excipients

Using natural alternative excipients for tableting and capsule filling

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This article discusses the importance of finding organic substitutes to traditional excipients and presents a study that used premixed natural excipients to incorporate an oily substance into a powder for encapsulation.

A large number of dietary supplements are available in solid oral dosage forms. Vitamin and mineral supplements can be easily pressed into tablets by wet granulation or direct compression, but such tablet formulations require good binders. Commonly used binders in tablet formulations include cellulosic materials, such as hydroxypropyl cellulose (HPC) or microcrystalline cellulose (MCC), or synthetic polymers, such as polyvinyl pyrrolidone (PVP). For organically oriented consumers, however, these excipients sound synthetic and unnatural.

The trend toward organic foods has been evident for several years as consumers develop a greater awareness of organic products [1]. Dietary supplement manufacturers are also slowly changing to organic formulations, as consumers increasingly look to avoid chemical or synthetic ingredients. Therefore, dietary supplement manufacturers are under increasing pressure to replace traditional binders with more natural-sounding ingredients.

The same challenge applies to fillers, flow agents, lubricants, disintegrants, and pigments, including magnesium stearate, stearic acid, silica, and synthetic colors. This move toward more natural ingredients is part of the so-called "Clean Label" movement, which also attaches importance to the sustainability of raw materials.

Pharmaceutical manufacturers are also beginning to use more natural ingredients as excipients due to their increasing availability, relatively low costs, lower toxicity, and fewer side effects. The application of natural ingredients in pharmaceuticals is expected to expand in the coming years along with consumer demand. The aging population in developed countries is expected to increase the future rate of chronic disease and stimulate demand for pharmaceuticals. At the same time, consumers are looking to natural products to improve their general well-being and prevent illness [2].

By working closely with their ingredient suppliers, tablet manufacturers can successfully change a formulation from a synthetic binder to natural or organic ingredients.

Replacing synthetic binders

Binders give cohesion to the loose particles or granules in a tablet formulation. This ensures that the tablet remains intact after compression. To replace conventional binders such as HPC, MCC, and PVP, a natural binder must be able to produce tablets with the same mechanical strength and release properties. Table 1 shows some starches, gums, mucilages, and dried fruits that have binding capacity as well as other characteristics, such as filler and disintegrant properties, and that could be used as alternatives to synthetic binders.

By working closely with their ingredient suppliers, tablet manufacturers can successfully change a formulation from a synthetic binder to natural or organic ingredients. A natural ingredient cannot replace a synthetic ingredient 1:1, however. Users usually must add several natural raw materials in different concentrations to a formulation to achieve the desired binding properties. Customer-specific premixes made from various certified natural raw materials, on the other hand, can simplify development, handling, and the manufacturing process.

Natural disintegrants

Disintegrants are substances or mixtures of substances formulators add to a formulation to increase the dispersion or breakup of tablets and capsules into smaller particles for fast dissolution. Popular synthetic superdisintegrants include cross-linked PVP, MCC, croscarmellose sodium, and sodium starch glycolate, all of which are chemical-sounding names that are unsuitable for clean label products. More natural sounding raw materials that can act as disintegrants include: mucilage of ispaghula or psyllium husks, cress, gum karaya, fenugreek seed and gum of locust bean, chitin and chitosan, gellan, agar, alginates, oat fiber, xanthan, cucurbita maxima pulp powder, hibiscus rosa-sinensis Linn, and mango peel pectin.

As with dry binders, 1:1 disintegrant replacement is not possible in most cases. A dry powdered premix compound based on natural and certified organic ingredients (such as Biogrund's CompactCel DIS) can replace synthetic disintegrants in tablet, capsule, and granule formulations and enable the rapid break-up upon contact with moisture required by a fast-release solid oral dosage form.

From oil to powder to capsules naturally

Manufacturers are increasingly looking to add natural sources of vitamins, probiotics, omega 3-6-9 fatty acids, antioxidants, amino acids, and hemp to their natural supplement products. These nutrients often come in the form of an oil or oily powder. For oily powders, microencapsulation can be beneficial, especially if the oily powder is then filled into hard capsules, which allows precision dosing of ingredients or nutrients. Flavor and odor masking can minimize unpleasant tastes and smells associated with certain nutrients. Protection from mois-

Table 1

Example sources of natural binders

Source	Material
Animal	Chitosan and chitin, chondroitin sulphate
Marine	Agar, alginic acid, laminarin
Microbial (bacteria & fungi)	Xanthan, dextran
Plant	Shrub/tree exudates (gum Arabica, gum ghatti)
Seed gums	Guar gum, locust gum
Extracts	Pectin, larch gum
Tubers and roots	Potato starch

Table 2

Formulation 1

Ingredients (ratio 1:1)	Percentage	Target weight (milligrams)	Oil content	
			(milligrams)	(% w/w)
Oil-powder blend (25% oil w/w)	50	292	78	12.50
Flow aid (CompactCel FLO 305.17, Biogrund)	50	292		
Total	100	584		

Table 3

Capsule set 1 (Dosing disk thickness = 19.7 millimeters, size 0 HPMC capsules)

Tamping pin height (millimeters)	7	10	13	16	19
Powder bowl height (millimeters)	15	15	20	20	20
Machine speed (rpm)	110	100	110	140	100
Mean (milligrams)	532	562	584	572	513
Standard deviation (milligrams)	48	31	22	25	54
Relative standard deviation (%)	9.06	5.52	3.75	4.39	10.63

Table 4

Formulation 2

Ingredients (ratio 1:2)	Percentage	Target weight (milligrams)	Oil content	
			(milligrams)	(% w/w)
Oil-powder blend (25% oil w/w)	37.67	220	55	9.42
Flow aid (CompactCel FLO 305.17, Biogrund)	62.33	364		
Total	100	584		

Table 5

Capsule set 2 (Dosing disk thickness = 19.7 millimeters, size 0 HPMC capsules)

Tamping pin height (millimeters)	7	10	13	16	19
Powder bowl height (millimeters)	20	20	25	30	30
Machine speed (rpm)	110	140	110	110	140
Mean (milligrams)	564	508	559	563	553
Standard deviation (milligrams)	19	22	13	13	14
Relative standard deviation (%)	3.36	4.34	2.26	2.23	5.59

ture, acids, heat, and oxygen is also critical, as it enhances stability, bioavailability, and delivery. The powder must also be easy to handle and free flowing.

The following study examined the possibility of incorporating oily substances into a powder for encapsulation using only natural ingredients. The study simulated the following three applications using sunflower oil as an oil substitute:

1) 20 milligrams of hemp in a size 0 capsule;
2) 22.5 international units (IU) of vitamin E and approximately 15 milligrams of vitamin D3 in a size 1 capsule; and
3) 30 million colony forming units (CFU) of probiotics in a size 0 capsule using oil to make the probiotics more stable.

Materials and methods

To incorporate the sunflower oil into powder, the oil was blended into a natural and organic premixed moisture-absorbing dry binder (CompactCel MAB, Biogrund) using a high-shear mixer at a ratio of 1:3 oil to powder. The oil was added to the binder a little at a time to guarantee a homogeneous distribution and avoid clumping.

Three different trials using two different formulations were performed with the oily powder (Tables 2 and 4). For the encapsulation process, a Syntegon (formerly Bosch) GKF 705 was used, with different tamping pin heights, bowl fill heights, and machine speeds (rpm) (Tables 3 and 5). As the results show, the right speed, tamping pin height, and formulation is crucial when encapsulating an oil-powder blend into hard capsules.

Results and discussion

As previously mentioned, three applications served as the basis for the simulation (Table 6).

In the nutraceutical industry, a relative standard deviation (RSD) below 5 percent of filled capsules is acceptable. The results of capsule set 1 (ratio 1:1) showed an RSD of 3.75 percent. This indicates that for formulation 1, the right combination of process parameters was able to achieve good powder flow and consistently filled capsules.

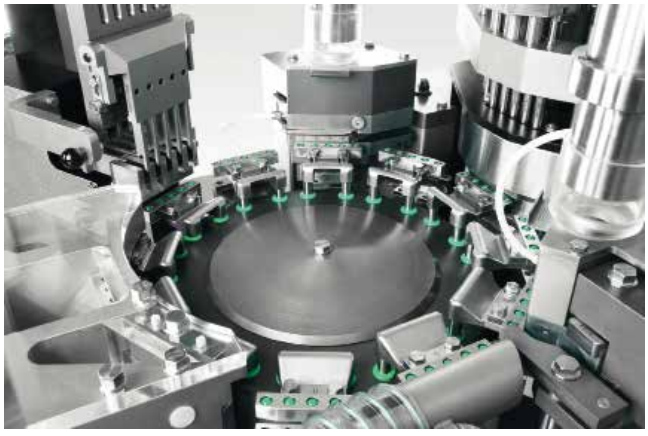

Photo 1: The formulations studied were encapsulated using a Syntegon GKF 705 capsule filler.

Table 6

Applications simulated in study

Substance	Target	Details	Capsule size	Oil content
Hemp	20 mg	~30 mg of oil (containing 20 mg of CBD)	Size 0 500 mg	6% of oil must be in the capsule
Vitamin E	22.5 IU vitamin E, ~15 mg vitamin D3 in 1 capsule	~15 mg of oil (containing 15 mg of vitamin E)	Size 1 350 mg	~4% of oil must be in the capsule
Probiotics	30 million CFU	~30 mg of oil (containing 30 million CFU of probiotics)	Size 0 500 mg	6% of oil must be in the capsule

In the pharmaceutical industry, an RSD below 3 percent of filled capsules is acceptable. The results of capsule set 2 (ratio 1:2) showed an RSD of 2.23 percent. This indicates that for formulation 2, the right combination of process parameters was able to achieve good powder flow and consistently filled capsules.

As these results demonstrate, the natural powder blend CompactCel MAB can absorb 12.5 (set 1) and 9.5 (set 2) percent oil and be filled into hard capsules. These percentages are much greater than the assumed percentages for the simulated applications (6 percent for hemp, 4 percent for vitamin E, and 6 percent for probiotics).

Comparing these results with the underlying applications, it is evident that filling an oil-to-powder mixture into hard capsules is a straightforward process and a viable alternative dosage form to liquid-filled capsules, softgels, or pure oil, assuming that the process uses the right equipment, parameters, and ingredients.

A natural substitute exists for each synthetic filler, binder, flow agent, lubricant, and disintegrant commonly used to formulate solid oral dosage forms. However, as previously stated, a 1:1 replacement in the formulation is not always sufficient to replace 100 percent of the synthetic excipient's functionality. *T&C*

References

1. Survey data from the Organic Trade Association, ota.com/organic-market-overview/organic-industry-survey.

2. CBI—Ministry of Foreign Affairs, www.cbi.eu/market-information/natural-ingredients-health-products/what-demand.

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