Mechanical Forming of Herbal Tablets

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AN OVERVIEW OF HERBS IN MALAYSIA

The use of traditional medicine as the primary alternative for healing as well as its usage as complementary medicine goes back beyond recorded history. This interesting phenomenon has allowed traditional herbs to be brought forward continuously throughout the centuries without fading in popularity.

In fact, according to BERNAMA (2006a), annual sales for traditional medicine increased from US$385 million (RM1 billion) to US$1.29 billion (RM45 billion) from 2000 to 2005. Indeed, the herbal medicine industry is expected to grow faster than the general economy at more than 15% to 20% per year (BERNAMA, 2006b). Examples of some of the herbs that are commonly used worldwide include garlic *(Allium sativum)*, ginkgo *(Ginkgo biloba)*, ginseng *(Panax ginseng)*, saw palmetto *(Serena repens)* and St. John's wort *(Hypericum perforatum)*.

Figure 1: Andrographis paniculata plant

In Malaysia, we have our own local favourites. The *Eurycoma longifolia jack* is just one of the many popular local herbs with multiple uses. The country has been blessed with an abundant variety of medicinal plants (Ang and Lee, 2006). Malaysia's rainforest currently supports more than 20,000 plant species, among which 2,000 plant types are reported to have several therapeutic and chemical properties (Indu and Ng, 2000) such as improving blood circulation and reducing blood sugar levels. Examples of these herbs include *mengkudu (Morinda Citrifolia)*, *misai kucing (Orthosiphon Stammineus)*, *pegaga (Certella asiatica)*, *hempedu bumi (Andrographis paniculata*, see Figure 1*)*, *tongkat ali (Eurycoma longifolia jack)* and *kacip fatimah (Labisia pumila)*.

ENGINEERING ASPECTS

Knowledge will facilitate Malaysia's emergence as a global medicinal herbal producer, and the country is currently making an aggressive effort to gain knowledge in three major areas: agricultural practice, pharmacology and processing technology (engineering). Among these three areas, processing technology (engineering) needs special attention given the fact that scientific data must always be converted into engineering data before the technical feasibility and economic viability of products can be determined. Table 1 shows the main stages involved in Malaysian herbal production based on an engineering approach (Abdul Aziz *et al.*, 2005).

Table 1: Engineering aspects of herbal production (Abdul Aziz et al., 2005)

Stage	Engineering Contribution
planting and harvesting	sensors and monitoring; harvesting equipment
pre-processing	grinding, drying and storage; quality tests
processing	extraction methods; online sensors; chemical analysis optimisation; process synthesis and design; new extraction methods; batch process optimisation
value addition and final processing	spray or freeze drying; mixing and formulation; batch processing; product engineering; final form production; capsule and tablets

AN EXAMPLE - *EURYCOMA LONGIFOLIA JACK*

Almost all parts of the plant *Eurycoma longifolia jack* (Figure 2) are used in traditional medicine; however, it is the roots that are mainly used in the preparation of herbal medicine. Significantly, *Eurycoma longifolia jack*, also known as *tongkat ali* in Malaysia, has strong potential to be developed beyond local consumption and into a globally accepted herbal medicine. In traditional usage, these herbs are directly boiled and consumed orally. In modern usage, however, the products of *Eurycoma longifolia jack* are sold as dietary supplements in the form of capsules, pills and pastes. It is also used as an active ingredient in canned energy boosters or energy drinks.

Interestingly, this herb has found use as a supplement to regular coffee, chocolate drinks and tea mixtures found in hawker stalls, department stores, pharmacies and even in hotel cafes. Food manufacturers brought this herb to the public's attention with an even more creative approach, *i.e.* in the form of an active ingredient which is added in small amounts into biscuits and ice cream.

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These trendy marketing schemes have helped inform the public indirectly of the many potential uses of this herb. In light of its increasing popularity, the need for competent monitoring of its quality and for scientific research concerning quality assurance and control (QA/QC) is paramount on many fronts, including botanical, chemical and manufacturing-related issues, or biological and clinical aspects, in order to guarantee the value, safety and effectiveness of the herbal products.

TABLETS

Tablets are becoming an increasingly popular form of making herbs readily accessible to consumers. Tablets are not only the most common form of drug administration, but also a way to deliver an accurate dosage of, in this context, the bioactive compound of the herbs. The tablet form offers various additional advantages including chemical and physical stability, and acceptable shelf life.

There are many practical reasons for adopting the tablet form. First, tablets are easy to ingest for the otherwise reluctant patient, and the accurate dosage it offers assures a high level of satisfaction. Second, the varieties of shapes and colours made available allow the tablets to be uniquely identifiable; these tablets are also suitable for (marking by) the debossing technique, which is favoured by commercial manufacturers. Third, tablets tend to absorb little moisture and remain physically and chemically stable. Finally, the tablet form is more resistant to damage compared to other dosage forms, is convenient for packaging, shipping and administering, and is advantageous in terms of manufacturing speed and cost (Prafull, 2006).

However, tablets have some disadvantages as well. Bioavailability is a potential problem as dissolution must precede absorption. For example, tablets for immediate release must disintegrate rapidly (in less than 10 minutes) after ingestion in order for the active ingredient to dissolve easily (Prafull, 2006). Furthermore, gastrointestinal irritation can occur as a result of a high concentration of the active ingredient and, according to a previous research, some patients reportedly had difficulty ingesting tablets because of its size and shape (Prafull, 2006).

Figure 2: Eurycoma longifolia jack plant

Table 2: Characteristics of Various Tablet Types (Prafull, 2006)

Types	Characteristics
Immediate Release Uncoated Tablet	• generally has no taste or stability issues
Coated Tablet	• used for taste, stability and identification • typically coated with water-soluble/dispersible polymer-mixture of hydroxypropyl cellulose/ hydroxypropylmethyl cellulose
Enteric-Coated Tablets	• used for drug inactivated or destroyed in the stomach; or for those causing irritation to the gastric mucosa • tablet passes through the stomach but disintegrates in the intestines where absorption takes place • excipients used for enteric coating include cellulose acetate phthalate, mixtures of fats and fatty acids
Multiple Compressed Tablets	• multiple-layered tablets produced by using more than one compression cycle • each layer contains a different drug and each may be coloured differently
Controlled Release Tablets	• improved therapy, less toxicity, improved patient compliance and use of polymers such as methacrylates
Sublingual Tablets	• small, flat ovals such as nitroglycerin • ideal tablets for the absorption of drugs which are destroyed by gastric juice or undergo first pass metabolism
Chewable Tablets	• disintegrate rapidly when chewed • best for patients who have difficulty swallowing • best used when there is no access to water • commonly used for multiple vitamins and antacids
Effervescent Tablets	• product contains sodium bicarbonate and citric acid • chemical reaction causes carbon dioxide to occur subsequent to adding water, which helps to disintegrate and produces effervescence that hastens dissolution (antacids)

Given its increasing popularity, it is also important to be mindful of the assortment of tablets that are presently available in the market. The tablets can be classified into eight types with respect to the method of production and type of usage, namely, immediate release uncoated tablets, coated tablets, enteric-coated tablets, multiple compressed tablets, controlled release tablets, sublingual tablets, chewable tablets and effervescent tablets. The important characteristics of these tablet types are listed in Table 2.

UNIAXIAL DIE COMPACTION

The processing of a tablet is similar to the processing of other powdery compacts, and it is divided into four different steps: die filling, compression, decompression and ejection, as shown in Figure 3. The first step is die filling whereby the powder mixture is poured under gravity into the feed shoe running over the die opening. In the compression step, the powder is compressed uniaxially by means of a plunger pressing against the upper punch (Figure 3b). For decompression, the plunger (force transmitter) is removed

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from the upper punch to allow tablet relaxation, an elasticity phenomenon, to take place (Figure 3c).

Tablet relaxation is defined as the ability of materials to return to their original state upon the removal of applied forces, and causes the distance between the upper and lower punches to increase (Anonymous, 2005). Finally, in ejection, the compressed powder, now in tablet form, is removed from the die. The behaviour of the powder during the aforementioned four steps will determine the properties of the tablet. Therefore, understanding the mechanical behaviour of powders during each individual step is crucial.

TABLET TESTING

The tensile strength of the tablets is among the essential parameters to be determined at room temperature by diametral compression using a universal testing machine in a procedure also known as indirect tensile strength test (Fell and Newton, 1970). In this test, the compression mechanism of the particles and the evolution of the tablet's micro structures are evaluated using a type of piston compression equation, developed by such workers as Heckel (1961), Kawakita and Lüdde (1970/71), and Walker (1923).

The Heckel equation is widely used for relating the relative density of the powder bed during compression to the applied pressure. The Kawakita and Lüdde equation, on the other hand, has been used to study powder compression using the degree of volume reduction. The Walker equation has reported experimental data on the compressibility of powders and expresses the volume ratio as a function of applied pressure. In addition to these studies, the physical properties of the powder are also investigated in terms of mean particle size, particle shape, density, flowability, morphology (see Figures 4 and 5) and moisture content.

Other quality control tests are also carried out to determine the quality of the tablets in aspects such as dissolution and friability. These data could prove to be useful to agricultural and food engineering researchers as well as to members of the public who wish to know more about the mechanical properties of herbal powders.

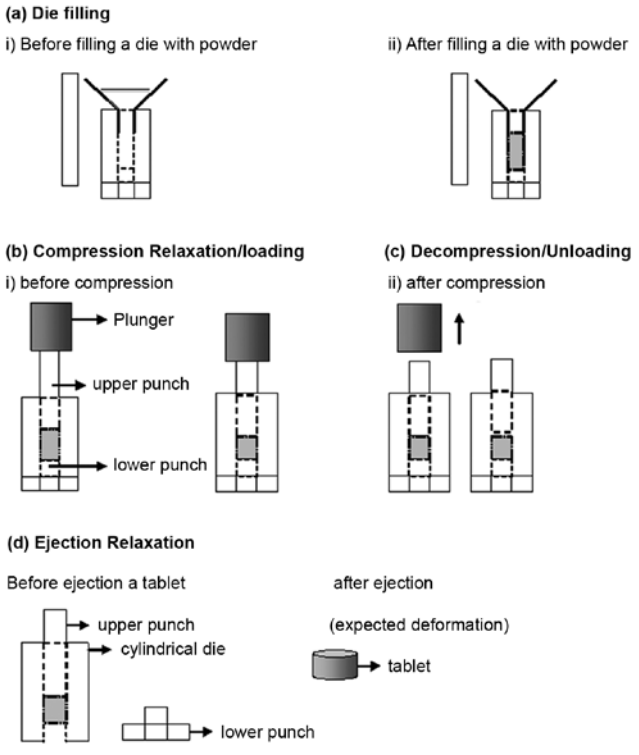

Figure 3: Schematic representation of the major processing stages for compression using uniaxial die compaction. (a) die-filling; (b) compression; (c) decompression and (d) ejection

THE FORMULATION OF TABLETS

Microcrystalline cellulose (MCC) is commonly used as a filler-binder in direct compression because of its good bonding properties. MCC is also claimed to have disintegrating and lubricating properties. The high compactibility of MCC has been attributed to its relatively high propensity for plastic deformation, which enables large surfaces to come close to each other and a large number of bonds, mainly intermolecular forces, to be established between the particles (Reier and Shangraw, 1966; Lamberson and Raynor, 1976; Karehill and Nyström, 1990; Nyström *et al.*, 1993).

The contribution of mechanical interlocking to the mechanical strength has also been suggested (Karehill and Nyström, 1990). Thus, it has excellent binding properties as a dry binder. During compression, MCC is believed to undergo stress relief deformation by several mechanisms. It produces hard tablets with low applied forces and can be used alone or in combination with other directly compressible excipients such as lactose and starches. All of these factors make MCC a commonly used binder in direct compression method.

Other frequently used binders in direct compression include starches and their derivatives, such as pregelatinised and granulated starches. A typical feature of many of the filler-binders used in direct compression is that it undergoes plastic deformation during compression. One exception is dibasic calcium phosphate dihydrate, which fragments quite extensively (Mohammed *et al.*, 2006). Because of its brittle nature, it is less ductile and thus includes less compactable materials, as noted by Mohammed *et al.* (2006). As a result, the bonding properties of this compound are moderate compared with other filler-binders; however, it is practically unaffected by lubricants, which is a clear advantage.

Lactose is also used in direct compression; however, it exhibits relatively poor bonding properties in comparison to other filler-binders. By modifying lactose, for example, by spray drying, a material with enhanced bonding properties is obtained (Bolhuis and Chowhan, 1996). This study finds that the binder that has the most suitable characteristics is MCC. The characteristics of MCC are fully described in the United States Pharmacopeia XXIV/National Formulary 19, 1999.

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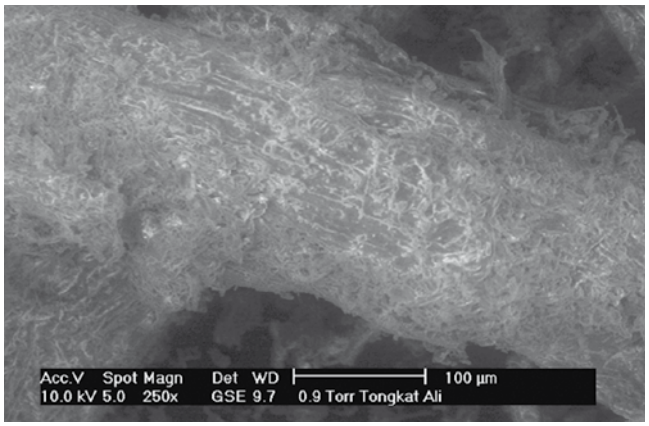

Figure 4: SEM images of andrographis Eurycoma longifolia jack extract powders

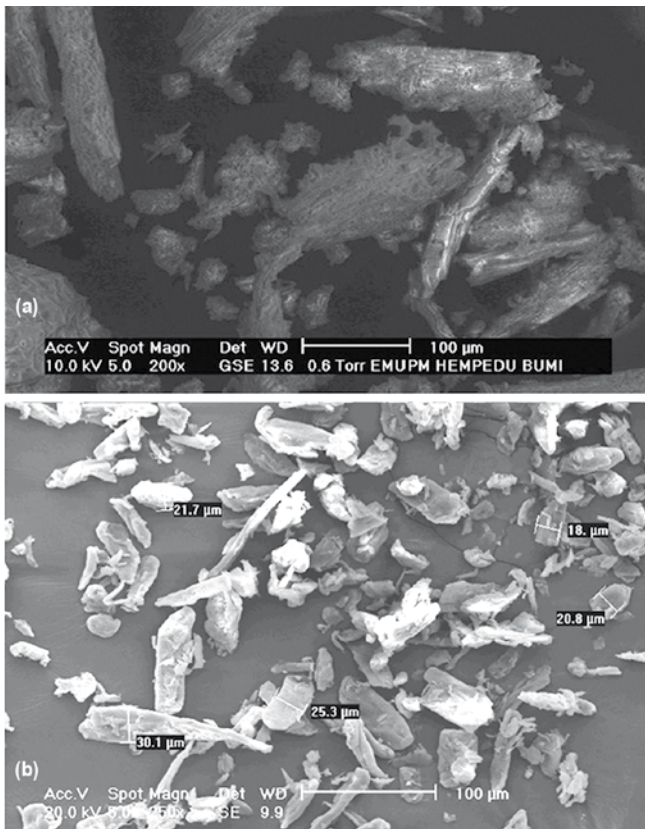

Figure 5: SEM images of andrographis paniculata powders. (a) ground and (b) extract

CONCLUSION

Tablets are becoming an increasingly popular form of making herbs readily accessible to consumers. Tablets are not only the most common form for administering drugs, but also a way to deliver an accurate dosage of, in this context, the bioactive compound of the herbs. The tablet form offers various additional advantages, such as chemical and physical stability, and acceptable shelf life. Advancements in the knowledge of processing technology (engineering) are necessary for the transfer of scientific data into engineering data to take place and for the technical feasibility and economic viability of the products to be determined. ■

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