Capsules continue to be a favored drug delivery vehicle for early-stage development of solid oral dosage forms. They offer formulation flexibility, are compatible with various active pharmaceutical ingredient (API) forms, and can expedite clinical evaluation.

By 2014, 10 to 15 percent of FDA approved drug products were capsule formulations. In 2007, only 5 percent were. Capsules made from gelatin—which is derived from animals—have been the dominant capsule in the pharmaceutical industry and that will likely continue. Capsules
made from hydroxypropyl methylcellulose (HPMC), however, offer a number of advantages and are having a great impact on the market. HPMC capsules originated in Japan in 1990, and the first US patent on them was issued in 1993. Throughout the 1990s and early 2000s, HPMC capsules slowly gained market acceptance and began to encroach on gelatin capsule market share. Several factors helped HPMC, including the perception that consuming gelatin could lead to bovine spongiform encephalopathy and transmissible spongiform encephalopathy disease (BSE/TSE), commonly known as “mad cow” disease. Other headwinds included fluctuations in the price of gelatin, consumer preference toward vegetarian capsules, and technical difficulties, including crosslinking and brittleness from moisture loss.

Capsules can also be made from other plant-based materials, such as pullulan and starch, but HPMC capsules offer several technical benefits, including low moisture content, no crosslinking, and better stability. While gelatin has many desirable properties, pharmaceutical and nutraceutical developers are using more HPMC capsules in new products. By 2019, it is expected that gelatin capsules will exhibit a marginal 2 percent decline in demand.

Gelatin capsules market

The gelatin used in capsules is made from the bones and hide of cattle and pigs. In fact, the gelatin capsule industry consumes roughly 90 to 95 percent of all bovine-bone gelatin production and, in 2015, about 628 billion gelatin capsules—both soft and hard—were made. Within the gelatin capsule market segment, demand for hard gelatin capsules (HGCs) is growing faster than for soft gelatin capsules (softgels) due to their higher adoption rate. The HGC segment is mature but is still expected to grow at a compound annual growth rate (CAGR) of 3 to 4 percent.

Challenges in the gelatin capsule industry

The animal origin of gelatin, price fluctuations, and technical limitations have hampered growth in the gelatin capsule market. In 2012 to 2014, overall prices of pharmaceutical-grade gelatin increased 10 to 15 percent due to increased demand from competing industries and a reduced slaughter level. The price of bovine-bone gelatin used in HGCs increased by 13 to 15 percent in 2013 from the prior year due to increased demand for raw bones from the competing meat and bone meal industry. Fears of BSE/TSE have affected the gelatin industry, but according to all scientific bodies, there is no risk of contracting the disease from gelatin capsules due to the high temperature and pH of the manufacturing process. Gelatin derived from pigs is also widely used in manufacturing HGCs, but outbreaks of porcine epidemic diarrhea (PED) in the USA in 2014 led to a temporary hike in global porcine gelatin prices. The situation is now under control and the price of porcine gelatin is expected to remain stable. Porcine gelatin also faces religious objection.

As a result of stronger demand for the raw materials of gelatin from other industries, more regulations, perceived risk of BSE/TSE and PED, and climatic conditions that affect the availability of cattle, gelatin prices increased, which led to increases in the price of HGCs. That motivated pharmaceutical and nutraceutical companies to evaluate HPMC capsules as an alternative.

Opportunities in HPMC capsules

There has been more consumer demand for plant-derived materials in the pharmaceutical and nutraceutical industries. That development, coupled with the factors cited above, have given suppliers of HPMC capsules the opportunity to grow, and the HPMC capsule market is expected to increase at a rate of 10 to 15 percent between 2014 and 2019. The gelatin capsule market is expected to grow at 3 to 4 percent over the same period.

The use of HPMC capsule shells in nutraceuticals and over-the-counter formulations has grown. According to surveys conducted by Capsugel in 2013, about 40 percent of users said that they would prefer dietary supplements in vegetarian capsules instead of HGCs. Triggered by the influx in demand for capsules that aren’t sourced from animals—often stemming from the dietary or cultural needs of customers—HPMC capsules are poised to capture additional market share from HGCs. HPMC capsules are forecast to grow from a 3 to 4 percent market share in 2014 to a 9 to 10 percent market share by 2019.

While consumers are pushing for alternatives, so are regulators. In April 2016, India’s Central Drugs Standard Control Organization proposed banning gelatin capsules in favor of cellulose-based capsules. However, regulatory constraints, the small number of qualified HPMC capsule suppliers, lack of domestic pharmaceutical-grade HPMC, and the higher price of HPMC are likely to work against this proposal. No final decision has been made.

Advantages of using HPMC capsules in pharmaceutical applications

Initially, suppliers had more success selling HPMC capsules to nutraceutical companies over pharmaceutical companies because it was easier for them to adopt a new
capacities in Europe for HPMCs. In summary, in Romania, enabling the company to develop low-cost production capacity in Europe for HGCs. In February of this year, Qualicaps acquired Genix Industria Farmaceutica in Brazil, giving it the dominant position in the important and growing Brazilian market.

In August 2014, CapsCanada invested more than $10 million in a new manufacturing facility in Canada. In 2011, Suheung Capsules, a South Korean supplier, added a production line to meet demand from vegetarians and people in the Middle East who prefer non-gelatin capsules.

In 2015, an Indian supplier of gelatin and HPMC capsules, Natural Capsules, announced plans to invest 1.5 billion rupees to upgrade its manufacturing facility, including converting some of its existing gelatin lines to HPMC at its Bangalore site. Another Indian supplier, Sunil Healthcare, recently launched HPMC capsules and has begun supplying overseas markets.

Raw materials

The raw materials—gelatin and HPMC—are the major cost for producing capsules. For HGCs, gelatin accounts for 45 to 50 percent of production cost, and for HPMC capsules, HPMC typically accounts for 50 to 60 percent of the production cost. Table 1 lists the market sizes for pharmaceutical-grade HPMC and gelatin and notes what portion of production is used in making capsules.

The price of HPMC has been relatively stable, with a marginal increase of 3 to 4 percent in the last 2 years. Gelatin prices have increased more over the last 2 to 3 years, causing the price of HGCs to increase 5 to 10 percent. The increase in the cost of gelatin has been attributed to supply constraints and higher demand for raw materials from the leather, food, and other industries.

Challenges facing HPMC capsules

Price challenge. The process to make gelatin capsules is simply more efficient. While HPMC offers a number of advantages over traditional gelatin, it also has drawbacks, including cost. See tables 2 and 3. HPMC capsules are more expensive than their gelatin counterparts, largely due to lower production yields, or conversion ratios, compared to gelatin. For example, manufacturing 1 million capsules requires roughly 126 kilograms of HPMC but only 85 kilograms of gelatin. As a result, the prices of HPMC capsules are four to five times higher than those of HGCs. But as

### Table 1

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<th>Raw material</th>
<th>Global market, usage in pharmaceutical industry</th>
<th>Portion used in pharmaceuticals globally</th>
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<tbody>
<tr>
<td>HPMC</td>
<td>35-40 kilotons</td>
<td>20%. Of that portion, 58% is used as an excipient in tablets and 42% in capsule shells.</td>
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<tr>
<td>Gelatin</td>
<td>113 kilotons</td>
<td>28%. Of that portion 85% is used in capsule shells and 15% in vaccines and blood plasma expander.</td>
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</table>

Note: Information gathered from private correspondence
more companies opt to use HPMC capsules, their price is expected to decline over the next 4 to 5 years.

The price of HPMC capsules used in DPI applications is approximately $8 to $10 per 1,000 capsules due to the stringent requirements and specialized manufacturing processes needed to meet inhalation specifications. DPI applications generally use a size 3 capsule.

**Technical challenges.** The process for making HPMC capsules also takes longer and is more technologically intensive than the HGC process. That contributes to the higher price of HPMC capsules. According to one supplier we spoke with, there is also less flexibility in the HPMC process because suspensions must be consumed within 20 hours, whereas gelatin solutions can be used 72 hours after preparation.

**Conclusion**

In the last 3 years, only three of the 29 capsule-based drug products approved by FDA used an HPMC capsule shell. Clearly, gelatin remains the largest segment in the capsule market, with an estimated 90 percent share. But the growth of HPMC capsules is outpacing that of HGCs because acceptance in the nutraceutical industry and customer demand have prompted pharmaceutical companies to give them more consideration.

At the moment, pricing of HPMC capsules is the major challenge. But as more companies adopt them due to their technical advantages over HGCs, it is expected that suppliers will increase manufacturing capacity and that companies currently making only gelatin capsules will enter the HPMC capsule market. In short, use of HPMC capsules is likely to grow at a faster rate compared to HGCs, perhaps even becoming the preferred choice for use in clinical trials and new development projects.

**References**


### Table 2

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<thead>
<tr>
<th>Approximate prices of gelatin capsule shells</th>
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<td>Market</td>
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Note: Information gathered from private correspondence

### Table 3

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<th>Approximate prices of HPMC capsules used in dietary supplements</th>
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<td>Market</td>
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Further reading
