MICROENCAPSULATION

1. Introduction

Microencapsulation is the coating of small solid particles, liquid droplets, or gas bubbles with a thin film of coating or shell material. In this article, the term microcapsule is used to describe particles with diameters between 1 and 1000 μm. Particles <1 μm are called nanoparticles; particles >1000 μm can be called microgranules or macrocapsules.

Many terms have been used to describe the contents of a microcapsule: active agent, actives, core material, fill, internal phase (IP), nucleus, and payload. Many terms have also been used to describe the material from which the capsule is formed: carrier, coating, membrane, shell, or wall. In this article, the material being encapsulated is called the core material; the material from which the capsule is formed is called the shell material.

Although virtually any coating material conceptually is a candidate microcapsule shell material, most commercial microcapsules produced to date utilize a relatively small number of different shell materials. Table 1 lists representative examples of these materials along with typical applications. Microcapsule shell material selection for a specific application is determined by a number of factors including cost, availability, processing ease, and inherent barrier properties. Shell materials for pharmaceutical, food, and personal care products are limited to materials that are approved by regulatory agencies responsible for such products. Defining an optimal shell material for a given application can be complex, since many interacting parameters determine success of a given capsule shell material. Fortunately, many suppliers of candidate shell materials provide valuable information concerning the use of their products in various encapsulation processes.

Microcapsules can have a wide range of geometries and structures. Figure 1 illustrates three possible capsule structures. Parameters used to characterize microcapsules include particle size, size distribution, geometry, actives content, storage stability, and core material release rate. Characterization studies provide valuable insight into the nature of various types of capsules and how they function in specific applications.

Research and development activity throughout the world dedicated to advancing microcapsulation technology is producing a steadily increasing number of commercially successful products that utilize microcapsules. Many established encapsulation processes like spray drying and fluidized bed coating are being refined and improved while new processes continue to be developed. Various reviews of this subject exist (1–6). Pan coating, a well-established means of producing coated particles for the pharmaceutical industry is not discussed because produces particles >1000 μm.

2. Encapsulation Processes

Because there are so many encapsulation processes, various schemes have been created in order to classify them. Some schemes classify encapsulation processes

Table 1. **Shell Materials Used to Produce Commercially Significant Microcapsules**

Shell material	Regulatory status	Chemical class	Encapsulation process	Applications
gum arabic	edible	polysaccharide	spray drying	food flavors
gelatin	edible	protein	spray drying	vitamins
gelatin–gumarabic[b]	nonedible[a]	protein–polysaccharide complex	complex coacervation	carbonless paper
ethylcellulose	edible	cellulose ether	Wurster process or polymer–polymer incompatibility	oral pharmaceuticals
polyurea or polyamide	nonedible	cross-linked polymer	interfacial polymerization	agrochemicals and carbonless paper
aminoplasts	nonedible	cross-linked polymer	*in situ* polymerization	carbonless paper, fragrances, and adhesives
maltodextrins	edible	low molecular weight carbohydrate	spray drying and desolvation	food flavors
hydrogenated vegetable oils	edible	glycerides	fluidized bed	assorted food ingredients

[a] For intended application, ie, carbonless paper.
[b] Treated with glutaraldehyde.

as chemical or physical even though so-called chemical processes may be based exclusively on physical phenomena while physical processes may involve chemical reactions. This author prefers to simply classify encapsulation processes as Type A or B. Type A processes are defined as those in which capsule formation occurs entirely in a liquid-filled stirred tank or tubular reactor. Type B processes are processes in which capsule formation occurs because a coating is sprayed or deposited in some manner onto the surface of a liquid or solid core material dispersed in a gas phase or vacuum. This latter category includes processes in which liquid droplets containing core material are sprayed into a gas

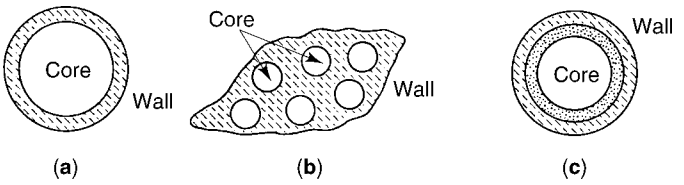

Fig. 1. Schematic diagrams of several possible capsule structures: (**a**) continuous core–shell microcapsule in which a single continuous shell surrounds a continuous region of core material; (**b**) multinuclear microcapsule in which a number of small domains of core material are distributed uniformly throughout a matrix of shell material; and (**c**) continuous core capsule with two different shells.

phase and subsequently solidified to produce microcapsules. Emulsion and dispersion stabilization play a key role in the success of both Type A and B processes.

Differences in some Type A and B processes can be subtle, but significant. For example, solvent evaporation is a key step in spray dry encapsulation protocols (Type B) and protocols involving solvent evaporation from an emulsion (Type A). The difference in these protocols is that evaporation in the former case occurs directly from a liquid to a gas phase, whereas in the latter case evaporation involves transfer of a volatile liquid from a dispersed phase to a continuous liquid phase from which it is subsequently evaporated. Another example is encapsulation by gelation. In Type A gelation processes, the droplets that are gelled and become microcapsules are formed by dispersion in a liquid phase and are gelled in this phase. In Type B gelation processes, droplets formed by atomization or extrusion into a gas phase are subsequently gelled either in the gas phase or a liquid gelling bath.

Representative examples of both types of processes follow. Type B processes tend to be promoted by organizations that sell and service equipment for producing microcapsules. Most Type A processes are developed and used in-house by organizations that produce microcapsules.

2.1. Type A Processes. This process occurs in aqueous media and is used primarily to encapsulate water-immiscible liquids or water-insoluble solids (4,5). In the complex coacervation of gelatin with gum arabic (Fig. 2), a water-insoluble core material is dispersed to a desired drop size in a warm gelatin solution. After gum arabic and water are added to this emulsion, pH of the aqueous phase is typically adjusted to pH 4.0–4.5. This causes a liquid complex coacervate of gelatin, gum arabic, and water to form. When the coacervate adsorbs

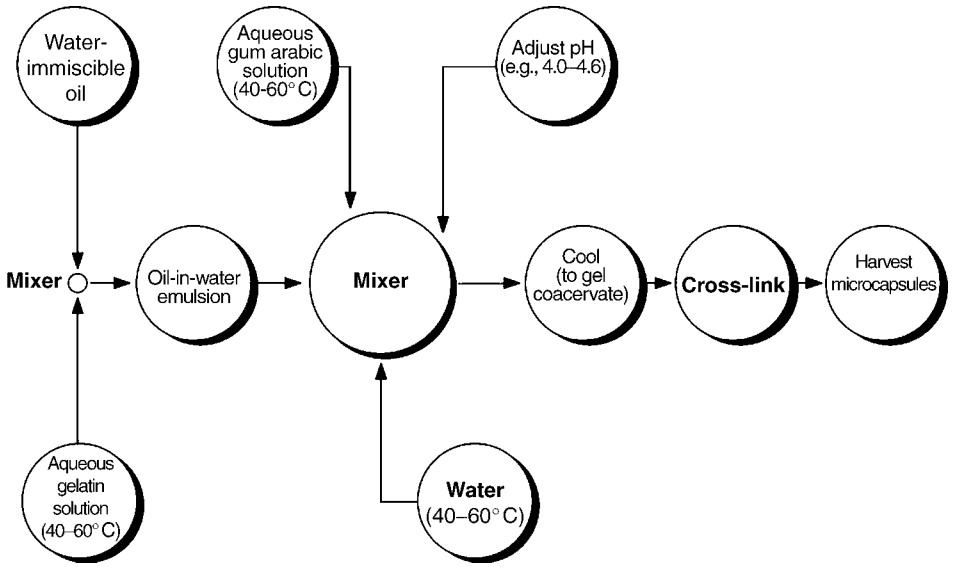

Fig. 2. Flow diagram of a typical encapsulation process based on the complex coacervation of gelatin with gum arabic.

on the surface of the core material, a liquid complex coacervate film surrounds the dispersed core material thereby forming embryo microcapsules. The system is subsequently cooled, often $<10^{\circ}C$, thereby gelling the liquid coacervate shell. After gelation, the coacervate gel typically is chemically cross-linked. For many years, glutaraldehyde was the preferred cross-linking agent, but an enzyme, transglutaminase, has now emerged as a candidate cross-linking agent, particularly when the capsules are for food or cosmetic applications.

Many pairs of oppositely charged polyelectrolytes are able to form a liquid complex coacervate suitable for microcapsule formation. Gelatin normally is the positively charged polyion, because it is readily available and forms suitable complex coacervates with a wide range of polyanions. Polyanions typically used include gum arabic, polyphosphate, poly(acrylic acid), and alginate.

Chemically cross-linked complex coacervate capsule shells generally are highly water swollen, but can be dried in a spray dryer or fluidized-bed dryer. If such capsule shells are treated with urea and formaldehyde under acidic conditions, these materials polymerize within the water-swollen complex coacervate capsule shell greatly thereby increasing the degree of chemical cross-linking, reducing water content of the shell and enhancing ease of drying to a free-flow powder.

A wide variety of capsules loaded with water-immiscible or water-insoluble materials have been prepared by complex coacervation. Capsule size typically ranges from 20 to 1000 μm, but capsules outside this range can be prepared. Although core contents often are 80–95 wt%; capsules with lower loadings can be made. Complex coacervation processes are adversely affected by active agents that have finite water solubility, are surface active, or are unstable at pH values of 4.0–5.0. The shell of dry complex coacervate capsules is sensitive to variations in atmospheric moisture content and becomes plasticized at elevated humidities.

2.2. Simple Coacervation. Aqueous solutions of water-soluble polymers are phase-separated in aqueous media when sufficient salt is added to such solutions. This phenomenon is called simple coacervation. As long as phase separation produces a liquid polymer-rich phase, simple coacervation can be used to produce microcapsules (5). Microcapsules with a gelatin or poly(vinyl alcohol) shell have been formed in this manner. The use of poly(vinyl alcohol) as a capsule shell material is of great interest in various applications because it is a widely available synthetic polymer with excellent oxygen and oil barrier properties.

Two chemically different polymers dissolved in a common solvent usually are incompatible. That is, they spontaneously separate into two liquid phases with each phase containing predominately one polymer. When a core material insoluble in the solvent is dispersed in such systems, it is spontaneously coated by a thin film of the liquid phase that contains the polymer designed to be the capsule shell material; this polymer must be preferentially adsorbed by the core material that is not difficult to arrange. Microcapsules are harvested by desolvating this coating either by chemical cross-linking or addition of a nonsolvent (Fig. 3) (4,5). In the latter case, the embryonic capsule as slurry is often added to a very large excess of nonsolvent in order to minimize capsule agglomeration during isolation.

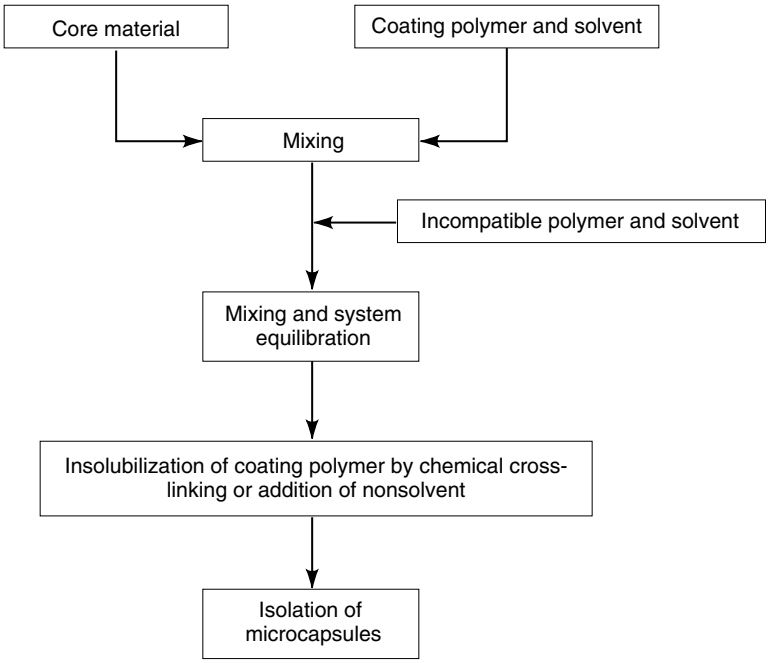

Fig. 3. Flow diagram of typical encapsulation process based on polymer–polymer incompatibility.

Polymer–polymer incompatibility encapsulation processes can be carried out in aqueous or nonaqueous media, but thus far have primarily been carried out in organic media. Core materials encapsulated tend to be polar solids with a finite degree of water solubility. Ethylcellulose historically has been the shell material used. Biodegradable shell materials such as poly(D,L-lactide) and lactide–glycolide copolymers have received much attention. In these latter cases, the object has been to produce biodegradable capsules that carry proteins or polypeptides. Such capsules tend to be <100 μm in diameter and are for oral or parenteral administration (7).

Many types of polymerization reactions can be made to occur at interfaces or produce polymers that concentrate at interfaces thereby producing microcapsules. Accordingly, this approach to encapsulation has steadily developed into a versatile family of encapsulation processes. Figure 4 schematically illustrates five types of encapsulation processes that utilize these types of reactions.

Figure 4**a** represents interfacial polymerization encapsulation processes in which shell formation occurs at the core material—continuous phase interface due to reactants in each phase diffusing and rapidly reacting there to produce a capsule shell (1,8). The continuous phase normally contains a dispersing agent in order to facilitate formation of the dispersion. The dispersed core phase encapsulated can be water, or a water-immiscible solvent. The reactant(s) and coreactant(s) in such processes generally are various multifunctional acid chlorides, isocyanates, amines, and alcohols. For water-immiscible core materials, a multifunctional acid chloride, isocyanate or a combination of these

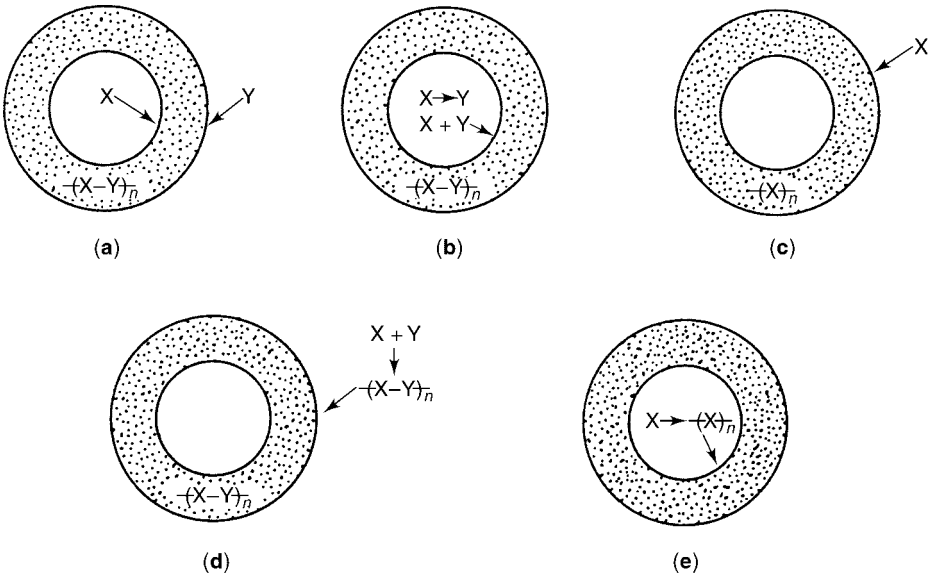

Fig. 4. Schematic diagrams that illustrate the different types of interfacial polymerization reactions used to form microcapsules. Reactants: X, Y; polymerization product: $(X–Y)–n$ or $–(X–)_n$. See text for descriptions of cases (**a**–**e**).

reactants, is dissolved in the core and a multifunctional amine(s) or alcohol(s) is dissolved in the aqueous phase used to disperse the core material. For water or water-miscible core materials, the multifunctional amine(s) or alcohol(s) is dissolved in the core and a multifunctional acid chloride(s) or isocyanate(s) is dissolved in the continuous phase. Both cases have been used to produce capsules.

Figure 5 illustrates the type of encapsulation process shown in Fig. 4**a** when the core material is a water-immiscible liquid. Reactant X, a multifunctional acid

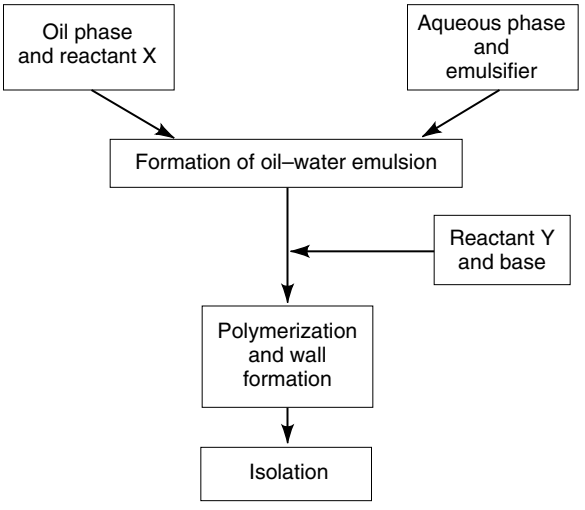

Fig. 5. Flow diagram of typical interfacial polymerization encapsulation process in which reactants X and Y are dissolved in separate mutually immiscible phases (see Fig. 4**a**).

chloride, isocyanate, or combination of these reactants, is dissolved in the core material. The resulting mixture is emulsified in an aqueous phase that contains an emulsifier such as partially hydrolyzed poly(vinyl alcohol) or a lignosulfonate. Reactant Y, a multifunctional amine or combination of amines such as ethylenediamine, hexamethylenediamine, or triethylenetetramine, is added to the aqueous phase thereby initiating interfacial polymerization and formation of a capsule shell. If reactant X is an acid chloride, base is added to the aqueous phase in order to act as an acid scavenger.

A key feature of encapsulation processes (Figs. 4**a** and 5) is that the reagents for the interfacial polymerization reaction responsible for shell formation are present in two mutually immiscible liquids. They must diffuse to the interface in order to react. Once reaction is initiated, the capsule shell that forms becomes a barrier to diffusion and ultimately begins to limit the rate of the interfacial polymerization reaction. This, in turn, influences morphology and uniformity of thickness of the capsule shell. Kinetic analyses of the process have been published (8). A drawback to the technology for some applications is that aggressive or highly reactive molecules must be dissolved in the core material in order to produce microcapsules. Such molecules can react with sensitive core materials.

Figure 4**b** represents the case where a reactant dissolved in the dispersed phase reacts with the continuous phase to produce a coreactant. The coreactant and any remaining unreacted original reactant left in the dispersed phase then proceed to react with each other at the dispersed phase side of the interface and produce a capsule shell. Capsule shell formation occurs entirely because of reaction of reactants present in the droplets of dispersed phase. No reactant is added to the aqueous phase. As in the case of the process described by Fig. 4**a**, a reactive species must be dissolved in the core material in order to produce a capsule shell.

A specific example of the process represented by Fig. 4**b** occurs when a multifunctional isocyanate is dissolved in a liquid, water-immiscible core material and the mixture produced is dispersed in an aqueous phase that contains a dispersing agent. The aqueous phase reacts with some of the isocyanate groups to produce primary amine functionalities. These amino groups react with unreacted isocyanate groups to produce a polyurea capsule shell (9).

Figure 4**c** illustrates interfacial polymerization encapsulation processes in which the reactant(s) that polymerize to form the capsule shell is transported exclusively from the continuous phase of the system to the dispersed phase–continuous phase interface where polymerization occurs and a capsule shell is produced. This type of encapsulation process has been carried out at liquid–liquid and solid–liquid interfaces. An example of the liquid–liquid case is the spontaneous polymerization reaction of cyanoacrylate monomers at the water–solvent interface formed by dispersing water in a continuous solvent phase (10). The poly(alkyl cyanoacrylate) produced by this spontaneous reaction encapsulates the dispersed water droplets. An example of the solid–liquid process is where a core material is dispersed in aqueous media that contains a water-immiscible surfactant along with a controlled amount of surfactant. A water-immiscible monomer that polymerizes by free-radical polymerization is added to the system and free-radical polymerization localized at the core material–aqueous phase interface is initiated thereby generating a capsule shell (11).

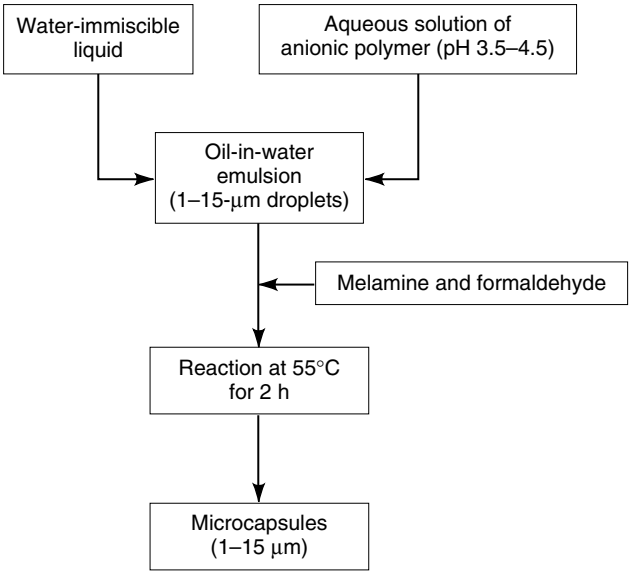

Fig. 6. Flow diagram of microencapsulation process that utilizes acid-catalyzed *in situ* polymerization of melamine or urea with formaldehyde to form a capsule shell (see Fig. 4**d**).

Figure 4**c** also describes the spontaneous polymerization of *p*-xylylene diradicals on the surface of solid particles dispersed in a gas phase that contains this reactive monomer (12) (see XYLYLENE PLOYMERS). The poly(*p*-xylylene) polymer produced forms a continuous capsule shell that is highly impermeable to transport of many penetrants including water. This is an expensive encapsulation process, but it has produced capsules with impressive barrier properties. It is a Type B encapsulation process, but is included here for the sake of completeness.

Figure 4**d** represents *in situ* encapsulation processes (13,14), an example of which is presented in more detail in Fig. 6 (14). The first step is to disperse a water-immiscible liquid or solid core material in an aqueous phase that contains urea, melamine, water-soluble urea–formaldehyde condensate, or water-soluble urea–melamine condensate. In many cases, the aqueous phase also contains a system modifier that enhances deposition of the aminoplast capsule shell (14). This is an anionic polymer or copolymer (Fig. 6). Shell formation occurs once formaldehyde is added and the aqueous phase acidified, eg, pH 2–4.5. The system is heated for several hours at 40–60°C.

A unique feature of *in situ* encapsulation technology is that polymerization occurs in the aqueous phase thereby producing a condensation product that deposits on the surface of the dispersed core material where polymerization continues. This ultimately produces a water-insoluble, highly cross-linked polymer capsule shell. The polymerization chemistry occurs entirely on the aqueous phase side of the interface, so reactive agents do not have to be dissolved in the core material. The process has been commercialized and produces a range of commercial capsules.

Figure 4**e** represents interfacial polymerization processes in which a solution of water-immiscible vinyl monomer(s), vinyl monomer initiator, and core material is dispersed in an aqueous phase that contains a dispersing agent. Polymerization is then initiated, eg, by heating. The polymer produced within the droplets of core material is designed to precipitate or deposit at the core material–aqueous phase interface thereby producing a microcapsule shell. Although this technology was disclosed many years ago, it has not received much use, presumably because the capsules produced do not have acceptable barrier properties.

This encapsulation technology involves removing a volatile solvent from either an oil-in-water, oil-in-oil, or water-in-oil-in-water emulsion (4,15). In most cases, the shell material is dissolved in a volatile solvent such as methylene chloride or ethyl acetate. The active agent to be encapsulated is either dissolved, dispersed, or emulsified into this solution. Water-soluble core materials like hormonal polypeptides are dissolved in water that contains a thickening agent before dispersion in the volatile solvent phase that contains the shell material. This dispersed aqueous phase is gelled thermally to entrap the polypeptide in the dispersed aqueous phase before solvent evaporation occurs (16).

Once the active agent is dispersed in the volatile solvent phase, the dispersion produced typically is emulsified into an aqueous phase that contains a dispersing agent. Solvent used to dissolve the shell material is subsequently removed from this emulsion at atmospheric or reduced pressure. Significantly, solvent evaporation processes can be based on non-aqueous media. In such cases, a volatile organic solvent is removed by evaporation from an organic solvent that has low volatility.

The microcapsules produced by solvent evaporation processes can range in size from $<1\,\mu m$ to over several hundred micrometers. The technique is used often to form drug-loaded microparticles from biodegradable polymer shell materials (15,16). Significantly, solvent removal from the dispersed phase of a solvent evaporation process occurs by partitioning or extraction of volatile solvent into the continuous phase of the emulsion rather than direct evaporation into a gas phase. Solvent is removed from the continuous phase by evaporation. Because of this, a range of mass-transfer events can occur during the solvent evaporation process. These may have a negative effect on microcapsule formation, such as causing loss of core material to the continuous phase. Because of this, solvent evaporation encapsulation processes have also been described as solvent removal, in-liquid drying, or emulsion solvent evaporation encapsulation processes.

A variety of Type A encapsulation processes have used centrifugal force or submerged nozzles to produce microcapsules. For example, a device in which a perforated cup was immersed in an oil bath and spun at a fixed rate has been described (17). An emulsion of core and shell material fed into the spinning cup is thrown in droplet form into the oil outside the spinning cup by centrifugal force. Such droplets are gelled by cooling to thereby yield gel beads loaded with an oil that are subsequently dried.

Capsules have also been produced by extruding in droplet form a liquid core and liquid shell formulation through a submerged two- or three-fluid nozzle into a moving stream of carrier fluid. The liquid shell formulation is gelled, usually by cooling, to yield gel beads that can be dried (18). By using a three-fluid nozzle,

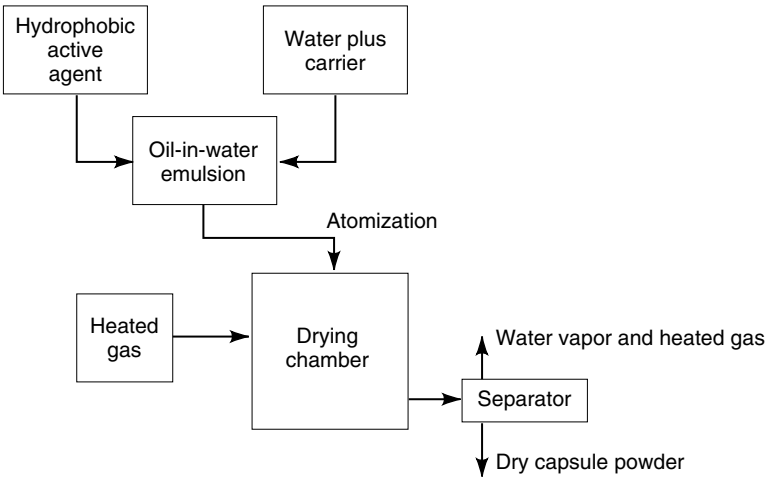

Fig. 7. Flow diagram of a typical spray-dry encapsulation process.

capsules with unique multiple shell structures can be produced. To date, Type A centrifugal force and submerged nozzle encapsulation processes have been used primarily for the encapsulation of various vitamin or flavor oils, and probiotics. The capsules tend to be relatively large and typically are formed from natural shell materials capable of being gelled thermally.

2.3. Type B Processes. Spray-dry encapsulation processes (Fig. 7) consist of spraying an intimate mixture of core and shell material into a heated chamber where rapid desolvation occurs to thereby produce microcapsules (19,20). The first step in such processes is to form a solution of the carrier or shell material in the solvent from which spray drying is to be done. Water is the most common solvent for spray drying. Any film-forming shell material can, in principle, be used, but water-soluble polymers such as gum arabic, modified starch, and hydrolyzed gelatin are used most often. Solutions of these shell materials at 50 wt% solids have sufficiently low viscosities that they still can be atomized without difficulty. It is not unusual to blend gum arabic and modified starch with maltodextrins, sucrose, or sorbitol.

The second step is to disperse the core material being encapsulated in the solution of shell material. The core material usually is a hydrophobic or water-immiscible oil, although solid powders have been encapsulated. A suitable emulsifier is used to aid formation of the dispersion or emulsion. In the case of oil core materials, the oil phase is typically reduced to a drop size of 1–3 μm. This is done in order to minimize free oil on the surface of the dried capsules. Once a suitable dispersion or emulsion has been prepared, it is sprayed into a heated chamber. The small droplets produced have a high surface area and are rapidly converted to a fine powder by desolvation in the chamber. Residence time in the spray-drying chamber is 30 s or less. Inlet and outlet air temperatures are important process parameters as is relative humidity of the inlet air stream.

Capsules produced by spray drying often have a diameter of 10–40 μm. They may be individual particles or aggregates. In either case, capsule geometry varies from irregular to spherical. Core material loadings of commercial

spray-dried capsules typically are 20–30 wt%, although loadings as high as 60 wt% have been reported. The core material is dispersed as small droplets or particles throughout spray-dried capsules. Hydrocolloid carriers such as gum arabic and modified starch produce spray-dried capsules that are dispersible in cold water, but warm or hot water is needed to dissolve them completely. Maltodextrins and hydrolyzed gelatins give capsules soluble in cold and hot water.

Spray-dry encapsulation is a low cost process capable of producing a range of microcapsules in good yield. It is often used to produce commercial capsules loaded with fragrance or flavor oils. A number of research workers have prepared drug-loaded biodegradable capsules by spray drying from nonaqueous media (20). This technology has steadily improved over the years, but the capsules produced may contain a small amount of free or unencapsulated active agent. If this active agent is an oil that contains components capable of oxidizing on storage, an objectionable odor or taste may be produced. Another problem is loss of volatiles during the atomization and drying steps if the active agent contains low boiling, polar active agents such as ethyl acetate and acetaldehyde. Such agents can be difficult to encapsulate by this technology. Their retention is favored by maximizing initial concentration of carrier material.

Spray chilling, cooling, and congealing are essentially variations of conventional spray drying. These processes use a chilled gas to solidify molten capsule shell material formulations rather than volatilize a solvent as is done in the case of spray drying (21,22). Various fats, waxes, fatty alcohols, or fatty acids are used as shell materials. In such encapsulation procedures, the active agent is dispersed in a molten shell material with the aid of an emulsifier if necessary (see EMULSIFIERS). This dispersion is atomized through heated nozzles into a cooling chamber analogous to that shown in Fig. 7. The shell material is solidified by cooling and solid particles are isolated. If the chamber is at room temperature, the coating material has a melting point between 45 and 122°C. If the chamber is cooled, material melting at 32–43°C can be used. Particles produced by this method have water-insoluble shells. The influence of processing temperature on shell material polymorphism, a phenomenon characteristic of many fats, has been discussed (23).

Fluidized-bed encapsulation technology involves spraying shell material in solution or hot melt form onto solid particles suspended in a stream of heated gas, usually air (2,6,24). Although several types of fluidized-bed units exist, so-called top and bottom spray units have been used most often to produce microcapsules. In top-spray units, hot melt shell materials such as fats and waxes are sprayed onto the top of a fluidized-bed of solid particles (25). The coated particles are subsequently cooled producing capsules with a solid shell. This technology is used to prepare a variety of encapsulated water-soluble food and pharmaceutical ingredients. Top-spray units generally are not recommended for applying solutions of shell material because the spray droplets move countercurrent to the gas stream that suspends the fluidized bed. This favors solvent evaporation and deposition of a poor coating of shell material.

In bottom-spray or Wurster units (Fig. 8), the coating material is sprayed as a solution into the bottom of a column of fluidized particles. The freshly coated particles are carried away from the nozzle by the airstream and up into the coating chamber where the coating solidifies due to evaporation of solvent. At the top

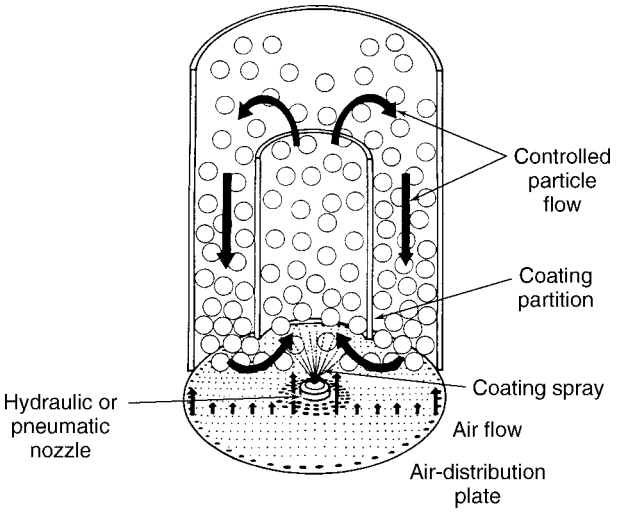

Fig. 8. Schematic diagram of a Wurster coating chamber. (Courtesy of the Coating Place.)

of the column or spout, the particles settle. They ultimately fall back to the bottom of the chamber where they are guided once again by the airstream past the spray nozzle and up into the coating chamber. The cycle is repeated until a desired capsule shell thickness has been reached. Coating uniformity and final coated particle size are strongly influenced by the nozzle(s) used to apply the coating formulation. This technology is routinely used to encapsulate solids, especially pharmaceuticals (qv). It can coat a wide variety of particles, including irregularly shaped particles. The technology generally produces capsules >100–150 μm, but can produce coated particles <100 μm. An important feature of the Wurster process is that it can be used to apply a wide range of coating materials and multiple layers of different coating materials. Candidate coating materials include various water-soluble polymers or hydrocolloids, solvent–soluble polymers, sugars, and pseudolatices. The latter are aqueous dispersions of small polymer particles that fuse together during desolvation to form a continuous capsule shell.

Several Type B encapsulation processes utilize centrifugal force to form microcapsules. In one process, two mutually immiscible liquids, the core and shell material, are pumped through a two-fluid nozzle that is spun rapidly (26). The two-fluid column produced breaks up spontaneously into a series of droplets. Each droplet contains a core region surrounded by a continuous film of fluidized-shell material. The shell is solidified either by cooling or by immersion in a gelling bath to produce microcapsules that can be harvested. In the former case, the shell material is typically a molten wax or fat that has relatively low melt viscosity and solidifies by cooling as it falls away from the nozzle. It may contain a small amount of polymer added in order to toughen the final capsule shell. The core material is typically water or an aqueous solution. In the latter case, the fluidized-shell material typically is an aqueous sodium alginate solution. This solution is gelled ionically by immersion in an aqueous $CaCl_2$ solution

to form a gel bead that can subsequently be dried and isolated. The core material is a water-immiscible liquid. This type of encapsulation technology tends to favor production of larger microcapsules. The lower particle size limit is ~250 μm; the upper particle size limit is several millimeters.

A second Type B encapsulation process that uses centrifugal force is called rotational suspension separation (6). It utilizes a rapidly spinning disk to produce particles of core material surrounded by shell material. The fluidized-shell material formulation, often a wax, fat, or solution of a polymer in these materials, is mixed with particles of core material. The resulting dispersion is fed onto a rotating disk placed at the top of a chamber. Individual particles of liquid-coated droplets are flung off the edge of this disk into the chamber producing solid particles of core material enclosed in a thin film of liquid-shell material. The shell formulation solidifies as the embryonic capsules fall to the bottom of the chamber producing solid microcapsules. Droplets of pure coating material are also flung off the edge of the disk, and fall in a circumferential area or zone below the disk at a closer distance to the disk than the capsules.

A number of hot melt shell formulations have been applied in this manner to produce a range of capsules. It is claimed that the process is capable of rapidly producing capsules <100 μm in large amounts at low cost. Candidate core materials must act like solids on the rotating disk and should have a spherical geometry. Candidate coating formulations must solidify rapidly on cooling and not have high viscosities. For these reasons, preferred shell formulations typically are waxes and fats or polymer solutions in these materials.

This encapsulation technology (Fig. 9) has been used to produce commercial water-soluble capsules loaded with a range of flavor compounds (27,28). Water-soluble shell materials used are maltodextrins, sugars, and gums (qv). The shell material is dissolved in as little water as possible and the core material is dispersed in this solution. Heat, up to 124°C, is used to reduce the viscosity of the shell formulation so that dispersion can be achieved readily. The dispersion of core material and shell formulation is either extruded or atomized into a desolvation solvent. Preferred desolvation solvents are water-miscible alcohols such as 2-propanol or polyglycols. This step solidifies the particles. Because the core materials used in this process are miscible with the desolvation solvents used,

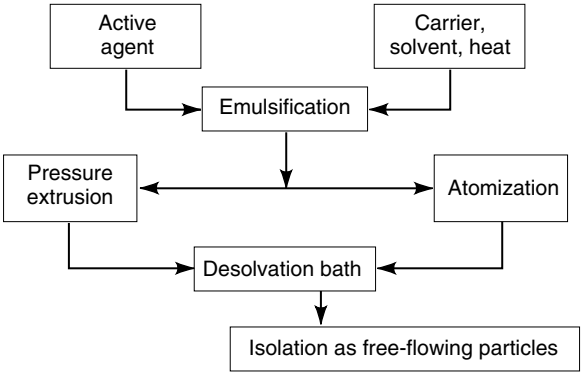

Fig. 9. Desolvation process.

capsules with no free core material are produced. Such capsules have excellent storage stability properties. The problem with this approach to encapsulation has been that it uses solvents other than water that must be recycled. It also produces capsules with relatively low core loadings. Core loadings as high as 15% can be achieved, but forming stable emulsions in the concentrated hot aqueous core solutions used poses serious problems.

A steady stream of encapsulation technologies continues to appear in the patent literature. Some are simply modifications or improvements of established technologies, whereas others are novel new technologies like very low temperature casting (29), deposition of coating material from a supercritical fluid (30), and polymer phase separation induced by evaporation of a volatile solvent from a two component solvent mixture (31).

3. Applications

Microcapsules are incorporated in a number of products produced by the pharmaceutical, graphic arts, food, agrochemical, cosmetic, and adhesive industries. In order to illustrate the wide range of microcapsule applications, it is appropriate to describe briefly a number of commercial microcapsule-based products and the role that microcapsules play in these products.

Carbonless copy paper was the first large-scale commercial application of microcapsules. This product has consumed thousands of tons of capsules annually for many years, although the rate of usage has begun to decline significantly. Figure 10, a schematic diagram of a three-part business form, illustrates the concept of carbonless copy paper. The bottom surface of the top sheet of this form (sheet A) and the second sheet (sheet B) is coated with a layer of small microcapsules. The coating includes inert spacer particles, often starch particles, that are larger than the microcapsules. They protect the microcapsules from

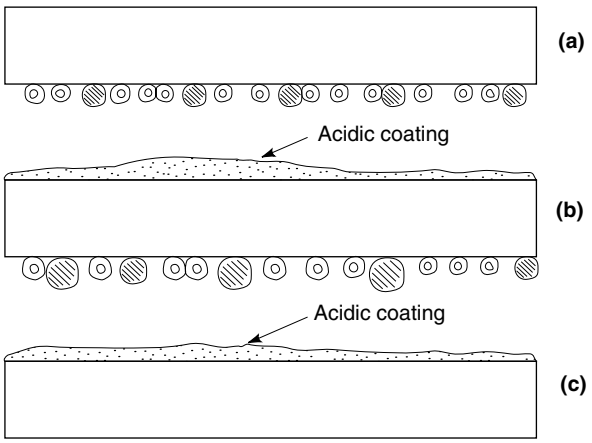

Fig. 10. Cross-section of a three-part business form prepared from carbonless copy paper where are microcapsules and are starch: (**a**), CB sheet; (**b**), CFB sheet; and (**c**), CF sheet.

premature rupture. The capsules, filled with a colorless solution of 2–6% leuco dye dissolved in a high boiling organic solvent, rupture under pressures encountered in normal handwriting or impact printing. The dye solution released is transferred from the bottom surface of sheets A and B to the top surface of sheets B and C, respectively, where it reacts to form an image. The reactive coating on the top surface of sheets B and C contains acidic sites that activate leuco dyes. Reactive materials used often are attapulgite clay (see CLAYS, USES) or phenolic resins. Sheet A in Fig. 10 is called a coated back (CB) sheet; sheet B, a coated front back (CFB) sheet; and sheet C, a coated front (CF) sheet. The capsules and reactive coating can be coated on the same paper surface. In this case, the product is called self-contained carbonless copy paper.

Blythe and co-workers (32) discuss the industrial and commercial aspects of microcapsules for carbonless paper. Such capsules must be small enough to give a sharp image on the reactive coating of the transfer sheet and large enough to be broken by pressures encountered in normal writing and impact printing. The upper size limit is $\sim$20 μm, since capsules larger than this produce a fuzzy image. The lower size limit is $\sim$1–2 μm. Capsules smaller than this tend to fall into the crevices of the paper where they are protected from breakage. Capsules that meet these size requirements and are able to retain leuco dye solutions can be produced by complex coacervation, interfacial polymerization, or *in situ* polymerization. Solvents for dyes used in carbonless copy paper are high boiling (>200°C) organic liquids that experience minimal solvent loss during product storage. Candidate solvents include benzylated ethylbenzene, benzyl butyl phthlate, isopropylbiphenyl, and diisopropylnaphthalene. Solcent choice is determined by cost, availability, toxicity, ability to dissolve the dye system, produce the desired color intensity on the transfer sheet, and form acceptable microcapsules.

Microcapsules have many imaging applications other than carbonless paper. They are used in toners for electrophotography, thermomsensitive printing papers, various thermosensitice recording products, photosensitive recording materials, and thermo-fixing phootosensitive paper (33). Encapsulated liquid crystal formulations coated on polyester film produce a variety of temperature sensitive display products while polyester film coated with capsules loaded with leuco dyes is used as a means of measuring line and force pressures. So-called microencapsulated electronic inks have received much publicity in recent years. They consist of microencapsulated electrophoretic media that change color (eg, black to white) when an electric field is applied to thin microcapsule layers placed between thin electrodes. This color change occurs, because the microcapsules contain a mixture of two color compoonents dispersed in a dielectric fluid. The two color components can conceptually be two different colored particles (eg, white titanium dioxide and carbon black) or particles of one color (eg, titanium dioxide) dispersed in a dyed dielectric fluid. In either case, application of an external electrical field causes the color components to migrate or separate inside the microcapsules thereby forming different colored images. Such inks make it possible to create flexible electronic paper displays that require low power and can receive and display information electronically (34–36).

The concept of microencapsulation has intrigued the pharmaceutical industry for many years, because it offers the possibility of providing a number of

important new oral and parenteral dosage forms. Microcapsules in oral dosage forms can conceptually taste-mask bitter pharmaceuticals, provide extended release *in vivo*, provide enteric release, improve the stability of incompatible drug mixtures, provide resistance to oxidation, reduce volatility, and distribute a drug in many small carrier particles so that effects of the drug on the sensitive walls of the stomach are minimized. Microencapsulated parenteral formulations can provide prolonged delivery of drugs with short half-lives *in vivo* and perhaps even achieve targeted drug delivery. For these reasons, microencapsulation has received much attention by pharmaceutical scientists (37) and yielded a number of commercial pharmaceutical formulations. Initially, many of the microcapsules in these formulations had an ethylcellulose shell and were produced by a polymer–polymer phase-separation process carried out in hot cyclohexane (5). More recent formulations tend to have an acrylic copolymer coating and are prepared by using a fluidized-bed coating process. Core materials encapsulated tend to be solids with finite water solubility. Encapsulated potassium chloride, KCl, has been used extensively because the KCl dispersed in many small capsules minimizes high localized KCl concentrations that can irritate the lining of the stomach and induce bleeding. Encapsulated aspirin for arthritic patients is an example of using microencapsulation to extend time of release of a drug in the gastrointestinal tract (see GASTROINTESTINAL AGENTS). In this case, the encapsulated aspirin formulation provides overnight relief. Finally, encapsulated oral acetaminophen formulations for children are used to provide taste-masking. One application that has received much attention in recent years is the development of microcapsules with a biodegradable poly(lactide-glycoilide) copolymer shell for delivery of vaccines (38,39).

Several commercial parenteral formulations utilize microcapsules. The core materials are polypeptides with hormonal activity. The shell materials are poly(lactide-glycolide) copolymers. The capsules are produced by solvent evaporation, polymer–polymer phase separation, or spray-dry encapsulation processes. Core material release can occur over a 30–90 day period *in vivo*, although not at a constant rate.

Injectable encapsulated leuprolide acetate formulations (LUPRON DEPOT) have developed into a major tool for treating cancer of the prostrate. LUPRON DEPOT dosages that last 30 and 90 days *in vivo* are available. Biodegradable poly(lactide-glycolide) polymers are the shell materials used to form these microcapsules. The capsules are produced by removing volatile solvent from a water-in-oil-in-water emulsion. Okada reviewed their preparation and release behavior (16). An encapsulated formulation of bromocryptin [25614-03-3] is used to inhibit milk production in women after pregnancy. Injectable biodegradable microcapsules loaded with fertility control agents have been under development for a number of years and have been carried to various stages of clinical development (40) (see CONTRACEPTIVES).

The development of injectable microcapsules for delivery of chemotherapy agents remains an active area of research. The ultimate goal is to achieve targeted delivery of chemotherapy agents to specific sites in the body, ideally by injection of drug-loaded microcapsules that would seek out and destroy diseased cells. Intra-arterial infusion chemotherapy is a direct approach to targeted delivery. The clinical applications of microspheres and microcapsules in

embolization and chemotherapy have been assessed (41) (see CHEMOTHERAPEUTICS, ANTICANCER).

The use of microcapsules for a variety of biomedical and biological applications has been promoted for many years (42,43). Several biomedical microcapsule applications are in clinical use or have approached clinical use. One application is the use of liquid-filled microcapsules or microbubbles as ultrasound contrast agents. Such microcapsules can be formed in several different ways (44). Perfluorocarbon-gas-filled microbubbles with a human albumin shell (45) are U. S. Food and Drug Administration (FDA) approved.

Another biomedical application is the encapsulation of live mammalian cells for transplantation into humans. The purpose of encapsulation is to protect the transplanted cells or organisms from rejection by the host. The capsule shell must prevent entrance of harmful agents into the capsule, allow free transport of nutrients necessary for cell functioning into the capsule, and allow desirable cellular products to freely escape from the capsule. This type of encapsulation has been carried out with a number of different types of live cells, but studies with encapsulated pancreatic islets or islets of Langerhans are most common. The alginate– poly(L-lysine) encapsulation process originally developed in 1981 (46) catalyzed much of the cell encapsulation work carried out since. In 1993, Vos and co-workers (47) reviewed the obstacles that must be overcome for successful application of microcapsules in islet transplantation. Work on this approach to islet transplantation has continued. Vos and co-workers (48), recently reported a study of the long-term biocompatibility, chemistry and function of encapsulated pancreatic islets. These authors report that capsules prepared with purified alginate are biocompatible and stable *in vivo* up to 2 years after implantation. Yin and co-workers (49), describe microcapsules loaded with hepatocytes for use in a bioartificial liver assist device.

The microencapsulation or immobilization of a variety of live cells and organisms has been examined. The capsules prepared often are $>1000\,\mu m$ and may not have a well-defined capsule shell, but they are designed to provide many of the capabilities traditionally associated with microcapsules. Rokstad and co-workers (50) evaluated several different types of alginate microcapsules that contained endostatin secreting cells. Park and Chang (51) reviewed the microencapsulation of microbial cells. Goosen discussed the animal cell encapsulation (52). A wide range of applications has been explored including the use of alginate microcapsules gel beads to shorten the handling time for preparing champagne.

Other biomedical and biological applications of microcapsules exist. For example, the encapsulation of enzymes continues to attract interest even though loss of enzyme activity due to harshness of the encapsulation protocols used has been a persistent problem (53). Microencapsulated activated carbons can be used as sorbents to remove metabolic wastes and/or toxins from blood (54). The use of microcapsules in antibody hormone immunoassays has been reviewed (55). The encapsulation of hemoglobin as a red blood substitute has received much attention because of Acquired immune deficiency syndrome (AIDS) and blood transfusions (56).

A number of food ingredients or additives have been encapsulated and are available commercially. Solid ingredients encapsulated are typically

water-soluble and are often encapsulated with a hydrophobic hot melt coating material applied by a fluidized-bed coating process. Preferred hydrophobic coating materials are partially hydrogenated vegetable oils of varying melting points, monoglycerides, and diglycerides. If a hydrophilic coating is used, it tends to be gum arabic, modified starch or mixtures of these materials with a maltodextrin. Such capsules typically are produced by spray drying. All coating materials used are well-accepted food-grade products (see FOOD ADDITIVES).

Several reviews (57–59) and books (60,61) examine in some detail many aspects of the formation, properties and uses of microencapsulated food ingredients. Encapsulation is designed to provide taste-masking, possibly a degree of prolonged release, stabilization of the core material against oxidation, and minimization of reaction with other ingredients in the final product. Dziezak discussed the function of a number of commercially available encapsulated solid food ingredients (62). Acidulants like citric and lactic acid encapsulated in partially hydrogenated vegetable oil are used in meat processing where they provide direct acidification and shorten processing time. Sodium acid pyrophosphate encapsulated in hydrogenated vegetable oil is used in frozen cake batters in order to aid mixing and reduce gas release during batter make-up. In both types of applications, release of core material occurs during a heating cycle that melts the shell formulation and releases the core material. Figure 11 illustrates the nature of commercial NaCl-loaded microcapsules with a lipid coating produced by fluidized-bed coating.

Acidulants like citric, lactic, and fumaric acids encapsulated in a water-soluble maltodextrin shell formulation are used in dry mix beverages and desserts as well as prepared premixes for the baking and dairy industries. The maltodextrin coating is designed to minimize hygroscopicity, reduce dusting, and minimize reactions with incompatible ingredients. It dissolves in the presence of liquid water to rapidly release the contents of the capsules during a mixing

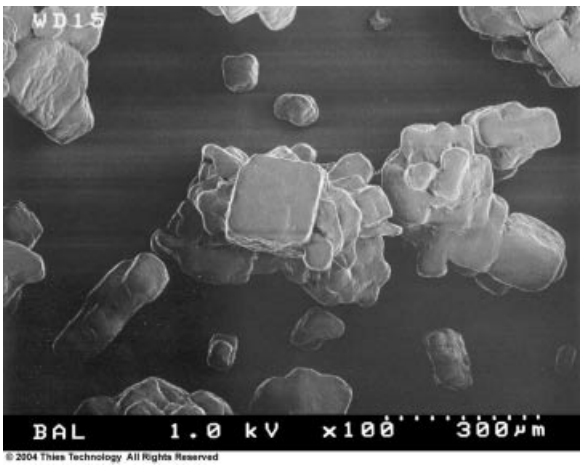

Fig. 11. Scanning electron micrograph of commercial NaCl microcapsules with a lipid coating produced by fluidized-bed coating. Magnification: x. ©2004 Thies Technology.

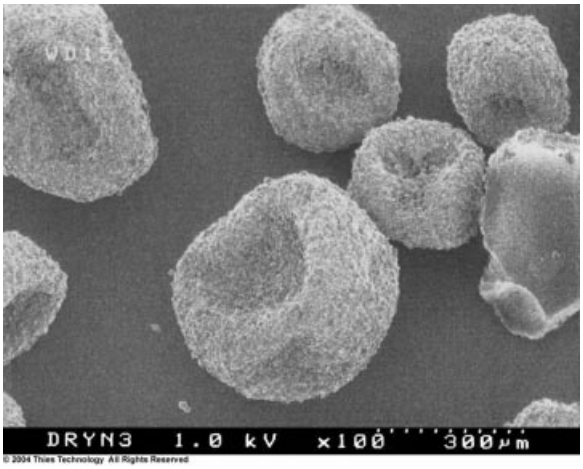

Fig. 12. Scanning electron photomicrograph of commercial PFUA-loaded microcapsules. ©2004 Thies Technology.

cycle. Figure 12 is a photomicrogrpah of commercial spray dried microcapsules that contain an oxygen-sensitive supplement oil.

Various iron compounds have been encapsulated in order to provide food products with enhanced iron contents. Boccio and co-workers (63) studied the bioavailability in mice and storage stability in milk of ferrous sulfate encapsulated with a lecithin shell. They report high bioavailability of the encapslated ferrous sulfate and found that the capsule-containing milk was stable to heat processing (100°C, 30 min) as well as 6 months storage at room temperature.

Calcium proprionate [4075-81-4], and sodium bicarbonate [144-55-8] encapsulated in hydrogenated vegetable oil are used in chemically leavened products. Release typically occurs during the baking cycle due to melting of the hydrogenated shell material. Sodium bicarbonate encapsulated with maltodextrin is used in dry mix baking and other chemically leavened products (see BAKERY PROCESSES, CHEMICAL LEAVENING AGENTS). In this case, release occurs during the mixing step. Sodium chloride [7647-14-5] encapsulated in a hydrogenated vegetable shell is used in various meat products, yeast-containing mixes, and assorted doughs. The capsules are designed to minimize inhibition of yeast activity, rancidity, and excessive salt binding during product storage.

Liquid food ingredients encapsulated traditionally have been oil-soluble flavors, spices, and vitamins (qv). However, in recent years the encapsulation of 3-*n* polyunsaturated fatty acids (PUFAs) for improved cardiovascular health has received much interest. Fish oils contain desired PUFAs and are microencapsulated in order to increase resistance of the PUFAs to oxidation. Encapsulation also provides taste masking. A human feeding study established that the *n*-3 PUFAs in a microencapsulated fish oil have the same desired effect on platlet *n*-3 fatty acid profile as unencapsulated fish oil (64). Figure 12 is a photomicrograph of commercial capsules loaded with PUFAs.

Hydrophobic flavors, food oils, and fats are often encapsulated with a water-soluble shell material applied by spray drying from water (65), but gelatin-based shells formed by complex coacervation can also be used (66). Water-soluble shell

materials applied by spray drying include milk protein (casein), modified starches, gum arabic, maltodextrins or blends of these polysaccharide polymers with maltodextrins. Vitamins are encapsulated with zero bloom strength gelatin by spray drying.

A range of spray-dried flavor-filled capsules with water-soluble shell formulations are used in various dry beverage mixes and other dry food products. Flavors containing ethyl acetate and other low boiling point components pose problems for successful spray-dry encapsulation. Such components are either lost during the initial emulsification process or during the actual dewatering step as a result of azeotrope formation. Another problem with spray-dry encapsulation is the formation of free surface oil. The rapid desolvation that occurs in the drying chamber can produce blow holes in the capsules essentially leaving a small amount of flavor oil or free or surface oil which oxidizes on storage and detrimentally affects product quality. This effect generally limits the flavor content of capsules produced by spray drying to 20–30 wt%. Another approach to the encapsulation of food flavors is desolvation by pressure extrusion. The rod-like particles produced in this manner typically have a relatively low loading (8–10 wt%) although higher loadings (15%) have been reported. The advantage of this technology is that it yields essentially defect-free particles with superb shelf-life storage stability. Macrocapsules loaded with a flavor oil are produced by drop-wise extrusion through a submerged multifluid nozzle. Figure 13**a** shows the outer surface of commercial capsules produced in this manner. Figure 13**b** is a photomicrograph of a cut capsule that shows the thickness of the capsule shell and lack of macrosopic defects in the shell. Another approach to the encapsulation of food flavors, spray chilling, should be particularly well suited to the encapsulation of aqueous flavor compositions. Release occurs during a product heating cycle, eg, bake or microwave.

The food industry increasingly has realized that microencapsulation offers much potential for the development of new products. For example, A. Talwlkar and K. Kailasapathy (67) discuss the effect of microencapsulation on oxygen toxicity in probiotic bacteria, another appplication area of current

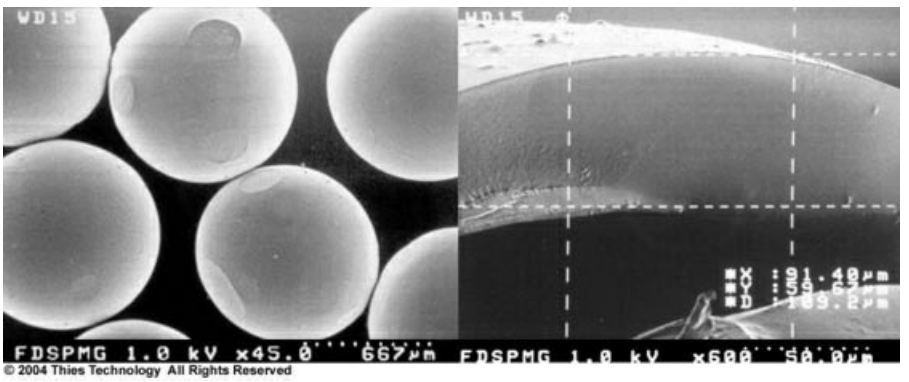

Fig. 13. Scanning electron photomicrographs of commercial flavor-loaded macrocapsules produced by dropwise extrusion through a multifluid submerged nozzle. (A) Outer surface of the capsules. Magnification: x. (B) Cut macrocapsule that shows uniformity and thickness of the capsule shell. Magnification: x. ©2004 Thies Technology.

interest. Hegenbart gives a valuable discussion of the problems that must be overcome when an effort is made to develop microcapsule formulations for use in food products (68).

The microencapsulation of pesticides (qv) herbicides (qv) and other pest control agents has been an active area of development. Several books or book chapters (69–72) summarize much of these efforts. Wilkins (69, pp. 314, 315) and Tsuji (71) list commercial microencapsulated formulations of pest control agents available in 1990 and 1999, respectively. Most of the microcapsules in these formulations are prepared by interfacial polymerization.

Pest control agents are microencapsulated in order to prolong activity while reducing mammalian toxicity, volatilization losses, phytotoxicity, environmental degradation, and movement in the soil. Ideally, encapsulation would also reduce the amount of agrochemical needed. Penncap-M was the first of several encapsulated pesticide formulations commercialized by Atochem North America (Pennwalt) (8). It is sold as an emulsifiable concentrate of encapsulated methyl parathion. The 30–50-μm capsules are prepared by interfacial polymerization. Encapsulation reduces mammalian toxicity of methyl parathion and prolongs its activity. Significantly, the use of highly toxic pesticides, including microencapsulated forms like Penncap-M, is declining. Microencapsulated chlorpyriphos is no longer sold in the United States.

A significant trend in current agrochemical development work is the ongoing transition from highly toxic pesticides to pest control agents with markedly less mammalian toxicity. Examples of the latter include insect pheromones to disrupt mating, insect growth regulators, and pyrethins. Microencapsulation enhances the effectiveness of these compounds. For example, methoprene [40596-69-8], a mosquito growth regulator, has been sold as an encapsulated formulation that provides release over a 5–7-day period in the field. A microencapsulated pyrethin formulation is used to control crawling insects, such as cockroaches. The capsules are sold as an aqueous-based suspension that provides protection for at least 30 days. Field tests indicate effectiveness of the encapsulated pyrethin compares favorably with several nonencapsulated pesticides although the capsule formulation leaves a visible residue. Encapsulated fenitrothion [122-14-5] is also available commercially. The capsules are 20 μm in diameter and have a polyurethane shell formed by interfacial polymerization (73). Commrcial microencapsulated pheromone formulations are available and provide pheromone release in the field for 14–28 days. Figure 14 is a photomicrograph of the outer surface of pheromone-loaded microcapsules produced by interfacial polymerization.

The encapsulation of biopesticides has been studied for many years, but the author is not aware of any commercialed encapsulated biopesticide formulations. Hunter-Fujita and co-workers (74) summarize the techniques and shell materials used to produce past encapsulated biopesticide formulations. More recently, Behle and co-workers (75) describe the storage stability and field activity of a spray dried nucleopolyhedrovirus formulation. Cost and long-term stability of encapsulated biopesticides remain issues to be resolved.

Several encapsulated herbicide formulations exist. Encapsulated alachlor herbicide has been sold as a liquid or dry granule formulation. The capsules, produced by interfacial polymerization, are spherical with a diameter of 2–15 μm.

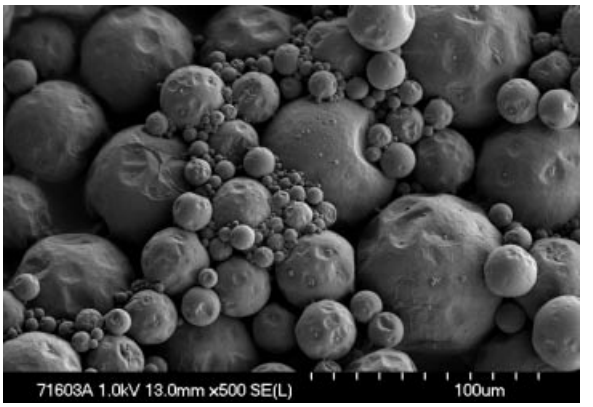

Fig. 14. Scanning electron photomicrograph of pheromone-loaded microcapsules produced by interfacial polymerization. Magnification: x. ©2004 Thies Technology.

Two thiocarbamate herbicides, EPTC and vernolate [1929-77-7], were encapsulated by interfacial polymerization because they are volatile compounds. When applied in unencapsulated form, they must be incorporated in the soil within 2 h in order to provide effective weed control. When applied as a microencapsulated formulation, the rate of volatilization is lower and soil incorporation can be delayed 24 h (76). Microencapsulation of clomazone reduces the risk of bleaching of nontargeted foilage (77).

Various workers have explored the use of microencapsulation as a means of preparing formulations for feeding fish at various stages of development (78). Encapsulated fish food is currently commercially available (79).

Many encapsulated consumer and industrial products exist. Advertising inserts that utilize encapsulated perfumes and flavors contain a coating of scent-filled capsules which break and release scent when the insert is torn open. This product is widely used as a marketing tool, primarily for new perfumes. Various paper products are coated with scent-filled capsules that break when the coated area is rubbed.

Microcapsules are present in a number of personal care and cosmetic products (80). For example, deodorants may contain capsules that release their core contents due to moisture developed because of sweating. Microcapsules are incorporated in various cosmetic creams, powders, and personal cleansing products. Kiyama (81) summarizes the preparation and use of poy(vinyl alcohol) microcapsules in cosmetic products. Miyazawa and co-workers (82), describe the formation of agar capsules designed for cosmetic use. They note that residual glutaraldehyde in capsules with gelatin shells formed by complex coacervation may be an issue for microcapsules intended for cosmetic applications.

Microcapsules are used in several film coatings other than carbonless paper. Encapsulated liquid crystal formulations coated on polyester film produce a variety of temperature sensitive display products including thermometers. Polyester film coated with capsules loaded with leuco dyes analogous to those used in carbonless copy paper is used as a means of measuring line and force pressures.

Microcapsules loaded with phase change materials (PCMs) have been incorporated into various textiles (83). They provide enhanced heat capacity capablity

not easily achieved in other ways. Nelson (84) discusses a variety of textile applications of microcapsules including encapsulated PCMs. Encapsulated PCMs offer much promise as a means of improving the thermal capacity of various heat transfer fluids (85).

Several groups have described the fabrication of microcapsules loaded with a catalyst. Catalysts encapsulated include palladium(II) acetate (86) and osmuim tetraoxide (87). Microencapsulated catalysts are described as effective, easily isolated from a reaction system by filtration and reusable. Shchukin and co-workers (88), recognized that chemical processes can be performed within microcapsules to produce unique products that are retained within the microcapsules. They produced crystalline WO_3 nanoparticles inside microcapsules with a polyelectrolyte shell.

Pernot and co-workers (89) discussed a number of one- and two-component adhesive systems that utilize microencapsules. A majority of fasteners used in automobiles are coated with microcapsules loaded with an adhesive. When the fastener is installed, a fraction of the capsules in the coating rupture releasing the adhesive payload. The adhesive essentially glues the fasteners in place preventing them from becoming loose and causing rattles. The capsules are designed so that only a fraction of them break each time a fastener is taken off and put back. The on/off cycle can be repeated three or four times.

Encapsulated ammonium polyphosphate [10124-31-9] incorporated in plastics acts as a fire retardant. In Japan, microcapsules loaded with naramycin are incorporated into poly(vinyl chloride) (PVC). The capsule-loaded PVC is used to coat a range of electrical cables. Rodents bite and gnaw on cables coated with PVC free of capsules ultimately causing power interruptions, but when rodents bite into cables coated with capsule-loaded PVC coatings, they break the capsules in the coating thereby releasing the naramycin [66-81-9], a taste repellent to the rodents. The encapsulation of fillers and pigments for engineering plastics as well as inks and toners is an active area of development (90).

The oil industry uses microencapsulated oil-field chemicals. For example, microencapsulated breaker is delivered into a subterranean formation where it breaks the fracturing liquid used to stimulate the recovery of fluids such as crude oil or natural gas. Examples of breakers encapsulated include oxidizers, enzymes, and various mineral or organic acids.

Microcapsules designed to serve as inertial confinement fusion targets represent an intriguing potential capsule application that is currently under active development. Schultz and co-workers (91) reviewed the status of this effort in the United States in 1999. Capsules for this application must meet strict spherical geometry and shell thickness uniformity requirements. Tsai and co-workers (92) note that desired properties of candidate shell materials include high gas permeability, high Young's modulus and tensile strength, and good optical transparency. They described the formation of candidate capsules with a polyimide shell by vapor deposition polymerization.

Creation of novel microencapsulation technology and applications of microcapsules are goals that many research and development groups are pursuing globally. Technical deficiencies of current capsules, unanticipated problems in marketing, and poor product design are problems that handicapped past efforts. The growing number of products that utilize microcapsules indicates these issues are increasingly resolved successfully.

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