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Review Article

Microencapsulation and Nanoencapsulation: A Review

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ABSTARCT

Encapsulation is a process of enclosing the substances within an inert material which protects from environment as well as control drug release. Recently, two type of encapsulation has been performed in several research. Nanoencapsulation is the coating of various substances within another material at sizes on the nano scale. Microencapsulation is similar to nanoencapsulation aside from it involving larger particles and having been done for a greater period of time than nanoencapsulation. Encapsulation is a new technology that has wide applications in pharmaceutical industries, agrochemical, food industries and cosmetics. In this review, the difference between micro and nano encapsulation has been explained. This article gives an overview of different methods and reason for encapsulation. The advantages and disadvantages of micro and nano encapsulation technology were also clearly mentioned in this paper.

Keywords: Microencapsulation, Nanoencapsulation, Core material, Polymers, Control drug release.

INTRODUCTION

Microencapsulation is a rapidly expanding technology in which very tiny droplets or particles of liquid or solid material are surrounded or coated with a continuous film of polymeric material[1]. The microencapsulation procedure was introduced by Bungen burg de Jon and Kan, (1931)[2]. Microencapsulation are involved in converting liquids to solids, which alter colloidal and surface properties, provide environmental protection and control the release characteristics of different coated materials[3,4,5]. Most of the microencapsulated product have diameters between 1 to 1000 µm[6]. A large number of core materials like live cells, adhesives, flavors, agrochemicals, enzymes, pharmaceuticals etc., can be encapsulated. The scanning electron microscopy is used to reveal the structural features of microencapsulated compound[7].

Nanoencapsulation is defined as a technology to encapsulate substances in miniature and refers to bioactive packing at the nanoscale range[8]. The delivery of any bioactive compound to various sites within the body is directly affected by the particle size[9,10]. Thus, nanoencapsulation has the potential to enhance bioavailability, improve controlled release, and enable precision targeting of the bioactive compounds in a greater extent than microencapsulation[11]. Nanoparticles are colloidal-sized particles with diameters ranging from 10 to 1,000 nm and are expressed both as nano capsules and nanospheres[12]. Nanocapsules are vesicular systems in which the bioactive compound is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems where the bioactive compound is uniformly dispersed (Figure. 1)[13]. Nanoencapsulation of therapeutic agents increases their efficiency, specificity and targeting ability[14].

Reason for Microencapsulation

The primary reason for microencapsulation is found to be either for sustained or prolonged drug release.

This technique has been widely used for masking taste and odor of many drugs to improve patient compliance.

The liquid drugs can be converted into a free flowing powder.

The drugs which are sensitive to moisture light and oxygen can be protected by microencapsulation.

Incompatibility among the drugs can be prevented by microencapsulation.

The drugs, which are volatile in nature and vaporize at room temperature, can be prevented by microencapsulation.

Many drugs have been microencapsulated to reduce toxicity and GI irritation including ferrous sulphate and KCl.

Alteration in site of absorption can also be achieved by microencapsulation.

Microencapsulation can be employed to change the site of absorption. This application has been useful for those drugs which have the toxicity at lower pH.

Microencapsulation of vitamin A palmitate provides the enhanced stability, as prevents from oxidation[15,16].

Core Materials for Microencapsulation

The core material are the specific material to be coated which can be liquid or solid in nature. The composition of the core material can be varied, as the liquid core can include dispersed and/or dissolved materials. The solid core be active constituents, stabilizers, diluents, excipients, and release-rate retardants or accelerators. The ability to

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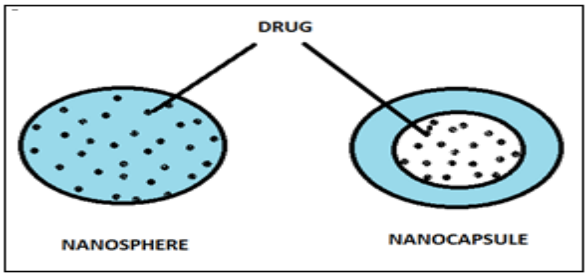

Figure 1: Structure of nanosphere and nanocapsule

vary the core material composition provides definite flexibility and utilization of this characteristic often allows effectual design and development of the desired microcapsule properties[3]. The core material and its characteristics were illustrated in Table 1.

Core Materials for Nanoencapsulation

Core materials such as lipophilic and hydrophilic nutraceuticals compound are used for nanoencapsulation. Hydrophilic compounds are soluble in water but insoluble in lipids and organic solvents, whereas, lipophilic compounds are insoluble in water but soluble in lipids and organic solvents. Some nanoencapsulated hydrophilic compounds are ascorbic acid, polyphenols etc [17,18,19,20]. Nanoencapsulated lipophilic compounds includes lycopene, beta- carotene, lutein, phytosterols and docosahexaenoic acid[17,21,22,23].

Coating Materials for Microencapsulation

The coating material should be capable of forming a film that is cohesive with the core material; be chemically compatible and nonreactive with the core material; and provide the desired coating properties, such as strength, flexibility, impermeability, optical properties, and stability. The coating materials used in microencapsulation methods are amenable, to some extent, to in situ modification. The ideal characteristics of coating material are as stabilization of core material, inert toward active ingredients, controlled release under specific conditions, film forming, pliable, tasteless, stable and non-hygroscopic, no high viscosity, and economic, soluble in an aqueous media or solvent and melting and the coating should be flexible, brittle, hard, thin etc. Examples of coating materials are:

Synthetic polymers

Non-biodegradable polymers e.g. Poly methyl methacrylate (PMMA), Acrolein, Glycidyl methacrylate Epoxy polymers[24,25].

Biodegradable polymers e.g. Lactides, Glycolides & their co polymers[26] Poly alkyl cyanoacrylates Polyanhydrides.

Natural polymers

Proteins: albumin, gelatin and collagen[27].

Carbohydrates: agarose, carrageenan, chitosan, starch[28] and

Chemically modified carbohydrates: poly dextran, poly starch[29].

Coating Materials for Nanoencapsulation

Polymers used in preparation of nanoparticles

The polymers should be compatible with the body in the terms of adaptability (non-toxicity) and (non-antigenicity) and should be biodegradable and biocompatible[30].

Natural polymers

The most commonly used natural polymers in preparation of polymeric nanoparticles are Chitosan, Gelatin, Sodium alginate and Albumin[31].

Synthetic polymers

There are many synthetic polymers like Polylactides(PLA), Polyglycolides(PGA), Poly(lactide co-glycolides) (PLGA), Polyanhydrides, Polyorthoesters, Polycyanoacrylates, Polycaprolactone, Poly glutamic acid, Poly malic acid, Poly(N-vinyl pyrrolidone), Poly(methyl methacrylate), Poly(vinyl alcohol), Poly(acrylic acid), Poly acrylamide, Poly(ethylene glycol), Poly(methacrylic acid) etc[31].

Different Methods of Microencapsulation

Air suspension coating
Coacervation phase separation
Centrifugal extrusion process
Spray drying and spray congealing
Pan coating method
Solvent evaporation techniques
Polymerization process

Air Suspension Coating

Air suspension coating consists of the dispersing of solid particulate core materials in a supporting air stream and the spray coating of the air suspended particles. Within coating chambers, particles are suspended on an upward moving air stream. The design of the chamber and its operating parameters effect a re-circulating flow of the particles through the coating zone portion of the chamber, where is a coating material, usually a polymer solution is spry-applied to the moving particles[32].

Coacervation Phase Separation

Microencapsulation by coacervation phase separation consists of three steps[33]:

Formation of three immiscible phases; a liquid manufacturing phase, a core material phase and a coating material phase.

Deposition of the liquid polymer coating on the core material.

Rigidizing the coating usually by thermal, cross linking or desolation techniques to form a microcapsule.

Centrifugal Extrusion Method

Liquids are encapsulated using a rotating extrusion head containing concentric nozzles. In this process, a jet of core liquid is surrounded by a sheath of wall solution or melt. As the jet moves through the air it breaks, into droplets of core, each coated with the coating material solution. While the droplets are in flight, molten coating material may be hardened or a solvent may be evaporated from the coating material solution. Since most of the droplets are within ± 10% of the mean diameter, they land in a narrow ring around the spray nozzle. Hence, if needed, the capsules can be hardened after formation by catching them in a ring-shaped hardening bath[16].

Spray Drying and Spray Congealing

Spray drying and spray congealing processes are similar in that both involve dispersing the core material in liquefied coating substance and spraying or introducing the core coating mixture into some environmental condition, whereby relatively rapid solidification of the coating is

Table 1: Core material and its characteristics[6]

Core Material	Characteristic Property	Purpose of Encapsulation	Final Product Form
Acetaminophen	Slightly water soluble solid	Taste-masking	Tablet
Activated Charcoal	Adsorbent	Selective absorption	Dry powder
Aspirin	Slightly water soluble solid	Taste masking, sustained release; reduce gastric irritation; separation of incompatibles	Tablet or capsule
Islet of Langer Hans	Viable cells	Sustained normalization of diabetic condition	Injected
Isosorbide di nitrate	Water soluble solid	Sustained release	Capsule
Liquid crystals	Liquid	Conversion of liquid to solid; stabilization	Flexible film for thermal mapping of anatomy
Menthol/methyl salicylate camphor mixture	Volatile solution	Reduction of volatility; sustained release	Lotion
Progesterone	Slightly water soluble solid	Sustained release	Varied
Potassium chloride	Highly water soluble solid	Reduced gastric irritation	Capsule
Urease	Water soluble enzyme	Perm selectivity of enzyme, substrate and reaction products	Dispersion
Vitamin-A Palmitate	Non-volatile liquid	Stabilization to oxidation	Dry powder

affected. The principle difference between the two methods is the means by which coating solidification is accomplished. Coating solidification in the case of spray during is effected by rapid evaporation of solvent in which the coating material is dissolved. Coating solidification in spray congealing method, however, is accomplished by thermally congealing a molten coating material or by solidifying the dissolved coating by introducing the coating core material mixture into a nonsolvent. Removal of the nonsolvent or solvent from the coated product is then accomplished by sorption extraction or evaporation techniques[34,35.]

Pan Coating Method

The pan coating process, widely used in the pharmaceutical industry, is among the oldest industrial procedures for forming small, coated particles. The particles are tumbled in a pan while the coating material is applied slowly. With respect to microencapsulation, solid particles greater than 600 μm in size are generally considered essential for effective coating. In practice, the coating is applied as a solution or as an atomized spray to the desired solid core material in the coating pan. Usually, to remove the coating solvent, warm air is passed over the coated materials as the coatings are being applied in the coating pans. In some cases, final solvent removal is accomplished in drying oven [36,16].

Solvent Evaporation Techniques

This technique has been carried out in a liquid manufacturing vehicle. The microcapsule coating is dissolved in a volatile solvent, which is immiscible with the liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation, the core coating material mixture is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microcapsule. The mixture is then heated (if necessary) to evaporate the solvent for the polymer. In the case in which the core material is dispersed in the polymer solution, polymer shrinks around the core. In the case in which core material is dissolved in the coating polymer solution, a matrix - type microcapsule is formed. Once all the solvent for the polymer is evaporated, the liquid vehicle temperature is reduced to ambient temperature (if required) with continued agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrates or isolated as powders. The solvent evaporation technique to produce microcapsules is applicable to a wide variety of liquid and solid core materials. The core materials may be either water - soluble or water - insoluble materials. A variety of film - forming polymers can be used as coatings[37].

Polymerization Process

The method involves the reaction of monomeric unit located at the interface existing between a core material and a continuous phase in which the core material is dispersed. The continuous or core material supporting phase is usually a liquid or gas and therefore the polymerization reaction occurs at a liquid-liquid, liquid-gas, solid-liquid or solid-gas interface[38].

Nanoencapsulation Techniques

Nanoencapsulation techniques use either top-down or bottom-up approaches for the development of nanomaterials.

Top-down approach

A top-down approach involves the application of precise tools that allow size reduction and structure shaping for desired application of the nanomaterials being developed. Techniques such as emulsification and emulsification–solvent evaporation are used under the top-down approach[39].

Bottom-up approach

In the bottom-up approach, materials are constructed by self-assembly and self-organization of molecules, which were influenced by many factors including pH, temperature, concentration, and ionic strength[39]. Supercritical fluid technique, inclusion complexation,

Table 2: Advantages and Disadvantages of Some Encapsulation Methods.

Encapsulation Method	Principle	Advantages	Disadvantages
Spray drying	Dispersion of the core material in a entrapment material, followed by atomization and spraying of the mixture in a hot air desiccant into a chamber	a) Low process cost; b)Wide choice of coating material; c)Good encapsulation efficiency; d) Good stability of the finished product; e)Possibility of large-scale production in continuous mode	a) Can degraded highly temperature sensitive compounds; b) Control of the particle size is difficult; c) Yields for small batches are moderate
Spray cooling/chilling	The same of the spray drying differing only that the air desiccant is cold	Temperature-sensitive compounds can be encapsulated	Difficult control of the particle size; moderate yields for small batches; special handling and storage conditions can be required
Simple extrusion	Forcing a core material in a molten wall material mass through a die (laboratory scale) or a series of dies of a desired cross section into a bath of desiccant liquid. The coating material hardens on contacting liquids, entrapping the active substances	a) The material is totally surrounded by the wall material; b) Any residual core is washed from the outside; c) It is a relatively low-temperature entrapping method	a) The capsule must be separated from the liquid bath and dried; b) It is difficult to obtain capsules in extremely viscous carrier material melts
Centrifugal extrusion	Similar of simple extrusion differing that the core material and coating material form a unified jet flow only at the end through a nozzle with a coaxial opening (coextrusion) by centrifugal force	The same of simple extrusion	The same of simple extrusion
Ionic gelation	Coating material with dissolved core material is extruded as drops within an ionic solution. The capsules are formed by ionic interaction	Organic solvents and extreme conditions of temperature and pH are avoided	a) Mainly used on a laboratory scale; b) The capsules, in general, have high porosity which promotes intensive burst
Thermal gelation	The principle is almost the same of ionic gelation' principle, nonetheless there is no necessity of an ionic solution to form a gelled drop, the gelation is only due to thermal parameters	The same of ionic gelation	The same of ionic gelation
Fluidized bed coating	This technique relies upon by nozzle spraying the coating material into a fluidized bed of core material in a hot environment	a) Low cost process; b) It allows specific capsule size distribution and low porosities into the product	Degradation of highly temperature- sensitive compounds
Lyophilizaton/ Freeze drying	The entrapment occurs by lyophilization of an emulsion solution containing a core material and a coating material	Thermosensitive substances that are unstable in aqueous solutions may be efficiently encapsulated by this technique	a) Long processing time; b) expensive process costs; c) expensive storage and transport of the capsules

Inclusion complexation	Particular apolar molecules are entrapped through a hydrophobic interaction inside the β-Cyclodextrin cavity replacing water molecules	Very efficient to protect unstable and high added value apolar compounds such as flavors	a) Encapsulation restricted to apolar compounds with a suitable molecular dimensions; b) β cyclodextrin price is expensive; c) frequently undesirable release of the formed complex
Emulsion polymerization	Core material is dissolved into polymerization solution. The monomers are polymerized to form capsules in an aqueous solution	Micro-nanocapules with narrow size distribution can be obtained	a) Difficult control of the capsule formation (polymerization)
Coacervation	The entrapment is due to the deposition of a liquid coating material around the core material by electrostatic attraction	Can be used to encapsulate heat-sensitive ingredients due to done at room temperature	a) Toxic chemical agents are used; b)The complex coacervates are highly unstable; c) There are residual solvents and coacervating agents on the capsules surfaces; d) spheres low size range; e)expensive and complex method
Emulsion Phase Separation	The core material is added in the polar or apolar layer of an oil-in-water emulsion - O/W or water-in-oil - W/O emulsion. The emulsions are prepared using a surfactant	a) Polar, non-polar (apolar), and amphiphilic can be incorporated; b) emulsions can either be used directly in their "wet" state	a) Instable when exposed to environmental stresses, such as heating, drying, etc; b) limited number of emulsifiers that can be used
Liposome entrapment	Phospholipids are dispersed in an aqueous phase spontaneously formation a liposome. A core material is entrapment into a liposome	a) Either aqueous or lipid soluble material can be encapsulated; b) suitable to high water activity applications; c) efficient controlled delivery	Mainly used on a laboratory scale

coacervation, and nanoprecipitation comes under the bottom-up approach[40,41].

Hydrophilic and lipophilic nanoencapsulation techniques

Nanoencapsualtion techniques can also be used for encapsulation of various hydrophilic and lipophilic bioactive compounds. Emulsification, coacervation, and supercritical fluid technique are used for encapsulation of both hydrophilic and lipophilic compounds[42,43,44]. However, inclusion complexation, emulsification–solvent evaporation, and nanoprecipitation techniques are mostly used for lipophilic compounds[45].

Advantages of Microencapsulation

The microencapsulated ingredients can be added at any time in the processing and remain unaltered.

Food products have increased nutritional and health benefits[32].

Reliable to deliver the drug to the target site with specificity and to maintain the desired concentration at the site of interest without untoward effects.

Solid biodegradable microspheres have the potential throughout the particle matrix for the controlled release of drug.

Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs to the tumor.

The size, surface charge and surface hydrophilicity of microspheres have been found to be important in determining the fate of particles *in vivo*[46].

Advantages of Nanoencapsulation

Protection of API from degradation.

Targeted drug delivery with surface coating or conjugation.

PEGylation for extended circulation time.

Modification to surface charge can promote cell entry.

Surface function for cell entry.

Fluorescent labelling for imaging[47].

Applications of Microencapsulation

It has wide application in Cell immobilization: i.e. In plant cell cultures, Human tissue is turned into bio-artificial

organs, in continuous fermentation processes and Drug delivery: Controlled release delivery systems.
Microencapsulation techniques is used in beverage production.
This technique is used for protecting the molecules from other compounds
Microencapsulation also protect liquid crystals
It is employed for Quality and safety in food, agricultural & environmental sectors.
Play a major role in textiles**:** means of imparting finishes[48].
Applications of Nanoencapsulation
The basic reason for nanoencapsulation is to protect the core material and to then release it when it is required. Applications for this include:
Targeted drug delivery systems that release the drug only when the drug has arrived at the site in the body where it is required.
Timed release drug delivery where the nanoencapsulation material slowly allows the drug to be released into the body – such as nasal delivery of insulin. The coating material can be customized to determine the rate of delivery.
Embedded fragrances for branded perfumed clothing.
Food additions and food enhancements such as Omega-3 fatty acid additions to bread that do not alter taste.
Increasing shelf life and stability of products like vitamins.

CONCLUSION

There has been substantiate growing interest towards the evaluation of medicinal activity of astaxanthin and its potent use in the nutraceutical as food supplements. However, the unstable nature in the structure of astaxanthin limits its biomedical application. This can be overcome by converting astaxanthin to astaxanthin esters or by encapsulating the astaxanthin. Hence, this paper is mooted out to explore various methods and techniques available for the both micro- and nano- encapsulation of astaxanthin. The pros and cons of various encapsulating agents and encapsulation methods were also discussed. Hence, prospective research should be accomplished to explore the effects of encapsulated astaxanthin on various biological activities and their uses in nutraceutical and pharmaceutical industries.

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