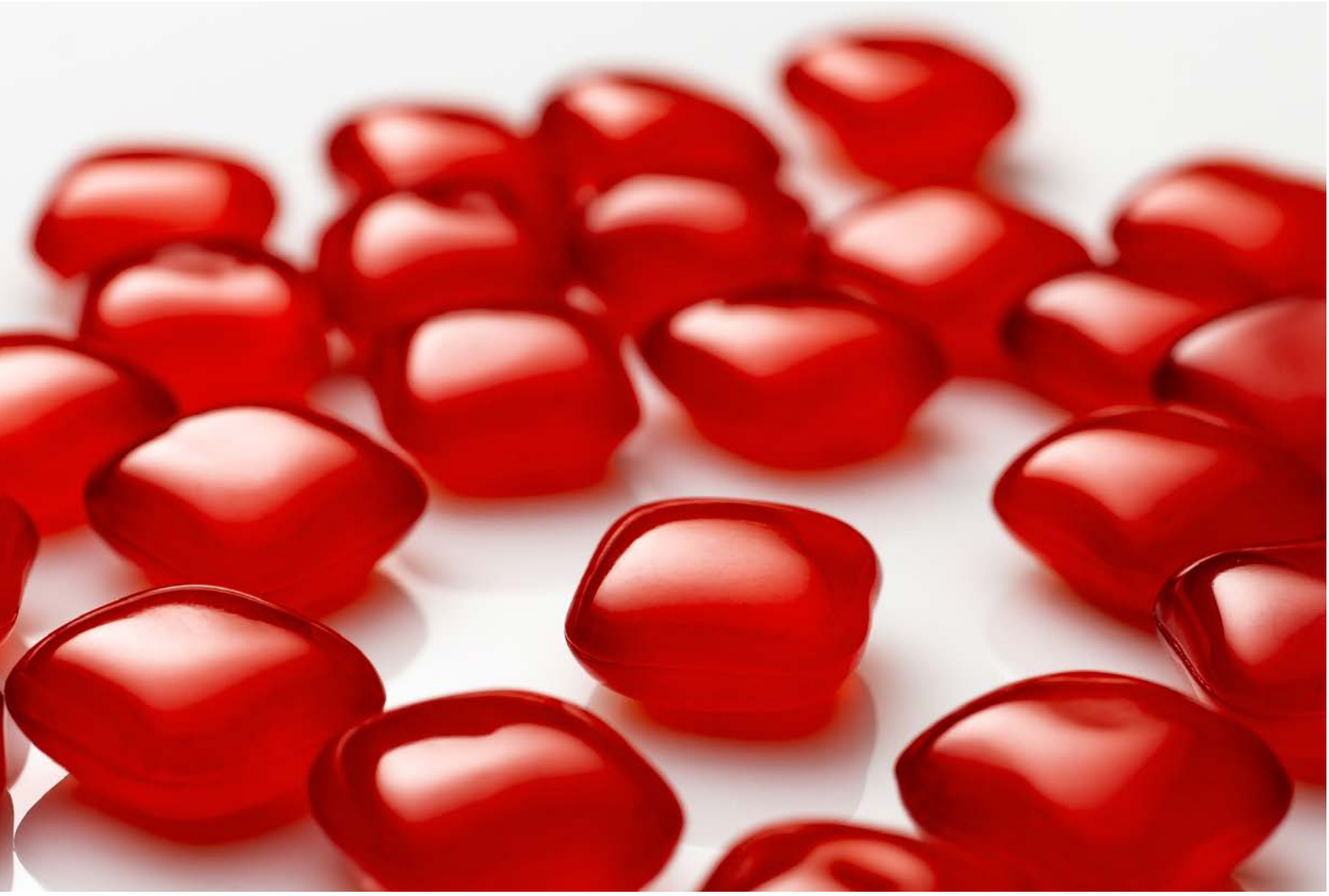
ThermoFisher SCIENTIFIC



MADE WITH

INSIGHT & INNOVATION

WHITEPAPER

Debunking myths and misconceptions about softgels

Kaspar van den Dries

Senior Director of Science and Innovation, Thermo Fisher Scientific

Abstract

Softgels are a popular dosage form among consumers because of their easy swallowability and quick onset of action. Pharmaceutical developers often do not consider softgels to be the best choice for prescription drug formulations, however, instead favoring tablets and hard-shell capsules. The disconnect between consumer and formulator preferences for prescription drugs may be due in part to misconceptions surrounding the development process for softgels and their perceived limitations. Here, we take a look at some common myths about softgels and explore why drug developers may want to reconsider their go-to delivery methods.

Myth: Softgels are expensive and complicated to manufacture

Contrary to popular belief, softgels are comparable with other oral solid dosage forms in terms of price and manufacturing complexity. The reason why is that the active pharmaceutical ingredient (API) drives the cost of most formulations, not the delivery method. In fact, internal benchmarking at Thermo Fisher Scientific shows that softgels are priced the same as or less expensively than other oral solid dosage forms like tablets or capsules. An exception to the rule might be tablets made inexpensively through direct compression, though few novel APIs can be successfully manufactured in this manner. Rather, most new tablet formulations require complex production processes that drive up the cost of the finished product.

The fact that softgels pricing is very competitive with that of tablets and capsules should come as no surprise. One need only examine the selection of over-the-counter (OTC) drugs available at grocery stores and pharmacies to see the large number of softgel formulations available. If softgels were truly more expensive and complicated to manufacture than other oral delivery formats, they would not comprise such a large share of the OTC market and with such variety.

Myth: Softgels are not as stable as tablets and capsules

Stability challenges are not unique to softgels; they can occur with any formulation, including tablets and capsules. A main factor in a formulation's stability is how excipients interact with the API, and thus addressing such issues requires similar compatibility testing and adjustments across all oral solid dosage forms alike. Of note, softgels have an edge over tablets in terms of stability in some cases. By nature, gelatin is impermeable to oxygen and thus softgels can better protect oxygen-sensitive APIs than a typical tablet formulation.

A main factor in a formulation's stability is how excipients interact with the API, and thus addressing such issues requires similar compatibility testing and adjustments across all oral solid dosage forms alike.

Myth: Softgels are not really appropriate for prescription drugs

It is a misperception that softgels are not suitable for the prescription drug market. Billions of softgels are produced every year for prescription drugs, so there is a substantial market for these kinds of formulations.

One cannot deny that tablets and capsules dominate the prescription drug market, however. The tendency of formulators to choose tablets and capsules over softgels could be rooted in their training at universities, where the focus of lessons is typically technologies like tablets, hard gelatin capsules, creams, ointments, and liquid solutions, with much less emphasis on softgel manufacturing and development.

If softgels are not a core part of the curricula, pharmaceutical scientists enter the workforce lacking familiarity with the technology and it might take years before they work with softgels firsthand. Thus, more education is needed about softgels—a mature, broadly used format that offers numerous benefits to formulators and consumers.

Myth: You should go with what you know—tablets

Many clients come to us to formulate their molecules as tablets because they are most familiar with this format. Sometimes, tablets are the perfect solution.

In other cases, such as with highly potent APIs, creating a tablet is extremely complex and the risk of producing a non-uniform tablet is very high. As such, softgels are a much better option for low-dose formulations.

Molecules have become increasingly complex and many have poor water solubility with sub-optimal bioavailability.

Softgels are also advantageous when the API's bioavailability is of concern. Molecules have become increasingly complex and many have poor water solubility with sub-optimal bioavailability.

These challenges may be addressed by using solubility enhancement techniques such as lipid-based systems—the basis of a softgel. With this technique, we can boost the API's bioavailability, increase exposure, and reduce the amount of API needed to achieve the desired effect in patients.

Myth: Softgels are mainly appropriate for nutraceuticals and OTC products

Softgels are broadly used in the nutraceutical and consumer healthcare fields. Nutraceuticals like vitamin D and vitamin A have excellent compatibility with softgel formulations, while polyunsaturated fatty acids such as omega-3s benefit from the oxidation prevention noted previously.

Softgels are also often preferred by consumers because they are easy to swallow as well as administer to others like children. Some softgels are also available in a chewable format, adding to improved patient acceptability and better compliance.

Since consumers can also be patients that require prescriptions, they have come to expect the same important benefits of softgels (e.g., swallowability, convenience, and quick onset of action) in prescription drugs as well.

Myth: Softgels are not as safe or effective as tablets and capsules

Softgels have the same safety or efficacy profile as tablets or capsules. Generally, the API is the biggest determining factor in the product's safety and efficacy, not the dosage form.

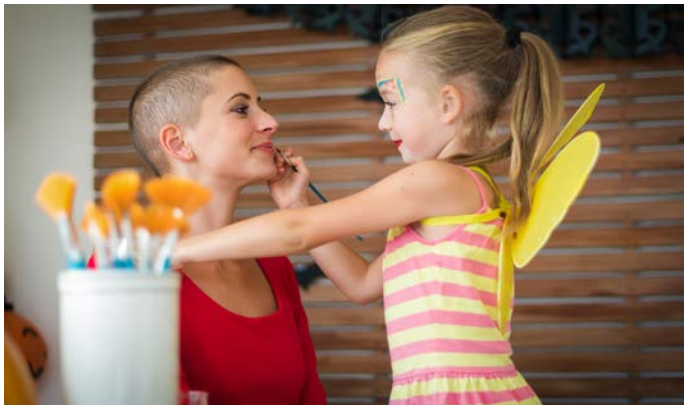
In some cases, softgels can actually improve a formulation's safety and efficacy, such as with drugs that suffer from food effects. In these cases, if the drug is in a tablet, it might be recommended that patients take the medication just before or after a meal, or two hours after or before a meal, to ensure safety and efficacy.

Softgels are also often preferred by consumers because they are easy to swallow as well as administer to others like children.

Conversely, by formulating the API into a lipid system as with softgels, food effects can be reduced and the effect of taking the drug with or without food varies less. Lipid systems help improve drug solubility in part by stimulating the similar physiologic events that occur when consuming the drug with food, although it is to a lesser degree.

Myth: Softgels are not suitable for all climate zones because of stability issues

We market softgels throughout the world including in countries with relatively mild climates such as in Western Europe and the United States, as well as in countries with Climate zone III and IV conditions (i.e., hot and dry conditions or hot and humid conditions). Softgels can easily withstand all these conditions, and we regularly test a formulation's stability in a variety of climate zones.



Summary

Many patients prefer softgels because of their easier swallowability and quick onset of action. Softgels are widely used in the nutraceutical and OTC drug markets and are increasingly found in prescription drugs. With benefits for formulating highly potent APIs or those with food effects, softgels should be a top option among formulators. More education is needed about the myths and misconceptions surrounding softgel development and manufacturability so that developers will not hesitate to use this patient-friendly format for OTC and prescription drugs alike.

About us

Thermo Fisher Scientific provides industry-leading pharma services solutions for drug development, clinical trial logistics and commercial manufacturing to customers through our Patheon brand. With more than 65 locations around the world, we provide integrated, end-to-end capabilities across all phases of development, including API, biologics, viral vectors, cGMP plasmids, formulation, clinical trials solutions, logistics services and commercial manufacturing and packaging. We give pharma and biotech companies of all sizes instant access to a global network of facilities and technical experts across the Americas, Europe, Asia and Australia. Our global leadership is built on a reputation for scientific and technical excellence. We offer integrated drug development and clinical services tailored to fit your drug development journey through our Quick to Care™ program. As a leading pharma services provider, we deliver unrivaled quality, reliability and compliance. Together with our customers, we're rapidly turning pharmaceutical possibilities into realities.

Kaspar van den Dries, PhD

Senior Director, Science and Innovation, Thermo Fisher Scientific

Dr. van den Dries currently serves as Senior Director and Principle Scientist, Solid Dose Development at Thermo Fisher Scientific. With a Master's Degree in Pharmaceutical Sciences (University of Utrecht, the Netherlands) and a PhD degree in high shear granulation, Dr. van den Dries has spent a large portion of his career solving formulation and process challenges in solid dosage forms for, amongst others, poorly soluble compounds at Organon, Schering-Plough and Merck. In addition, Dr. van den Dries has experience serving as the global CMC project lead for the development, registration and commercialization of a late stage project that was ultimately selected as a pilot for quality-by-design, which included the implementation of quality risks management on in-line NIR blend control in commercial production. With extensive experience in pharmaceutical formulation development in softgel production, Dr. van den Dries eventually moved to Banner Pharmacaps, a well-established softgel manufacturer, as R&D Director to explore possibilities in drug delivery innovation based on soft gelatin technologies. This includes the upcoming regulatory approval of the first pharmaceutical chewable softgel formulation and the development of other delivery options based on softgels, which are in development in their R&D centers in Tilburg, the Netherlands, Mexico City and High Point, North Carolina.

+1 919 226 3200 • thermofisher.com/patheon • pharmaservices@thermofisher.com

Published 07/21

ThermoFisher SCIENTIFIC