USING THE FULL DESIGN SPACE POLY(VINYL ACETATE) PROVIDES IN THE FORMULATION OF DIRECTLY COMPRESSIBLE SUSTAINED RELEASE TABLETS

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Overview

In a June 2105 webinar titled "Using the full design space poly(vinyl acetate) provides in the formulation of directly compressible sustained release tablets," Thorsten Cech, Manager of the European Pharma Application Lab at BASF SE, presented a deep dive into how poly(vinyl acetate) (PVAc) opens up an array of options to formulators of directly compressible sustained release tablets.

Context

Sustained release tablets are challenging formulations to get right. The formulation must release the active pharmaceutical ingredient (API) over a prolonged period of time and be robust enough that this dissolution profile remains constant even if details of the processing change. In trying to achieve these goals, it is useful for formulators to have a strong sustained release agent that is suitable for use in a number of processing techniques.

PVAc fits these criteria. This is a very strong sustained release agent--it is used in chewing gums. And it comes in two distinct forms. Kollidon SR is a powdery material made up of 79% PVAc. The other two main components are poly(vinyl pyrrolidon) (PVP K30) and sodium lauryl sulphate (SDS), which make PVAc more brittle and thermodynamically stable in water. Kollicoat SR 30 D has a similar composition but is an aqueous polymer suitable for use in coating applications and as a binder in wet granulation.

Key Learnings

Using PVAc as a powder and an aqueous dispersion creates a vast design space

The availability of PVAc as a powder and aqueous dispersion is a boon for formulators of sustained release tablets. A formulator can use Kollidon SR in direct compression with an API to create a tablet with a certain release profile. Then, by taking the same mix and putting it through a wet granulation process, the formulator can create a tablet with exactly the same quantities of API, PVAc and other components, but with a dramatically different release profile. The aqueous form adds even more options.

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When working with a poorly-soluble API such as theophylline, this creates opportunities to tweak the release profile. A simple, direct compression formulation of theophylline and Kollidon SR will release 70% of the API within 24 hours. Using the same recipe in wet granulation in a high-shear mixer changes the porosity--but not the formulation--of the tablets. In the case of theophylline, the change to the porosity leads to 100% of the API being liberated after 24 hours.

Formulators can achieve similar results by inputting the same theophylline plus Kollidon SR recipe into an array of processes. Single pot technology changes the particle size and shape, but has no effect on the dissolution profile. Similarly, fluid bed granulation creates unevenly shaped particles that nonetheless release the API at the same rate as the aforementioned processes. Comparable drug release is achieved regardless of technology, opening up a vast design space to formulators.

THE VAST DESIGN SPACE ENABLED BY PVAc IS PARTICULARLY USEFUL WHEN WORKING WITH HIGHLY-SOLUBLE APIs.

Fluid bed granulation and Kollicoat SR 30 D turn soluble APIs into sustained release tablets

The vast design space enabled by PVAc is particularly useful when working with highly-soluble APIs. Caffeine, for example, is released much faster than theophylline, regardless of whether the tablet is made using direct compression, wet granulation or single pot technology. Such highly-soluble APIs are prone to over-wetting during processing, a phenomenon that causes the ingredient to dissolve and recrystallize on the surface. These crystals are released immediately when exposed to water.

Fluid bed granulation helps resolve over-wetting by continuously drying in parallel to the agglomeration process. This entails introducing hot process air and evaporating it immediately. When applied to caffeine, the process creates tablets with a more sustained release profile than the other techniques, but that still fall short of what is achievable with Kollidon SR. To lengthen the release profile further still, Kollicoat SR 30 D is added to the granulation liquid.

Kollicoat SR 30 D dries out the granulation process while also acting as a coating. In doing so, it prevents the over-wetting that blights other processing techniques and results in tablets with a true sustained release profile. Formulators can adjust the rate of release by varying the amount of PVAc that is added to the granulation liquid, allowing for precise control over a tablet's dissolution characteristics without changing its formulation.

Kollidon SR and Kollicoat SR 30 D eliminate compression as a crucial risk parameter in QbD

The release profiles for tablets containing theophylline, caffeine and other APIs when made using the wide array of processes discussed in this summary share some common characteristics. Crucially, one of the shared traits is a lack of correlation between the rate of dissolution of a tablet and the compression force that was applied to it during production. In many of the discussed examples, the dissolution charts for tablets made using five, 10 or 20 kilonewtons of force are identical.

For quality management teams, this is important. It means that even if the rotary press compression settings change during production, the tablets will still have the same release profile and as such will still meet the standards required for shipping to customers. The upshot from a Quality-by-Design (QbD) perspective is that compression force is removed from the list of crucial parameters in the risk analysis.

Summary

Through its experiments using Kollidon SR and Kollicoat SR 30 D in a variety of processes with a diverse range of APIs, BASF has established that PVAc opens up a vast design space to formulators of sustained release tablets. Uniquely, formulators can use PVAc to create tablets with wildly-different dissolution profiles from identical recipes, a capability that allows formulators to factor other needs into their decisions, such as the ability of single pot technology to cut employee exposure to APIs.

Attracted by such flexibility, companies have used PVAc in a range of development projects, some of which have resulted in approved and monographed products. This track record is complemented by BASF's own experiments to demonstrate the applicability of PVAc to many APIs. Collectively, these initiatives create a compelling body of evidence to support the status of PVAc as a go-to sustained release agent.

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BASF offers comprehensive solutions to the pharmaceutical industry, ranging from a broad, high-quality excipients portfolio to APIs. With its expertise in polymer chemistry, its worldwide R&D capabilities and the company's commitment to developing value-adding excipients, BASF continuously creates solutions to challenges related to Instant & Modified-Release, Solubilization, Soft Gels and Skin Delivery.

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