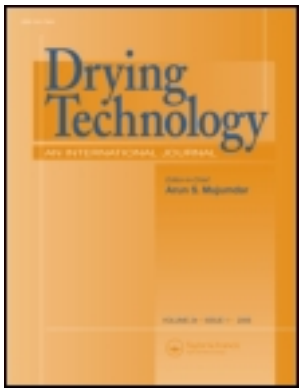

Drying Technology: An International Journal
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/ldrt20

MICROENCAPSULATION BY SPRAY DRYING

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Published online: 27 Apr 2007.

To cite this article: M. I Ré (1998) MICROENCAPSULATION BY SPRAY DRYING, Drying Technology: An International Journal, 16:6, 1195-1236, DOI: 10.1080/07373939808917460

To link to this article: http://dx.doi.org/10.1080/07373939808917460

DRYING TECHNOLOGY, 16(6), 1195–1236 (1998)

MICROENCAPSULATION BY SPRAY DRYING

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Key Words: drug delivery systems; entrapment; flavours; microcapsules; microspheres; retention; volatiles

ABSTRACT

Spray drying technique has been widely used for drying heat-sensitive foods, pharmaceuticals, and other substances, because of the solvent rapid evaporation from the droplets. Although most often considered a dehydration process, spray drying can also be used as an encapsulation method when it entraps 'active' material within a protective matrix, which is essentially inert to the material being encapsulated. Compared to the other conventional microencapsulation techniques, it offers the attractive advantage of producing microcapsules in a relatively simple continuous processing operation. This chapter will present a brief overview of the main considerations involved in the application of spray drying for microencapsulation, with a special emphasis given to microencapsulation of volatile materials. The potential use of spray drying microencapsulation for pharmaceutical applications, particularly the preparation of microparticulate drug delivery systems, will also be discussed.

I. INTRODUCTION

In the course of some twenty years, microencapsulation of small particles in envelopes of protective shell materials has become an established technology for coating and isolating liquid or solid substances until such time that their activity is needed.

The major reasons for the use of microencapsulation include:

- protection of the product from the surrounding environment (temperature, moisture, UV radiation, interaction with other materials),
- protection of the environment from the hazardous or toxic product, so that this kind of material can be more safely handled,
- decrease of the evaporation or transfer rate of the core material to the outside environment,
- dry handling - conversion of liquids and sticky solids to free-flowing powders (better mixing, prevent lumping),
- masking of the undesired properties of the active component, e.g. taste or odour masking, or masking the chemical properties such as pH or catalytic activity,
- control of the rate of release of the core material under desired conditions.

Virtually, any material that needs to be protected, isolated or controlled release can be encapsulated. The benefits of controlled release given by microcapsules are obvious for pharmaceutical applications. Several technical aims may be envisaged when developing a modified release form for an active constituent, such as the transport of a therapeutic agent selectively to the intended site of action in order to optimise the biological response, or the release of an active molecule into a selected environment following a predetermined kinetic profile. The release kinetics can be adjusted by the design of the system, and can for instance result in a constant plasma level within the therapeutic margin between the threshold of efficiency and the threshold of toxicity (1). The three actions - protection, targeting and release according to an appropriate kinetic profile - are sought in combination by means of microcapsules.

Microencapsulation and controlled release of flavours and fragrances have also revolutionised the food and fragrance industries, constantly interested in improving the flavour, aroma, stability, nutritive value, and appearance of their products. In these areas, the conversion of liquids to dry powders which are easy to handle was one of the first motivations for the use of microcapsules.

For food components, typical advantages offered by microencapsulation are a means to : protect sensitive food components from other food ingredients during storage, protect against nutritional loss and even add nutritive materials to foods after processing, incorporate unusual or time-release mechanisms into the formulation, mask or preserve flavours and aromas, and finally provide an additional attractiveness for the display and merchandising of food products (greater flexibility and control in developing foods that are more flavourful and nutritious, to better meet the expectations of today's consumers). Examples of food additives which may benefit from encapsulation and

controlled release are preservatives, colours, sweeteners, enzymes, antioxidants, flavours, nutrients and cross-linking agents.

For essential oils and fragrances, microencapsulation is used for a number of other reasons including delayed release of perfume volatiles, prevention of chemical degradation or interactions with incompatible components, incorporation into dry systems, modulation of odour release and volatility losses. Protection aspects are very important. Indeed, essential oils and fine fragrances may consist of more than 200 different elements, and although some of them can be present at minuscule levels, they may nonetheless be intrinsic for the aesthetic qualities of the formulation, and must therefore be preserved. A uniform release of fragrance components is also desired without any fractionation which could change the aroma.

Following the pharmaceutical, food and fragrance industries, several other areas of industrial activity have also been expanding the use of microcapsules, in particular the parachemical industry (for encapsulation of catalysts, release of bactericidal agents, colouring agents) and the agrochemical industry (for release of pesticides, protection of seeds).

Many different methods have been proposed for the production of microcapsules. In general, these methods can be divided into three groups known as (2):

physicochemical processes: simple or complex coacervation (aqueous phase separation), emulsion-solvent evaporation (organic phase separation), emulsion-solidification, liposome entrapment.
chemical processes: interfacial polymerisation, molecular inclusion.
physical processes: spray drying, spray coating, prilling, extrusion, etc.

The choice of the encapsulation process for a specific application is based on parameters such as : mean particle size required, physical/chemical properties of both core and coating, applications for the microencapsulated material, desired release mechanisms, industrial manufacturing scale envisaged and the acceptable process cost.

This chapter will present a brief overview of the main considerations involved in microencapsulation by spray drying. A special emphasis will be given to microencapsulation of volatile materials. The potential use of spray drying microencapsulation for pharmaceutical applications, particularly, the preparation of microparticulate drug delivery systems will also be discussed.

2. MICROCAPSULES TERMINOLOGY

The term microencapsulation has been interpreted broadly to include microcapsules, microparticles, nanocapsules, entrapped or embedded active substances. Two main groups of microcapsules architecture can be distinguished, based on the way the active core (solid particles, droplets of liquids) is distributed within the system (1) :

a) those in which, the core is largely concentrated near the centre, surrounded by a definite and continuous film of the coating material,
b) those in which, the core is uniformly dispersed throughout a matrix.

In pharmaceutical and medicinal applications, an attempt has been made to use the terms *microcapsule* and *microsphere* for definitions (a) and (b), respectively. The microcapsules defined by (a) are often referred to as *reservoir* capsules, while those defined by (b) are called *matrix* design.

Microcapsules (*reservoir* or *matrix*) have a size between 0,2 and 5000 μm, in contrast to macrocapsules which are bigger than 5000 μm. Capsules smaller than 0,2 μm are often termed nanocapsules (3). A number of different terms are used to describe the interior contents of microcapsules including core, core material, ingredient, substrate, active agent. The coating material also termed carrier (or shell, coat, wall) material, encapsulating matrix (or agent) can be selected from a wide variety of natural or synthetic polymers, depending on the active agent to be coated and the characteristics desired in the final microcapsules.

In general, the microcapsules produced by spray drying are of the *matrix* type. The core exists as microparticles or microdroplets distributed within the dry solid matrix. In spite of increasing attempts to distinguish the encapsulated from the entrapped products (4), spray drying is formally regarded as a microencapsulation process. Although capsule size distribution during microencapsulation is a function of many process parameters, spray drying typically results in microcapsules less than 100 μm in size.

Microcapsules are typically formulated with the expectation that the core will either be released relatively quickly in a burst fashion, or in a controlled and gradual manner. In general, the release depends upon the type and geometry of the capsule, and the nature of the coating material used to form the microcapsules. These factors determine the mechanisms of core release from the microcapsules, which may be based on solvent effects, diffusion,degradation or particle fractures (2).

Solvent release and diffusion are the mechanisms of release most commonly associated with the spray dried microcapsules. Solvent release is based upon the

solubilisation of the capsule wall (typically with water for lipophilic materials), followed by subsequent release of the core material. Release rate may be regulated by controlling the rate of wall solubility, pH effects or changes in the ionic strength of the dissolution medium (2,3).

Diffusional release depends upon the possible interactions between the core and the wall material and the rate at which the active core is able to pass through the outer wall. Characteristics of the microcapsules wall such as chemical structure, thickness, pores size and surface integrity play a determinant role in the core diffusion rate.

An other factor which has a critical importance in influencing diffusion, and thus core release is the physical state of the wall material. Matrices in the amorphous glass structure are considered quite impermeable to diffusion while matrices in the rubbery state are more amenable to diffusion of solutes. Therefore, the glass/rubber transition of a matrix material is also a relevant consideration in evaluating release properties. Changes in the particles structure initiated by a transition from the amorphous 'glassy' to the amorphous 'rubbery' state as the system is plasticized, may eventually result in crystallisation or collapse of the matrix.

A general review of the various chemical and physical properties of microcapsules associated with release of the encapsulated material has been published in the literature (5). The reader can refer to this review for more details concerning the different mechanisms for controlled core-release. These considerations are outside the scope of the present paper.

3. MICROENCAPSULATION BY SPRAY DRYING

3.1. PROCESS

Spray drying is by definition the transformation of a feed from a fluid state (solution, dispersion or paste) into a dried particulate form by spraying the feed into a hot drying medium (6). It is a continuous processing operation involving a combination of several stages namely, atomisation, mixing of spray and air, evaporation and product separation.

Selection of the atomiser is one of the most important choices in spray dryer design and has a significant effect upon the size distribution of the final dried particles. The most important atomiser characteristics from the standpoint of product quality are uniformity of drop-size, control of drop-size distribution, and homogeneity of the spray. Atomisers common forms are pressure atomisers, centrifugal (wheel) atomisers and pneumatic (two-fluid) atomisers.

Droplet drying is complicated due to wide drop-size distributions and complex air-spray mixing patterns. Any single droplet may encounter a unique temperature-humidity history as it travels through the dryer.

Droplet drying is complicated further by a transfer from external to internal mass-transfer control. On the formation of the drop, loss of moisture is controlled by the gas-phase resistance. In this period, called constant-rate or constant-activity period, the water activity at the drop surface remains nearly constant. If the partial pressure of water vapour in the bulk air has not built up to a substantial value, the water-vapour partial pressure driving force for mass transfer in the gas boundary layer surrounding the drop remains constant, and the evaporation rate per unit area of drop surface is constant. The drop temperature is the wet-bulb temperature of the drying air, as moisture is lost in proportion to the heat gained.

As drying continues, a gradient in water concentration builds up within the drop, the water activity at the surface decreases, and the surface dries out. This brings about the falling-rate period, in which drying is rate-limited by moisture transport within drops. The relative lengths of the constant-rate and the falling-rate periods vary according to the conditions in the spray dryer and the material being dried.

Once a dry skin has been formed, the droplet temperature starts to increase from the wet bulb to the air temperature. At temperatures reaching or exceeding the boiling point of water, substantial internal voidage and particle inflation tend to occur. These morphological changes reflect the development of large partial pressures and mole fractions of water vapour as the drop temperature increases, joining air bubbles firstly formed through internal desorption of dissolved air (7,8) or, come from mechanical entrainment into the liquid drop during atomisation (9). A driving force of dissolved gases from the feed during drying will occur as water is evaporated and as the drop temperature rises, lowering the solubility of air (10).

Once the particle is dry enough, the final shape sets into place, and any final evaporation of water occurs. A comprehensive practical review of spray drying for substances in general is the handbook of Masters (6). For a more thorough review on the subject with emphasis on an appraisal of the influence of these individual stages on product quality, the reader can be referred to King et al (10).

Although most often considered a dehydration process successfully employed for the drying of solutions, slurries and pastes, spray drying can also be used as an encapsulation method when it entraps 'active' material within a protective matrix, which is essentially inert to the material being encapsulated.

The preparation of the dispersion or emulsion to be processed is the first step involved into the process of encapsulation by spray drying. The process starts with the preparation of a solution of the solid matrix to which the active material to be encapsulated will be incorporated. The matrix selected according to the microcapsules final application is dissolved in a solvent, where the active core is usually insoluble (solid) or immiscible (liquid).

The active core is then added to the wall solution. A vigorous mixing gives a dispersion (for solids) or an emulsion (for droplet liquids). In the latter, the emulsion created should have small oil droplets to improve its stability and prevents droplets coalescence during the drying process. In fact, most of the active materials (especially the flavours) are in liquid state and are insoluble in aqueous solutions. They are thus encapsulated from their emulsions, which are usually of the oil-in-water type.

The core/wall material mixture (emulsion or dispersion) is fed into the spray dryer, where it is submitted to the typical and well-known successive stages of the drying process (7):

First, the core/wall material mixture is transformed into droplets by an atomiser. Second, hot air flowing in either a concurrent or counter-current direction contacts the atomised particles and evaporates the water. Since spray drying is a very fast process, the physical composition of the drop is fixed and reflected in the structure of the resulting powder particles. The dried particles, consisting of dry matrices in which the core material is held in a micro dispersion, fall through the gaseous medium to the bottom of the dryer and are collected.

Successful spray drying microencapsulation relies on achieving high retention of the core material during processing and storage.

Core material leaves the drying droplets mainly at stages prior to the formation of the dry crust on the surface of the droplets. Losses of volatile core are governed by diffusion within the liquid phase. Once a dry crust has formed, further losses can occur if the core material can pass through the crust by means of diffusion in the solid, or through pores or channels.

Losses of non-volatile core may also occur during drying of the drops. Droplets (or particles) of non-volatile substances that are present at the surface of the drops leaving the atomiser, or those that migrate to the surface prior to the formation of dry crust around the drying particles, may be swept off the particle surface.

3.2. MICROENCAPSULATION OF VOLATILE MATERIALS

3.2.1. Background

Microencapsulation of volatile materials by spray drying presents the challenge of removing water by vaporisation, while retaining substances that are much more volatile than water. This is the case of most organic compounds.

For some specific applications (such as food flavours and aroma components), volatile substances with different volatilities relative to water are associated in a complex bouquet. In these cases, the task of retaining the volatile substances is still more complicated because it requires a balanced retention of all of the substances that are associated in the bouquet.

Food liquids contain small concentrations of many organic compounds which give the food its characteristic flavour and aroma. Most of these compounds are highly volatile with respect to water and may be lost easily to a great extent during drying. A need to optimise the retention of balanced flavour and aroma during drying of food products motivated the considerable research that has been carried out over the past 30 years on the mechanisms of loss of volatile compounds in spray drying, as well as in the drying of single, suspended drops (11,12,13).

As a first approximation, the liquid foods have been considered as pseudo-ternary systems consisting of water and dissolved solids containing trace amounts of volatile organic components (14). According to this, model food systems are commonly constituted of carbohydrate solutions with one or more model aroma components added in very low concentrations, close to those occurring naturally in foods. Summaries of these researches are provided by several authors (7,15,16). Excellent reviews with the theoretical description of aroma retention and recovery during concentration and drying processes are also given in the literature (17,18).

In fact, the well-known concept of selective diffusion was generated by Thijssen and co-workers in the course of their studies on drying of liquid foods. This concept is based on the fact that the diffusion coefficient of water in concentrated solutions behaves differently from the diffusion coefficients of other substances.

Thijssen and Rulkens (19) noted that retention of the volatile compounds in spray-dried foods are considerably higher than what would be predicted from equilibrium considerations alone, because of the rate-limiting effect of liquid phase diffusion to the surface of the drop. As the water concentration at the droplet surface decreases, the diffusion coefficients of the volatile components decrease by several orders of magnitude, more sharply than that of water.

While water continues to diffuse at a significant rate, the volatiles diffuse at a negligible rate. Below some water content, the surface of the drying drop reaches a moisture content no longer permeable to most volatiles organic, but quite permeable to the relatively smaller, water molecules. Therefore, this dry surface acts as a semipermeable membrane permitting the continued loss (or diffusion) of water, but efficiently retaining (or stopping) organic molecules.

A desirable goal is to ensure that the surface of droplets reaches a critical moisture content at an early point in drying, so that the surface become impermeable while there is still a large concentration of volatile substances within the drops. To achieve this situation, it is required to have entered the falling-rate period of drying where substantial gradients of water concentration are developed within the drops.

According to the selective diffusion concept, in spray drying, favourable conditions for obtaining high volatiles retention can be created due to the rapid decrease of the water concentration at the drying droplet surface in contact with a hot air stream. Once the surface of the drops have dried sufficiently, losses of volatile compounds from drops are governed by diffusion within the liquid phase. Selective diffusion comes into effect, as the diffusion coefficients of organic compounds in the surface region become much lower than the one of water.

The retention of volatiles in spray drying can still be improved if a high concentration of dissolved solids is built up on the surfaces of drops early enough in the drying process. Therefore, feed concentration and drying temperature are very important because of their effect on crust formation. Increasing the feed concentration markedly improve the volatiles retention as it lower the diffusion coefficients of the dissolved solids and reduce the initial concentration gradient needed to achieve the critical surface concentration to allow selective diffusion to occur. Hotter air would result in better volatiles retention since faster drying would impose steeper internal water concentration gradients,but this must be balanced against the possibility of greater thermal degradation.

On the other hand, additional losses of volatiles can occur during the process, preventing or destroying the retaining action of the selective diffusion mechanism. These losses can occur during atomisation and drop formation, as well as from expansion and crust cracking of drops during the later stages of drying in a spray dryer (7,20).

Volatile losses can occur in the immediate vicinity of the atomiser, due to the high surface areas and mass transfer coefficients involved in atomisation, to the turbulence and the secondary flows within the sheets and ligaments of liquid that are drop precursors (21,22).

It is also known that complex changes in the size, shape and appearance of drops occur during spray drying (23,24,25). These morphological developments during periods of expansion and crattering of drops can expose surfaces and interior liquid with consequent potential for further loss of volatiles which have been imprisoned by selective diffusion.

Studies upon drying of single droplets have provided information on both diffusional and additional losses of volatiles due to morphological changes during drying (26,27). The first quantitative demonstration of major losses accompanying changes in drop morphology was made by Verderber and King, in 1992 (27). These authors developed a method to measure losses of a highly volatile tracer as a function of time during the drying of a suspended drop, while simultaneously observing and recording changes in morphology of the drop as drying proceeded. The appearance of the drop during drying was recorded with a video camera. The results clearly display the onset of the volatiles selective diffusion phenomenon : there was an initial release of the volatile in the early stages of drying before the onset of selective diffusion, after which there was little or no release until changes occurred in morphology of the droplets. There was also an additional loss of the volatile component later in the drying process, coincident with expansions and surface eruptions.

From these substantial advances in understanding the mechanisms of losses of volatiles during drying of food liquids, many practical processing rules and several avenues for controlling the retention of trace volatile compounds during spray drying are identified and analysed in the literature (7,18). In fact, deriving processing rules for obtaining high aroma retention in spray drying is directed to the promotion of the selective diffusion concept, thereby reducing the additional losses mentioned above.

As mentioned earlier, for most of the model systems used, the volatiles were present in concentrations close to those occurring naturally in foods (of the order of several ppm). Owing to its very low concentration, it has been considered that the aroma component hardly affects the mass transfer of water and dissolved solids during drying in these systems (18).

Somewhat more complicated is the retention of volatile compounds which are present under a dispersion form, i.e. during the drying and microencapsulation of volatiles from their emulsions. In this case, the retention may be affected by other factors such as the dependence of the water and volatiles diffusivity upon the volatiles concentration, the water solubility of the volatiles, as well as the much stronger interactions that may occur between dissolved solids and volatiles, which may thus affect the mechanisms of diffusion and/or loss of these components.

3.2.2. Factors influencing the Microencapsulation of an Organic Emulsified Phase

To improve the understanding of the ways in which the retention of volatile materials is affected during the spray drying microencapsulation of an organic emulsified phase, measurements of volatile retention in relation to process variables although requiring considerable effort, has been a common approach to the problem.

The process parameters which have been stated as influencing the volatiles retention during the process are (28) :

- *properties of the volatile compounds* (molecular weight, vapour pressure, concentration in the emulsion)
- *properties of the capsule wall material* (type, molecular weight)
- *properties of the emulsion* (dissolved solids content, viscosity, oil droplet size distribution)
- *drying process conditions* (atomised droplet size, dryer inlet and outlet air temperatures, drying air velocity, dryer feed temperature, humidity of the dryer inlet air)
- *spray dried particle morphology* (shape, mean particle size, integrity, porosity, bulk volume).

The effect of some of them as regards the importance of their role in obtaining satisfactory microcapsules is discussed hereafter. The factors considered are :

- type of capsule wall material
- concentration and nature of the volatile to be retained
- concentration and viscosity of the emulsion
- emulsion size
- dryer inlet air temperature
- capsule morphology

For the influence of the other process variables not discussed here, the reader is referred to several review papers on control of food quality (10,29,30) and encapsulation of food flavourings (28).

Type of Capsule Wall Materials

Numerous materials are commercially available for use as flavour encapsulating agents. The most widely used are selected from the following types (2):

- carbohydrates (starch, maltodextrins, corn syrup solids, cyclodextrins),
- cellulose esters and ethers (carboxy methylcellulose, methylcellulose, ethylcellulose),
- gums (gum acacia, agar, sodium alginate),
- lipids (wax, paraffin, fats, oils),
- proteins (gelatin, soy protein, whey protein).

For spray drying microencapsulation, the choice of the encapsulating agent is critical as the material will influence emulsion stability before drying, flowability, mechanical stability and shelf-life after drying. Therefore, wall materials are chosen so as to meet as closely as possible the following properties: high solubility, effective emulsification and film forming characteristics, efficient drying properties, and low viscosity even at highly concentrated solution.

Among the available materials, the major encapsulating agents used for spray drying applications are gums (essentially gum acacia), emulsifying starches and hydrolysed starches.

Gum Acacia

Gum acacia, also known as gum arabic, is defined as the gummy exudate flowing naturally or obtained by incision of the trunk and branches of Acacia Senegal or other species (31).

Gum acacia has been the encapsulating agent of choice for many years, particularly, due to its specific characteristics like film forming and emulsifying properties. It is a polymer consisting primarily of D-glucuronic acid, L-rhamnose, D-galactose and L-arabinose, with about 5% protein (2). This protein fraction is responsible for the emulsification properties of the gum since it acts as an interface between oil and water. The film forming properties comes from the arabinogalactan fraction of the gum. The low viscosity and consequently high solubility of this portion is likely responsible for the barrier film that is formed after the evaporation of water during drying (31).

Gum acacia provides very good volatiles retention during the drying process as shown in spray drying microencapsulation of citrus oil (31,32), esters (33), and of citral and linalyl acetate (34), among others. In recent years, despite its emulsification ability and good retention of volatiles for flavour encapsulation, its high cost, limited availability, and the impurities associated with it, have been deterrents to the use of gum arabic.

Starches

Hydrolysed starches (maltodextrins, corn syrup solids) and modified starches are extensively used for spray drying encapsulation of food ingredients due to their aqueous solubility, low viscosity and ease of drying conditions. However, maltodextrins and corn syrup solids do not usually result in good retention of volatile compounds during the spray drying process. The reason which is often cited to explain the poor retention obtained with these two encapsulating agents, is their poor film-forming abilities (2,35,36).

Chemically modified starches (i.e., incorporating a lipophilic group into their molecules and having emulsifying properties) have been shown in numerous studies (37,38), to yield very good retention of volatiles during drying.

An example of the different encapsulation abilities for an hydrolysed and a modified starch is given in Table 1. The characteristics of emulsions constituted by a model volatile component (Allylguaiacol) as the oil phase, and by solutions of either maltodextrin (DE 10) or modified starch as the aqueous phase, as well as the characteristics of the spray dried encapsulated powders obtained from these emulsions are presented. In these systems, a wall material to oil ratio of 5:2 was fixed and, the emulsions were prepared with a dry solids content of 46%.

First of all, one can see on Table 1 that the emulsion prepared with modified starch was less viscous, and had a smaller particle size than the one made with maltodextrin.

Second, the results show that the modified starch gave high total oil retention (94%), better than maltodextrin (67%). Since maltodextrin has no emulsification properties, it produces coarse emulsions that result in poor oil retention during drying.

Blends of Hydrolysed Starches with Gum Arabic or Modified Starches

Blends of commercially available carriers have also been evaluated by several authors, with the aim to obtain an effective microencapsulation.

Informations suggesting the advantage of using mixtures of maltodextrins, and either gum arabic or modified starches have been reported.

A mixture of gum arabic and maltodextrin was reported to be effective for the microencapsulation of cardamom oil (39). These authors tried various combinations to achieve high levels of oil retention. A wall material to oil ratio of 4:1 was fixed. They

TABLE 1
CHARACTERISTICS of EMULSIONS and POWDERS (from Ré and Liu (37))

WALL MATERIAL	EMULSION		POWDERS	
	viscosity of emulsion 20°C (cp)	mean droplet size, d_{32} (μm)	particle size range of microcapsules (μm)	retention total oil * (% w/w)
maltodextrin DE 10	220.0	5.2	5.3 - 48.1	67.0
modified starch	160.0	1.6	4.2 - 48.6	94.0

* determined by Clevenger distillation method

found that combinations of maltodextrin and gum acacia in the ratio 1:2.3 gave the best quality capsules.

Bhandari et al (34) reported good retention levels for a mixture of two volatile materials, citral and linalyl acetate in the proportion of 4:1, using blends of gum arabic and maltodextrin in different proportions. The emulsion was prepared with a dry solids content of 50%. They used a spray drying system able to dry liquids at very high viscosities. This is referred to as the Leaflash spray drying technique. This system uses very hot air (300 to 400°C) and is able to dry very viscous liquids at high dry solids content. They reported that the retention of volatiles was higher for higher gum content in the blends.

Blends of maltodextrin and gum acacia have also been used to encapsulate citrus oil. Thevenet (31) tested four different ratios of acacia gum to maltodextrin (1:0; 1:1, 1:3, 1:5). An emulsion was prepared by mixing citrus oil (20% w/w of wall solids) into a hydrated gum/maltodextrin blend (40% solids w/w). The blend of maltodextrin and gum acacia in the ratio 1:1 gave high volatiles retention.

The combination of maltodextrin and modified starch also decreases the cost of the encapsulating material and enhances the emulsification ability of the encapsulating system.

A mixture of maltodextrin and modified starch was evaluated for spray drying microencapsulation of a model volatile system, Allylguaiacol (40). In their work, the authors prepared various emulsions using blends of maltodextrin (DE 10) and modified

starch in different proportions into which the oil was emulsified (12% w/w of wall solids). The emulsions were prepared with a dry solids content of 40% (solids w/w).

Table 2 presents the characteristics of both the emulsions and the spray dried encapsulated powders, as well as the oil retention levels. It can be seen that for a constant solids content in the emulsion, the variation of the proportion of maltodextrin to modified starch from 1.5:1 up to 3:1 led to a reduction of the viscosity, whilst the increase of this ratio from 3:1 up to 4.5:1 resulted in a viscosity increase.

The evolution of both the total oil and the surface oil retention levels, as a function of the maltodextrin to modified starch ratio, is also presented on Table 2. It can be observed that the maltodextrin concentration increase, corresponding to a variation of maltodextrin to modified starch ratio from 1.5:1 to 3.1, reduced the retention capability of the microcapsules. On the other hand, a ratio increase from 3:1 to 4.5:1 hardly affected the retention level.

The substitution of part of gum arabic or modified starches by maltodextrin aims at reducing the cost of the support material. However, the film forming and emulsifying properties of either gum arabic or modified starches cannot be ignored. One should therefore always determine the optimal proportions for which the retention of the volatiles would also be unaffected.

Blends of Hydrolised Starches with Proteins and Lipids

Researchers are also investigating proteins and lipids, both in combination with carbohydrates as encapsulating blend materials.

Milk proteins (whey proteins, caseins) have excellent nutritional value and possess numerous functional properties which are important for the formation of edible films, such as their solubility in water and ability to act as emulsifiers (41). Mixtures of whey protein with natural or modified carbohydrates have been evaluated for spray drying microencapsulation.

Sheu and Rosenberg (42) have shown that combinations of whey protein and high DE maltodextrins and corn syrup solids were effective wall systems for microencapsulation of volatiles. They emulsified a model ester (ethyl caprylate) into the wall solutions (25% solids w/w) at a proportion of 30% (w/w of wall solids). A whey protein to carbohydrates ratio of 1:9 gave an ester retention around 90%. According to these results, mixtures of whey proteins and carbohydrates appear to provide the appropriate functionality profile for successful microencapsulation of volatile materials.

TABLE 2
CHARACTERISTICS of EMULSIONS and POWDERS (from Onimaru et al (40))

EMULSION				POWDERS		
proportion maltodextrin/ modified starch (w/w)	emulsion viscosity 20°C (cp)	mean droplet size, d_{32} (μm)	particle size range of microcapsules (μm)	total oil [1] retention (%w/w)	inner oil retention [2] (%w/w)	inner to total oil retention ratio (%)
1.5:1	1173	4.2	5.8 - 44.7	88.0	85.0	96.0
3.0:1	406	2.2	4.3 - 34.3	85.0	77.0	91.0
4.5:1	716	2.5	5.8 - 45.5	84.0	77.0	91.5

[1] determined by Clevenger distillation method

[2] determined by Clevenger distillation method after washing capsules (without destruction) with pentane, and remove the extractable oil surface.

Among the lipids, lecithins represent a potential material to be used blended with other coating materials. It is known that lecithins play a significant role as a surface-active substance in the production of emulsions (2).

Combinations of maltodextrin and soy protein, as well as maltodextrin and soy lecithin were also evaluated by Ré and co-workers (37,43) as encapsulating systems. From some of their results shown here (Table 3), one can see that the total oil retention level obtained by using a wall system consisting of maltodextrin was larger than the value found for the maltodextrin/protein combination, but lower than for the maltodextrin/soy lecithin system.

One can say that in the combined systems, the carbohydrate (maltodextrin) acted as a matrix-forming material, while the added agent, the lipid (soy lecithin) or the protein (soy protein), served as an emulsifying agent.

The inclusion of soy protein in the dryer feed matrix of maltodextrin reduced oil retention. This behaviour could be attributed to the extent to which the interactions between soy protein and maltodextrin adversely affected the emulsification properties of the wall system and drying properties. On the other hand, inclusion of the lecithin in the wall material formulation containing maltodextrin could improve the amount of encapsulated core, probably by improving emulsion stability before drying. The results suggest that soy lecithin can be used as a wall constituent in order to improve the

microencapsulating properties of some commercially available encapsulating agents with poor emulsifying properties.

Observations regarding the mean droplet size in the emulsions with the combined systems (Table 3) suggest that, like as for the single systems, retention level was also improved (in part) by reducing the droplet size of the core material.

Wall Materials as Protectors Against Oxidation

As shown up to now, the development of improved carrier material has been an active area of recent researches. In addition to achieving higher volatile retention, another important aspect of encapsulation efficiency is the improvement of the oxidative stability of the core material, in particular for the flavour oils.

For an ideal encapsulation process, the entire core material will be within the wall. Controlling the volatiles on the particle surface is important, since any volatiles not encapsulated but absorbed on the surface of the encapsulation matrix, is subject to evaporation and/or oxidation. While extractable surface core is not a direct indicator of oxidative stability (i.e., shelf-life), powders with high levels of surface core may be associated with poor stability (44).

The carbohydrates commonly used as wall materials vary greatly in protecting encapsulated volatiles against oxidation A comparative study of the protective effect of gum arabic, modified starch and corn syrup solids (DE 25) in spray drying orange peel oil microencapsulation, was carried out by Westing et al (45). While the encapsulation ability of the modified starch was reported to be equal to, or even greater than gum arabic, it provided a poorer protection against the oil oxidation. Corn syrup solids provided the best protection to the oil. This is in agreement with other investigators which have shown that hydrolysed starches with increasing DE provide protection against oxidative deterioration (46).

It has been suggested that the protection afforded by the higher DE products could be due to the presence of the smaller oligosacharides, which promote oxidative stability by forming a much more effective oxygen barrier (28,47).

New Developments on Wall Materials

An area of research of increasing interest is the development of alternative and inexpensive polymers that would be considered 'natural' like gum arabic, and that could encapsulate flavours with high volatile retention (similar efficiency as gum arabic) and better shelf life stability.

TABLE 3
CHARACTERISTICS of EMULSIONS and POWDERS (from Ré and Liu (37))

COMBINATION OF WALL MATERIALS	EMULSIONS			POWDERS	
	proportion matrix/ added agent	emulsion viscosity 20°C (cp)	mean droplet size, d_{32} (μm)	particle size range of microcapsules (μm)	retention level* (%)
maltodextrin	10:0	220.0	5.2	5.3 - 48.1	67.0
maltodextrin and soy protein	9:1	144.0	5.7	3.8 - 37.0	53.0
maltodextrin and soy lecithin	9:1	22.0	1.2	3.3 - 31.1	82.0

* determined by Clevenger distillation method

To this end, Beristain and Vernon-Carter (48,49) evaluated the performance of mesquite gum as compared to gum arabic in the spray drying encapsulation of orange peel oil. Mesquite gum is the exudate from a small leguminous shrub *Prosopis juliflora*, which grows in south western United States and northern Mexico. It has been reported as being very effective in stabilising o/w emulsions due to its ability to form gel-like protective films around the oil drops (50). The performance of this gum was compared to gum arabic in the encapsulation of orange peel oil, and it was shown that arabic-mesquite blends (1.5:1) have a very good flavour encapsulation ability (93,5 %).

On the other hand, different species of gum acacia are also being developed and different formulations with these species are being evaluated to produce encapsulation matrices which could provide protection against oxidation of encapsulated citrus oils during storage (32).

In the last few years, milk proteins have also been explored for their potential as new encapsulating material (51,52,53,54). Their functional properties have shown new avenues for their use, in order to improve food quality and shelf-life as they can be readily incorporated in food systems.

Concentration and Nature of Volatile Components

Using the highest possible core-to-wall material ratio that provides high core retention on the microcapsules is advantageous, because the effect of wall material on

physicochemical characteristics of the product (to which microcapsules will be incorporated) could be minimised.

A typical wall to core material ratio of 4:1 is usually adopted in most of published reports (39,55), as well as in many practical cases. This ratio has been reported optimal for encapsulating materials like gum arabic, and for other carbohydrate derivatives (28).

An example of the influence of the core material concentration on its retention in a carbohydrate matrix is given in Figure 1. The variations of both total and inner volatile retentions are given as a function of the initial dispersed oil load in the feed emulsion. The matrix consisted of a mixture of maltodextrin and modified starch in the proportion 3:1. As it can be seen, the increase of the oil load in the feed emulsion affects the retention. Total oil retention decreases with the increase of the wall to oil ratio from 1.5:1 to 5:1. On the other hand, the oil retention inside the wall capsules increases up to a wall to oil ratio of 3.2:1. The higher wall to oil ratio used (5:1) leads to a poorer inner retention. Therefore, for this system, an optimal wall to core material ratio to ensure the best encapsulation efficiency is located around 3.2:1.

A decrease in volatiles total retention and an increase in volatiles retained on the surface of powder particles was also observed by Bhandari et al (34), when the wall to oil ratio was decreased from 4:1 to 3:1. In spite of this trend, in some specific applications higher volatile loads would also provide higher retention. For example, Sheu and Rosenberg (42) obtained high ethyl caprylate retention in a whey protein/ carbohydrate combined wall system for an ester load of 30% (w/w), corresponding to a wall to core ratio of 2.3:1.

Some evidences of the fact that core material properties affect the core's retention are also reported in the literature.

First of all, the influence of both molecular weight and vapour pressure of the volatile compounds on their retention during spray drying is known and well documented in the literature (14,17). Molecular weight is a reasonable representation of molecular size, directly related to molecular diffusivity. The increase of molecular size generally results in slower diffusion rate; subsequently, the molecules will take more time to reach the particle size during drying, and the retention will increase. Vapour pressure (or volatility) plays a secondary role in determining volatiles retention, due to its influence in controlling volatile losses until the drying droplet surface becomes semipermeable. The final result is that the small, very volatile molecules will be lost to a greater extent than the larger less volatile molecules (28).

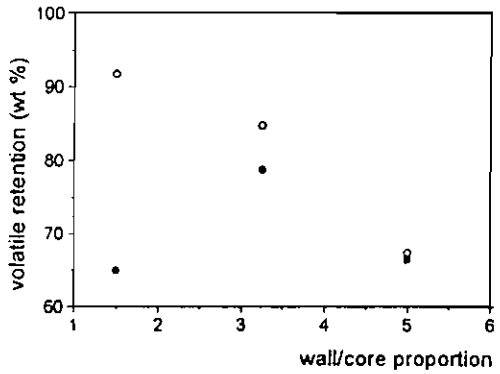


FIGURE 1 - Retention of Allylguaiacol by a Combined Matrix during Spray Drying Microencapsulation, as a Function of the Wall to Core Ratio. (o) - total oil retention; (•)-inner oil retention.; (Emulsion Composition: Maltodextrin/Modified Starch Matrix (3:1); 40% solids w/w . Drying Inlet Air Temperature: 130°C; data from Onimaru et al (40)).

The retention of a volatile compound may also be affected by its solubility in water. As the water solubility of the volatile increases, the volatile losses increase due to the ability of the water fraction soluble of the volatile to diffuse through the selective membrane, even at late stages of the drying process.

Indeed, Ban (56) observed that the retention, in gum arabic matrix, of volatiles with very low solubility (methyl benzoate and L-carvone) was different from that of volatiles with moderate solubility (benzyl alcohol and benzaldehyde). In addition, for volatiles with very low solubility, the retention was nearly independent of dissolved solid concentration, whilst for volatiles with moderate solubility, it decreased steadily with a decrease in initial dissolved solids content. Rosenberg et al (33) studied the influence of the core load on the retention of several esters in gum arabic encapsulation matrix, by varying the ester concentration from 10 to 30 % (w/w of wall solids). They found that retentions, in gum arabic, of partially water soluble esters (ethyl propionate and ethyl butirate) were less good than for esters of lower polarity (ethyl caproate). From their results, they considered that the retention of volatiles that are at least partially water soluble, is controlled by a combination of molecular diffusivity of the water-soluble fractions of the esters, and by droplet stripping that occurs in the early stages of drying.

Besides factors such as volatility, diffusivity and solubility of the volatile compounds through the matrix, another factor that should be taken into account in spray drying microencapsulation is the possible interactions between the volatiles and the matrix. This

may involve physical and/or physicochemical interactions including formation of insoluble complexes, molecular association of the encapsulating matrix with the volatile through hydrogen bonds, among others. These interactions may have an effect on the formation of the interfacial film at the interface O/W, which stabilises the emulsion. This area needs to be further studied in order to improve the current knowledge of the mechanism by which concentrated solutions of encapsulating matrices retain volatiles during spray drying process.

Total Solids Content in the Emulsion

It is well known that the primary factor determining the retention of volatiles during drying is the dissolved solids content in the feed. Increase in total solids concentration results in increase of the emulsion viscosity. Higher viscosity prevents the circulation movement in the drops, resulting in a rapid skin formation.

The tendency to improve retention by increasing the total solids content in the emulsions has been reported in the literature. While some workers observed that an increase of solids content results in a continuous increase in volatiles retention, since viscosity remains low enough for good atomisation (33,39), others have also reported that each encapsulating material has a characteristic optimum concentration for maximum retention (34,57).

The increase in solids content of the emulsion could also affect the amount of volatiles actually entrapped into the spray dried capsules (34,40). Figure 2 shows the influence of the emulsion total solids content upon the total and the inner oil retention level of microcapsules produced from emulsions consisting of Allylguaiacol, as the oil phase (24% w/w), and of a blend of maltodextrin DE 10 and soy lecithin (3:1) as encapsulation matrix.

The increase in solids content of the emulsion corresponded to reduced volatiles retained on the surface of the particles. Similar results were also reported by Bhandari et al (34). Higher feed concentration resulted, in both cases, in larger droplets formed from more viscous emulsions. Bhandari et al (34) attributed the better volatiles retention into the capsules to the increase in particle size, that provided less surface area to volume ratio. However, the increase of both viscosity and droplet size should have opposing effects, which will be discussed hereafter.

Viscosity of the Emulsion

As discussed up to now, increasing the dissolved solids concentration in the feed is considered to be a powerful process parameter for achieving an improvement of volatiles

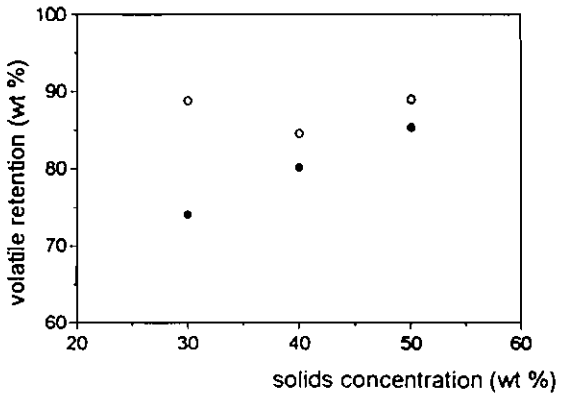


FIGURE 2 - Retention of Allylguaiacol by a Combined Matrix during Spray Drying Microencapsulation, as a Function of the Solids Content in the Emulsion. (o) - total oil retention; (•) - inner oil retention: (Emulsion Composition: Maltodextrin/Modified Starch Matrix (3:1); Wall to core material (3.2:1) . Drying Inlet Air Temperature: 130°C; data from Onimaru et al (40)

retention. However, there are restrictions because of opposing effects related to the consequential increase of the viscosity. The role of viscosity of the atomised droplets is thus very important in determining volatiles retention.

Firstly, viscosity can exert an effect on volatiles retention during drying by influencing circulation currents within the drying droplet. If viscosity is low, internal mixing may occur during drying, which delays formation of the semipermeable surface. Internal mixing may bring the volatiles to the surface of the droplet, and thus cause losses of volatiles to the drying air. Increasing the viscosity feed may reduce internal mixing and thus increase volatiles retention.

Based only on the reduction of internal mixing and the reduction of the time for film formation around the droplets, one would expect, for a given feed solid content, a greater volatiles retention for a higher viscosity feed than for a low viscosity feed material. To confirm this assumption, some authors added thickeners (<1% w/w of wall solids) like carboxymethylcellulose, gums, sodium alginate or gelatin to the emulsion, in order to increase the viscosity without significantly changing the feed solids content.

To illustrate a trend commonly observed, the effect of the feed emulsion viscosity on the volatiles retention is shown in Table 4. The viscosity was increased by addition of sodium alginate (up to 0.5% w/w wall solids) to an encapsulating matrix consisting of a

TABLE 4
CHARACTERISTICS of EMULSIONS and SPRAY DRIED MICROENCAPSULATED POWDERS (from Silva and Ré (58))

Sodium alginate, %	viscosity of emulsion 20 °C (cp)	mean droplet size, d_{32} (μm)	particle size range of microcapsules (μm)	total retention level* (%)
0	53.4	0.5	2.4 - 26.2	77.5
0.05	60.3	2.0	2.4 - 29.4	82.3
0.12	105.5	3.3	2.9 - 31.1	86.6
0.15	124.6	3.5	3.1 - 35.9	74.2
0.25	226.3	3.7	2.9 - 46.9	69.8
0.50	653.3	5.6	3.4 - 64.0	54.7

* determined by Clevenger distillation method

blend of maltodextrin DE 10 and soy lecithin (3:1), to which Allylguaiacol was added as the oil phase (24% w/w of wall solids). By means of addition of sodium alginate, the viscosity was increased from 53 to 653 cp, resulting in an increase of emulsion size and dried capsule size (also in Table 4).

Increasing the viscosity by means of sodium alginate improved retention up to an optimum, beyond which retention levels dropped. Similar results were observed by Rosenberg et al (33) during microencapsulation of esters by spray drying, when incorporating sodium alginate to a gum arabic support matrix. Thus, viscosity may be increased to an optimal value to improve retention. Increasing of the emulsion viscosity up to this optimum will suppress the internal circulations and oscillations of droplets, and will put the selective diffusion into action earlier. A further increase causes a decrease of the retention, due to a longer exposure during atomisation, and difficulties in droplet formation.

Secondly, it is known that more viscous feeds will produce larger droplet sizes (25,34). The results presented in Table 4 also suggest the existence of an optimal droplet size to achieve maximal volatiles retention. Similar results showing that the volatiles retention increased first with the increase in particle size to a maximum value, and subsequently decreased significantly, were found by Chang et al (59).

The existence of an optimal droplet size to achieve maximal volatiles retention can be logically explained. While large particles have a reduced surface area to volume ratio,

which would result in better core retention, they also imply a longer time for film formation around the large drying droplets in the drying process. The longer the time necessary for film formation, the greater the loss of volatile substances. These two competing factors will thus determine the overall effect of particle size upon volatiles retention.

However, some different findings about the role of atomised droplets size in determining volatiles retention have been presented through various papers. Indeed, several authors have reported that a large particles size may improve volatiles retention during drying (28,60). On the other hand, Reineccius and Coulter (61) could find no effect of particle size on retention. Later, Reineccius (28) attributed this result to the high level of solids concentration feed, for which the effect of particle size on retention would not be significant. These conflicting data can be mainly attributed to variations in the drying design, or means to achieve varied droplet size distributions (59).

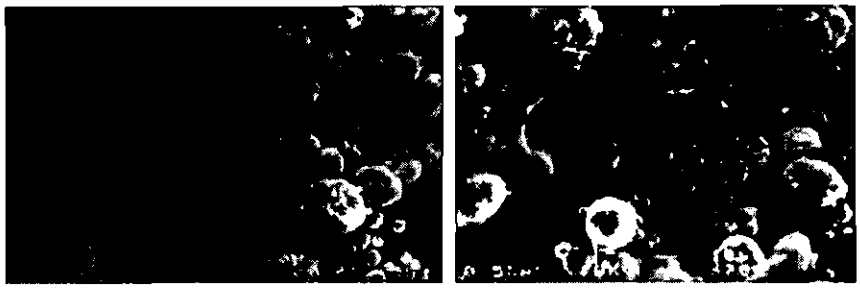
At higher viscosities, difficulties on drop formation result in the formation of irregular particles (oval, cylindrical and stringy) as shown in Figure 3. The presence of irregular particles was also observed by Bhandari et al (34) during spray drying of highly viscous emulsions.

On the other hand, surface imperfections have been well documented in the literature, when slow process of film formation of drying droplets is encountered. Therefore, decreases on retention observed for larger particles could also be related to the surface morphology. In fact, the damage of the particles surface integrity (fissures, shrinkage) observed mainly for larger particles, which result in an increase of their surface area, may contribute to the increase of the unencapsulated (or surface) core, as observed by Chang et al (59).

The importance of the duration for film formation around the droplets can be illustrated by the microencapsulation of the model volatile compound used by Silva and Ré (58) in a wall matrix constituted only by sodium alginate (7.0 % w/w of wall solids). The outer structure of microcapsules in which no retention was found is shown in Figure 4. It is characterised by the presence of some large holes in a thin wall. This indicates that the loss of the volatiles may have occurred before the wall solidification.

In summary, it appears obvious that emulsion viscosity plays an important role in determining volatiles retention into the capsules, due to its large influence on the control of volatile losses until the drying droplet surface becomes semipermeable.

From these considerations, Onimaru et al (40) observed that their experimental results (obtained from an extensive study about the influence of the emulsion



magnification - 700 X
0,12 % sodium alginate
emulsion viscosity (20°C) = 105 cp
total retention = 87%

magnification - 700 X
0,50 % sodium alginate
emulsion viscosity (20°C) = 653 cp
total retention = 55%

FIGURE 3 - SEM Micrographs of Spray Dried Microcapsules containing Allylguaiacol prepared from different Emulsion Viscosities (modified by adding a thickener)

magnification - 5000 X

magnification - 3000 X

FIGURE 4 - SEM Micrographs of Sodium Alginate Spray Dried Microcapsules containing Allylguaiacol (from Silva and Ré (58))

composition on the volatiles retention), could be better analysed when taking into account the indirect effect of the viscosity linked to the variation of the parameters which were considered (total solids content, volatiles load, proportion of constituents in a blended matrix). They concluded that, for a given encapsulating system,the encapsulating effectiveness may be related to the emulsion viscosity as shown in Figure 5. Increasing emulsion viscosity by means of changes on the emulsion composition improved the ability to entrap the core material up to an optimum beyond which the real encapsulation ability dropped, because of the reasons already discussed hereabove.

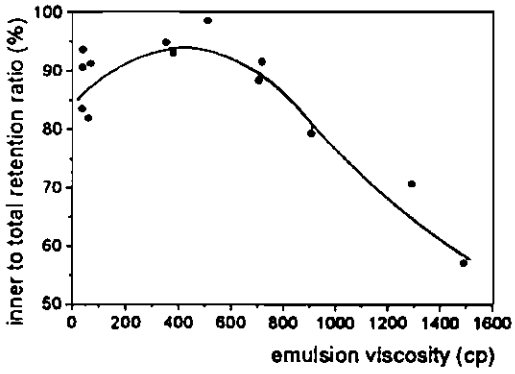


FIGURE 5 - Effect of the Emulsion Viscosity on the True Ability (Inner To Total Retention) of a Combined Matrix to encapsulate Allylguaiacol during Spray Drying.; (Emulsion Composition: Maltodextrin/Modified Starch Ratio - from 1.5:1 to 5:1; Core Material Load - from 15 to 40% w/w of wall solids; Total Solids Content - from 30 to 50% w/w. Drying Inlet Air Temperature: 130°C; data from Onimaru et al (40))

The search of the best emulsion composition to ensure the optimal retention for a given system (i.e., high levels of volatile retention on the powder and into the wall of the capsules) should therefore be conducted taking into account the existence of an adequate range of viscosity, which is itself closely related to the other retention-related variables (composition and process aspects).

Emulsion Size

A first advantage of producing a finer emulsion is that the emulsion is more stable. A stable emulsion of core material in the wall solution is critical in microencapsulation.

To obtain an emulsion with fine droplets (< 2.0 μm), an encapsulating agent with good emulsifying properties should be employed. The emulsifying agent lowers surface tension of the droplets and forms a barrier which helps to prevent coalescence of the droplets. The dispersed droplet size, referred to as emulsion size, can yet be reduced in the spray dryer feed matrix by more vigorous mixing or homogenisation.

The emulsion size may be an important parameter in determining the stability of the emulsion prior to drying, but may also affect the characteristics of the final spray dried microencapsulated powder.

The effect of emulsion size on the retention and shelf-life of spray dried citrus oil has been well investigated by Rish and Reineccius (62), using gum arabic as encapsulating materials. Different emulsions were created by mixing of the oil and the matrix solution to various extents. It was also observed that a smaller emulsion size yielded a higher percent total retention of orange oil in the dried powders. Similar results suggesting that retention of volatiles during microencapsulation could be enhanced by reducing the emulsion size have also been reported (36,37,42).

Besides this, another advantage pointed out by Rish and Reineccius (62), was that smaller emulsions also yielded dried powders which had less unencapsulated (or surface) oil. As mentioned earlier, the oil on the surface of the dried microcapsules has no protection against oxidation. Therefore, finer emulsions may contribute to keep the core into a product within acceptable levels for a longer period of time, although this does not correspond to a longer shelf-life, or a higher resistance to oxidation in the product (the greater surface area of the droplets embedded in the encapsulating matrix provides greater possibility for oxidation once oxygen has permeated the spray dried particles).

While the emulsion size is only one factor which can influence the characteristics of the spray dried microcapsules, it may be possible to use this property in conjunction with other data to obtain better emulsion stability and higher core load.

Dryer Inlet Air Temperature

The influence of dryer inlet air temperature on volatiles retention during spray drying microencapsulation has also been the subject of a considerable number of studies.

Increasing the air temperature also increases the rate of the film formation upon the surface of the drying drop, thereby increasing volatiles retention (63). Another favourable effect observed when increasing the inlet air temperature was a decrease in volatiles content on the surface of powder particles (34). A rapid drying rate would also probably make the crust layer more firm and no further core migration would occur towards the surface.

However, as the inlet air temperature increases, volatiles retention increases until a temperature is reached which is sufficiently high to form steam in the interior of the drying drop resulting in its expansion. At temperatures equal or higher than this 'ballooning temperature', the positive effect of increase retention by enhancing the onset of selective diffusion may be completely overruled by additional losses due to inflation/deflation of droplets. This temperature is primarily a function of the encapsulating matrix and the dryer design (28).

Capsule Morphology

It has been shown, up to now, that successful spray drying microencapsulation is dependent on a complex interplays of several process variables, in particular, the ability of the encapsulating matrix to protect the core material. Therefore, a closer observation of the microcapsules morphology could improve the understanding of how the core material is organised and protected within the microcapsules, and subsequently, to provide indirect information on the encapsulation ability of the wall material.

Besides this, other properties of a microencapsulated material result from its morphology, such as the core release rate which depends upon the porosity and the surface integrity, and/or the flow properties of spray dried powders that are linked to the outer topography of the particles.

Informations on the porosity and surface integrity of the spray dried encapsulated powders have been obtained by scanning electron microscopy (37,40,42,43). Several techniques have also been developed to provide information about the inner microstructure of the microcapsules (64). Figure 6 shows a representative sample of microcapsules with high volatile retention (> 90%). These are spherical bodies with outer surfaces free of cracks but characterised by the presence of dents, which were probably formed by shrinkage of the droplets during the early stages of the drying process.

Typical inner structures of microcapsules obtained from emulsions are shown in Figure 7. The core material is in the form of small droplets embedded in the wall matrix. In the centre of the capsules, a large void can also be observed which occupies most of the capsule volume.

Formation of the central void is related to the expansion of the capsule. It has been commonly observed in spray dried powders and has been studied by several authors. The mechanisms associated with the formation of these central voids are related to expansion of the particles during the latter stages of the drying process (8,23,24).

In a preliminary analysis, it appears that the morphology of the initial emulsion (droplet size distribution) is preserved within the capsules. In order to confirm this assumption, which is frequently considered in the literature (33,37), for the microcapsules presented in Figure 7b, the size-distribution of the encapsulated core material was measured immediately after dissolution of the spray dried powder in water, and compared to the size-distribution of the droplets emulsion measured before drying.

In fact, as can be observed in Figure 8, the small droplets embedded in the dry matrix are very close in size distribution to the dispersed phase in the emulsion prior to

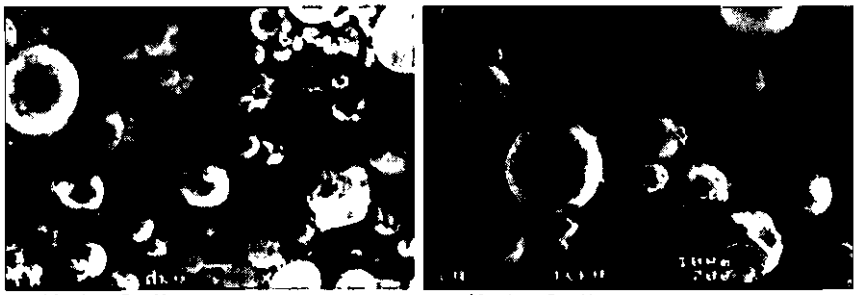


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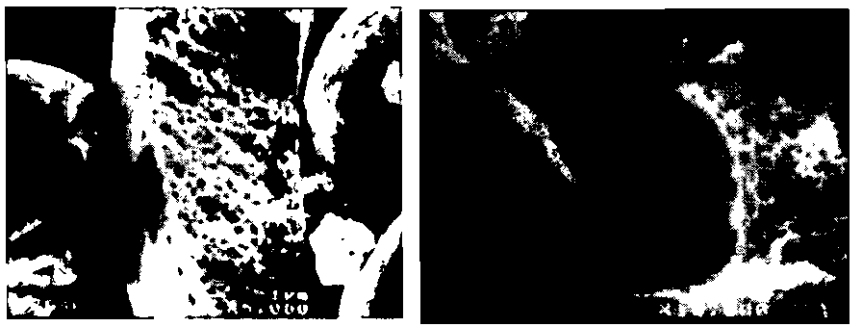
FIGURE 6 - SEM Micrographs of Spray Dried Microcapsules containing Allylguaiacol
(Emulsion Composition: Maltodextrin/Modified Starch Matrix - 3:1; Core Material Load - 24% w/w of wall solids; Total Solids Content - 40 % w/w. Drying Inlet Air Temperature: 130°C)

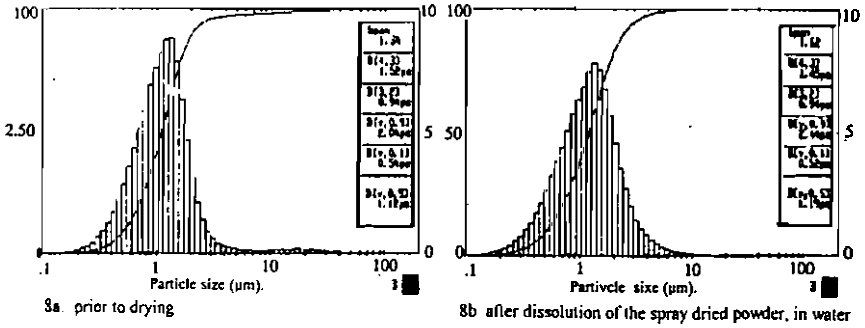


7a. magnification - 2500 X 7b. magnification - 10000 X

FIGURE 7 - Typical Inner Structures of Spray Dried Microcapsules
(Emulsion Composition: Maltodextrin/Modified Starch Matrix - 3:1; Core Material (Allylguaiacol) Load - 24% w/w of wall solids; Total Solids Content - 40 % w/w. Drying Inlet Air Temperature: 130°C)

drying. This may be attributed, in part, to the rapid formation of the external solidified skin that prevents the coalescence of the dispersed droplets, and in part, to a good stability of the emulsion before drying. Consequently, the emulsion stability before and during drying might influence the microcapsule wall structure and closely affects the functional properties of the microcapsules related to core loading and release kinetics.

As mentioned earlier, the balloon-like expansion of droplets may result in the formation of cracks and craters in the dry skin, as shown in Figure 9. The amounts of losses resulting from frothing, expansion, or the cratering of droplets are yet relatively unknown and uncharacterised.



8a. prior to drying

8b after dissolution of the spray dried powder, in water

FIGURE 8 - Droplets Size Distribution of the Core Material, Before and after Drying (Emulsion Composition: Maltodextrin/Modified Starch Matrix - 3:1; Core Material (Allylguaiacol) Load - 24% w/w of wall solids; Total Solids Content - 40 % w/w. Drying Inlet Air Temperature: 130°C)

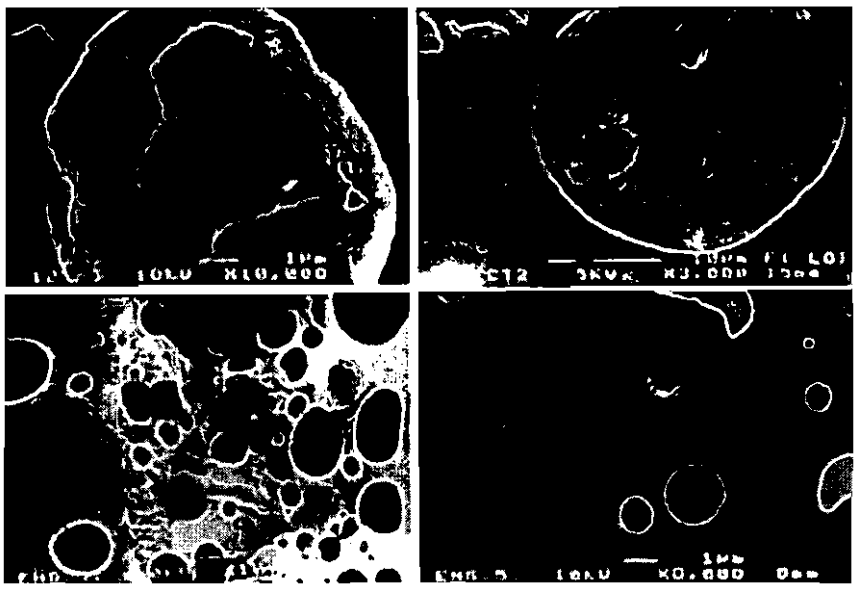


FIGURE 9 - High Magnification of Cracks in Spray Dried Microcapsules Surface

3.3 SPRAY DRYING AS A METHOD TO PREPARE MICROCAPSULES FOR CONTROLLED DRUG RELEASE

Fabricating drugs in a polymeric device is a common technique, where drug release is regulated either by diffusion though the polymer barrier, or by erosion of the polymer matrix. The preparation of microparticulate drug delivery systems of both natural and synthetic polymers can be carried out by several methods (65). Most of them are governed to a great extent by the solubility characteristics of the active compound and of the wall-forming polymer, and besides this, are often time-consuming and difficult to scale-up.

In comparison with a wide variety of microencapsulation techniques, spray drying may offer the advantage of realising the microencapsulation process in one step. In addition, it seems to come close to the properties desired for an ideal method of preparation of controlled release microparticles : spray drying offers rapidity, little dependency on the solubility characteristics of the drug and polymer, and is easy to scale-up. From these considerations, the evaluation of the spray drying potentiality as a method for encapsulation of drugs has been a research area of increasing interest.

Microcapsules containing an active drug can be prepared by spray drying from both homogeneous (solutions) or heterogeneous (suspensions) systems. In the case of solutions, the drug and the polymer are co-dissolved in a common solvent and spray dried. For suspensions, a polymer solution is initially prepared and the microparticles of the active drug are dispersed into the solution. The solution or suspension is fed to the spray dryer and atomised. Upon solvent evaporation, the polymer precipitates and entraps the solid dispersed (from suspensions) or the precipitated crystal (from solutions). As pointed out earlier in this chapter, this microcapsule structure is often called *microspheres* for pharmaceutical and medicinal applications.

Most of the applications involve an organic solvent. However, systems are increasingly developing towards the use of aqueous solutions or dispersions, instead of organic phases. The polymer used is then dissolved in a hydroalcoholic solution or suspended in water, with or without plasticizer, in different weight ratios with the drug. The obtained solution or suspension is spray-dried.

The choice of the coating polymer may be determined by the need for a soluble or biodegradable shell, depending on the route of the administration and elimination, as well as the region of the drug absorption. Considerations of toxicity, allergenicity and irritancy are of primary importance. The main categories of polymers used to obtain encapsulated drugs by spray drying are :

- cellulose derivatives such as cellulose acetate phthalate (66), sodium carboxymethyl cellulose (67,68), hydroxypropyl methyl cellulose (69), methyl cellulose and hydroxypropyl methylcellulose acetate succinate (68),
- biodegradable polymers such as poly(±)lactide (69,70) and polylactide-co-glycolide (70),
- polyacrilic acid (67) and methacrylic polymers such as Eudragit L100-55, Eudragit L30D, Eudragit NE 30D (71), and Eudragit RS (72).

The success of the process is related to the degree of drug encapsulation, as well as to the physicochemical characteristics of the spray dried microcapsules, which both depend upon factors such as the type of feed (i.e., drug in solution or dispersed as solid particles in the polymer solution) and the drug-to-polymer ratio.

In order to give a general overview upon the application of spray drying as a method to encapsulate active drugs, some experimental results concerning the influence of the parameters mentioned above for an effective drug encapsulation by spray drying, as well as examples of specific developments in this area, are presented hereafter.

3.3 1.Factors Influencing Properties of Microcapsules

Type of Feed

Different spray or formulation conditions may affect the predominance of the type of product formed and subsequently, the flow properties and the kinetics release profile of the entrapped drug.

It has been found that encapsulated products from a suspension feed have better flow properties and slower drug dissolution than the products from a solution feed. This may be attributed to the fact that different products are formed. In fact, most of the product from a solution feed contains drug crystals on the polymer surface. This morphology results from the initial formation of a polymeric solid crust, followed by the diffusion of water within the crust to the surface, carrying dissolved drug. During evaporation, drug crystals are deposited on the surface of the microcapsules (68). The drug protrusions on the polymer surface give a higher degree of roughness to the dried product, and result in a rapid drug release. On the other hand, the predominant dried products from a suspension feed are usually microencapsulated drug crystals (enclosed into the polymer), with fairly smooth surfaces compared to the solution feed spray dried product.

The major problem encountered in the spray drying of polymer solutions is the formation of fibres as a result of insufficient forces present to break up the liquid filament into droplets. Studies have shown that the successful dispersion of the filament into polymer droplets depends greatly on the type of polymer, and to a lesser degree, on the viscosity of the spray solution (69). The intermolecular bond between polymer chains, as well as the polymer-solvent interaction, may play a role (73).

Drug to Polymer Ratio

As mentioned earlier, the degree of encapsulation depends among other factors on the drug to polymer ratio. The increase of the amount of unencapsulated drug with an increase in the initial drug load was observed by Bodmeier and Chen (69) in the preparation of spray-dried drug-poly(±)lactide (PLA) microparticles from solutions and suspensions. They either dissolved progesterone, or suspended theophylline in DL-PLA/methylene chloride solution, and spray dried to form microspheres of less than 5 μm. In the case of solutions, the drug and PLA were co-dissolved in a common organic solvent and spray-dried. Microparticles of theophyline was used as the model compound for the spray drying of drug suspensions.

Similar results were reported by Takeuchi et al (71) during spray drying microencapsulation of theophylline with acrylic polymers (Eudragit L100-55 and Eudragit E30D). The poorer degree of drug encapsulation found for low polymer content (drug to polymer ratio of 8:3) was attributed to the presence of agglomerates of drug crystals with the polymer, whilst for higher polymer contents (drug to polymer ratio of 1:1or 1:3), the drug crystals were entrapped in the polymer matrix.

The shape and surface topography of the spray-dried particles is also affected by the drug-to-polymer ratio in the formulation. As the polymer content increases, the drug is less exposed at the particle surface, and the dried product has a smoother surface (71).

Transformation of drug crystals into amorphous state, or decrease in drug cristallinity with increase in polymer content can also occur when the drug is initially dissolved in the polymer solution. The nature of the solvent, the temperature of solvent evaporation, and the presence of a polymer may all change the polymorphic form.

Bodmeier and Chen (69) reported that spray dried progesterone is predominantly in its alpha-form of crystal, but when progesterone was spray dried in combination with PLA polymer, the beta-form crystals increased with an increase in the inlet temperature of the spray drier.

Takeuchi et al (71) observed that the cristallinity of the drug (theoplylline) entrapped in the spray dried particles decreased with the increase in the initial polymer

concentration (Eudragit L100-55), and the complete transformation of the drug into amorphous state was observed with a drug to polymer ratio of 1:3. These authors related the changes in drug cristallinity to the effect of the polymer solution viscosity on the kinetics of drug crystallisation, i.e., crystallisation of drug was assumed to be restricted by a viscous polymer solution formed during the drying process and by the rapid solvent evaporation.

3.3.2. Spray Drying as an Alternative Method to the Conventional Microencapsulation Techniques

The potential use of spray drying technique in the preparation of microparticles as an alternative method to the conventional microencapsulation techniques such as solvent evaporation techniques or phase separation, has been investigated by several authors.

Some advantages of the spray drying technique with respect to the solvent evaporation method have been evidenced in the case of the progesterone microencapsulation.

Progesterone has been entrapped within poly(±)lactide (PLA) microspheres by the solvent evaporation technique (74). One problem encountered with this method was the spontaneous crystallisation of progesterone in the aqueous phase. Progesterone partitioned into the external aqueous phase and precipitated after the evaporation of the organic solvent was complete. The drug-loaded microspheres had to be prepared by an interrupted solvent evaporation method, or had to be separated from the free drug crystals by a washing step. This problem did not occur during spray drying of progesterone-PLA solutions (69). In this case, the drug and PLA were co-dissolved in a common organic solvent and spray-dried. The external phase was hot air and the drug was not lost due to partitioning.

In addition, there are some differences between the spray drying and solvent evaporation methods which can be important when selecting a technique for a specific drug microencapsulation. They are :

- the particle size (microcapsules prepared by spray drying are in most cases an order of magnitude smaller than those prepared by solvent evaporation),
- the drying rate, which goes from several seconds in spray drying to several hours in solvent evaporation.

Spray drying was also evaluated for encapsulation of water soluble drugs using biodegradable polymers (75). Injectable microcapsules prepared to ensure the sustained

release of the drug could be obtained by this technique, instead of more commonly used techniques, such as phase separation.

Another application of spray drying for drug microencapsulation reported in the literature is the preparation of mucoadhesive microspheres for nasal administration. Low drug content is often a problem when mucoadhesive microspheres are prepared. However, with the spray drying technique it was possible to charge the amount of the drug incorporated (dissodium cromoglycate, DSCG) in the microspheres prepared with either polyacrylic acid or sodium carboxymethylcellulose polymers (67). The mucoadhesive microspheres size ranged from 3,2 to 5,7 microns.

4. CONCLUSIONS

The evolution of microencapsulation processes towards greater productivity and simplification of formulations ensures the attractiveness of spray drying as a microencapsulation method. Besides advantages such as low processing costs and readily available equipment, it generally provides good protection to the core material, and there is a wide variety of available wall materials.

Spray drying microencapsulation remains one of the most widely used among the current processes in food industry. The major encapsulating agents used are gum arabic, modified and hydrolysed starches. Each one of these available materials has its own strengths and weaknesses. Blends of these materials may be more effective than the individual materials alone. Research of new blends and/or new materials (inexpensive and 'natural' polymers) is continuing with the aim of yielding higher volatile retention and better oxidative stability of the spray dried microcapsules.

Emulsion stability is one of the utmost importance for the efficient entrapment of active compounds. The original structure of the emulsion has a deep effect on size, morphology and porosity of the final dry powder, and subsequently on core loading and release kinetics. Factors related to the composition and characteristics of the emulsion which should be considered to ensure high levels of core retention in this process are the type of encapsulating agent (to take into account the extent to which each material affects emulsion characteristics and drying properties), as well as the volatility, the diffusivity and the solubility of the core material in the matrix.

In evaluating materials encapsulant properties, comparisons based on dryer feeds of equal viscosity (with consideration of their aqueous solubility) rather than equal solids may present a true picture of encapsulating abilities.

However, much remains to be done in the volatiles encapsulation area. The most representative characteristics of the final microcapsules are core load, particle size, morphology and kinetics of core release. Additional researches are needed to evaluate the physicochemical factors associated with the retention and release of organic compounds from the traditional spray dried encapsulating matrices, in order to better understand how and why retention, losses, and the final and desired release of the active material occur. Subjects of interest for further studies in this area include the following:

- improvement of physical data of organic compounds such as activity and diffusion coefficients in aqueous solution. The data on diffusion coefficients of organic compounds as a function of temperature, composition (water and compounds content) are necessary to allow a quantitative comparison between experimental and theoretical work in spray drying. Only some of these data are available today.
- relationships of diffusion coefficients of molecular species of varying size to bulk properties such as the viscosity of the encapsulating matrix.
- physicochemical interactions of organic compounds in complex media (particularly, in carbohydrate solutions highly concentrated).
- mechanisms of volatile release from encapsulated powders, including evaluation of diffusion and effects of encapsulating matrices phase transitions on volatile release.

Also, spray drying is a potentially suitable technique for encapsulation of peptide and protein drugs. One of the main advantages offered by this technique for pharmaceutical applications is the realisation of the process in a relatively simple continuous operation. The successful results reported through the studies mentioned in this chapter encourage further development of this technique for preparation of biodegradable microparticles for pharmaceutical and medicinal uses.

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