CHAPTER 2
LITERATURE REVIEW

2.1 Herbal

Herbal medicine is defined in the Drug Act of 1967 as "The drug from botanic, animals or minerals which is not mixed or transformed" (Royal decree committee offices, 1967). In general, most herbal medicines used for primary health care are herbal plants. Five major parts of herbal plants used for medicines include fruit, leaf, stem, root and flower. Parts of these plants have a different structure and different role to a plant. In addition, each section also contains different quantities of basic components. The basic components that may affect to herbal tablet formulation in each part are included in Table 2.1.

Table 2.1 The common quantity of the basic component that is found in each part of plant. (Soontornchainaksaeng, 2005; Hiranramdet, 1992)

Parts of plants	Starch	Fiber	Volatile oil
1. Underground part	+++	+	+++
2. Stem	+	+++	+
3. Leaf	+	+	++
4. Fruit	+++	+	+

Note: + indicates the quantity of the basic component found in each section:

+++ large quantity
++ medium quantity
+ small quantity

2.1.1 Herbal basic component

2.1.1.1 Starches

Starch constitutes the principal form of carbohydrate reserve in the green plant and it is found especially in seeds and underground organs. The green parts of plants exposed to sunlight contain small granules of transitional starch which arise from photosynthesis. During the hours of darkness they are removed to the storage organs.

Starch occurs in the form of granules (starch grains) the shape and size of which are characteristic of the species as is also the ratio of the content of the principal constituents, amylose and amylopectin. (Evans, 2002)

2.1.1.2 Volatile oils

Volatile oils are the odorous principles found in various plant parts. Because they evaporate when exposed to the air at ordinary temperatures, they are called volatile oils, ethereal oils, or essential oils. The last term is applied because volatile oils represent the “essence” or odoriferous constituents of the plant. Volatile oils are colorless as a rule, particularly when they are fresh, but on long standing they may oxidize and resinify, thus darkening. They should be stored in a cool, dry place in tightly stoppered, preferably full (not half-emptied) amber glass containers.

Depending on the plant family, volatile oil may occur in specialized secretory structures such as glandular hairs (Labiatae), modified parenchymal cells (Piperaceae), oil-tubes called vittae (Umbelliferae), or in lysigenous or shizogenous passages (Pinaceae, Rutaceae). They may be formed directly by the protoplasm, by decomposition of the resinogenous layer of the cell wall, or by the hydrolysis of certain glycosides. In the conifers, volatile oils may occur in all parts of plants. Volatile oils may act as repellents to insects, thus preventing the destruction of the flower and leaf; or they may surve as insect attractants, thus aiding in cross-fertilization of the flowers. (Tyler et al., 1988)

2.1.1.3 Fibers

Tissue composed of spindle-shaped or elongated cells with pointed ends is known as prosenshyma. When cells of this kind are thick-walled, they are known as fibers. The cell wall may be composed of almost pure cellulose or may show various degrees of lignification in the form of sclerotic or sclerenchymatous fibres.

Fibers are developed from the single cell, the fiber initial, which during its development grows rapidly in the axial direction. During this period of growth the tips of the elongating cells may push past one another, a process known as ‘gliding growth’ and made possible by a modification in the state of the middle lamella. Most mature fibers are unicellular, but occasionally transverse septa develop (e.g. ginger).

Fibers are best differentiated on the basis of the tissue in which they occur (i.e. as cortical fibres, pericyclic fibres, xylem fibres, xylem fibres or phloem fibers). (Evans, 2002)

2.1.2 Fundamental and standard information of 19 selected herbals

(Vichiara et al., 1995 & 2000; ASEAN countries, 1993; Faculty of pharmacy, Mahidol university,1986; Norman et al.1992)

2.1.2.1 Fruit

(1) *Phyllanthus emblica* Linn.

Thai name: Ma-kham-pom

Family: EUPHORBIACEAE

Loss on drying: not more than 9%

Total ash: not more than 4%

Acid-insoluble ash: not more than 1%

Constituents: ascorbic acid, rutin, mucic acid, gallic acid, phyllemblic acid, and protein

Ethnomedical uses: expectorant, laxative with secondary astringent action and antiscorbutic

(2) *Solanum trilobatum* Linn.

Thai name: Ma-waeng-krueo

Family: SOLANACEAE

Loss on drying: not more than 6%

Acid-insoluble ash: not more than 1%

Constituents: solasodine

Ethnomedical uses: expectorant

(3) *Terminalia chebula* Retz.

Thai name: Sa-maw-thai

Family: COMBRETACEAE

Loss on drying: not more than 11%

Total ash: not more than 3.5%

Acid-insoluble ash: not more than 0.6%

Constituents: tannin: chebulinic acid, chebulic acid, tannic acid and gallic acid; β-sitosterol, saponins and fixed oil

Ethnomedical uses: laxative, carminative, astringent and expectorant

(4) *Piper nigrum* Linn.

Thai name: Phrik-thai-dam

Family: PIPERACEAE

Loss on drying: not more than 14%

Total ash: not more than 7%

Acid-insoluble ash: not more than 1.5%

Constituents: volatile oil, crystalline alkaloids: piperine and piperttine; minor alkaloids: chavicine, piperyline, piperoleines A, B and C, and piperanine

Ethnomedical uses: aromatic, stomachic and carminative

(5) *Morinda citrifolia* L.

Thai name: Yo

Family: RUBIACEAE

Loss on drying: not more than 10%

Total ash: not more than 7%

Acid-insoluble ash: not more than 2%

Constituents: morindin, malic acid, citric acid, glucose and gum.

Ethnomedical uses: anthelmintic, expectorant, laxative for fresh ripe fruit and skin antiseptic for dried unripe fruit

2.1.2.2 Underground part

(1) *Zingiber officinale* Rosc.

Thai name: Khing

Family: ZINGIBERACEAE

Loss on drying: not more than 14%

Total ash: not more than 14%

Acid-insoluble ash: not more than 5%

Constituents: starch, oleoresin, volatile oil, fat and fatty acid, phosphatidylcholine, lysophosphatidylcholine, acetylcholine, phenylethyl alcohol, N-eicosane (dodecyl), N-heneicosane and paradol

Ethnomedical uses: carminative, antipyretic and antiemetic

(2) *Curcuma longa* Linn.

Thai name: Kha-min-chan

Family: ZINGIBERACEAE

Loss on drying: not more than 16%

Total ash: not more than 9%

Acid-insoluble ash: not more than 4%

Constituents: turmeric yields about 7% of a yellow volatile oil containing turmerone and zingiberene as major constituents and many other sesquiterpenes and monoterpenes; yellow coloring matter including curcumin or diferuloylmethane, desmethoxycurcumin, and bismethoxycurcumin.

Ethnomedical uses: Externally for the treatment of skin diseases, wound healing, antipruritic, internally as antidiarrheal, carminative, stomachic and antipyretic

(3) *Acorus calamus* Linn.

Thai name: Wann-nam

Family: ARACEAE

Loss on drying: not more than 13%

Total ash: not more than 9%

Acid-insoluble ash: not more than 2%

Constituents: asarone, calamol, acoramone, as aryl aldehyde, phenyl propane derivative of isoeugenol methyl ether, calamine, camphor, 1,4 cineol, 1,8 cineol, pinene, calamendiol, preisocalamendiol, isocalamendiol, epishyobunone, isohyobunone, shyobunone, acoronene, epoxy isoacoragermacrone, acoragermacrone, acolamone, isoacolamone and essential oil

Ethnomedical uses: Rhizome has been used as carminative, aromatic bitter, emetic, antidysenteric, antiasthmatic, flavoring agent and for the treatment of sore throat.

(4) *Eurycoma longifolia* Jack.

Thai name: Plaa-lai-phuek

Family: SIMAROUBACEAE

Loss on drying: not more than 11%

Total ash: not more than 4%

Acid-insoluble ash: not more than 2%

Constituents: eurycomalactone, β-sitosterol, campesterol, stigmasterol, saponin, laurylcolactone A, laurylcolactone B

Ethnomedical uses: A decoction of root has been used as a remedy for intermittent fevers.

(5) *Glycyrrhiza glabra* Linn.

Thai name: Cha-em-thet

Family: PAPILIONACEAE

Loss on drying: not more than 12%

Total ash: not more than 7%

Acid-insoluble ash: not more than 2%

Constituents: triterpene saponins, flavonoids, coumarins, stilbenes, gum and wax

Ethnomedical uses: expectorant, prevent of the gastrointestinal disorders and carminative

2.1.2.3 Leaf

(1) *Cassia angustifolia* Vahl.

Thai name: Ma-khaam-khaek

Family: CAESALPINIACEAE

Loss on drying: not more than 9%

Total ash: not more than 16%

Acid-insoluble ash: not more than 4%

Constituents: anthraquinones, sennosides, sennidin, anthrone glycosides, dianthrone, rhein, isorhamnetin, kaempferol, oxalic acid, D-(+)-tartaric acid, pinitol

Ethnomedical uses: purgative

(2) *Andrographis paniculata* Wall.Ex Nees.

Thai name: Fa-thalaai-jone

Family: ACANTHACEAE

Loss on drying: not more than 10%

Total ash: not more than 15%

Acid-insoluble ash: not more than 4%

Constituents: 5-hydroxy-7, 8, 2', 3', tetramethoxyflavone, andrographolide sodium bisulfite, andrographolide, polyphenols, caffeic acid, chlorogenic acid,

dicaffeoylquinic acid, neoandrographolide, andrographin, panicolin, apigenin and 4, 7-dimethyl ether

Ethnomedical uses: treatment of the gastrointestinal disorders

(3) *Centella asiatica* (L.) Urban.

Thai name: Bua-bok

Family: UMBELLIFERAE

Loss on drying: not more than 6%

Total ash: not more than 16%

Acid-insoluble ash: not more than 1%

Constituents: triterpenoids, asiatic acid, asiaticoside, brahmic acid, brahmonoside, brahmoside, centellic acid, centelloside, centoic acid, indocentoic acid, thankunic acid, thankuiside, isobrahmic acid, madecassoside, madecassic acid, madecassol, centic acid, oxyasiaticoside, alkaloids, carbohydrates, D-arabinose, D-glucose, L-rhamnose, centellose, pectin, mesoinositol, resin, vitamin C and oil

Ethnomedical uses: anti-inflammation and wound healing

(4) *Pluchea indica* (L.) Less.

Thai name: Khlu

Family: COMPOSITAE

Loss on drying: not more than 8%

Total ash: not more than 11%

Acid-insoluble ash: not more than 1%

Constituents: volatile oil and alkaloids

Ethnomedical uses: deodorant, diaphoretic and dysentery

(5) *Citrus hystrix* DC.

Thai name: Ma-grood

Family: RUTACEAE

Loss on drying: not more than 11%

Total ash: not more than 17%

Acid-insoluble ash: not more than 3%

Constituents: Volatile oil: citronellal, citronellol and citronellol acetate, sabinene, α-,γ-terpinene, cymene and linalool; indole alkaloids: diosmin; rutin and hesperidin

Ethnomedical uses: flavouring agent and carminative

2.1.2.4 Stem

(1) *Tinospora crispa* Miers.

Thai name: Bo-ra-pet

Family: MENISPERMACEAE

Loss on drying: not more than 4%

Total ash: not more than 8%

Acid-insoluble ash: not more than 2%

Constituents: picroretin, N-transferuloyltyramine, N-cis-feruloyltyramine, tintotuberide, phytosterol, methylepentose and alkaloids

Ethnomedical uses: antimalarial, bitter tonic and treatment of skin diseases

(2) *Cinnamomum verum* J.S.

Thai name: Ob-choei-thet

Family: LAURACEAE

Loss on drying: not more than 15.5%

Acid-insoluble ash: not more than 6%

Total ash: not more than 4%

Constituents: volatile oil, phenolic, gum, mucilage, resin, and starch.

Ethnomedical uses: food appetizer, carminative, astringent, antiemetic and expectorant

(3) *Caesalpinia sappan* Linn.

Thai name: Fang

Family: LEGUMINOSAE

Loss on drying: not more than 12%

Acid-insoluble ash: not more than 0.84%

Total ash: not more than 0.06%

Constituents: flavonoids, volatile oil, tannins, campesterol and stigmasterol

Ethnomedical uses: pain reliever and antibacterial

(4) *Derris scandens* Benth.

Thai name: Thao-wan-priang

Family: PAPILIONACEAE

Loss on drying: not more than 9%

Acid-insoluble ash: not more than 10%

Total ash: not more than 4%

Constituents: lonchocarpic acid, scaudenin and gum

Ethnomedical uses: The stem has been used as an expectorant, diuretic, antipyretic and antidysentery.

2.2 Tablets

Tablets are one of the most widely used pharmaceutical formulations at present because it is easy to use, convenient portable and low priced. In addition, the drug dose that the patient receives is accurate and regular when compared to other oral route formulations. Tablets should have the following properties (Natpoonwat et al., 2002).

2.2.1 They are appropriately hard. They should not be too weak in order to prevent breaks during the production process, packaging and transport. If they are too hard the time to disintegrate is too long. This property can be examined using a hardness and friability test.

2.2.2 They are consistent in weight and the amount of drug in each tablet. This property can be examined from weight variation or content uniformity.

2.2.3 They have good bioavailability which can be examined from disintegration and dissolution test.

2.2.4 They are elegant.

2.2.5 They contain efficacy and drug stability.

Tablets production can be classified into 3 processes:

1 Wet granulation process

2 Dry granulation process

3 Direct compression process

Limmattawapiratt S. (2002) provides the considerations for choosing the tablets production process for herbal powder as follows:

1 Herbal quantity per 1 tablet If herbal dosage of tablet is not very high, flow and compression properties of the herbal powder may not have much influence because excipients can be used to improve these properties. However, if the drugs have a high dosage, flow and compression properties have an important role because they have an effect on the production. Powder, which has good flow and compression

properties, can be prepared by direct compression process. If the powder has a poor flow property but can be compressed, the dry granulation process is applied. While the powder with poor flow and compression properties, the wet granulation process is applied. Most herbals have poor flow and compression properties because of some components. For example, *C. longa* has a lot of volatile oil which makes it difficult to prepare tablets and cannot be compressed. Before preparing tablets they must be prepared as granules. The wet granulation process is suitable in this case.

2 Powder's bulk density Some herbals have a dosage that is not very high and there is a low density. This makes for a large volume that can't be compressed immediately. In this case, granules should be prepared before preparing tablets.

3 Active drug's stability Drugs that have instability from moisture, should not be prepared as wet granules with water as part. In this case, solvent that's not water based such as alcohol or direct compression process may be used if possible. If the drugs are sensitive to heat, the process used should avoid from high tempurature, and dry granulation or direct compression should be used. If heat cannot be avoided, it should be taken in short time increments. This can be done by using a binder that uses alcohol as a solvent to shorten the time to dry granules or select a suitable drying instrument.

4 Drug's dissolution Several types of herbal have a main substance with slightly soluble and hydrophobic properties. If prepared by wet granulation process with water, the tablets will dissolve better, when compared with the dry granulation process. However, when compared with the direct compression process in which drugs aren't captured in granules, the drug is released faster. Therefore, the selection process may require a trial comparing the two methods.

Even though the effect of the herbal powder component on the tablet production process selection has been suggested, no information that explicitly support the research is available. Therefore, it is necessary to have additional information to understand the results of the trial. A review of various articles and research found that there was little research related to the development of herbal powder tablets formulation as follows:

Patra and colleaques (2008) studied on tablets formulation development of *Rauwolfia serpentina* powder compared tablets preparation by direct compression and

wet granulation process. The results from the Kawakita analysis revealed improved flowability for formulations prepared by direct compression and wet granulation technique. The Heckel plot showed that *R. serpentina* powder is soft in nature, poor in die filling and deforms by initial fragmentation whereas granules and direct compression formulation showed a higher degree of plasticity and fragmentation. The Leuenberger equation revealed a higher value for maximum tensile strength in case of granule over direct compression formulation, indicating that tablets prepared by the wet granulation process have greater hardness than when prepared by the direct compression process. Both wet granulation and direct compression method could be used successfully for developing tablet formulation of *R. serpentina* root powder, but the granules showed better flowability, compressibility and compactibility compared to direct compression formulation.

Patra and colleaques (2008) studied on the flowability and compressibility of *Asparagus racemosus* root powder and tablet formulations. The root powder showed very poor flowability and compressibility. The Kawakita analysis revealed improved flowability for formulations prepared by direct compression which mixed glidant and wet granulation techniques. The compression behavior was analyzed by Heckel equations. Granules showed a higher degree of fragmentation and plasticity than powder and direct compression formulations. A study on compression properties using Leuenberger equation showed the compression susceptibility parameter for compaction formed by direct compression and wet granulation implied that the maximum crushing strength was reached faster at lower pressure of compression as opposed to powder. In summary, filling glidant in preparing tablets by direct compression and wet granulation process can improve flow and compaction properties of *A. racemosus* root powder.