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Review on - Microencapsulation

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ABSTRACT
Microparticles, tiny particles carrying drugs, have some great advantages for delivering medications. They protect the drug from things that could break it down, like enzymes. Also, we can control how fast the drug is released over a long time, making it convenient for patients. It's easier to give than other long-lasting forms like implants. Plus, we can design it to match exactly what the patient needs. This article explores these tiny drug carriers and how they've improved medical treatments. This paper dives into how microparticles can make drug delivery more efficient, improve release patterns, and hit the right targets. It also covers some basic info to understand how these tiny capsules work in drug delivery.Microencapsulation is a method where tiny particles (ranging from really tiny to a bit larger) of solids, liquids, or gases are wrapped in a thin layer of another material. This is often done with drugs in medicine to control their release and protect them. The inner material is called the core, and the outer layer is the coating.
Keywords: Microcapsulation , coating material , microcapsule ,microsphare ,coat material

INTRODUCTION

Microencapsulation is a process where tiny droplets or particles of liquid or solid materials are coated with a continuous film of polymers. This procedure was first introduced in 1931 by researchers Bungenburg de Jon and Kan. It involves converting liquids into solids, altering their properties, protecting them, and controlling how their contents are released. Microencapsulated products are small entities with an active core surrounded by a shell or embedded in a matrix. These shells are typically made of organic polymers, but waxes and lipids are also used. These microencapsulated products vary in size from 1 to 1000 μm in diameter and can contain 10-90% of the core material. They are used for encapsulating various materials like live cells, adhesives, flavors, agrochemicals, enzymes, and pharmaceuticals. Scanning electron microscopy is used to examine their complex structural features

Principles of Microencapsulation:

•Microencapsulation involves the creation of micro-sized capsules, which are often composed of polymers, lipids, or other materials.

• These capsules encapsulate a core material, which can be a solid, liquid, or even a gas.

The protective shell or coating serves to control the release of the core material, protecting it from external factors

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Fig . Microencapsulation

Advantages of microencapsulation:-

1. Controlled Release: It allows for controlled and sustained release of the encapsulated material, ensuring a gradual and prolonged effect
2. Improved Bioavailability: It can enhance the bioavailability of certain substances, facilitating better absorption and utilization by the body
3 Taste and Odor Masking: Microencapsulation helps mask unpleasant tastes or odors associated with certain ingredients, improving the overall palatability of products.
4Targeted Delivery: Enables targeted delivery of substances to specific sites within the body or in a particular environment, enhancing therapeutic or functional outcomes.

Disadvantage of Microencapsulation:-

1.Release Control: Achieving precise control over the release of the encapsulated substance can be difficult, impacting the effectiveness
2. Raw Material Compatibility: Not all substances can be easily encapsulated, and compatibility issues with certain materials may arise during the process.
3. Scale-up Challenges: Transitioning from lab-scale to industrial-scale production can pose challenges, affecting the efficiency
4. Stability Issues: The stability of microcapsules may be compromised under certain conditions, such as exposure to high temperatures

Microencapsulation serves various purposes in pharmaceuticals:

1. It is primarily used to control the gradual release of drugs over time.
2. It is widely employed to mask the taste and odor of certain medications, enhancing patient adherence, such as with Paracetamol or Nitrofurantoin to cover their unpleasant taste.
3. This technique can transform liquid medications into easily handled powdered form.
4. Microencapsulation helps protect drugs sensitive to moisture, light, or oxygen. For instance, it safeguards Nifedipine from light-induced degradation.
5. It prevents interactions between drugs that can be incompatible.
6. Volatile drugs like Aspirin and Peppermint oil, which might evaporate at room temperature, can be preserved through microencapsulation.
7. It can reduce toxicity and gastrointestinal irritation caused by substances like KCL and Ferrous sulfate.
8. Microencapsulation can alter the site of drug absorption, which is beneficial for medications with toxicity at lower pH levels.
9. As per studies by Smith and Anderson, microencapsulated Vitamin A palmitate offers improved stability and protection from oxidation.

In microencapsulation, two key components are involved:

1 **Core Material**: This refers to the primary substance that needs to be encapsulated, and it can be either in liquid or solid form. The core material's composition can vary, including the presence of dispersed or dissolved substances. In the case of solid cores, it may consist of active ingredients, stabilizers, diluents,

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excipients, and substances that control the release rate, either slowing it down or accelerating it. The ability to adjust the composition of the core material offers flexibility and plays a crucial role in designing and developing the desired properties of microcapsules.

2 **Coating Material:** The coating material is responsible for forming a film that adheres well to the core material. It should also be chemically compatible and non-reactive with the core material, ensuring stability. Additionally, the coating material should remain inert when in contact with active ingredients, and it should provide controlled release under specific conditions. The coating itself can have various characteristics, such as being flexible, brittle, hard, thin, and so on. It should be readily available and cost-effective. Ultimately, the coating material contributes to achieving the desired coating properties

3. **Microsphers**: microspheres are small spherical particles or capsules that are used to encapsulate active substances, such as drugs or chemicals, within a protective shell or coating. These microspheres are designed to release the encapsulated substance gradually over time, allowing for controlled and sustained delivery. They are commonly used in pharmaceuticals, food science, and various other industries to improve the stability, solubility, and targeted delivery of the enclosed materials.

2.1Coatingmaterial properties

Coating materials used in various applications possess specific characteristics and functions. These include:

1. Ensuring the stability of the core material they cover.
2. Remaining inert or unreactive with the active ingredients within.
3. Releasing the contents in a controlled manner under specific conditions.
4. Having the ability to form a pliable, tasteless, and stable film.
5. Being non-hygroscopic (not absorbing moisture), maintaining a reasonable viscosity, and being cost-effective.
6. Exhibiting flexibility, brittleness, hardness, thinness, or other desired physical attributes.

Examples :-of such coating materials include water-soluble resins like gelatin, gum arabic, starch, polyvinylpyrrolidone, carboxymethylcellulose, hydroxyethylcellulose, methylcellulose, l alcohol, and polyacrylic acid.

TECHNIQUES TO MANUFACTURE OF MICROCAPSULES

Microencapsulation encompasses diverse processes: chemical, physiochemical, electrostatic, and mechanical. In chemical processes, interfacial and in situ polymerization play roles. Physiochemical processes span coacervation-phase separation, complex emulsion, meltable dispersion, and powder bed methods. Mechanical processes embrace the air-suspension method, pan coating, spray drying, spray congealing, micro-orifice system, rotary fluidization bed granulator, and sometimes spheronization.

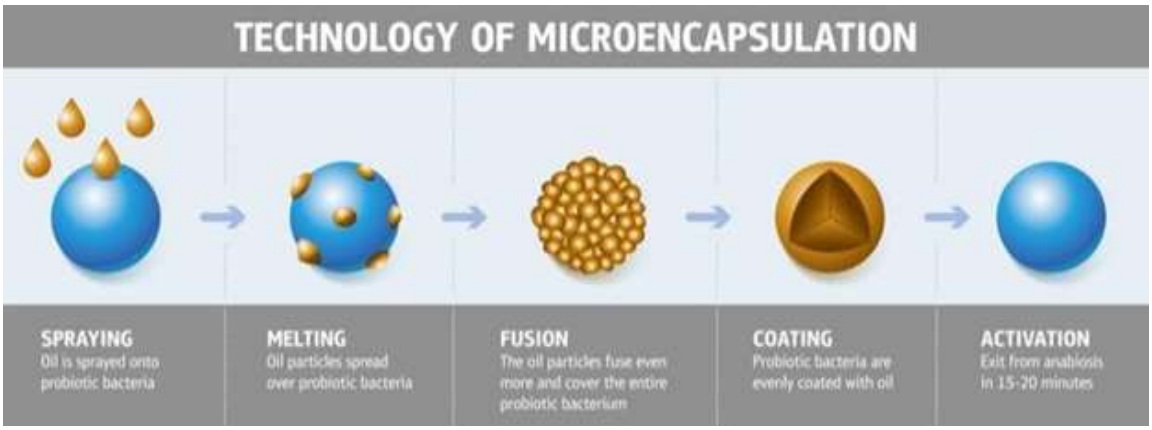

Fig. Technology of microencapsulation

For instance, sustained-release polymer microcapsules with drugs of varying solubility can be formed by utilizing colloidal polymer dispersion in an all-water environment, providing an

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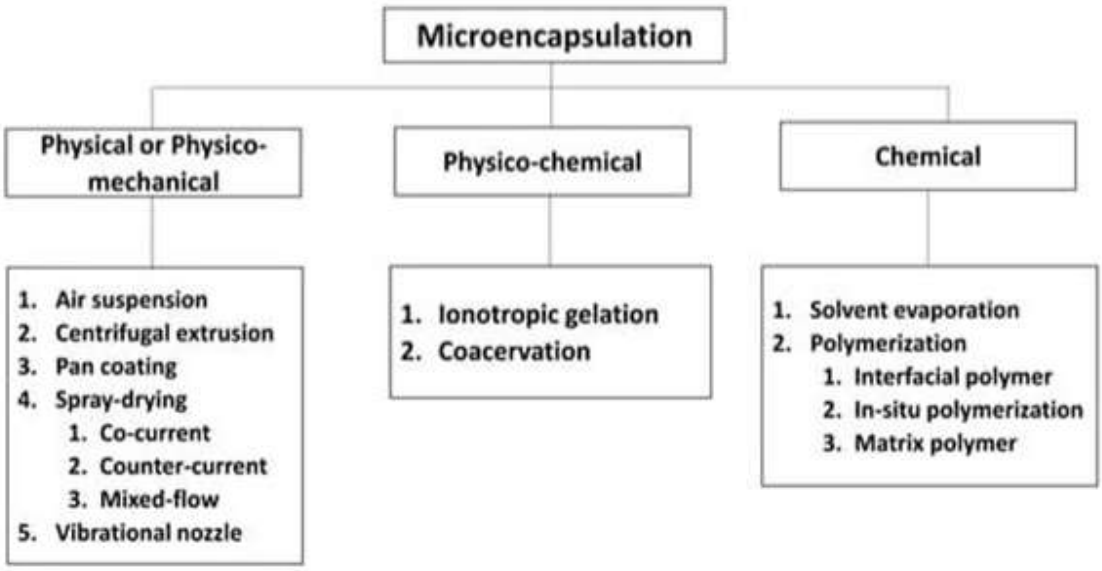
alternative to traditional microencapsulation techniques.

In interfacial polymerization, a monomer undergoes polymerization at the interface of two immiscible substances. When the internal phase is a liquid, the monomer can be dispersed or solubilized in this phase, forming an emulsion in the external phase. A cross-linking agent may be added to the external phase to achieve the desired particle size. The majority of polymerization occurs at the interface due to the migration of the monomer from the internal to the external phase.Electrostatic methods of microencapsulation bring together the wall material and the material to be encapsulated when both are aerosolized. The wall material must be liquid during the encapsulation stage and capable of surrounding the core material. The aerosols produced must be oppositely charged. This process involves three chambers for atomization of the wall and core material, as well as mixing, with oppositely charged ions generated and deposited on the liquid drops during atomization.Mechanical methods for microencapsulation utilize specialized equipment. The microcapsules produced result from mechanical procedures rather than a well-defined physical or chemical phenomenon. One commonly employed mechanical method is the multiorifice-centrifugal process, developed by the Southwest Research Institute. This process uses centrifugal forces to propel a core material particle through an enveloping microencapsulation membrane, impacting mechanical microencapsulation. The multiorifice-centrifugal process is capable of microencapsulating liquids and solids of varying size ranges, using diverse coating materials.



1.**Physical methods**

1.1**Air -suspension**

Air-suspension coating is a technique used to create microcapsules by floating tiny particles in an upward-moving stream of air. A perforated plate with holes, both inside and outside a cylinder, supports these particles. The air, often heated, makes the particles rise, and as it slows down at the top, they settle back down. This process can be repeated, and the particles pass through the cylinder multiple times in a short period. This method is versatile and can use various coating materials such as solutions, emulsions, or hot melts to encapsulate very small particles. However, it may lead to these particles clumping together into larger ones during the process.

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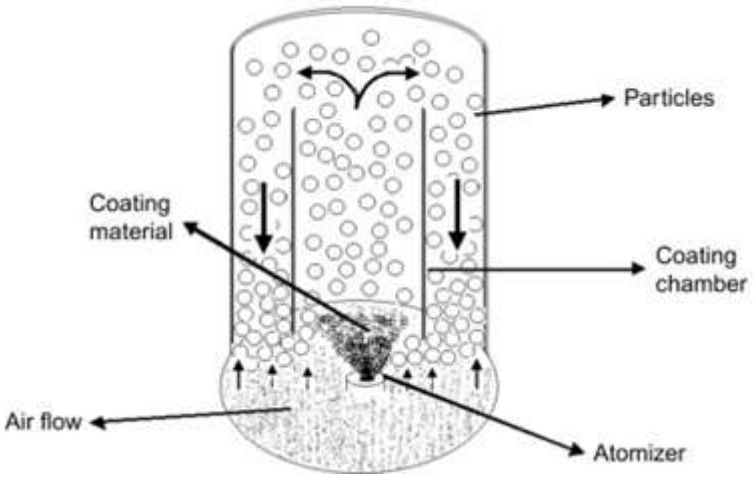

Fig air suspension method

1.2.**Centrifugal extension**

Centrifugal extrusion is a technique that involves using a rotating extrusion head with concentric nozzles to encapsulate liquids. In this process, a core liquid is jetted out and surrounded by a layer of wall solution or molten material. As the core liquid travels through the air, it naturally breaks into droplets due to Rayleigh instability, and these droplets get coated with the wall solution. While these droplets are in the air, the molten wall can solidify, or the solvent in the wall solution can evaporate. Most of these droplets have sizes close to the average diameter, so they tend to land in a ring around the spray nozzle. If needed, the capsules can be further solidified by placing them in a ring-shaped hardening bath after formation. This method is highly effective for producing particles with diameters ranging from 500 to 2,000 µm. It's essential to understand that this process is suitable only for liquid or slurry materials.

Moreover, it allows for high production rates, potentially yielding up to 23 kg of microcapsules per hour per nozzle in a head that can have multiple nozzle

1.3 **Pan coating**

Pan coating is a well-established method in the pharmaceutical industry for making small particles or tablets with a protective layer. It works by applying a coating material to a moving pile of particles and using warm air to help the liquid in the coating dry up. The particles are mixed around in a pan or similar device while the coating material is added gradually.Pan coating is a really old but still commonly used method in the pharmaceutical industry. It's used to make small particles or tablets with a protective covering. During this process, the particles are rolled around in a pan or something similar while the protective covering is applied gradually.

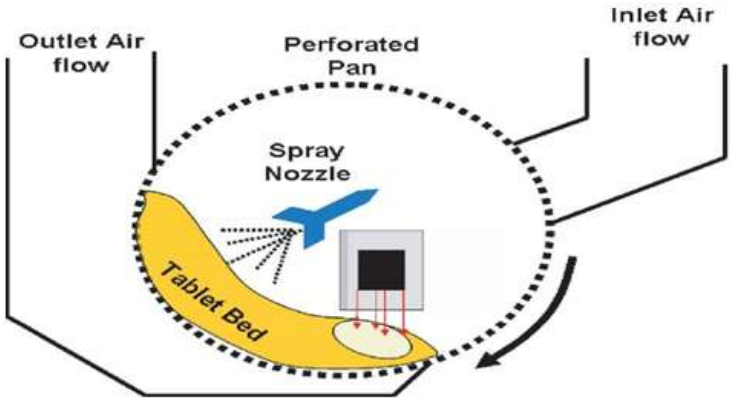

Fig. Pan coating

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When it comes to making tiny medicine beads that release the drug slowly, this method is great. It's often used to coat medicines onto tiny spherical things like **sugar** seeds and then add protective layers made of different materials. For this to work well, the particles should be larger than 600 microns.

1.4.Spray draying

Spray drying is a widely adopted technology in the food and pharmaceutical industries because it's versatile, cost-effective, efficient, easy to scale up, and produces high-quality powdered products. It has been extensively used for encapsulating various bioactive food components like proteins, fats, vitamins, enzymes, pigments, and flavors over many years. However, it's not suitable for heat-sensitive products such as microorganisms and essential oils because the high temperatures involved can cause them to evaporate or be damaged. In spray drying for microencapsulation, you create an emulsion, solution, or suspension and then turn it into a dry powder.

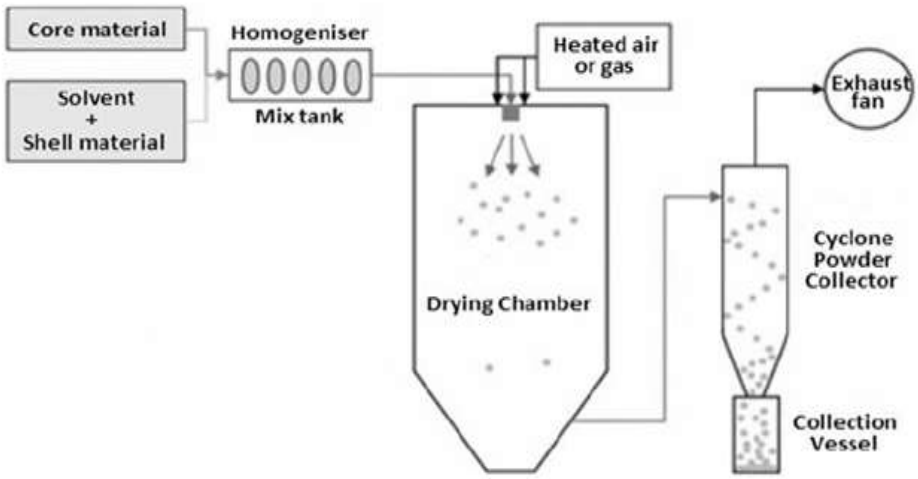

Fig. Spray draying

1.5. **Fludized– bed technology:-**

Fluidized-bed technology is widely utilized in microencapsulation for solid core materials, including liquids absorbed into porous solids. This method, commonly applied in pharmaceuticals, involves suspending solid particles on an air jet and then enveloping them with a spray of liquid coating. The capsules are transported to an area where their shells solidify through cooling or solvent vaporization. This process, known as the Wurster process when the spray nozzle is positioned at the bottom of the fluidized-bed, repeats the steps of suspension, spraying, and cooling until the desired capsule-wall thickness is achieved.

2.**Chemical method**

2.1.Interfacial Polymerization

Interfacial polymerization is a process where two substances involved in polycondensation come together at an interface and react swiftly. This method relies on the classic Schotten-Baumann reaction, which occurs between an acid chloride and a substance that possesses an active hydrogen, such as an amine or alcohol. This reaction results in the creation of materials like polyesters, polyurea, and polyurethane. When the right conditions are met, thin, pliable barriers form quickly at this meeting point. To illustrate, you'd mix a pesticide solution with a diacid chloride in water and then introduce an aqueous solution that contains an amine and a polyfunctional isocyanate. A base is used to counteract the acidity produced during the reaction. The end result is the immediate formation of condensed polymer walls at the interface of the tiny droplets within the emulsion.

2.2.Insitu polymerization

In in situ polymerization, the protective shell around the core material is formed by combining and transforming small building blocks (monomers) into a solid shell. This process occurs entirely within the surrounding material and at the boundary created by the core material and its surroundings. Initially, a small starter material is created, and over time, it grows and forms a solid

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shell on the surface of the core material, creating a protective coating.

2.3.matrix polymer

In various manufacturing processes, a central material is encased in a plastic-like substance. One way to do this is through a simple technique called spray-drying, where the material is shaped as the solvent in the plastic-like substance dries up. Alternatively, the plastic-like substance can solidify due to a chemical change.

For example, Chang uses this method to create tiny capsules that contain protein solutions. He mixes the protein with a specific liquid, and these capsules can selectively let certain substances pass through. He's shown this by using the capsules to turn blood urea into ammonia while keeping the enzyme inside them when used in a medical shunt system. Many groups are employing polymerization methods to achieve this process of making tiny protective capsules.

3.Coacervation phase separation:

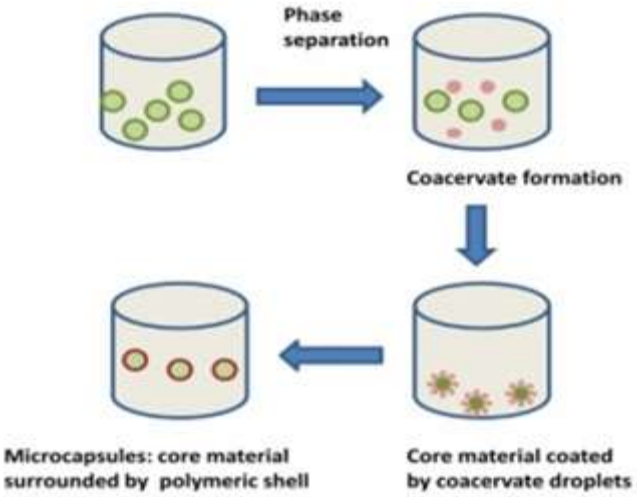

Fig . Phases of coacervation

Microencapsulation using coacervation phase separation involves three main steps:-

1.Formation of Phases: Three types of substances are involved: a liquid for making the product, the material inside (core), and a coating material and substances don't mix well initially .

2.Coating Formation: The liquid coating material is added to the core material.The coating is made by applying the liquid polymer around the core.

3. Making it Solid: The coating is solidified using methods like heat, chemical reactions, or removing solvents and forms tiny capsules.

There are two methods for coacervation are available.

1. Simple Process:

Using a single polymer, induce phase separation by subjecting it to conditions that lead to desolvation.

2. Complex Process:

Utilizing two hydrophilic polymers with opposing charges, induce separation and deposition on droplets through charge neutralization. After coacervates form, stabilize the polymer complexes by cross-linking with glutaraldehyde.

Characterization of microcapsules

1. Size and Morphology: Determine the size, shape, and surface characteristics of the microcapsules. Techniques like microscopy (e.g., SEM or TEM) can be used for this purpose.
2. Shell Thickness: Measure the thickness of the microcapsule shell to ensure it meets the desired specifications. This can be done using microscopy and image analysis.
3. Core Material Content: Analyze the amount and distribution of the core material within the microcapsules. Techniques like spectroscopy, chromatography, or titration can be used.

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4. Release Properties: Evaluate the release kinetics of the core material from the microcapsules. This involves studying how and when the core material is released under various conditions
5. Physical Stability: Assess the stability of microcapsules over time, including factors like aggregation, sedimentation, and changes in appearance.
6. Chemical Composition: Analyze the chemical composition of the microcapsule shell and core material to ensure they meet quality standards.
7. Release Triggering: Investigate the stimuli or conditions required to trigger the release of the core material from the microcapsules. This is important in applications where controlled release is necessary
8. Rheological Properties: Analyze the rheological behavior of microcapsule suspensions or dispersions, which can affect their processing and application in products like paints or coatings.
9. Spectroscopic Analysis: Employ techniques like infrared spectroscopy (FTIR) or nuclear magnetic resonance (NMR) to understand the chemical structure and interactions within the microcapsules.

Drug release machanisum:

The release mechanism in microencapsulation depends on the type of shell or coating material used and the specific application. Here are some common release mechanisms:

1. **Diffusion**: In diffusion-controlled release, the core material diffuses through the shell over time. The rate of diffusion depends on the properties of the core material and the shell material. The medicine inside dissolves into the coating and then seeps out. How fast it happens depends on how quickly the coating lets the medicine in, how fast the medicine dissolves, and how rapidly it leaks out.Higuchi's EquationThere's a fancy formula to describe this process, considering things like how much medicine there is, how well it dissolves, and features of the coating. But to keep it simple, we can say the amount of medicine released over time depends on these factors.This is a common mechanism in many microencapsulation applications.
2. **Chemical Reaction**: Some microcapsules are designed to release their contents through a chemical reaction. For example, pH-sensitive capsules may release their payload when exposed to a specific pH level, such as in the acidic environment of the stomach.
3. **Temperature**:Temperature-sensitive microcapsules can release their contents when exposed to specific temperature conditions. This is often used in self-heating or self-cooling packaging and medical applications.
4. **Mechanical Disruption**: Microcapsules can be designed to break open when subjected to mechanical stress. For example, microcapsules in scratch-and-sniff stickers release their aroma when the sticker is scratched.
5. **Enzyme Activation**: Some microcapsules are designed to release their contents in the presence of specific enzymes. This is common in pharmaceuticals and targeted drug delivery systems.
6. **Electrostatic or Magnetic Triggers**: Electric or magnetic fields can be used to trigger the release of materials from microcapsules in certain applications.
7. **Osmotic Pressure**: Osmotic pressure can be employed to push the contents out of the microcapsule. This is used in controlled drug delivery systems.
8. **Erosion**: At times, the coating wears away due to factors like pH or enzymes, impacting how the medicine is released.

Recent advances in microencapsulation

Recent progress:

Recent progress in microencapsulation involves clever ways to create tiny particles for delivering things like drugs. Scientists are working on improving how they make these small particles, paying attention to the methods and materials used. The aim is to carefully manage factors such as the kind of particles, their size, and how they interact with each other, all tailored for specific purposes.

A standout approach Is using tiny, biodegradable polymeric particles, often made through a process called emulsion solvent evaporation. This method allows for a slow and controlled release of drugs, safeguarding them from breaking down. Researchers have been applying these techniques in different areas, such as delivering drugs to the eyes, creating microspheres with antibiotics for swallowing, and enclosing things like hormones and DNA.

These advancements are making drug delivery systems better, providing answers for controlled release, making medicines taste better, and shielding the body from harmful drug effects. The versatile use of polymeric carriers, whether

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they break down or not, highlights how valuable microencapsulation is in the world of medicine.

Example:

1. **Biodegradable Polymeric Microparticles**: Utilizing emulsion solvent evaporation, researchers create biodegradable polymeric microparticles. This method is employed for sustained drug delivery. For instance, in ocular drug delivery, these microparticles protect drugs from degradation.

2. **Antibiotic-Containing Microspheres**:

Microencapsulation has been applied to create antibiotic-containing microspheres for oral administration. This offers controlled release, enhancing the efficacy of the antibiotic.

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