Excipients are generally considered inert additives included in drug formulation to help in the manufacturing and use of the dosage form. Yet, evidence indicates they are not inert, and drug excipient interaction can give rise to many problems. For one class of excipients, ion exchange resins, the interactions can actually be used to control the rate and site of drug dissolution.

Ion exchange resins are polymeric materials that contain basic or acidic groups that interact with ionizable molecules and create insoluble salts. The resins—elusive to industry until now—have been used as active ingredients in drug formulations; as excipients for tablet disintegration, taste-masking, controlled release, extended release and drug stabilization; and in pharmaceutical manufacturing for drug isolation, drug purification and catalysis of reactions. The resins are insoluble solids that are not absorbed by the body, so are very safe.

The drug-resin complex, known as a resinate, can be used in suspension or isolated as a dry, solid, free-flowing, stable compound. The drug is released from the resinate upon exposure to physiological fluids. The nature and extent of the interaction between the drug and the resin depend on factors such as pK of the drug and the resin, ionic strength, pH of the fluid, solubility of the drug and chemical structure of the resin. Examples of drugs that have used ion exchange resins in formulation include dextromethorphan, ranitidine, paroxetine, diclofenac, and ibuprofen.

Ion exchange resins allow formulators to achieve some very desirable results:

- **Effective Taste-masking**—The drug resinate has no taste because it is insoluble, if the drug is not released during passage through the mouth. A liquid paroxetine formulation uses this approach.
- **Controlled release**—The release rate of the drug from the resinate can be manipulated. A slower rate of dissolution of pure drug allows extended release—up to several hours. Further control can be induced by applying a coating to the resinate.

A novel approach to the extended release application has been developed recently. The drug and resin are simply mixed together in the dosage form, eliminating the need to manufacture the resinate. Drug loading occurs in vivo because of the drug-resin interaction, but is slowly released as dissolved drug is absorbed by the body. When comparing diclofenac resinate and a diclofenac/resin mixture, one can see that the dissolution

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### Physical Properties of Pharmaceutical Ion Exchange Resins

- Fine, free-flowing powders
- Commercially available particle size of 25-150 microns
- Contain functional groups that exchange ions
- Insoluble in all solvents
- Not absorbed by the body
- Manufactured under cGMP

### Dissolution of Indomethacin

<table>
<thead>
<tr>
<th>Time (mins)</th>
<th>% Released</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>61</td>
</tr>
<tr>
<td>20</td>
<td>78</td>
</tr>
<tr>
<td>45</td>
<td>97</td>
</tr>
<tr>
<td>120</td>
<td>100</td>
</tr>
</tbody>
</table>

USP specification for indomethacin capsules: not less than 80% in 20 minutes
rate curves are essentially identical (Fig. 2). Eliminating the need for manufacture and characterization of a resinate reduces the manufacturing cost, development cost and time-to-market.

Simple resinates give a characteristic release-rate profile that is roughly exponential (Fig. 1), preventing their use when a more exotic profile is needed. Recently this situation changed with a unique formulation7. By mixing a resin (unloaded) with a drug resinate, the shape of the release curve was changed significantly. Under some conditions, the inventors achieved an almost constant release rate during a period of several hours (Fig. 3). Compared with some other methods developed for controlled release, this is a very convenient and low-cost option.

**Rapid Dissolution**—The slow dissolution of poorly soluble drugs is a well-known problem responsible for poor bioavailability. The release rate of such drugs from resinates can be much faster than the dissolution rate of the pure drug (Table 2). The commercially available product indomethacin uses micronization of the drug powder to achieve rapid dissolution. Not all poorly soluble drugs are amenable to micronization because of problems including low melting point, dust formation and agglomeration. Ion exchange resinates are a convenient alternative.

**Hygroscopic drugs**—Another recent discovery7 is the use of ion exchange resinates to eliminate problems associated with hygroscopicity, and even deliquescence. Resinate water uptake is significantly less than for the pure drug, and with deliquescent drugs, resinates remain free-flowing under normal environmental conditions.

These examples are certainly not an exhaustive list of the use of ion exchange resinates, but they do serve to demonstrate their benefits. Second only to the use of cellulose excipients for their multiple applications, ion exchange resinates have been called the best-kept secret in the pharmaceutical industry. Their mechanism of action is sufficiently well understood that the drug-resin interaction can be manipulated to create many different effects. The technology should be included in the toolbox of every pharmaceutical formulator.

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