, particle aggregation, and Ostwald ripening,

leading to uneven drug distribution and reduced efficacy over time.

2.Complex Manufacturing Process: Preparing micro suspensions often requires specialized equipment and techniques such as high-pressure homogenization or milling, increasing production costs and complexity.

3.Limited Drug Loading: Although micro suspensions allow for higher drug loading than solutions, there is still a limit to how much drug can be suspended without causing viscosity or stability issues.

4.Need for Preservatives and Stabilizers: To prevent microbial growth and physical instability, micro suspensions often require the addition of preservatives, surfactants, and stabilizers, which can increase formulation complexity and potential for side effects.

5.Risk of Particle Growth: Over time, particles in the suspension can grow or aggregate, which may lead to changes in drug release profiles or reduction in bioavailability.

6.Difficult to Formulate for Certain Drugs: Some drugs may not remain stable in suspension due to chemical degradation or may require solubilization, making them unsuitable for this type of formulation.

7.Viscosity Issues: High concentrations of suspended particles can increase the viscosity of the formulation, making it difficult to handle, administer, or inject, particularly for parenteral routes.

8.Risk of Clogging in Delivery Devices: For injectable micro suspensions, there is a risk of particles clogging needles or infusion devices, which could disrupt drug delivery and require special attention to particle size control.

9.Patient Acceptability: In some cases, patients may experience discomfort or irritation, especially with injectable or ophthalmic micro suspensions, due to the presence of particles.

10.Storage and Handling Concerns: Micro suspensions may require specific storage conditions to maintain stability, such as refrigeration, and they may need to be shaken before administration to ensure uniform dosing.

11.Potential for Adverse Immune Reactions: For parenteral suspensions, the presence of particulate matter can trigger immune responses or inflammatory reactions, especially when injected.

Method of preparation :

1.Wet Milling: Involves grinding the drug in a liquid medium using beads or balls to achieve the desired particle size.

2.High-Pressure Homogenization: Utilizes high pressure to force the drug suspension through a narrow gap, resulting in size reduction and better distribution of particles.

3.Ultrasonication: Applies ultrasonic waves to create cavitation bubbles in the liquid, which collapse and disrupt larger particles, reducing their size.

4.Co-solvency Method: Involves dissolving the drug in a suitable solvent mixture and then precipitating it out to form a micro suspension.

5.Spray Drying: A method where a liquid suspension is sprayed into a hot gas, leading

to rapid evaporation of the solvent and forming micro-sized particles.

6.Emulsification: Involves dispersing the drug in an emulsifying agent to create a micro suspension, commonly used when the drug is insoluble in water.

7.Solvent Evaporation: Involves dissolving the drug in a volatile solvent, which is then evaporated to leave behind a micro suspension.

This are the methods to prepare the micro suspension formulation.

Formulation:

In the formulation of micro suspension the active ingredient are suspended in the liquid medium.

The active ingredient of isoniazid is isoniazid it self (API)

The (API) is suspended in liquid medium

Liquid medium are used like:

1. Water: Often used as a solvent or dispersing medium due to its availability and compatibility with many substances
2. Ethylene Glycol: Commonly used for its solubilizing properties and ability to stabilize suspensions.
3. Glycerin: A viscous liquid that can enhance stability and improve the texture of suspensions.
4. Polyethylene Glycol (PEG): Used to improve solubility and stability of the active ingredients.
5. Vegetable Oils: Used in pharmaceutical and cosmetic formulations for their emulsifying and solubilizing properties.

It is used as a disperse medium.

Steps:

The three steps that can be taken to ensure formulation of an elegant pharmaceutical

Suspension are:

1. Control particle size. On a small scale, this can be done using a mortar and pestle, to grind Down ingredients to a fine powder
2. Use a thickening agent to increase viscosity of vehicle, using suspending agents of Viscosity
3. Use a wetting agent.

Micro suspension of an antibiotic:

This study developed and tested an ofloxacin micro suspension, suitable for various routes of administration due to its rapid breakdown. Suspensions are more stable than solutions and are ideal for poorly water-soluble drugs. The drug's properties were confirmed through various analyses, and multiple formulations were created using different excipients. The micro suspension had smooth, spherical particles around 200 nm in size and was evaluated for physical properties, drug content, release rate, and stability. The optimized formulation showed promising results for stability and drug release.

Method of preparation:

Physicochemical Characterization and Drug Identification:

Physicochemical characterization of the drug provides The information to identify the nature of the drug Substance.

Spectroscopic Studies (UV spectral analysis):

A Shimadzu spectrophotometer was used to gather Ultraviolet and visible spectra (UV–Vis) in the 200–400 nm Range, in 0.1 N Hcl was created for this research.

Preparation of Stock Solution:

Dissolving 50 mg of Ofloxacin in 50 ml of 0.1 N Hcl Produced a stock solution of Ofloxacin (1000 g/ml). The dilutions ranged from 3 to 15 g/ml. Using a Shimadzu-1700 Pharma spec UV- visible spectrophotometer, the solution was kept in the wavelength range of 200-400 nm to determine the maximum absorbance of Ofloxacin

Applications of micro suspension:

Pharmaceutical micro suspensions are a form of drug delivery system where active pharmaceutical ingredients (APIs) are suspended in a liquid medium at a microscopic size. They have several important applications in the pharmaceutical field.

Improved Solubility and Bioavailability: Micro suspensions are often used for drugs with poor water solubility. By reducing the particle size, the surface area of the drug increases, leading to improved dissolution rates and bioavailability when taken orally.

Sustained or Controlled Release: Micro suspensions can be designed for slow or controlled release of the drug, allowing for prolonged therapeutic effects and reduced dosing frequency. This is useful in treatments that require long-term or consistent drug levels in the bloodstream

Enhanced Stability: Drugs that are chemically unstable in solution can be formulated as micro suspensions to improve their stability. This helps in avoiding degradation of the drug in the gastrointestinal tract or during storage.

Parenteral Drug Delivery: Micro suspensions are commonly used for injectable formulations, particularly for drugs that are not suitable for oral delivery. They provide a way to administer drugs via subcutaneous, intramuscular, or intravenous routes with precise control over particle size, ensuring safety and efficacy.

Topical Drug Delivery: Micro suspensions are often used in dermatological products like creams and ointments for localized delivery of APIs. This allows the drug to penetrate the skin more effectively and reach the targeted site.

Targeted Drug Delivery: Micro suspensions can be used in targeted drug delivery systems, where the drug is directed to a specific site in the body, minimizing side effects and enhancing therapeutic outcomes. This is especially useful in cancer therapy and site-specific treatments.

Ophthalmic Suspensions: Micro suspensions are widely used in eye drops to improve the retention of the drug on the ocular surface and enhance its absorption into the eye. This is crucial for treating

conditions like glaucoma, infections, and inflammation.

Paediatric and Geriatric Formulations: Liquid-based micro suspensions are preferred for patients who have difficulty swallowing solid dosage forms, such as children and the elderly. These formulations can be easily administered and dosed accurately.

Micro suspension use in treatment of verity of disease:

Micro suspensions are increasingly used in the treatment of various diseases due to their ability to enhance drug solubility, stability, and bioavailability. Here are some key applications of micro suspensions in treating different diseases:

Cancer Treatment : Micro suspensions are used for delivering poorly soluble chemotherapeutic agents. By reducing the particle size, the drug can more effectively penetrate tumours and maintain a higher concentration at the target site. This can improve the efficacy of the treatment while reducing systemic toxicity. For example, paclitaxel, a common cancer drug, is often formulated as a micro suspension.

Infectious Diseases: Antibiotics and antifungal drugs that have low solubility can be formulated as micro suspensions to enhance their bioavailability. For instance, micro suspensions of antifungals like amphotericin B are used to treat systemic fungal infections with fewer side effects compared to traditional formulations.

Respiratory Diseases: Micro suspensions are also used in inhalation therapies for respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD). The small particle size ensures better penetration into the lungs, leading to more effective treatment. Inhalable steroids and bronchodilators are often delivered in micro suspension form.

Cardiovascular Diseases: Certain cardiovascular drugs, such as antihypertensive and anticoagulants, are prepared as micro suspensions to enhance their absorption and therapeutic effect. This is particularly useful for drugs that have erratic absorption profiles when taken orally in conventional forms.

Dermatological Conditions: Micro suspensions are used in topical formulations for treating skin diseases like psoriasis, eczema, and acne. These formulations allow the drug to penetrate deeper into the skin, providing more effective relief while minimizing systemic side effects.

Ophthalmic Conditions: For diseases like glaucoma, dry eye syndrome, and bacterial infections of the eye, micro suspensions can improve the retention time of the drug on the ocular surface, leading to enhanced therapeutic outcomes. Drugs like corticosteroids or antibiotics are often delivered via ophthalmic micro suspensions.

Neurological Disorders :Micro suspensions can be used to deliver drugs to the brain for the treatment of neurological diseases such as Parkinson's and Alzheimer's. The improved bioavailability and targeted delivery help in crossing the blood-brain barrier, making treatments more effective.

Gastrointestinal Disorders: Drugs used to treat conditions like Crohn's disease, ulcerative colitis, and irritable bowel syndrome can be delivered as micro suspensions to enhance absorption in the gastrointestinal tract. This helps in providing better control over symptoms with a reduced risk of side effects.

Hormonal Disorders: In hormone replacement therapies or for the treatment of endocrine disorders, micro suspensions can be used to administer poorly soluble hormones like testosterone or estradiol. These formulations offer a sustained release, providing a more stable hormonal level over time.

Paediatric and Geriatric Use: Micro suspensions are particularly beneficial in paediatric and geriatric populations, where swallowing solid oral dosage forms may be difficult. Liquid micro suspensions provide a more manageable form for administration and ensure proper dosing.

Evaluation of MicroSuspension:

1. Particle Size

- We measure how big the particles are and how evenly they're spread out. This matters because small particles stay floating in the liquid, while bigger ones might sink or float to the top.

2. Stability

- We check if the particles are staying mixed or if they're separating. Stable suspensions don't settle or form clumps quickly.
- **Zeta potential** is a measure of how much the particles push away from each other. The more they push away, the more stable the suspension.
- Sometimes we add substances that keep particles apart, so they don't clump together.

3. Thickness and Flow

- We measure how thick or runny the liquid is. A thicker liquid can keep particles suspended longer. We also look at how it flows when stirred or moved.

4. Amount of Solid Particles

- We check how much solid material is mixed in with the liquid. This can be done by drying out the liquid and weighing the solids left behind.

5. Clumping

- We look to see if particles are sticking together to form bigger chunks, which could make the suspension less effective.

6. Appearance

- We evaluate how clear or cloudy the suspension is. This gives us an idea of how well the particles are spread out.
- We also check if the color of the suspension stays the same, especially if it's important for its use.

7. Reaction to Environment

- We test how the suspension holds up when the pH (acidity) or

temperature changes. This helps predict how it will behave in different conditions.

- We also run tests over time to see if it stays stable during storage.

8. Specific Use Testing

- Depending on what the suspension is for, we might test how well it does its job—like how a medicine works or how a coating performs.

Conclusion:

Micro suspension form of drug are more effective than other form of drug . they have more bioavailability than other, more stable than other dosage form, more stable more effective than other dosage form, Use to treat different varieties of disease, they have small particle size (range in micrometres) particles suspended in liquid medium. In this type of formulation they have control release of drug, flexibility of administration etc. micro suspension form given better therapeutic effect then other dosage form.

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