

Air Suspension Encapsulation of Moisture-Sensitive
Particles Using Aqueous Systems

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For Presentation at Symposium
on Microencapsulation
Process and Applications

American Chemical Society
Division of Organic Coatings
and Plastics Chemistry

Chicago, IL
August 27-31, 1973

This work was initiated in the interests of eliminating the use of organic solvents in the application of coatings onto solid particles. While it was anticipated that moisture-sensitive substrates might interact with aqueous coating systems used for encapsulation, it was also realized that the successful utilization of aqueous systems offered economic advantages compared to the use of organic solvents.

For example, if one applies a coating material costing \$2.50 per pound from 5% solution in a solvent costing \$0.13 per pound, the cost of the solvent can equal the cost of the coating material. If the cost of the coating material is less than \$2.50 per pound, the solvent is frequently the largest single cost.

There is also growing concern over solvent emissions and permissible solvents. While solvent recovery can drastically reduce emissions and frequently reduce solvent costs, such recovery requires capital investment. If it were possible to avoid the use of solvents, substantial savings would be possible. Others¹ have described selective coating systems using various ratios of alcohol and water; however, this study utilized completely aqueous coating systems.

A number of useful coating materials can be formulated and applied in aqueous solutions, emulsions, or suspensions. The use of water as the sole solvent has been limited by the fact that many of the materials to be encapsulated are soluble in, or sensitive to, water.

The pharmaceutical industry has been sugar-coating tablets from aqueous systems for many years; in the process, however, encapsulation of water-sensitive tablets is preceded by the application of a moisture-resistant seal coat such as shellac or cellulose acetate phthalate (CAP) to protect the core. A study of various films used for seal coating has recently been released by Shin-Etsu Chemical Company².

We have used the Wurster Air Suspension Coating Process in our own studies because it employs very rapid drying kinetics. The process simultaneously applies and dries encapsulating materials onto particles supported by an upward moving air stream. The movement of particles within the coating chamber is controlled, producing a cyclic flow pattern into which the coating material is atomized. Each time the particles are cycled through the coating zone they receive an additional increment of coating. The process is continued until the desired coating level is attained. The particles exhibit uniform build-up of coating as the run progresses.

In the Wurster Process, drying conditions are a function of the humidity, temperature, and flow volume of the processing air stream, a significant and unique aspect of this process that differentiates it from other encapsulating techniques. The volume of processing air is determined by the size, shape and density of the material being encapsulated. The temperature of the processing air is limited by the sensitivity of either the core material or the coating itself. This information can be used to determine the drying capacity for aqueous systems. Psychrometric charts can be used to determine the desired moisture content of the air supply, the amount of moisture the air can hold at given temperature, and by difference the drying capacity of the air.

¹ Film-Coating Technology: Dr. C. A. Signorino, Colorcon, Inc., Moyer Boulevard, West Point, Pennsylvania 19486: 1973

² Water Sealing of Sugar-Coated Tablets with Pharmacoat 606; Shin-Etsu Chemical Co. (Biddle-Sawyer Corporation, 2 Penn Plaza, New York, NY 10001)

The Wurster Process is commonly used for encapsulating and film-coating particles from organic solvents. Pharmaceutical particles and tablets are commonly coated with cellulose-derived films using solvents such as alcohols, chlorinated hydrocarbons and ketones. Shellac, waxes, and glycerides have similarly been applied to foodstuffs. More recently the encapsulation of materials soluble in, or sensitive to the solvent system has been accomplished using the Wurster Process: e.g., warfarin, an anticoagulant rodenticide soluble in organic solvents, has been encapsulated using an alcohol/chlorinated solvent-based system.

The product to be encapsulated can be affected in several ways by an aqueous encapsulation system. A material may:

Dissolve	Sugar, salt
Change states of hydration	$\text{FeSO}_4 \cdot 4\text{H}_2\text{O} \rightarrow \text{FeSO}_4 \cdot 5\text{H}_2\text{O}$
Exhibit Instability	$\text{NaHCO}_3 + \text{RCOOH} \rightarrow \text{RCOO}^- \text{Na}^+ \text{CO}_2 + \text{H}_2\text{O}$

Aqueous coating systems can be grouped into the following categories:

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|---|---|
| 1. Water-soluble compounds | Sugars, salts |
| 2. Water-soluble polymers | Hydroxypropyl cellulose, hydroxypropyl methyl cellulose |
| 3. Water-dispersible colloids | Gums, starches |
| 4. Emulsions of water-insoluble materials | Polyvinylidene chloride polystyrene butadiene |
| 5. Suspensions of water-insoluble materials | Calcium carbonate, silica |

The water-soluble polymer hydroxypropyl cellulose (HPC) was selected for this study because of its established position in the pharmaceutical industry, and a polyvinylidene chloride (PVDC) emulsion was also selected for comparison of aqueous solution and emulsion types of encapsulating systems.

Initially, tests were made on placebo tablets at several moisture levels to determine the feasibility of encapsulating from aqueous systems without increasing the moisture content of the final product. Analytical data were obtained for tablets at three moisture levels to determine whether moisture was added during encapsulation with the selected polymer system.

<u>Tablets</u>	<u>Percent Moisture</u>		
Uncoated	3.2	2.5	1.0
Coated, HPC	3.1	1.4	1.0
Coated, PVDC	2.9	1.6	1.1

The moisture content of the final product is a function of the operating conditions used. The chart shown contains data obtained under normal drying conditions and indicates that under these conditions little or no moisture was added to the product. When drying conditions were inadequate, the moisture content of the product did increase.

Another series of experiments was conducted to determine the effect of aqueous coating systems on materials known to be sensitive to water. Ascorbic acid and acetylsalicylic acid

tablets³ were selected because both are water-sensitive and both have degradation products readily determined by standard analytical methods.

Decomposition products were determined within 10 to 14 days after encapsulation and again after an accelerated storage cycle of 30 days at room temperature, followed by 30 days at 37°C, followed by 60 days at room temperature. All samples were stored in sealed glass containers.

The Vitamin C tablets used in this study contained 50 mg ascorbic acid each. They were coated with HPC and analyzed for dehydroascorbic acid, the decomposition product of ascorbic acid. The data show no significant increase in the amount of dehydroascorbic acid as a result of encapsulation with an aqueous system. The analysis is accurate to ± 0.05 mg.

<u>Decomposition of Vitamin C</u> (mg. Dehydroascorbic acid/50 mg. Vitamin C)		
<u>Tablets</u>	<u>10-14 Days</u>	<u>Accelerated storage</u>
Uncoated	0.19 mg.	0.12 mg.
Coated	0.15	0.17

The same coating experiment was conducted using aspirin tablets containing 325 mg. of unstabilized acetylsalicylic acid and analyzed for the decomposition product, salicylic acid. In this test a more distinct pattern is observed, which reflects the effect of varying the coating conditions.

<u>Decomposition of Aspirin</u> (% Salicylic acid)			
<u>Tablets</u>	<u>Process Air Temperature</u>	<u>10-14 Days</u>	<u>Accelerated storage</u>
Uncoated		0.09%	0.23%
Coated, A	130°F	0.14	0.48
Coated, B	115°F	0.12	0.18
Coated, C	110°F	0.12	0.84

The difference in salicylic acid content of Samples A, B, and C correlate with process temperatures used during encapsulation. These tests indicate that either excessive heat (A), or inadequate drying (C) are undesirable and contribute to instability.

It is observed in Sample B that under properly controlled conditions it is possible to apply aqueous coating systems with a minimum of hydrolysis to the product.

Studies with each of these systems have demonstrated that solvent release characteristics, concentration, and molecular weight of the polymer, as well as processing conditions and

³ Tablets were supplied by courtesy of Eli Lilly and Company, Indianapolis, Indiana

equilibrium moisture content of the film, are all factors, which can affect the quality of the encapsulated product.

Water-based encapsulating systems, which have been applied by the Wurster Process include:

Cellulose Derivatives:

Methyl cellulose (MC)	Hydroxypropyl methyl
Ethyl cellulose (EC)	Cellulose (HPMC)
Hydroxypropyl cellulose (HPC)	Hydroxypropyl methyl
Cellulose acetate phthalate (CAP)	Cellulose phthalate (HPMCP)

Others:

Chitosan	Hydrolyzed cereal solids
Eudragit E	Polyvinylidene chloride
AEA Sank yo	Polystyrene butadiene
Shellac	Acetylated glycerides
Carbowax	Carrageenan
Acrylics	Polyvinyl acetate
Gelatins	Casein
Starches	Milk solids
Dextrins	Whey
Clays	Soy protein

Although this study of aqueous systems has centered on pharmaceutical products, it is apparent that potential areas of application can include:

- * Encapsulation of food ingredients to maintain activity.
- * Encapsulation of flavors and essential oils to improve shelf life of dry products.
- * Encapsulation of dehydrated products.
- * Encapsulation of seeds with no loss of seed viability.
- * Encapsulation of metals without corrosion damage.
- * Combination of reactive ingredients into products activated by moisture.
- * Application of colorants onto powders or crystalline products.

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