

Overcoming formulation difficulties

How does the pharmaceutical world meet the challenge of the ever-increasing pace in drug development? One shortcut solution for formulators is to use high-performing excipients.

Colorcon

THE CHANGING LANDSCAPE OF THE PHARMACEUTICAL INDUSTRY IS increasing the commercial pressure on R&D groups to shorten time to market for new products. As a result, formulators are demanding more functionality and performance from their pharmaceutical excipients. These ingredients now play a critical role in achieving stability, reducing costs and improving manufacturing efficiencies. They must also produce a robust dosage form that is unaffected by variations in process parameters or other ingredients.

Faced with shorter development cycles and more complex active pharmaceutical ingredients (APIs), formulators cannot afford the luxury of investigating new excipients. They need to use proven ingredients in the development of new tablets or capsules, and rely heavily on the producers of these ingredients to identify new applications.

Enhancing drug formulation

Excipient products from Colorcon have been shown to offer unique synergies with many common ingredients. For example, combining the Colorcon excipient Starch 1500 with microcrystalline cellulose results in very compactable formulations with excellent dissolution. This minimises the need for superdisintegrants that can affect stability. The flow properties and friability of lactose blends can also be greatly improved. Moreover, incorporating specially designed pregelatinised starch products can reduce the amount of lubricants, which are known to cause over-blending problems, and affect dissolution and film coating quality.

As APIs become more sophisticated, many of them are effective at low-dose concentrations and are often micronised. But low-dose medicines can be a challenge to formulate due to problems with content uniformity and physical stability. Traditionally, these drugs have been manufactured through wet granulation to assure that each tablet contains the proper amount of active material. This process can, however, be costly and time-consuming because of the many steps involved. If water has a detrimental effect on the drug, solvents must be used — thus increasing the cost and difficulty of the process.

Colorcon technical experts have helped many of their customers develop direct compression manufacturing

processes for these drugs through the use of Starch 1500. Content uniformity is achieved by first preparing a preblend of the API and Starch 1500, followed by the addition of the remaining ingredients and tableting. The granular morphology of this unique excipient combined with its inherent moisture content produces an ordered mix through adhesion and hydrogen bonding.

Humidity control

Moisture-sensitive drugs present another challenge to formulators. Potential problems associated with these APIs include reduced flow properties, as well as changes in dissolution rates, chemical stability and physical stability (in terms of colour, for example). Some ways to protect moisture-sensitive products involve humidity-controlled manufacturing conditions, protective packaging, moisture barrier film coating and, most importantly, selecting excipients that minimise moisture sensitivity. In this selection process, it is important to understand the difference between moisture content and water activity.

Total moisture content is, typically, measured by loss on drying. However, this method does not distinguish between bound moisture (unavailable for chemical interactions) and unbound moisture (available for chemical interactions). A better measure is water activity or equilibrium relative humidity, which shows only the unbound water that is free to interact with the drug.

For example, although the moisture content of Starch 1500 is higher than some other excipients', the water content is considerably lower. Therefore, it will equilibrate slower when exposed to moisture conditions and may, preferentially, bind the moisture, preventing interaction with the drug. Starch 1500 has been used to develop formulations with proven stability for many moisture-sensitive APIs, including aspirin and ranitidine. These robust formulations have helped lower costs by reducing the need for special manufacturing conditions and expensive packaging.

As formulators turn to proven excipients and vendors to meet today's challenges, Starch 1500 and Colorcon offer a long history of reliability and efficacy, and continue to provide benefits in the development of new applications. ■■■

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