

Formulating TCMs: East meets West

Gus Labella, Global Technical Services Manager, Colorcon
info@colorcon.com

As consumers increasingly turn to natural supplements to combat ageing, address malnutrition or just feel better about managing their hectic lifestyles, the manufacture and sale of herbal and natural health products has become a fast-growing global business. The worldwide nutrition industry grew 8.4% in 2003 to reach sales of \$182 billion. Supplement sales rose to 5.9%, contributing \$60 billion to the total. According to research by Nutrition Business Journal, the largest markets are the United States (\$20 billion), followed by Europe (\$15 billion) and Japan (\$10 billion).¹ Traditional Chinese medicines (TCMs) are playing an increasingly important role in the development of the alternative pharmacopoeia. Yet, to appeal to the modern, Western consumer, cutting-edge formulation technology must be combined with ancient Eastern herbalism. This article describes how formulated coated tablets can make TCMs more palatable.



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Natural ingredients such as ginseng, lotus leaf and tengtea extract have been used successfully for thousands of years in China to alleviate common ailments ranging from toothache and sore throat to insomnia and appendicitis. The use of herbs, along with acupuncture and massage to treat the body holistically, has

been termed traditional Chinese medicine (TCM). TCM uses flowers, seeds, fruits, leaves, bark and roots to formulate medicines; the herbs are characterized by property, flavour, channel tropism (selective therapeutic effects on particular organs) and action. Treatment of common ailments with nutritional supplements is thought to be less harsh to the body and may cause fewer side-effects because they contain natural ingredients. Many TCM products are produced and sold as gelatin capsules; however, this dosage form is less appealing to consumers and is more expensive and less efficient to manufacture. Many of the nutritional ingredients used in traditional Chinese medicines are hard to compress or have unpleasant odours and flavours that, ideally, should be masked, though producers of these medications continue to supply them in encapsulated forms.

This article presents Colorcon's experience in assisting companies that manufacture encapsulated TCM products to evaluate their core formulations, and develop and produce film-coated tablets that are less objectionable and more identifiable to the consumer — as well as being easier to swallow. Case histories cited in the article include improving the disintegration of a herb-blend tablet indicated for weight loss (1) and optimizing the hardness/taste/mouth-feel formulation of a herbal (tengtea) lozenge product indicated for sore throat (2).

Case #1: Improved Herb-Blend Weight Loss Formulation

In the development of TCM tablets, there is always a conflict between disintegration time and tablet hardness. The challenge becomes even more complex when there is little room in the formulation for specialty excipients.

The manufacturer of a common TCM product indicated for weight loss supplied the herbal blend to the market as a capsule, but wanted to produce a film-coated tablet that was more acceptable to the consumer. The formula contained a mixture of 22.5% spray-dried extract and 67.5% crude herb powder, which left only 10% of the formulation for excipients. The initial tablet formulation developed by the manufacturer had a long disintegration time and unacceptable hardness. The multifunctional excipient, Starch 1500 (Colorcon), was selected as an excipient to improve disintegration time as well as hardness, and a manufacturing process of high shear granulation was used. The product formulation is shown in Table I.

First, the active blend and starch excipient were mixed together in the granulator bowl for 3 minutes at an impeller speed of 500 rpm. A sucrose binder solution was prepared at 20% in deionized water. While the granulation binder was added, the impeller speed was increased to 800 rpm and the chopper speed was set at 1500 rpm. The granulation mix time was 2 minutes.

The resulting granules were dried in an oven to a target moisture content of 4% and the dried granules were passed through a 16-mesh sieve. Magnesium stearate was blended with the sized granulation. Tablets were produced on a Rimek Mini Press-II using 10 mm shallow concave tooling at a compaction force of 15 kN. The tablets were then film-coated using Opadry II.

The use of Starch 1500 in the manufacturing process provided the improved disintegration and desired hardness at low concentrations (Table II). In addition, the tablet developed was able to withstand the film coating process, resulting in a more elegant dosage form. Figure 1 shows the dissolution profile of the finished tablets.

Case #2: Improving a Herb-Blend Sore Throat Lozenge

The challenge facing the client manufacturer for this study was to formulate a robust herb-blend lozenge product indicated for sore throat by direct compression from a hard-to-compress herb. In addition to core hardness, the lozenge needed to have a good taste and a pleasant mouth-feel to the consumer; in this instance, a creamy texture was desired. Taste and palatability are critical to patient compliance; drugs that have a bitter taste often lead to consumer rejection of the product in favour of a more desirable one. Acceptance and compliance can be improved by using a film-coating that is sweetened, flavoured, or at least masks the taste of the active ingredients and gives a neutral reaction on the tongue without affecting the disintegration and dissolution profile. Film coating of the tablet was also needed for moisture protection and to give a more elegant appearance. To do this, Starch 1500 was incorporated into the formulation, which provided lubrication and enhanced both the flow and the binding functionality needed for direct-compression manufacturing.

Ingredients	Per cent (w/w)
Active Blend	90.00
American ginseng extract	
Ginseng extract	
Lotus leaf extract	
Largehead Atratyloides rhizome extract	
Rhubarb powder	
Starch 1500	7.00
Magnesium stearate	0.50
Sucrose	2.5
(used as binder solution at 15% in water)	
Total	100.00

Table I: Weight loss product formulation

Property	Improved formulation	Initial tablet formulation
Weight	280 mg	280 mg
Diameter	10.0 mm	9.0 mm
Thickness	3.9 mm	4.9 mm
Hardness	65 N	130 N
Friability	0.13%	0.25%
Disintegration time	14 min	25 min

Table II: Weight loss tablet properties

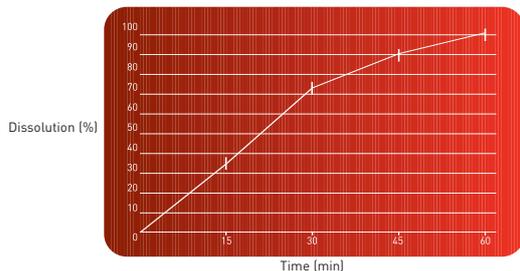


Figure 1: Dissolution profile of weight loss tablets

Ingredient	Percent (w/w)
Tengtea extract	14.00
Maltodextrin	50.00
Starch 1500	20.00
Lactose	14.00
Aspartame	0.50
Silica	0.50
Magnesium stearate	0.50
Lemon flavour	0.50
Total	100.00

Table III: Tengtea extract formulation composition

Angle of repose (powder blend)	36.2°
Flow time (powder blend)	18.2 s
Tablet weight	500 mg
Diameter	11.0 mm
Thickness	5.1 mm
Hardness	70 N
Ejection force	112.5 N
Friability	0.1%
Disintegration time	15 min

Table IV: Lozenge tablet properties

Formulation Assistance

Colorcon, a global company that develops, manufactures and supplies specialty chemicals, excipients and advanced coating systems for pharmaceutical dosage forms, has provided technical assistance to companies that develop solid oral dosage TCM formulations. From a technical service facility in Shanghai, China, and similar technical facilities around the globe that work with ingredients used in traditional Chinese medicines, Colorcon has helped manufacturers to evaluate their older core formulations, improve them and develop new formulations that can be made into film-coated tablets that are less objectionable and more identifiable to the consumer. Colorcon has provided advice on what excipient ingredients could be used, as well as how various active ingredients can affect outcomes in tablet formulations — such as friability, disintegration time, hardness, moisture problems and compressibility. Coated tablets are often favourably compared with capsules because it is less expensive to manufacture tablets than capsules, and tablets are perceived to be more palatable and easier to swallow than capsules.

Film-coating has proven to be a fast and inexpensive method of enhancing a tablet while providing other benefits, which include the following:

- odour/taste masking
- the dosage form is easier to swallow
- heightened safety through better product identification
- improved product appearance
- reduced throat irritation
- reduced manufacturing costs.

The herbal product consisted of spray-dried tengtea powdered extract at a concentration of 14%. The active ingredient could not be processed by wet granulation because it became very sticky when exposed to water. To avoid a solvent granulation process, a formulation for direct compression was developed (Table III).

The direct compression manufacturing process was started by blending together the active powder and the starch excipient for approximately 5 minutes in a groove form mixer. Maltodextrin and lactose were added and blended for an additional 5 minutes, then the aspartame, silica, magnesium stearate and lemon flavour were added and mixed for an additional 5 minutes. Tablets were produced on a Rimek Mini Press-II using 11 mm shallow concave tooling at a compression force of 15 kN. Tablets were then coated with Opadry II (Colorcon), a custom-formulated, dry-blend system consisting of a combination of polymers and polysaccharides for aqueous film coating.

The resulting tablets had very low friability (excessively breakable), which is an important feature of a lozenge-

type product (Table IV). Final film-coating gave a smooth, high-gloss, uniform appearance to the tablets and provided moisture protection of the active ingredients. Gloss is usually associated with smoothness, so the tablet appeared to be easier to ingest. The combination of maltodextrin and Starch 1500 provided the desired consistency and texture for a pleasant mouth-feel for the consumer.

Conclusion

As stated previously, the major advantages of using film-coated tablets for TCM nutritional supplements include masking unpleasant tastes and odours, reduced throat irritation, improved safety through better product identification, better product appearance and acceptance, and reduced manufacturing costs. With technical assistance, manufacturers have been able to evaluate their core nutritional medicines and improve them by developing new formulations that can quickly, easily and inexpensively be made into film-coated tablets, effectively integrating their “traditional science” into the fast-growing nutritional supplement marketplace.

Reference

1. “Global Nutrition Industry IX, No. 10–11,” *Nutrition Business Journal* (October/November 2004).