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Microencapsulation: A Review

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Abstract— *This review article delves into the dynamic realm of microencapsulation, a technology that encapsulates active ingredients within microscopic particles. The membrane dissolves itself when stimulated, releasing the core at the desired time or place. Microencapsulation has many applications in the food, agricultural, pharmaceutical, and medical industries. It has been used in flavours, acids, oils, vitamins, and microorganisms. This article comprehensively explores various microencapsulation techniques, ranging from traditional methods to state of the art technologies. Microencapsulation offers the crucial functionality of controlling the release of food ingredients at precise locations and timings, ensuring optimal effectiveness. It examines the applications of microencapsulation in different industries including pharmaceutical, agriculture, food, printing, cosmetic, textile and defence. Also highlighting its impact on product stability, controlled release and enhanced performance in different areas of science and technology. In the realm of pharmaceuticals and various other industries, microencapsulation plays a crucial role in enhancing stability, protecting sensitive substances and regulating the release of active ingredients. Microencapsulation is garnering significant attention across various domains including commercial development and research.*

Keywords— *Microencapsulation technology, microcapsule, polymers, pharmaceuticals, techniques.*

I. INTRODUCTION

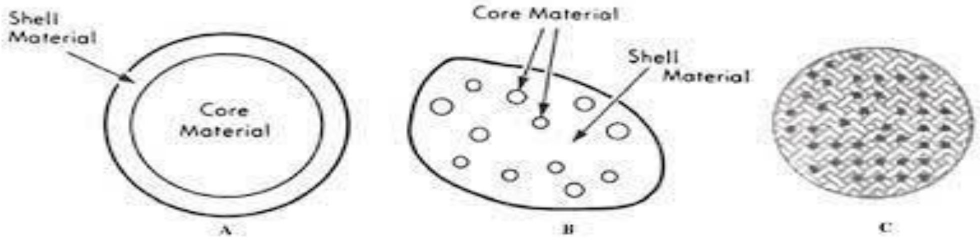
Microencapsulation involves encapsulating solid, liquid, or gaseous active ingredients within another material to shield them from the environment. The active ingredient becomes the core material, while the surrounding material forms the shell. This technique finds applications in various fields, including chemicals, pharmaceuticals, cosmetics, printing. For this reason, widespread interest has developed in microencapsulation technology. The Origins of microcapsule preparation trace back to the 1950s when Green and Schleicher pioneered the production of microencapsulated dyes using complex coacervation of gelatine and gum arabic. This innovation was aimed at manufacturing carbonless copy paper. Today, carbonless copy paper remains one of the foremost applications of microencapsulation technology and continues to be produced commercially. The advancements made in technologies for carbonless copy paper have subsequently paved the way for the development of numerous other microcapsule products in later years.

Microencapsulation has the capability to alter various properties of the encapsulated substance, including its color, shape, apparent density, volume, durability, reactivity, heat sensitivity, pressure sensitivity and photosensitivity. (Lamprecht & Bodmeier, n.d.) (C.A. Finch, Chem. Ind. (London) 1985, 752 – 756) It offers a method for transforming liquids into solids, altering the surface properties of alternative materials, providing environmental protection and controlling the release characteristics or availability of coated substances. (Khan et al., 2017)

During the 1960s, researchers reported the microencapsulation of cholesterol liquid crystal using complex coacervation of gelatine and acacia, leading to the creation of thermo sensitive display material. Additionally, J.L. Fergason developed the nematic curvilinear aligned phase (NCAP), liquid crystal display system achieved through the microencapsulation of nematic liquid crystal. This encapsulation technology has significantly contributed to expanding display areas and achieving wider viewing angles. In defence application, microencapsulation technology is utilized to create self healing composites, integral to aerospace structures. Additionally, it's employed in designing specialized fabrics for military personnel, enhancing their chemical protection against warfare agents. Thus, since the mid-1970s, microencapsulation has gained popularity not only in the pharmaceutical industry but also in various other products and daily life processes. (MOYER, 1949) (Cowsar, 1980)

II. MATERIALS INVOLVED IN MICROENCAPSULATION

Microencapsulation involves enveloping individual particles or droplets of solid or liquid material with a continuous polymeric film, resulting in the formation of microcapsules typically ranging from micrometers to millimetres in size. (Mali Snehal et al., 2013)



Core material:

The material to be coated

- May exist in liquid or solid form
- Liquid cores can consist of dissolved or dispersed material
- Composition of coating material:

1. Active constituents or Drug
2. Stabilizers
3. Release rate enhancers
4. Additives such as diluents (Mali Snehal et al., 2013)

A wide range of materials have been encapsulated. These comprises of:

1. Foods: Oils, Fats, Flavors, Spices
2. Pharmaceuticals: Proteins, Antidepressants, Antibiotics, Aspirin
3. Solvents: Paraffin, Esters, Ethers, Alcohols, Benzene, Toluene
4. Colorants: Dyes and pigments, especially leuco dyes for carbonless copying papers.
5. Agricultural chemicals: Insecticides, fertilizers, herbicides
6. Fragrances: Essences, menthol
7. Catalyst: Oxidants, curing agents, reducing agents, free radicals initiators
8. Adhesives: Epoxy resins, polysulphides, cyanoacrylates, thermally sensitive adhesive compositions
9. Others: Detergents, bleaches, fire retardants (Lamprecht & Bodmeier, n.d.)

Coating material:

The substance coats the core with the desired thickness and is compatible with the core material, aiding in its stabilization. It must also be inert toward active ingredients, enabling controlled release under specific conditions. The coating can vary in flexibility, brittleness, hardness etc. In addition, it should be abundantly and cheaply available. The composition typically includes an inert polymer, colouring agent, and plasticizer. (Mali Snehal et al., 2013)

Classification of coating materials:

- Water soluble resins –Gelatin, Starch, Hydroxy ethyl cellulose
- Water insoluble resins -Ethyl cellulose, Polyethylene , Polyamide , Poly methyl acrylate
- Waxes and lipids -Bees wax , Stearic acid ,Steryl alcohol (Print et al., 2021)

Properties of Coating Material:

- Microencapsulation helps stabilize the core material protecting it from degradation caused by external factors such as light, moisture and oxygen.

- The encapsulation process results in a film-forming, tasteless, pliable, and stable coating around the core material.
- The coating can exhibit various characteristics such as flexibility, hardness, brittleness, thickness depending on the desired properties of the microcapsule.
- Microencapsulation enables controlled release of the encapsulated substances under specific conditions, providing precise delivery of the active ingredients.
- The ideal characteristics of microencapsulation include being low viscosity, non-hygroscopic and cost effective, ensuring efficient production and storage of the encapsulated material.
- The material for microencapsulation should be soluble in aqueous media or solvent or capable of melting, facilitating the encapsulation process. (M. A. Garg et al., 2022)

Reasons for Microencapsulation:

1. Microencapsulation is primarily utilized for sustained or prolonged drug release. It's commonly employed to mask the taste and odour of medications, enhancing patient compliance. Additionally, this technique can convert liquid drug into free- flowing powders and stabilize drugs sensitive to oxygen, moisture or light. (Kumar et al., 2020)
2. Microencapsulation also helps to prevent incompatibilities among drugs and prevents the vaporizations of volatile drugs like methyl salicylate and peppermint oil.(Kumar et al., 2020)
3. Micro encapsulations have been employed to reduce the toxicity and gastrointestinal irritation of various drugs, including ferrous sulphate and potassium chloride. It can also facilitate alteration in the site of absorption. Toxic chemicals like insecticides can be microencapsulated to minimize the risk of sensitization of factory workers. Bakan and Anderson demonstrated that microencapsulated vitamin A palmitate exhibited enhanced stability. (Kumar et al., 2020)
4. Microencapsulation serves to protect reactive substances from the environment, shielding them from factors such as light, oxygen, moisture that may degrade or alter their properties. (Yongo et al., 2016)

Advantages of Microencapsulation:

- Micro-organisms and enzymes can be immobilized using microencapsulation techniques. For instance, enzymes have been encapsulated in cheese to expedite ripening and enhance flavour development, protecting them from low PH and ionic strength within the cheese environment. Similarly, encapsulation of micro-organisms has been employed to enhance the stability of starter cultures. (Mali Snehal et al., 2013)
- Microencapsulation provides protection against various environmental factors such as UV radiations, oxidation, heat, bases and acids. For example: it can be used to protect colorants and vitamins from degradation caused by these factors. (Mali Snehal et al., 2013)
- Microencapsulation can effectively mask taste and odour, improving the palatability and acceptability of various products, including pharmaceuticals and food supplements. (Mali Snehal et al., 2013) . Microencapsulation has the capability to mitigate the volatility, flavour and reactivity of food ingredients. (Jackson & Lee, 1991)
- There is an increasing demand for nutritious food for children, providing essential vitamins and minerals during their developmental years. Microencapsulation offers a solution to deliver these crucial ingredients in a child-friendly and palatable manner, enhancing their consumption and overall health. (Mali Snehal et al., 2013)
- It can enhance the visual aspect of products and contribute to innovative marketing concepts. By encapsulating ingredients that add visual appeal or unique properties, such as vibrant

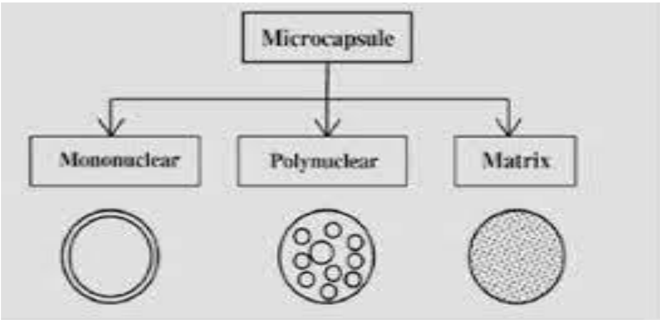
colors or enticing textures, companies can differentiate their products and attract consumers with novel offerings. (Mali Snehal et al., 2013)

- Pesticides are encapsulated to enable gradual release over time, allowing farmers to apply them in smaller amounts. This approach reduces the need for highly concentrated and toxic initial applications, as well as the necessity for repeated applications to combat efficacy loss due to factors like leaching, evaporation and degradation. (Mali Snehal et al., 2013)
- Microencapsulation improves shelf life by preventing degradative reactions such as degradation and oxidation, thereby maintaining the quality and efficacy of the encapsulated ingredients for longer periods. (Mali Snehal et al., 2013)
- Microencapsulation allows for the mixing of incompatible compounds, enabling the encapsulation of migraine medication and other substances that may not normally be compatible. (Mali Snehal et al., 2013)

Disadvantages of Microencapsulation:

- The microencapsulation technique may not be adaptable to all the types of core materials due to their inherent properties and compatibility with the encapsulation process. (T. Garg et al., 2012) (Leon L. 1991)
- In some cases, coating may be incomplete or discontinuous, leading to variations in the encapsulation process. (T. Garg et al., 2012) (Leon L. 1991)
- The microencapsulation process can be quite expensive due to the specialized equipment and materials required. (T. Garg et al., 2012) (Ansel H.C.)
- Sensitive pharmaceuticals cannot be utilized due to inadequate stability and shelf life resulting from microencapsulation. (T. Garg et al., 2012) (Ansel H.C.)
- Microencapsulation requires sterilization and necessitates carriers to be non-allergenic, biocompatible and biodegradable in nature, among other considerations. (T. Garg et al., 2012) (Leon L. 1991)
- Much of the information regarding microencapsulation remains patented, making it challenging to select suitable techniques and methodologies for individual applications. (T. Garg et al., 2012)
- Coated products may display non-reproducible and unstable release characteristics and could also be too bulky for certain applications. (T. Garg et al., 2012) (Ansel H.C.)
- Micro particles may not be suitable for parenteral applications due to size restrictions, limiting their use in certain medical treatments. (T. Garg et al., 2012) (Ansel H.C.)

Classification of Microencapsulation:



1. Mononuclear: Mononuclear microcapsules consist of a core-shell structure, with the shell surrounding the core. (M. A. Garg et al., 2022)
2. Poly-nuclear: Poly-nuclear capsules feature multiple cores enclosed within a single shell structure. (M. A. Garg et al., 2022)
3. Matrix type: In matrix encapsulation, the core material is uniformly distributed within the shell material. (M. A. Garg et al., 2022)

Important features of Microcapsules:

- The total surface area is inversely proportional to the diameter, as the diameter decreases, the surface area increases. (M. A. Garg et al., 2022)
- This large surface area is available for various processes such as adsorption, desorption, chemical reactions and light scattering.
  For instance, the total surface area of 1 cubic millimetre of hollow microcapsules with a diameter of 0.1mm has been reported to be

approximately 60 square meters. (M. A. Garg et al., 2022)

Techniques for manufacturing of micro- encapsulations:

(A): Physical Methods:

- Air suspension coating
- Spray drying
- Fluid Bed coating
- Pan coating
- Centrifugal extrusion
- Spray chilling
- Multi-Orifice centrifugal process

(B): Chemical Methods:

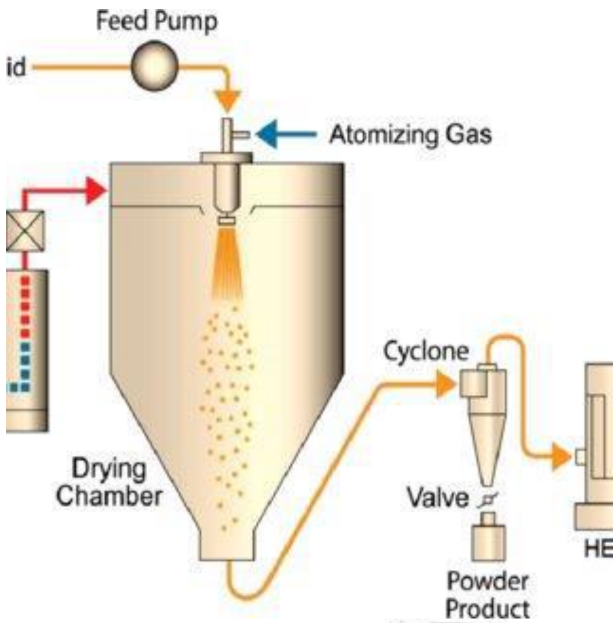
- In-situ Polymerization
- Coacervation Phase separation
- Matrix polymerization
- Solvent extraction
- Solvent evaporation

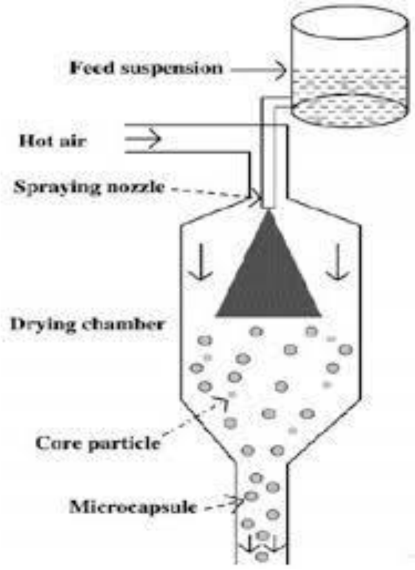
(A) Air suspension coating:

This technique, also known as Fluidized Bed Coating or Wurster coating, involves suspending particles in an upward-moving air stream. Solid, Non-volatile cores larger than 50 micrometers in size are placed at the bottom of the Fluid bed coater. The coating solution is sprayed while a non-turbulent, high-velocity air stream is introduced upward, fluidizing the solid cores and carrying them upwards. Most of the rising air (usually heated) flows inside the cylinder, causing the particles to rise rapidly. As the cores ascend, they are coated with the coating material, and the solvent evaporates. By the time they reach the upper chamber, the cores becomes heavier, the air expands, loses its pressure and can no longer carry the cores. This entire process takes just 10 seconds, and the cores continuously accumulate the coating with each passage. The process concurrently applies and dries the coating material onto fluidized cores. Air-suspension coating of particles with solutions or melts offers superior control and flexibility. (T. Garg et al., 2012) (Leon L., 1991) . The air suspension process presents a diverse range of candidate coating material for microencapsulation. (Jyothi Sri et al., 2012)

The process involves repeating the steps of suspending, spraying and cooling until the capsule walls reach the desired thickness. When the spray nozzle is positioned at the bottom of the fluidized bed of particles, this method is known as the Wurster process. Both the fluidized bed coating and the Wurster process are variations of the pan coating method. (Mali Snehal et al., 2013)

The rate of drying is directly proportional to the temperature of the airstream, which can be adjusted to further influence the properties of the coating. (M. A. Garg et al., 2022)





Advantages:

- Quick coating process
- Simple process requiring no expertise or skilled labor.
- Applicable to most solid cores regardless of size and shape, and compatible with a wide range of coating materials.
- Provides complete environmental protection, eliminating hazards to operators and minimizing the risk of contamination.

- The equipments are multipurpose and can be utilized for various applications such as drying, granulation, mixing and more.
- The coating can be applied in various forms including solutions, suspensions, emulsions or melts. (T. Garg et al., 2012)

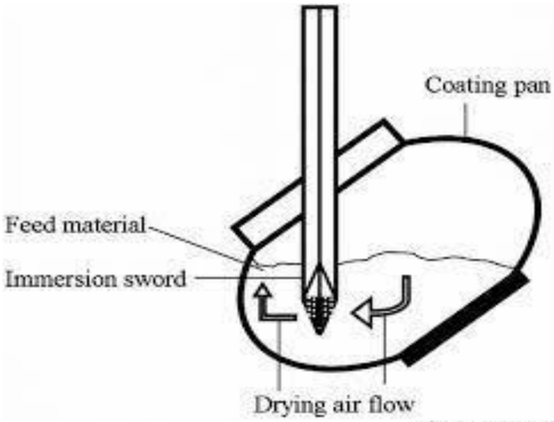
Disadvantages:

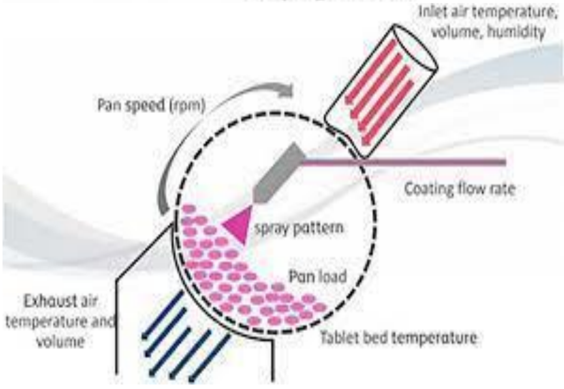
- The size of the cores must be greater than 50 micrometers, and the cores should be non-volatile.
- It is not appropriate for thermo sensitive cores.
- Decreased versatility.
- Higher equipment costs result in increased investment.
- Applicable only to solid cores. (T. Garg et al., 2012)

(B) Pan Coating:

The pan coating process, a longstanding method in the pharmaceutical industry, is one of the oldest industrial procedures for producing small, coated particles. During this process, particles are tumbled in a pan while the coating material is applied gradually. In microencapsulation, solid particles larger than 600 micrometers in size are typically deemed necessary for effective coating. In practice, the coating is typically applied as a solution or atomized spray onto the solid core material in the coating pan. Warm air is passed over the coating materials during application in the coating pans to remove the coating solvent. In some cases, final solvent removal is achieved in a drying oven. (Devi, 2016) (Kasturagi et al. 1995)

Product quality can be controlled by managing variables such as spray pattern, pressure, nozzle size, temperature, distance between the atomizer and the load, rotation speed, angle and the nature of the feed. Factors like the cost of the coating solution, rate of evaporation and the rate of application also play crucial roles. Hydraulic or Airless atomizers are typically preferred for pan coating processes. (T. Garg et al., 2012) (Deasy P., 1995)





Advantages:

- The microencapsulation process offers flexibility in terms of adapting to various core materials, coating materials and desired release characteristics, making it suitable for a wide range of applications. (T. Garg et al., 2012)
- Many companies already possess coating pans, which can be adapted for microencapsulation with relatively minimal modifications. (T. Garg et al., 2012)
- It can be applied to wide range of core and coating materials, offering versatility in formulation and application. (T. Garg et al., 2012)

Disadvantages:

- If roughness, irregularity and size distribution increase, coating quality decreases.
- Production time may extend into weeks, making the process time consuming. (T. Garg et al., 2012)
- Achieving the desired thickness and uniformity requires a significant amount of coating material, resulting in material loss. (T. Garg et al., 2012)

- Microencapsulation is a skilled operation that requires expertise and artistry to achieve optimal results. (T. Garg et al., 2012)
- Due to the large number of variables involved, technical difficulties can arise in obtaining satisfactory coating, making it challenging to control the process effectively. (T. Garg et al., 2012)
- There is a risk of atomization of particles in the atmosphere during the coating process. (T. Garg et al., 2012)
- Microencapsulation may be unattractive for fundamental research due to its more applied and practical nature, compared to more fundamental scientific inquiries. (T. Garg et al., 2012)
- Microencapsulation may not always be considered cost effective, particularly for applications with lower production volumes or where cheaper alternatives are available. (T. Garg et al., 2012)
- It cannot be applied to very fine particles due to limitations in the coating process. (T. Garg et al., 2012)

III. CONCLUSION

In conclusion, this review paper synthesizes the multifaceted landscape of microencapsulation in the pharmaceutical realm. By covering the background, methods, advantages, disadvantages etc, it serves as a valuable resource for researchers and industry professionals seeking a comprehensive understanding of microencapsulation's role in advancing pharmaceutical sciences.

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