ADVANCEMENTS IN TABLET COATING

By

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There is genuine hazard in attempting to discuss the latest advancements in any area. The danger is that the supposed “expert” may be talking to people who are really making advancements, which exceed those of the speaker. There are those in the audience who could readily expand upon my information and I encourage them to bring their information to the roundtable discussion.

In recent years there have been a number of developments in tablet coating technology. Some of these have been quite dramatic, but we need to take a historical perspective to determine just how dramatic they are. Technology that we consider almost routine today is really quite new to the pharmaceutical field.

Personally, my first contact with aqueous coating systems was in the period of 1967 through 1969. I then worked for a company, which makes packaging materials, on projects involving coatings applied to packaging materials for food contact. It was in this context that I was introduced to latex coatings. I remember my naivete and embarrassment because I could not quite understand how a coating could be diluted with water yet form a waterproof film when dried. I also remember asking more experienced chemists how this worked without receiving a good answer.

Although latex technology was new to me, it certainly was not new technology. In 1950, about 18 years before my introduction to the topic, 9 million gallons of latex paint were produced in the United States (1). Between 1950 and 1968 there were many changes and improvements in latex technology, and many new polymer combinations became commercially available. These polymers were used in developing coated papers (freezer wrap), textiles (rain gear and wallpaper), floor polishes, non-woven fabrics (filters), leather finishes, special concrete mixes, road paving materials, and glues, in addition to latex paints.

Up to about 1970, however, there had been no real use of latex technology, or aqueous coatings in general, in coating tablets. I feel that there were two concerns, which effectively inhibited aqueous coatings in the pharmaceutical industry:

1) A concern that many chemicals of pharmaceutical interest are unstable in the presence of water, especially at elevated temperature.

The pharmaceutical industry has long been concerned with delivering a safe and effective product to the market. Because of this we are concerned with shelf life and product degradation in stressful environments. Many products are routinely checked for stability and degradation, often by exposing them to conditions of high humidity and temperature. After many years of thinking high temperature and humidity as accelerating degradation and working diligently to minimized product exposure to such conditions it seemed quite natural to consider that exposing the product to water based coatings which must be dried with heat might be undesirable.
Although the pharmaceutical industry has a long history of sugar coating, and certainly used water-soluble cellulosic films in film coating prior to this time, many people were in the process of switching from sugar coating to film coating. Film coating usually meant films cast from organic solvents. Even water soluble films based on hydroxypropyl and hydroxypropyl methyl cellulose (HPC and HPMC) were normally applied from solvent mixtures to achieve short process times and glossy coatings.

2) A lack of coating materials based on these new technologies, which could be considered safe for ingestible products.

Water resistant polymers in latex form had not been developed with pharmaceutical applications in mind. Latex formulations then available generally were prepared using monomers, polymers and/or emulsifiers, which were not approved for ingestion. This was largely due to neglect of the comparatively small pharmaceutical market by those conversant with the technology.

In the early 70’s things began to happen. In 1970 and 1971 work was performed at Wisconsin Alumni Research Foundation (WARF) using latex systems to coat agricultural seeds. The success of this work led in 1971 and 1972 to trying to apply this technology to coating of pharmaceutical tablets. Published in 1973, (2) this work established that water sensitive products, aspirin and vitamin C, could be coated with water-based coatings without harming the product, if done carefully.

Table 1 shows the results of an early study demonstrating that tablets can be coated with water based systems without increasing the water content of the tablets. In this work the water content of the tablets actually dropped during coating.

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncoated tablets</td>
<td>3.2%</td>
<td>2.5%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Coated with HPC</td>
<td>3.1%</td>
<td>1.4%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Coated with Latex</td>
<td>2.9%</td>
<td>1.6%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

The data in table 2 show very little decomposition of aspirin to salicylic acid and vitamin C to dehydroascorbic acid after coating with HPC (Klucel) applied from aqueous solution. It was observed that use of excessive heat or over-wetting of the tablets did result in greater decomposition.

**TABLE 2**

<table>
<thead>
<tr>
<th>% DECOMPOSITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14 DAY</td>
</tr>
<tr>
<td>30 DAYS</td>
</tr>
</tbody>
</table>
### Table

<table>
<thead>
<tr>
<th>Material</th>
<th>@ RT</th>
<th>@ 37 C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncoated Aspirin</td>
<td>0.09%</td>
<td>0.23%</td>
</tr>
<tr>
<td>HPC coated Aspirin</td>
<td>0.12%</td>
<td>0.18%</td>
</tr>
<tr>
<td>Uncoated Vitamin C</td>
<td>0.38%</td>
<td>0.24%</td>
</tr>
<tr>
<td>HPC coated Vitamin C</td>
<td>0.30%</td>
<td>0.34%</td>
</tr>
</tbody>
</table>

The same year Signorino (3) reported work showing the usefulness of water/alcohol systems as a way to reduce the amount of organic solvent used. Also in 1973 Lehman and Dreher published a paper (4) describing the successful use of specially designed acrylic latices based on Eudragit® resins to coat tablets. At the January 1974 Arden House Conference, Dr. John Vanderhof of Lehigh University discussed wetting and film formation. This was important because it brought together people from the U.S. pharmaceutical industry with those knowledgeable about latex systems. In 1975 Jackson (5) reported no "commercial use of aqueous film coating" in the U.S. In 19975 Shinetsu (6) published data showing food stability for vitamins C and B1 and also for aspirin using HPMC applied from aqueous solution. Shinetsu did report slightly better stability when using lower viscosity grades of HPMC and when using slower spray rates (drier processing conditions).

In 1978 Hinkes (7) reported cost savings for companies, which had switched from using organic solvents to aqueous coating systems. The greatest savings were attributed to elimination of solvent costs.

The period 1978 through 1985 has seen the commercial development of several coating materials for use with aqueous systems. The first available were the Eudragit® resins mentioned above. These are manufactured by Rohm GmbH and are available in several forms. Eudragit E30D is a latex polymer, which dries to a water insoluble, but somewhat permeable film. Eudragit L30D is an enteric resin in latex form. Eudragit L100-55 is a powdered enteric resin, which is dispersed in water with the assistance of a base. Another early entry is HP-55F, a fine powder made with hydroxypropyl methyl cellulose phthalate by Shinetsu Chemical. HP-55F is also dispersed in water, along with a plasticizer, at time of use.

A dispersion of unplasticized ethylcellulose, known as Aquacoat® became available about 1980 through FMC Corporation. Although this is technically a pseudo-latex it is handled like conventional latex systems. Aquacoat must be plasticized prior to use. This requires a mixing step but permits one to tailor the coating as needed. FMC has published a large amount of data showing the effect of different plasticizers, plasticizer levels, processing conditions, and even the core being coated on the finished product. Recently Colorcon has begun marketing an aqueous ethylcellulose formulation under the name Surelease®. Because Surelease is preplasticized, mixing at time of use is simplified but the coating properties cannot be readily changed.

In the early 80's a water dispersable form of polyvinyl acetate phthalate known as Coateric® was brought to market by Colorcon. Since that time FMC has begun marketing a water dispersable form of cellulose acetate phthalate under the name Aquateric®.
The result of all the above activity is the availability of many products for aqueous coatings that were not available just 10 years ago.

"NEW" MATERIALS

Looking to the future we can anticipate some new developments in related areas, and also some new directions in coating formulations. It is my feeling that we will see further development, not only of new products and materials but also renewed and more creative use of some not so new coating materials.

Zein is one material, which seems to be finding new applications. Zein has had a troubled history since the early 70's. Several companies have gotten into and out of the business of supplying zein, which has created questions of availability. Zein seems at present to be reliably available from Freeman. What is most interesting is that new formulations based upon zein are becoming available after years of little activity. Zein is not readily soluble in single solvent systems. Because of this, zein is often formulated in mixed organic solvents or in mixed water/alcohol systems. Of current interest is Aqua-Zein®, which is an aqueous zein formulation containing no alcohol. This product is formulated using ammonia, which is driven off, and a plasticizer. Part of the plasticizer is also driven off, the balance being incorporated into the film.

Looking farther ahead I anticipate the development of high amylose starch and starch derivatives as coating materials. Dextrins, which are made from starch, have been used for a very long time as glazes in the confectionery trade. Although they work well as glazes they dissolve too quickly and lack film toughness to be highly useful for tablet coating. High amylose starch and starch derivatives yield tough films, which have excellent properties.

I feel that the situation concerning starches today is analogous to the status of latex technology of 10 - 15 years ago. Outside the pharmaceutical industry starch derivatives are widely used as "industrial gums" in papermaking, packaging materials, textile sizing and finishing, and adhesives.

One group of derivatized starches, the hydroxypropyl derivatives, are currently offered for food use. They have excellent film forming properties and are used in coating food products such as frozen french fries and in gum candies. High amylose starches are also used in making soluble packaging materials.

Some starch derivatives are presently limited by FDA restrictions on use as food ingredients, although they are considered suitable for food contact. This also is analogous to the limitations on about 15 years ago. I feel that in the next few years starches and their derivatives will be useful, inexpensive coating materials in the pharmaceutical industry also.

AUTOMATION

An area which has received a great deal of attention in recent years, and which will receive a great deal more, is automation. As an industry we have progressed from largely manual controls to individual automatic controls for each coating function. A few companies have
gone beyond this to integrate the automation so that the entire process can be staged and controlled from a central unit.

Currently several suppliers of equipment are developing and introducing automated systems which not only monitor and control each important parameter, but integrate the controls so that a change in one condition causes a corrective or compensating action elsewhere in the system. If the change is critical and cannot be compensated for, the system must shut itself down.

Perhaps of greatest interest is the fact the systems are designed not only to monitor the process itself but also to do the record keeping and to double check all ingredients. This introduces a quality assurance factor, which is a level above that previously available.

A separate presentation will discuss an automated coating system used with the Accela-Cota. I would like to take a few minutes to discuss an automated system designed especially for use with coating columns and which will be introduced formally under the name COMMANCI at the Chemical Exposition in New York in December. COMMANCI is an acronym derived as follows:

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COMPUTERIZED
MANUFACTURING
COATING PLACE
INC.
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For many years we have been working to identify the key variables in the coating process and developing the means to monitor and control them. This has taken time because in some cases it was necessary to control one function well before the effect of another function became apparent. Then it was necessary to devise a means of monitoring the new function, and eventually controlling it.

After the important items were identified and properly monitored and controlled, it was necessary to develop the logic to integrate the system. The system is designed with sufficient flexibility to permit experienced operators to make adjustments based on judgment, but also prevents operators from exceeding process specifications. This is accomplished by using several levels of authority within the program. At the highest level the Management Directory, screen 1, permits only those knowing the correct code to enter or change data concerning what is to be produced, formulation orders and process conditions, and lot identity.
The Supervisor Directory, screen 2, permits those with that code to call up lot numbers, formulation orders and other information, however this group may make only limited changes in control ranges.
The operator screen has the same display options as the supervisor screen, however operator codes permit changes only within preset ranges unless a supervisor or higher also authorizes the change.

To simplify quick readout of process data, a schematic graphic has been developed which clearly displays current process variables (Screen 3). An operator can see at a glance what current conditions are and the status of the process.

SCREEN 3
The central computer reads the individual controllers many times a minute and directs changes in control points per a Formulation Order which has been entered by the head of manufacturing. At directed intervals it dumps data to a permanent file. The program can print a voluminous data summary if requested. To avoid having to interpret reams of computer printout to determine just what the history of a particular batch may be, another graphic has been developed which tells at a glance the history of that batch. If greater precision is desired the printout is still available. Screen 4 shows the graphic for a coating run. The chart, actually in color for clarity, shows the entire process for a given batch of product.

SCREEN 4
The computer is not simply monitoring and controlling the process, it also creates a record by batch, does all calculations such as yield and accountability, creates hard copy as desired, cross checks each ingredient, and summarizes the batches to provide data on the entire product run. All materials, which are approved for use on that project, are also entered into memory. As each ingredient is weighed out and added the operator keys in the lot number and verifies the weight. If the weights or lot number cannot also be verified by the computer it will not accept the command and will not proceed to the next step.

None of us can truly predict the future, but I hope that this discussion of current and anticipated developments gives some of you a sense of what we are working on.


5) Jackson, Gerald J., Ph.D., *Aqueous Film Coating*. Presented at the Eastern Regional Meeting of the IPT Section, 1975.
