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# Soft Gel Capsules: An Elegant & Versatile Dosage Form © SIE

By Yousry Naguib, PhD

Soft gels (soft gelatin capsules) are becoming a popular dosage form for the administration of liquids, suspensions, pastes, and dry powders in the dietary supplement industry. Soft gels are easy to swallow, and have the ability to mask odors and unpleasant tastes. They have an elegant appearance, readily dissolve in the gastric juices of the digestive tract, and they may enhance the bioavailability of the active ingredient.

In a recent clinical trial, the dietary supplement Glucosol formulated in a soft gel capsule showed a 30 percent decrease in blood glucose levels compared to a 20 percent drop seen with dry-powder filled two-piece hard gelatin capsule formulation, suggesting that soft gel formulation of Glucosol improved its bioavailability.

## Definition and Characteristics

A soft gel capsule is a one-piece, hermetically sealed soft gelatin shell containing a liquid, a suspension or a semisolid; referred to as a fill. The soft gel shell is usually comprised of a film-forming material such as gelatin, and a water-dispersible

## Bringing Production In-house: Getting Prepared

**Supplement Industry Executive:** What advantages and challenges exist in bringing soft gel encapsulation production in house?

**Monte Monteleone:** First, if a dietary supplement manufacturer is already purchasing enough soft gels and the market exists for an increase of their soft gel product line, and if the company has good relationships with raw material suppliers, it would be highly advantageous to bring soft gel manufacturing in-house.

Producing soft gels is very unique—not just any manufacturer can do it. It is much easier to make tablets and two-piece capsule products. The challenges include achieving proper gel formulations that can vary, and also ensuring that the employees running the encapsulation machine and line are competent and well

or water-soluble plasticizer (to impart flexibility). The soft gel shell could also include minor additives such as coloring agents, flavors, sweeteners, medicaments, and preservatives. Soft gel capsules can also be enteric coated for certain applications.

Gelatin is derived mostly from collagen by thermal denaturing with the aid of diluted acid or alkali. Gelatin contains a mixture of water-soluble proteins (84-90 percent), mineral salts (1-2 percent), and water (8-15 percent). These proteins contain a significant amount of the amino acids: glycine, proline, hydroxyproline, glutamic acid, alanine, arginine, aspartic acid, lysine; in addition to other amino acids in smaller amounts.

There are two types of gelatins: type A, which is derived from pork skin by hydrolysis with an acid; and type B, which is derived from bones and animal skin by hydrolysis with an alkaline solution. Gelatin used in soft gels is a blend of both types, or used individually.

Gelatin is odorless, tasteless, colorless, and insoluble in most organic solvents (such as alcohols, acetone, chloroform), but soluble in glycerin, diluted acids and alkalis. Gelatin swells and absorbs room-temperature water, up to five to 10 times its weight. It dissolves in hot water, and forms a gel upon cooling. Gelatin is included on the FDA list of inactive ingredients.

trained. It is very difficult to learn the technique of taking a two-piece capsule formula and introducing oils to it to create a good flowing mixture to run efficiently on the soft gel encapsulation machine.

Soft gels have many advantages for the consumer, and for the manufacturer. The dosage is always the same from soft gel to soft gel, and the stability is much greater.

**SIE:** What is necessary to bring in a fully functioning soft gel encapsulation line?

**Monteleone:** A company would want to have a minimum of 24,000-square feet of space to house the soft gel manufacturing operation. This would be efficient for a one- or two-encapsulation machine operation. If the company wants to invest in building a site for soft gels, then I would recommend going beyond 24,000 square feet to have the capability of growth to meet increased production demands.

Equipment needs include: stainless-steel mixing tanks, a cold-milling operation for particle reducing, and evacuation for the removal of air in multivitamin products. Also needed are three ingredient-fill holding tanks, and four stainless-steel gelatin heating tanks, approximately 600 to 800 kilos each; a Kathabar system for drying and

The main source of gelatin is collagen, which is found in the skin and bones of animals such as deep-water fish. Most of the soft gel capsules on the market are made from an animal source, bovine or porcine. There are non-animal based forms of gelatin to meet the needs of those wishing alternatives to meat products for ethical or religious reasons. A vegetarian gelatin made from Irish moss, which is derived from seaweed and grows off the coast of Ireland, is available but is costlier than the animal-sourced gelatins.

**Manufacturing Process**

In the manufacturing process of making soft gel capsules, two gelatin ribbons pass between twin rotating die cylinders. As the ribbons meet, the liquid to be encapsulated is injected between them. The capsule halves are sealed and ejected by the continuous rotation of the cylinders. The shells containing the fill are then dried at room temperature so that the water content of each shell ranges from six to 10 percent.

**Dissolution**

The bioavailability of the bio-actives in the soft gel depends on the dissolution of both its shell and fill. Dissolution of a chemical compound in the aqueous environment of the gastrointestinal tract is often the rate-limiting step in its absorption. If a substance, such as oil, is insoluble in the acidic solution of the gastrointestinal tract, then its dissolution can be slow. However, if this substance is

dehumidification; trays for spreading the soft gels, inspection tables, standard polishing pan or a converted Pelligrini machine for the removal of the mineral oil residue that remains on the sof tgel; a sizing unit for the removal of any slugs and gel particles and for the removal of any over- and under-fills prior to packaging.

Once the aforementioned equipment is purchased for a one-machine operation, the manufacturer can then very easily convert to a two- or three-machine operation. Following this, the only purchases other than the machinery would be the gelatin itself.

The typical output of an eight- to nine-inch encapsulation machine is approximately 87,600 soft gels per hour. From my experience, most manufacturers run the machine(s) an average of 21 to 22 hours daily for such products such as vitamin E and fish oils.

Downtime includes changing gelatin and changing fill materials. If a company is running machinery under strict cGMP guidelines to produce OTC products, the machinery needs to be shut down for taking full sets of weights and verifying adjustments of ribbons for correct thickness.

Worldwide, there are about eight manufacturers of soft

administered in a vehicle in which it is soluble, then the absorption process may be enhanced. Polyethylene glycols, cyclodextrins, carboxymethylcellulose, and emulsifiers have been used to enhance solubility of substances in water.

Dissolution problems of the soft gel shell are less common; they may become apparent upon aging, which are attributed to the cross-linking of gelatin. The cross-linking causes the formation of a swollen, tough, rubbery, and water-insoluble material.

High humidity causes the capsules to become soft, tacky, and bloated and may increase the likelihood of moisture migration from the shell into the fill material. Such a transfer can cause chemical, physical and dissolution instability.

**Basic Formulations**

The formulation of capsule fill can be developed to fulfill the specifications and end-use requirements of the product. Capsulation of liquids that are immiscible with water and non-volatile, such as vegetable oils and vitamin E, are easy and require little or no formulation. However, solids that are not sufficiently soluble in liquids are capsulated as suspensions. Such materials should have a particle size of 80 mesh or finer.

Capsulation of suspensions is the most common form for a large group of dietary products. Suspension formulation

gel production equipment, there are three domestically: Soft Gel Solutions, Chatsworth Machine Co., and GIC Engineering. Basically, all machines produce soft gels in the same manner. They have rotating dies, and an independent wedge and pump that controls the fill.

**SIE:** What are the staffing needs for a full-line soft gel production division?

**Monteleone:** Producing soft gels is a very unique endeavor—it takes a lot of training to be able to produce these products and maintain quality throughout the operation. It takes four to six weeks to train an experienced two-piece encapsulator to learn the basics, before considering leaving him alone to run the equipment.

In the areas of blending and gelatin heating, the operator needs to know how to follow formulas and apply certain techniques; in soft gels, materials need to be blended a certain way. Particle size can be a big problem if not done correctly. Teaching employees how to achieve the proper particle size takes time.

I usually cross-train the blending and gelatin personnel so they can work in either area. In this application, training must be hands on—you can't sit in a meeting room and look at

requires a suspending agent to prevent the settling of the solids and to maintain homogeneity throughout capsulation. The most widely used suspending agent for oil-based formulation is wax (such as beeswax), and polyethylene glycols in a non-oil-base.

At Soft Gel Technologies (Los Angeles, CA), powdered extracts are usually combined with soybean oil (as a carrier), yellow beeswax (as a suspension and thickening agent), and lecithin (as a lubricant) for formulation in soft gels. The relative amounts of the extract and the other ingredients depend upon the desired extract dose to be administered.

**Limitations**

Filling of soft gel capsules with liquid and semi-solid materials is possible if the "fillings" selected do not dissolve the gelatin. Thus aqueous solutions would not be appropriate. But substances in which gelatin is not soluble are suitable.

The following types of compounds may not be suitable candidates for soft gel encapsulation:

• liquids that can easily migrate through the gelatin shell, such as water (more than 5 percent of the fill), and hygroscopic and volatile compounds

• aldehydes, which have the ability to harden the shell and hence affect its dissolution property

• acidic or alkaline solutions should be avoided, unless they are

pictures on a blackboard.

Regarding personnel distribution, I recommend staffing the soft gel encapsulating area with between 10 and 12 full-time employees for a three-shift operation. Two people on each shift for blending and gelatin areas (most companies with fewer than four encapsulating machines don't need these two operations performed on graveyard shift); one person per shift in the machine room area (total of three), and two inspectors, one for the sizer and one to polish and package.

Teaching maintenance is critical—it is essential for the employees to know how to properly dismantle the machines and to clean and reset them. Maintenance personnel can control whether the equipment runs smoothly or causes the company to lose money due to a lot of unnecessary downtime.

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adjusted to become neutral; acids and alkalis can cause hydrolysis and leakage of the gelatin shell

• water-soluble solid compounds that may affect the gelatin shell unless they are minor constituents of a formula or combined with a carrier that reduces their effect on the shell.

In summary, soft gels are a useful dosage form for dietary supplements; due to their elegant appearance and ability to hold dyes to make colorful capsules. They are easy to swallow and mask odors and unpleasant tastes. Soft gels can hold liquids, suspension, and pasty material. They may also enhance the bioavailability of active ingredients.***SIE***

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