

softgels

ARE SOFTGELS RIGHT FOR YOUR PRODUCT?

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Softgel capsules (or softgels) allow manufacturers to effectively deliver poorly soluble active pharmaceutical ingredients (APIs). This article discusses the benefits of using softgels as well as the manufacturing and handling considerations to keep in mind before selecting this dosage form.

Softgels have been available since 1935 when Robert Pauli Scherer patented the rotary die encapsulation process [1]. Since then, softgels have been used by the pharmaceutical industry for many applications, including the effective delivery of poorly soluble APIs. While the tech-

nology and process have been refined over the years, the basic manufacturing principle remains the same. Two flat polymer ribbons composed of gelatin, water, an opacifier, and a plasticizer are passed between two rotating dies. The dies form the ribbons into mating capsule shell halves while a pump inserts a solution (called a liquid fill) that contains an oil-soluble API. The machine then seals the shells and cuts out the filled capsules.

Softgels allow for the rapid absorption of APIs and generally require lower excipient amounts than tablets. Additionally, modern technologies allow for the production of softgels in a variety of shapes, colors, finishes, and flavors, which can aid in product differentiation, customer

appeal, and patient compliance. However, it is important that manufacturers understand softgels' strengths and weaknesses before choosing this dosage form.

Drug delivery characteristics

The primary reason pharmaceutical formulators and manufacturers use softgels is that this dosage form can effectively deliver poorly bioavailable APIs. According to some estimates, 40 percent of new chemical entities have poor biopharmaceutical properties, specifically due to low solubility [2].

Low solubility is a significant problem for drug developers because insoluble compounds—those designated as Biopharmaceutics Classification System (BCS) Class II or IV—are poorly absorbed by the human body, ultimately impacting a product's efficacy. Softgels can help resolve this problem because APIs contained in a solution are more readily absorbed and reach the site of action more easily than solid-form APIs.

Shell material

Despite softgels' utility, there are a number of considerations manufacturers need to keep in mind when producing softgel formulations. One major manufacturing constraint is that the gelatin shell is highly water soluble. During production, water is used to make gelatin pourable and after production the majority of the water is removed. However, the finished capsule shells still contain a water content of 4 to 10 percent [3].

In some respects, gelatin's solubility is an advantage. Because softgels rapidly dissolve when ingested, they are ideal for delivering fast-acting medicines. A drawback to gelatin's solubility is that it makes softgels very sensitive to heat and humidity. As a result, the shelf life of softgel formulations can vary considerably depending on storage conditions, which can pose potential stability problems for manufacturers and distributors in hot or humid climates.

Gelatin's solubility also impacts the types of APIs formulators can use because the liquid fill must be oil-based rather than water-based to prevent it from interacting with the outer shell. This requires excipients that can dissolve the API in an oily suspension. While gelatin—an animal-derived product—remains the most commonly used shell material, these solubility issues combined with demand for non-animal-based products have prompted companies to explore other shell materials. Alternatives are usually based on synthetic polymers or plant-derived hydrocolloids, with hydroxypropyl methylcellulose (HPMC) being one of the best-known examples.

Softgel design

Another reason that pharmaceutical companies choose softgel formulations is because the products can be tailored to improve patient compliance. For example, the shape of a softgel capsule can be modified to make it easier for patients to swallow. Likewise, manufacturers can incorporate taste-masking technologies into capsule shells to make otherwise unpalatable medicines more pleasant.

Still, it is important that companies always consider the shell material's potential interaction with the softgel's liquid fill. For example, certain shell colors can react with some API solutions, dramatically reducing the product's stability or resulting in leakage [4].

Production cost

Cost is another factor that pharmaceutical companies must consider when deciding whether or not to use softgels. Capsule fillers can be expensive to install for a company more accustomed to manufacturing traditional tablets [5]. Likewise, developing the liquid fill for a softgel pharmaceutical product can be time consuming and costly and is likely to involve specialty excipients.

Pharmaceutical companies can minimize these costs by outsourcing softgel development and production to a contract development and manufacturing organization (CDMO) with expertise in and existing capacity for softgel formulation.

Conclusion

In many cases, a softgel can be the ideal delivery system that improves the bioavailability of a poorly soluble API. After the initial setup costs and formulation development, softgels are relatively inexpensive to mass produce. In addition, they can minimize the amount of excipient required, deliver precise dosages, and make otherwise unpalatable medicines easier to swallow, aiding patient compliance.

However, like all dosage forms, softgels are not suitable for all products. It is important that pharmaceutical developers fully understand the stability characteristics and manufacturing considerations involved in making softgel products before selecting this dosage form. That being said, softgel expertise and production capacity is available, and skills in these areas are quickly becoming the benchmark of a modern, full-service CDMO. T&C

References

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