

## FROM SOLVENT TO AQUEOUS COATINGS

(Out of the Frying Pan....)

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A number of reasons exist for the current high level of interest in aqueous coating systems. The primary concern would seem to be government regulation. Over the years, solvent emissions regulation has become more and more stringent. New emissions are permitted only in special cases and usually only with 85% control, limiting both the expansion of existing solvent coating operations and the creation of new ones. Only recently has relaxation occurred in the exemption of Methylene Chloride in a number of states.

Industrial Hygiene rules have also been tightened. Limiting worker exposure to solvent vapors in the work place requires better ventilation, thereby increasing heating and air conditioning costs.

Another area of concern is the cost of the solvents, which can only be expected to rise in any long term projection.

If we eliminate organic mixtures, what is left? Hot melts and aqueous solutions. Although Hot Melts presently have application in the food field, they are still in their infancy in the pharmaceutical field. Therefore, we will deal mostly with aqueous systems.

Like other systems, aqueous coatings have some disadvantages. First, the selection of coating materials is limited to those which are water soluble or dispersable. Over the last two to three years several new products have become available. Aquacoat® (FMC), and aqueous form of Ethylcellulose; Coateric® (Colorcon), a water dispersable formulation of PVAP for enteric coating, and Eudragit L30D® (Rohm Pharma), also an enteric coating, are among them. Additional materials are expected to be introduced as more companies become active in aqueous coatings.

Once a coating is decided upon, a compatible plasticizer must be found. As shown in Figure 1, there are a large number of plasticizers, which can be considered. Water insoluble plasticizers can be used with some suspensions, latexes and dispersions.

FIGURE 1

PHTHALATE ESTERS

Cyclohexyl ethyl phthalate

Cyclohexyl methyl phthalate

+Dibutyl phthalate

+Diethyl phthalate

Diisopropyl phthalate

Dimethyl phthalate

+Dioctyl phthalate

Castor oil

MISCELLANEOUS ESTERS

Aetyl Tributyl Citrate

Acetyl Tiethyl citrate

Butyl stearate

+Dibutyl sebacate

Dibutyl tartrate

Diisobutyl adipate

+Glycerol Monostearate

Pegospere 100 M1

Methozyethyl oleate

Butoxyethyl Stearate

+Triethyl citrate

+Tributyl citrate

PHOSPHATE ESTERS

Santicizer 140

Tricresyl Phosphate

Triethyl Phosphate

Triphenyl phosphate

OILS

Lubricating oil

Mineral oils, refined

OILS(con't.)

Corn oil

Cottonseed oil

Durkex 500

OTHERS

Oleic Acid

-Stearic acid

-PEG 4000

-PEG 6000

Cetyl Alcohol

Myristyl Alcohol

Stearyl Alcohol

+Tributyryn (glycerol tributyrate)

By varying levels of coating (Figure 2), the plasticizer (Figure 3), and levels of plasticizer (Figure 4), a custom designed product can be obtained.

FIGURE 2

Release curves showing a decreasing rate of release as the coating level increases.  
(A latex plasticized with diethylphthalate)

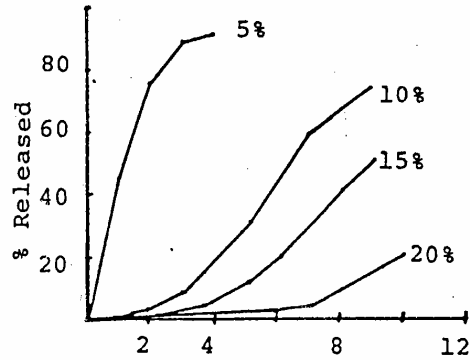


FIGURE 3

Comparison of the release rate for films plasticized with diethylphthalate (DEP) and Tributyrin

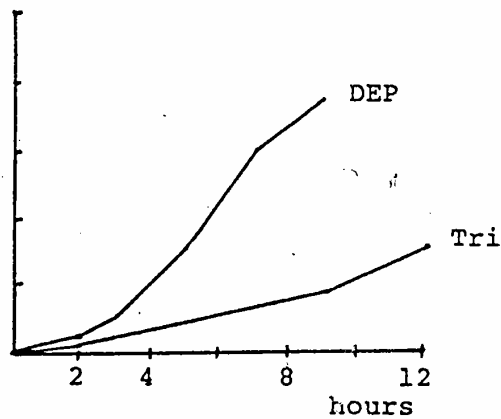
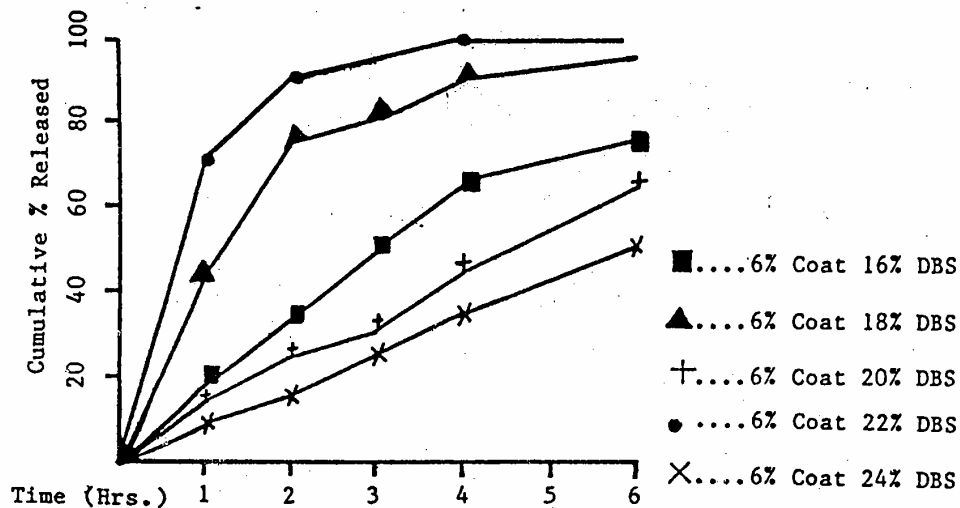


FIGURE 4

Effect of various coating levels with 6% coating on theophylline release rate from beads

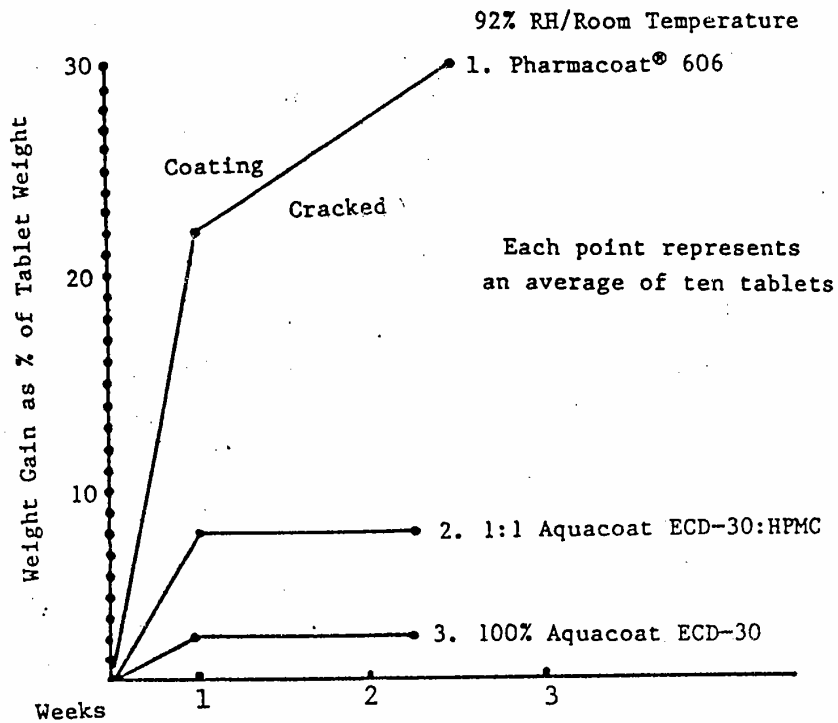


Keep in mind that water is less volatile than commonly used organic solvents, and may result in a higher energy cost to dry the coating. Exceptions do exist such as latexes which have a very low affinity for water, and therefore can be run at lower temperatures, higher rates.

The use of organic solvents raises the possibility of residual solvents in the finished product and it is important to be aware of the possible effects these would have on product stability or consumer health.

In addition to residual organic solvents in the product, residual water and moisture pickup in processing and storage are also of great concern (Figure 5). This can be limited with modification.

FIGURE 5



Although water is not considered a hazard itself, it can have adverse effects on many active ingredients resulting in dosage forms which are contaminated by degraded products (Figure 6 & 7). Microbial proliferation may be a problem in solution preparation and storage, cracked films may occur during processing or storage, and activity may be damaged if processing is not handled properly.

FIGURE 6

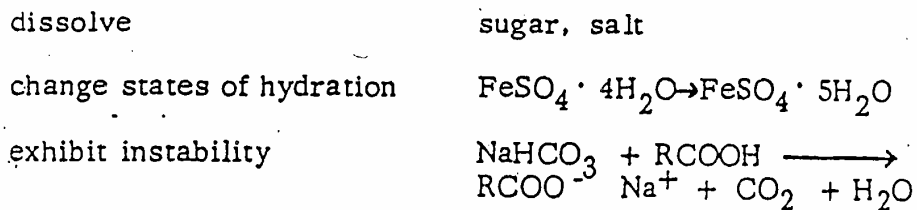


FIGURE 7

Microbiological proliferation of E. coli in test solutions

Microbiological proliferation of E. coli in test solutions

MEAN VARIABLE COLONY COUNT ( $\times 10^3$ ) NORMALIZED TO 1 ml SAMPLE

| Test | Polymer   | 0 hr | 8 hr | 1 day | 2 day | 5 day | 9 day | 14 day |
|------|---|------|------|-------|-------|-------|-------|--------|
| 1    | HPMC<br>Methocel E5 Grade (Dow)   | 2.1  | 2.7  | 1.3   | 2.3   | 66    | 130   | 102    |
|      | HPMC<br>Methocel E15 Grade (Dow)  | 2.1  | 2.2  | 1.3   | 1.1   | 0.1   | 0.0   | 0.0    |
|      | HPMC<br>Methocel E50 Grade (Dow)  | 2.0  | 2.8  | 2.1   | 1.2   | 0.1   | 0.0   | 0.0    |
|      | Sterile water control-  | 2.1  | 2.0  | 1.4   | 0.7   | 0.1   | 0.3   | 0.1    |
| 2    | HPMC  | 10   | 14   | 15    | 17    | 75    | 142   | 141    |
|      | HPMC  | 10   | 13   | 14    | 16    | 45    | 85    | 96     |
|      | HPMC  | 10   | 14   | 16    | 18    | 65    | 125   | 127    |
|      | Sterile water control-  | 10   | 9    | 6     | 3     | 2     | 1     | 1      |
| 3    | Pseudolatex-<br>Ethylcellulose latex, 20% Solids (Aquacoat: FMC)                | 9    | 0    | 0     | 0     | 0     | 0     | 0      |
|      | Pseudolatex-<br>Ethylcellulose latex, 30% Solids (Aquacoat: FMC)                | 8    | 0    | 0     | 0     | 0     | 0     | 0      |
|      | Methacrylic Copolymer-<br>Eudragit E-30D (Rohm Pharma)                          | 10   | 14   | 15    | 17    | 74    | 142   | 141    |
|      | Polymethacrylic acid/ester copolymer-<br>Eudragit L-30D (Enteric) (Rohm Pharma) | 10   | 13   | 14    | 16    | 45    | 85    | 96     |
|      | Sterile water control-  | 10   | 9    | 6     | 3     | 2     | 1     | 1      |
|      |   |      |      |       |       |       |       |        |

When a decision has been made to explore aqueous film coating as an alternative to organic solvents, what problems are likely to be encountered, and what can be done to resolve them?

Product appearance may change. The changes may be most apparent in color shades and thickness of coating levels when switching from solvent to aqueous coatings.

Aqueous films also tend to have a lower gloss level than the same polymers applied from organic solvents. In some cases this can be overcome by using a light "glaze" coat of HPMC modified with PEG's applied as a very dilute solution to improve gloss. Other problems such as logo filling, bridging, modeling and rough surfaces can be changed by modification in the coating, application, equipment or processing conditions.

During application, the aqueous film is relatively easy to damage. In a pan, damage can be minimized by reducing the pan speed to the point at which the tablets are just nicely cascading without being lifted or tumbled excessively. This may require modification of the pan drive. Many conventional pans are set at a fixed speed and even newer pans with variable speed drives are often limited as to how slow they are able to turn. Sugar pans may turn at 20 to 40 RPM depending upon size and even 60" vented pans are often run a 10 to 12 RPM for solvent film coating. By comparison, 3 to 4 RPM is usually sufficient for aqueous film coating.

Another item which often requires changing is the manner in which the coating is applied. Although some coatings, including shellac and sugar coatings, are ladelled on, ladelling of aqueous film coatings causes gross wetting of the cores. Organic based film coatings are often sprayed on using hydraulic or air atomizing nozzles. Aqueous solutions of materials such as HPMC are often more difficult to atomize well due to higher viscosities. Latex formulations will film-form under hydraulic pressures and plug the nozzles or bind the pumps. For these reasons, most aqueous coatings are applied using air atomizing nozzles. The ratio of air to fluid can be adjusted to obtain the desired degree of atomization and latex systems can be pumped without high shear or pressure.

Many commercial air atomizing nozzles are limited in that they are capable of atomizing only 100 ml/min of HPMC solution and doing it well. In conventional and vented pans this will probably require the use of multiple nozzles to keep the delivery rate per nozzle below this limit. As many as 8 nozzles have been used in large vented pans. Since some nozzles perform better at higher rates than others, the mist can be checked by passing a card through the spray and examining the card for large droplets. In our own trials in columns, we found it necessary to have a nozzle custom designed to obtain spray rates of 300-600 ml/min and still create a fine mist.

Because water is less volatile than most organics, drying is even more important for aqueous film coating. It is desirable to maximize the amount of air passing through the coating unit. This can be quite limited in conventional pans due to problems in creating even air flow in and out of the pan without distorting the spray pattern and the tumbling motion. This problem is greatly reduced in vented pans and columns because the air is directed to bring the spray into contact with the product. There is no minimum air volume required to coat successfully. However, the more air available, the faster the coating can be applied. Faster coating not only means shorter processing time, but also helps to minimize physical damage to the cores.

Although some water soluble polymers have comparatively high viscosities, other materials permit the use of relatively high solids ratios. Some dextrans and maltodextrins can be sprayed at 30% solids and even higher. Water disperseable polymers can be used at 15% polymer solids and latex formulations can be used between 30% and 50% solids.

Progress in aqueous film coating seems slow, but much has changed since 1973 when we described successful coating of vitamin C (Figure 8) and aspirin core (Figure 9) with aqueous films. New materials, improved equipment, and experience acquired make the future bright for aqueous systems.

FIGURE 8

Decomposition of Vitamin C  
(mg. dehydroascorbic acid/50mg. Vitamin C)

Tablets

10-14 Days

Accelerated Storage

|          |          |          |
|----------|----------|----------|
| Uncoated | 0.19 mg. | 0.12 mg. |
| Coated   | 0.15     | 0.17     |

FIGURE 9

Decomposition of Aspirin  
(% 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                       |