#### **CHAPTER 4**

### **RESULTS AND DISCUSSION**

## 4.1 Examination of Herbal Powders

HANG MA

The examination of herbal characteristics using macroscopic and microscopic methods in confirming types of medicinal plants revealed that all herbs used in this research were accurate and compatible with what presented in Thai Herbal Pharmacopoeia (Vichiara et al., 1995 & 2000) or Standard of Asean Herbal Medicine (ASEAN countries, 1993). The results of the sudy from this phase were shown in Fig 4.1-4.23. Regarding herb quality examination processed by measuring the total ash and the acid insoluble ash, it was found that all measured values are in accordance with the standard (Table 4.1).



### 4.1.1 Macroscopic characteristics

The macroscopic characteristics of herbal specimens classified by part used, namely fruit, underground part, leaf and stem were shown in Fig. 4.1-4.4.



(a) *P. emblica* (b) *S. trilobatum* (c) *T. chebula* (d) *P. nigrum* and(e) *M. citrifolia* 







**Fig 4.4** Macroscopic characteristics of crude drugs from herbal stem (a) *T. crispa* (b) *C. verum* (c) *C. sappan* and (d) *D. scandens* 

Investigation of herbal macroscopic characteristics showed that the morphology of herbal specimens used in the study was in agreement with those defined in the referenced documents (Vichiara et al., 1995 & 2000; Faculty of pharmacy, Mahidol university, 1986; Norman et al.1992)

### 4.1.2 Microscopic characteristics

The microscopic characteristic of herbal powder were shown in Fig 4.5-4.23



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## Fig 4.5 Powdered drug of the pericarp of P. emblica

- 1. Epicarp in surface view
- 2. Prismatic crystals
- 3. Fibrous sclereids
- 4. Thick-walled parenchyma containing reddish masses
- 5. Fibrous sclereids from seed coat
- 6. Grey masses

- 7. Sclereids
- 8. Reddish masses
- 9. Sclereids containing grey masses
- 10.Sclerenchyma sclereids from seed coat
- 11.Tannin granules



- Epidermis of pericarp in surface view
- 2. Thick walled parenchyma of pericarp
- 3. Sclerenchymatous layer of testa in surface view
- 4. Sclerenchymatous layer of testa in surface view from below
- 5. Endosperm with oil droplets
- 6. Embryo with oil droplets

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## Fig 4.7 Powdered drug of the fruit of T. chebula

- 1. Epidermis in sectional view
- 2. Epidermis in surface view
- 3. Fiber and starch grains
- 4. Ground parenchyma
- 5. Masses of brownish black material
- 6. Sclerenchyma of endocarp
- 7. Porous parenchyma
- 8. Sclereid

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- 9. Vessels stain with solution of phloroglucinol in 20 % HCl
- 10.Starch grains
- 11.Reticulate parenchyma
- 12.Oil globule stain with Sudan III solution
- 13.Parenchyma containing rosette aggregate crystal



Fig 4.8 Powdered drug of the fruit of P. nigrum

- 1. Stone cells
- 2. Perisperm tissue with starch granules and resin
- 3. Epidermal cells of epicarp
- 4. Typical stone cell stain with solution of phloroglucinol in 20 % HCl
- 5. Crystals of piperine
- 6. Starch granules
- 7. Polygonal cells of mesocarp





Fig 4.10 Powdered drug of the rhizome of Z. officinale

- 1. Parenchymatous cells with adherent starch granules
- 2. Part of fiber
- Cork in surface view underlying with parenchymatous cells containing starch granules

- 4. Parts of fibers with dentate walls, showing septa
- 5. Starch granules
- 6. Parts of reticulate vessel with associated pigment cell



### Fig 4.11 Powdered drug of the rhizome of C. longa

- 1. Cork in surface view
- 2. Spirally thickened vessel
- 3. Outer tissue in sectional view showing epidermis and cortex
- 4. Parenchymatous cell

- 5. Reticulately thickened vessel
- 6. Starch granules
- Parenchymatous cell filled gelatinised starch and yellow matter



## Fig 4.12 Powdered drug of the rhizome of A. calamus

- 1. Epidermis
- 2. Vessels
- 3. Fragment of parenchymatous cells in sectional view
- 4. Large oil cell
- 5. Starch granules stain with
- Iodine solution
- 6. Fibers with calcium oxalate prism sheath



Fig 4.13 Powdered drug of the root of E. longifolia

- 1. Cork in surface view
- 2. Mass of brownish pigments
- 3. Starch granules stain with Iodine solution
- 4. Fragment of fibers
- 5. Xylem parenchyma in longitudinal view
- 6. Xylem parenchyma in sectional view with starch granules
- 7. Xylem fibers and part of a medullary ray stain with

- solution of phloroglucinol in 20% HCl in radial-longitudinal view
- 8. Xylem fibers and part of a medullary ray in tangential-longitudinal view
- Fragment of large bordered pitted vessels stain with solution of phloroglucinol in 20% HCl
- 10.Stone cell
- 11.Fragment of parenchyma cells from the cortex



### Fig 4.14 Powdered drug of the root of G. glabra

- 1. Cork in surface view
- 2. Prism of calcium oxalate
- 3. Starch granules
- 4. Part of a medullary ray (m.r.) containing starch granules
- 5. Part of a single fiber
- 6. Fragment of a large vessel with elongated pits
- Part of a group of smaller vessels with bordered pits
- Part of medullary ray (m.r.) containing starch granules (s.t.)

- in tangential longitudinal section with part of fiber
- Part of a group of fibers with incomplete calcium oxalate prism sheath
- 10.Lignified xylem parenchyma with part of underlying bordered pitted
  - vessel
- 11.Fragment of a bordered pitted vessel
- 12.Part of a medullary ray in radial longitudinal section with part of a bordered pitted vessel



## Fig 4.15 Powdered drug of the leaf of *C. angustifolia*

- 1. Epidermis in surface view showing paracytic stomata and underlying palisade cells
- 2. Epidermis in surface view showing cicatrix and underlying palisade cells
- 3. Fragment of covering trichome
- 4. Rosette crystal of calcium

- 5. Epidermis in surface view with attached trichome
- 6. Xylem element from one of the larger veins stain with solution of phloroglucinol in 20 % HCl
- 7. Group of fibers with calcium oxalate prism sheaths

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## Fig 4.16 Powdered drug of the leaf of A. paniculata

- Lower epidermis of the leaf in surface view showing diacytic stomata, lithocyst cells and glandular trichome.
- 2. Elongated epidermis with lithocyst cells and stomata
- 3. Fragment of fibers

- Fragment of xylem tissues, showing xylem parenchyma and vessels
- 5. Glandular trichome

view

- 6. Epidermis at the edge of the
- leaf with mesophyll in surface

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## 0.05 mm

## Fig 4.17 Powdered drug of the leaf of C. asiatica

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- 1. Lower epidermis in surface view with anisocytic stomata
- 2. Part of the lamina in sectional view with rosette aggregates crystals
- 3. Part of stolon in longitudinal view showing vessels, fiber and parenchyma cells

- 4. Starch granule stain with Iodine solution
- 5. Prism of calcium oxalate
- 6. Part of stolon in surface view showing epidermal cells and cuticular striation
- 7. Epidermal cells
- 8. Part of lignified fiber

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3



### 0.05 mm

- Fig 4.19 Powdered drug of the leaf of *C. hystrix* 
  - 1. Epidermis and collenchyma in
    - sectional view
  - 2. Lamina in sectional view
  - 3. Upper epidermis in surface view
  - 4. Fibers

1

5. Lower epidermis in surface view showing stomata and the

underlying idioblasts containing prismatic crystals of calcium oxalate 6. Vessel

3

6

- 7. Prismatic crystals of calcium oxalate
- Epidermis of midrib in surface view

8

2

5



Fig 4.20 Powdered drug of the stem of T. crispa

- 1. Cortical parenchyma
- 2. Cork in surface view
- 3. Stone cells stain with solution
  - of phloroglucinol in 20 % HCl
  - 4. Parenchyma cells with
  - prismatic crystals
  - 5. Starch granules

Со

- 6. Phloem cells
- 7. Bordered pitted vessels
- 8. Reticulate vessel
- 9. Pitted vessel
- 10.Fragments of bast fibers with
- dentated wall
- 11.Xylem parenchyma with lignified wall



## Fig 4.21 Powdered drug of the stem bark of C. verum

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- 1. Fibers
- 2. Sclereid
- 3. Starch granules stain with
- Iodine solution and calcium associated oil cell
  - oxalate crystals
  - 4. Cork in surface view
- 5. Phloem parenchyma and oil าวทยาล
  - cell
  - 6. Part of a fiber with an
  - 7. A single oil cell



4. Prismatic crystal of calcium oxalate



## Fig 4.23 Powdered drug of the stem of *D. scandens*

- 1. Cork in surface view
- 2. Parenchymatous cells
- containing starch granules
- 3. Starch granules
- Prisms of calcium oxalate in parenchyma cells
- 5. Fragment of bordered pitted vessels stain with solution of phloroglucinol in 20 % HCl
- 6. Part of medullary ray with underlying xylem parenchyma

- Group of fibers with underlying medullary ray
- Group of fibers with part of calcium oxalate prism sheath
- Sclereid stain with solution of phloroglucinol in 20 % HCl
- 10.Part of medullary ray showing xylem parenchyma with underlying xylem fibers
- 11.Fragment of xylem parenchyma

Investigation of herbal microscopic characteristics showed that the histology of herbal specimens used in the study was in agreement with those defined in the referenced documents (Vichiara et al., 1995 & 2000; Faculty of pharmacy, Mahidol university, 1986; Norman et al.1992).

#### 4.2 Herbal Powder Composition

The herbal powder composition in each part of plants was quite different. Fiber was found at higher contents in stem and fruit than in leaf and underground part. The highest fiber content was found in *C. sappan* ( $55.03\pm0.05\%$ ), *T. chebula* ( $31.17\pm0.17\%$ ), *S. trilobatum* ( $30.28\pm0.23\%$ ) and *D. scandens* ( $30.17\pm0.12\%$ ), respectively (Table 4.1). The reason for this finding may be that both parts of plants need more strength than other parts do.

More starch content was found in underground part of plants than in other parts. The highest amount was found in *A. calamus* ( $44.45\pm0.34\%$ ), *E. longifolia* ( $39.39\pm0.69\%$ ), *Z. officinale* ( $32.75\pm0.65\%$ ) and *C. longa* ( $31.38\pm0.15\%$ ), respectively (Table 4.1). It could be considered that underground part is the part in which plants accumulate food in a form of starch granules.

Volatile oil was found in six plants including *P. nigrum* ( $1.43\pm0.21\%$ ), *Z. officinale* ( $1.53\pm0.12\%$ ), *C. longa* ( $6.83\pm0.29\%$ ), *A. calamus* ( $2.80\pm0.40\%$ ), *C. hystrix* ( $0.93\pm0.12\%$ ) and *C. verum* ( $0.82\pm0.03\%$ )(Table 4.1). Volatile oil is a secondary metabolite. It is a composition which is produced by a certain plant species and can be found in every part of the plants.

Sample Type	Total Ash % (w/w)		Acid Insoluble Ash %(w/w)		Volatile Oil Content %(v/w)		Fiber Content	Starch Content	Moisture Content
-	Standard	Experi mental	Standard	Experi mental	Standard	Experi mental	%(w/w)	%(w/w)	%(w/w)
Fruit		6			S N				
P. emblica	4.0	4.43±0.11	1.0	0.51±0.09	ND	ND	18.77±0.21	ND	5.56±0.09
S. trilobatum	-	12.21±0.02	1.0	0.64±0.06	ND	ND	30.28±0.23	0.86±0.01	6.08±0.03
T. chebula	6.5	6.72±0.04	1.0	1.05±1.49	ND	ND	31.17±0.17	1.17±0.26	5.66±0.02
P. nigrum	7.0	4.00±0.07	1.5	0.17±0.03	≥1.0	1.43±0.21	10.52±0.06	36.48±1.41	6.70±0.05
M. citrifolia	7.0	7.10±0.28	2.0	1.98±1.51	ND	ND	21.14±0.11	3.08±0.38	6.71±0.15
Underground part									
Z. officinale	8.0	8.14±0.56	1.8	0.88±0.63	2.0	1.53±0.12	7.97±0.13	32.75±0.65	6.78±0.51
C. longa	8.0	9.10±0.42	1.0	0.90±0.06	≥ 6.0	6.83±0.29	5.80±0.05	31.38±0.15	6.63±0.01
A. calamus	7.0	3.64±0.40	2.0	ND	≥1.2	2.80±0.40	7.95±0.06	44.45±0.34	7.37±0.03
E. longifolia	4.0	3.74±0.05	<b>E</b> 1.0	$1.06 \pm 0.06$	ND	ND	21.12±0.22	39.39±0.69	6.14±0.04
G. glabra	10.8	5.90±0.04	4.0	0.81±0.16	ND	ND	12.08±0.22	16.48±0.10	7.14±0.06
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	A		rig	h t s	ľ	ese	r v e		

 Table 4.1 Quantitative analysis and basic composition of herbal powder

Sample Type	Total As	h % (w/w)	Acid InsolubleVolatile OilAsh %(w/w)Content %(v/w)		Volatile Oil Content %(v/w)		Volatile OilFiberContent %(v/w)Content		Starch Content	Moisture Content
	Standard	Experi mental	Standard	Experi mental	Standard	Experi mental	%(w/w)	%(w/w)	%(w/w)	
Leaf		6			5					
C. angustifolia	16.0	11.57±0.04	4.0	0.86±0.39	ND	ND	8.19±0.29	5.06±0.29	$7.42 \pm 0.01$	
A. paniculata	19.0	21.47±0.10	4.0	3.74±0.12	ND	ND	14.75±0.10	0.73±0.03	7.32±0.01	
C. asiatica	17.0	18.15±0.19	1.0	1.24±0.73	ND	ND	11.44±0.09	0.53±0.38	6.11±0.08	
P. indica	15.0	16.35±0.10	1.0	1.01±0.18	ND	ND	22.38±0.08	ND	5.88±0.77	
C. hystrix	17.0	12.37±0.03	3.0	0.75±0.25	≥0.6	0.93±0.12	16.47±0.14	6.92±0.18	6.15±0.00	
Stem					1361					
T. crispa	9.0	9.37±0.30	1.0	1.12±0.03	ND	ND	13.65±0.04	34.87±0.02	$6.60 \pm 0.00$	
C. verum	3.4	3.43±0.03	0.2	0.11±0.07	≥ 0.8	0.82±0.03	19.77±0.06	11.04±0.32	8.07±0.01	
C. sappan	0.8	0.73±0.01	0.1	ND	ND	ND	55.03±0.05	0.81±0.12	5.83±0.06	
D. scandens	10.0	7.52±0.08	4.0	0.31±0.08	ND	ND	30.17±0.12	15.45±.017	6.31±0.02	

 Table 4.1 Quantitative analysis and basic composition of herbal powder (cont.)

All values are expressed as mean ± SD, n=3, ND: Not detected

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#### **4.3 Flow Properties**

The results of flow properties by measuring the repose angle, kawakita equation and flow rate were shown in Table 4.2. A large number of herbals have high values of repose angle and % compressibility ratio. It indicated the poor flowability (Table 4.3).

Kawakita plots (Plots of N/C versus N) for all herbal powders gave the linear relationship ( $r^2 \ge 0.99$ ) (Fig 4.24). Kawakita constants (a and 1/b) represent herbal powder behavior from bulk density state to the tap density state. Most powder exhibited high compressible value (a) showing the poor flowability; however, there were three herbal powders having low compressible value: *P. nigrum* (0.169), *C. longa* (0.201) and *Z. officinale* (0.242). Hence, these types of herbal powder had better flowability than others. 1/b value represents cohesiveness of the herbal powder. *C. angustifolia* (147.674) had the highest 1/b value, thus exhibited the most cohesiveness (Table 4.2). Flow rate could not be calculated for every herbal powder. As a whole, the flowability of almost all herbal powder used in this study was poor. It suggested the application of granulation method for tablet formulation.

The analysis of relationship between herbal powder composition and flowability using Kawakita constant values by a quadratic model revealed that the model as fit was not statistically significant (p > 0.05). It could be considered that the derived properties of herbal powder such as particle size and shape were more influential factors than the composition in the powder itself.

In order to improve the flowability of the herbal powder, the wet granulation was applied using 4 types of binders, namely 10% starch paste (SP), 5% starch paste + 5% gelatin solution (SG), 10% polyvinylpyrrolidone (PP) and 10% gelatin solution (GT). The compressibility ratios of the obtained granules were summarized in Table 4.3. The flow property of the granule changed from poor or passable for powder to good or excellent for granules.

The exemplary microscopic photographs in Figure 4.25 showed the comparison in characteristics of herbal powder and granules. The significant improvement in particle size was obviously observed. Moreover, it is well known that the shapes of the particles also affect the flow property. Particles which are square or fiber particles with a long shape have more difficulty to flow when compared to

particles with round shape. It can be seen that herbal powder granules are more spherical (Fig 4.25) and then gave better flowability as demonstrated by the lower compressibility ratio (Table 4.3).



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Intercep           (1/ab)           461         68.460           673         101.400           806         50.230           69         45.140	<b>at</b> 1/b 31.534 37.794 15.370 7.613	r <sup>2</sup> 0.997 0.997 0.999 0.999	(g/s) ND ND ND ND	(°) 32±2.65 43±1.00 44±0.58 42±0.58	Flow Property passable very poor very poor
(1/ab) 461 68.460 473 101.400 506 50.230 69 45.140 44.124	31.534 37.794 15.370 7.613	0.997 0.997 0.999 0.999	ND ND ND ND	32±2.65 43±1.00 44±0.58 42±0.58	passable very poor very poor
61     68.460       673     101.400       806     50.230       69     45.140	31.534 37.794 15.370 7.613	0.997 0.997 0.999 0.999	ND ND ND ND	32±2.65 43±1.00 44±0.58 42±0.58	passable very poor very poor
61     68.460       673     101.400       806     50.230       69     45.140	31.534 37.794 15.370 7.613	0.997 0.997 0.999 0.999	ND ND ND ND	32±2.65 43±1.00 44±0.58 42±0.58	passable very poor very poor
373       101.400         306       50.230         69       45.140         326       14.124	0 37.794 15.370 7.613	0.997 0.999 0.999	ND ND ND	43±1.00 44±0.58 42±0.58	very poor very poor
306         50.230           69         45.140           926         44.124	15.370 7.613	0.999 0.999	ND ND	44±0.58 42±0.58	very poor
69     45.140       44.124	7.613	0.999	ND	42±0.58	
14 104				/	very poor
44.134	14.822	0.997	ND	50±0.58	very poor
242 110.100	26.678	1.000	ND	50±1.73	very poor
201 100.100	20.169	0.999	ND	48±0.58	very poor
61.930	23.556	0.997	ND	51±0.58	very poor
882 109.700	41.854	0.995	ND	25±1.51	good
18 107.100	) 44.737	0.998	ND	42±1.73	very poor
	380     61.930       382     109.700       418     107.100	380       61.930       23.556         382       109.700       41.854         418       107.100       44.737	380       61.930       23.556       0.997         382       109.700       41.854       0.995         418       107.100       44.737       0.998	380         61.930         23.556         0.997         ND           382         109.700         41.854         0.995         ND           418         107.100         44.737         0.998         ND	380       61.930       23.556       0.997       ND       51±0.58         382       109.700       41.854       0.995       ND       25±1.51         418       107.100       44.737       0.998       ND       42±1.73



 Table 4.2 Flow properties of herbal powder (cont.)

Sample Type	Kawakita analysis				7	- Flow rate	<b>Repose angle</b>		
_	Slope	a	Intercept	1/b	$\mathbf{r}^2$	(g/s)	(°)	Flow	
	( <b>1</b> / <b>a</b> )	5	(1/ab)			3		Property	
Leaf				$(\mathbf{g})$					
C. angustifolia	1.806	0.554	266.700	147.674	0.891	ND	46±0.58	very poor	
A. paniculata	2.694	0.371	101.900	37.825	0.997	ND	29±1.81	good	
C. asiatica	2.310	0.433	81.570	35.312	0.996	ND	31±2.52	passable	
P. indica	3.290	0.304	70.340	21.380	0.999	ND	39±2.03	passable	
C. hystrix	2.745	0.364	60.440	22.018	0.999	ND	39±1.00	passable	
Stem					6				
T. crispa	2.655	0.377	96.430	36.320	0.998	ND	30±1.15	good	
C. verum	2.103	0.476	92.780	44.118	0.993	ND	35±0.58	passable	
C. sappan	2.747	0.364	104.700	38.114	0.999	ND	41±1.00	very poor	
D. scandens	3.300	0.303	115.700	35.061	0.999	ND 2	40±1.93	passable	

All values are expressed as mean  $\pm$  SD, n=3

ND: Not determinded (Determination was not possible due to powder could not flow through the funnel orifice)

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Sample Type	No bin	ıder	SI		SC	3	PF		G	Г
-	Compressi	Flow	Compressi	Flow	Compressi	Flow	Compressi	Flow	Compressi	Flow
	bility	Property	bility	Property	bility	Property	bility	Property	bility	Property
	Ratio (%)	G	Ratio (%)		Ratio (%)		Ratio (%)		Ratio (%)	
Fruit				Jun						
P. emblica	29±5.74	poor	10.20±2.29	good	9.28±1.86	excellent	10.20±2.35	good	8.25±1.17	excellent
S. trilobatum	24±2.78	passable	11.58±0.43	good	10.53±1.41	good	11.46±1.07	good	10.42±2.16	good
T. chebula	24±0.77	passable	11.22±3.09	good	10.23±2.42	good	11.44±1.54	good	10.27±0.45	good
P. nigrum	25±0.19	passable	10.53±0.68	good	9.47±1.64	excellent	10.42±0.56	good	9.38±0.67	excellent
M. citrifolia	23±1.26	passable	11.88±1.66	good	10.14±1.58	good	11.50±1.95	good	10.81±1.60	good
Underground par	·t									
Z. officinale	15±0.74	fair	8.51±0.81	excellent	8.51±1.54	excellent	7.45±0.95	excellent	6.45±1.23	excellent
C. longa	15±0.77	fair	9.28±1.67	excellent	8.33±2.68	excellent	9.28±1.57	excellent	8.42±1.51	excellent
A. calamus	22±1.07	passable	10.42±0.55	good	9.47±1.52	excellent	9.38±1.86	excellent	7.45±1.31	excellent
E. longifolia	29±2.08	poor	10.53±2.59	good	9.47±2.43	excellent	10.53±1.65	good	9.57±2.38	excellent
G. glabra	33±0.54	very poor	8.51±1.71	excellent	7.45±0.77	excellent	8.51±2.19	excellent	8.51±1.26	excellent
	C	opyrig	sht <sup>e</sup>	by C	hiang	Mai	Unive	ersity		
	Α		<b>rig</b>	h t	s r	e s	er۱	e d		

 Table 4.3 Compressibility ratio of herbal powder and herbal granules using different binders

Sample Type	No bin	der	SF		SG		PI	•	G	Г
_	Compressi	Flow	Compressi	Flow	Compressi	Flow	Compressi	Flow	Compressi	Flow
	bility	Property	bility	Property	bility	Property	bility	Property	bility	Property
	Ratio (%)	6	Ratio (%)		Ratio (%)		Ratio (%)		Ratio (%)	
Leaf				Juli						
C. angustifolia	16±3.46	fair	9.28±2.15	excellent	8.33±2.64	excellent	9.28±0.31	excellent	10.31±2.52	good
A. paniculata	22±3.77	passable	10.53±1.17	good	9.47±0.81	excellent	11.46±0.88	good	11.46±0.62	good
C. asiatica	25±4.22	poor	12.37±3.24	good	9.38±0.74	excellent	11.34±2.19	good	11.34±1.24	good
P. indica	21±4.09	passable	10.71±2.01	good	9.43±1.24	excellent	10.91±3.17	good	10.75±0.48	good
C. hystrix	23±1.61	passable	7.53±0.32	excellent	6.38±0.59	excellent	9.47±1.32	excellent	11.46±1.39	good
Stem										
T. crispa	27±3.02	poor	10.42±1.16	good	10.31±3.30	good	11.34±1.85	good	9.38±1.02	excellent
C. verum	25±2.05	poor	10.31±2.88	good	10.31±1.81	good	10.31±2.44	good	8.33±2.19	excellent
C. sappan	27±3.27	poor	10.64±0.74	good	10.53±2.77	good	11.58±1.97	good	9.57±1.06	excellent
D. scandens	26±4.95	poor	13.04±1.66	good	12.90±2.62	good	13.98±2.10	good	11.96±1.66	good

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**Table 4.3** Compressibility ratio of herbal powder and herbal granules using different binders (cont.)

All values are expressed as mean ± SD, n=3 by Chiang Mai University All rights reserved

#### 4.4 Compaction property

The compaction property of the herbal powder was evaluated by measuring the hardness of tablets compressed with a 15,000 N compression force, and the results are shown in Table 4.4. It was found that no compacted powder had hardness of over 40 N. Thus, it can be indicated that all herbal powder was not compressible enough for tablet production using direct compression or dry granulation. Therefore, it was obvious from the results of this study that wet granulation method was the most appropriate method in formulation of herbal powder tablets.

The analysis of relationship between herbal powder composition and compressibility using hardness value of tablets as a statistical tool in quadratic model revealed the following equation.

Hardness = 
$$3.291 - 0.221X_1 + 0.027X_2 - 1.272X_3 + 0.004X_1^2 - 0.002X_2^2$$
  
 $- 0.005X_3^2 + 0.003X_1X_2 - 0.024X_1X_3 + 0.041X_2X_3$ 

The coefficient of determination  $(r^2)$  of the regression equation was 0.920, indicating that the model as fitted explained 92.00% of the variability in hardness. The adjusted  $r^2$  for this equation model was 0.840 (sig = 0.001). According to this finding, it can be concluded that fiber, starch and volatile oil content are statistical significantly related to the hardness of tablet (p <0.05).

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Sample Type	Hardness (N)	Sample Type	Hardness (N)
Fruit		Underground part	
P. emblica	ND	Z. officinale	4.71±0.08
S. trilobatum	4.12±0.10	C. longa	17.06±0.28
T. chebula	5.39±0.04	A. calamus	2.55±0.05
P. nigrum	3.14±0.03	E. longifolia	1.86±0.03
M. citrifolia	2.75±0.05	G. glabra	18.73±0.31
Leaf	دررسینی	Stem	
C. angustifolia	15.69±0.17	T. crispa	4.02±0.04
A. paniculata	11.77±0.31	C. verum	3.92±0.09
C. asiatica	17.06±0.19	C. sappan	34.12±0.17
P. indica	7.35±0.09	D. scandens	16.87±0.22
C. hystrix	ND	FAL /	Ö

 Table 4.4 Hardness of the herbal tablets compressed with a 15,000 N compression force

All values are expressed as mean  $\pm$  SD, n=6, ND: Not determinded

NG MAI

#### **4.5 Formulation of herbal powders**

From herbal flowability and compactability tests, it can be concluded that all herbal powders were not compressible enough for tablet production using direct compression or dry granulation. Therefore, wet granulation method is the most appropriate method in formulation of herbal powder tablets. First of all, the adequacy of the lubricant in the formulation was investigated. The concentrations of glidant and lubricant used in the general formulation i.e, talcum 3% and magnesium stearate 0.5% were investigated by studying the maximum compression forces detected at the upper and lower punches during tablet compression as illustrated in Figure 4.26. The interpretation is based on the fact that if the compression force generated from the upper punch can transmitted effectively to the lower punch, or the compression force at the lower punch has a value closed to that of the upper punch, glidant and lubricant are present in sufficient concentrations in the system and the friction between granules or granules and die wall are minimized. The transmission ratio (R) or the ratio of the maximum upper punch force devided by the maximum lower puch force was used to represent the efficiency of the glidant and lubricant in the formulation. The results are shown in Table 4.5. It is obvious that all formulations had the transmission ratio of greater than 0.9, indicating that sufficient lubrication was available in all herbal formulations. Morover, the smooth and glossy surface was observed on the sides of the tablets. Therefore, it can be concluded that the concentrations of talcum and magnesium stearate at 3 % and 0.5 % were appropriate for all types of formulations in this study.


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 Table 4.5 The maximum lower and upper punch force and the pressure transmission ratio (R) of herbal tablet formulations using different binders

Sample Type		SP			SG	NAY I		РР	>" \		GT	
	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R C	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R
Fruit					IX							
P. emblica	14581	15201	0.97	15778	15994	0.99	15323	15753	0.97	15333	15410	1.00
	$\pm 548$	±498 °		±163	±192		±352	±298	7255	±249	±299	
S. trilobatum	15996	15575	0.94	15541	15333	1.01	15944	15863	1.01	15266	15554	0.98
	±365	±312		±253	±324		±232	±326		±405	±313	
T. chebula	15725	16344	1.02	14701	15742	0.93	15681	15732	1.00	15334	16121	0.95
	±231	±346		±448	±574		±332	±265		±398	±316	
P. nigrum	16064	15309	1.00	15352	16091	0.95	15929	15325	1.04	15302	15845	0.97
	±256	±342	1 5	±409	±347		±635	±513		$\pm 266$	±327	
M. citrifolia	15794	15437	0.99	15516	16125	0.96	15618	16814	0.93	14695	15333	0.96
	±462	±574		±363	±286	boo	±532	±465		±402	±516	
Underground p	art							57/				
Z. officinale	15873	16438	0.97	15605	15879	0.98	15577	16880	0.92	15087	15633	0.97
00	±237	±307		±374	±399	JN	±691	±546		±265	±272	
C. longa	14865	15876	0.94	15585	15759	0.99	15475	15525	1.00	15431	15902	0.97
0	±461	±378		±352	±339		±157	±217		±195	±325	
A. calamus	15823	15485	1.02	15144	15198	1.00	15312	15860	0.97	14492	15370	0.94
	±234	±364		±272	±275		±314	±464		±351	$\pm 409$	
E. longifolia	15922	15914	1.00	15383	15855	0.97	15541	15844	0.98	15213	15657	0.97
	±183	±241	•	±538	±442	•	$\pm 398$	±334	•	±187	±249	
G. glabra	15292	15413	0.99	15152	15282	0.99	15404	15373	1.00	15733	16024	0.98
-	±353	±419	/0	±236	±322		±341	±287		±373	±449	
		AI		rig	ht	S	re	s e i		e d		

 Table 4.5 The maximum lower and upper punch force and the pressure transmission ratio (R) of herbal tablet formulations using

different binders (cont.)

Sample Type		SP	9		SG	Mily E	$\bigcirc$	PP		GT			
	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R C	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R	Maximum Lower Punch Force (N)	Maximum Upper Punch Force (N)	R	
Leaf					13/								
C. angustifolia	14541	15962	0.91	15271	15951	0.96	15023	15517	0.97	16265	15925	1.02	
	±472	±364	12	±355	±299	- P'3	±417	±487	Gia	±427	$\pm 448$		
A. paniculata	15415	15781	0.98	14972	15034	1.00	15413	15887	0.97	15148	15432	0.98	
	±206	±308		±231	±285		±275	±326	~	±314	±213		
C. asiatica	14801	15632	0.95	14159	15513	0.91	15401	15628	0.99	16269	15865	1.03	
	±397	±325	T	±185	±249		±123	±206		±277	±346		
P. indica	15370	15583	0.99	15738	14944	1.05	15746	16131	0.98	15350	15751	0.97	
	±147	±234	$\mathbf{V}$	±532	±624		±343	±253		±291	±259		
C. hystrix	15475	16274	0.95	15067	15197	0.99	15477	15386	1.01	15867	15900	1.00	
2	±567	±671		±264	±402		±258	±371		±346	±.16		
Stem					Ar -		THAN						
T. crispa	15059	15172	0.99	15496	15804	0.98	15252	15593	0.98	15690	15937	0.98	
*	±246	±219		±459	±385		±385	±307		±559	±481		
C. verum	15378	15394	1.00	15525	15746	0.99	15755	16102	0.98	15586	15725	0.99	
	±119	±187		±214	±284		±293	±387		±324	±255		
C. sappan	15306	15543	0.98	15753	16173	0.97	15629	16096	0.97	15318	15495	0.99	
	±338	±419		±429	±395		±272	±415		$\pm 118$	±231		
D. scandens	14872	15007	0.99	15782	15437	1.02	15277	15667	0.98	15474	15756	0.98	
	±223	±247	righ	±335	±433	<u>niar</u>	±233	±254	<u>iver</u>	±259	±211		
All values are expressed as mean ± SD, n=6													

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The formulation development can be divided into 9 phases.

4.5.1 Development Phase I Effect of binders at a compression force of 15,000 N

Because of poor flowability and compactability of herbal powder, pharmaceutical excipients as well as the wet granulation process were required to enhance the powder properties. The basic formulation below was applied to study the effect of 4 types of binders, namely 10% starch paste (SP), 5% starch paste + 5% gelatin solution (SG), 10% polyvinylpyrrolidone (PP) and 10% gelatin solution (GT) on hardness of tablets. Magnesium stearate served as a lubricant during tableting. Purified talcum was employed as both glidant and antiadherant.

The basic formulation was as follows:

Formulation		
006	Amount per tablet (mg)	
Herbal powder	449.50	
Binder	33.00	
Talcum	15.00	
Magnesium stea	ate 2.50	

Compression force

15,000 N

The compression was performed with the instrumented tabletting machine by starting with a compression force of 15,000 N. The properties of formulated tablets are complied in Table 4.6.

It can be observed from Table 4.6 that formulations that had the hardness of greater than 40 N were as follows: Fruit

*S. trilobatum*: SP(47.74±0.14 N) and GT(44.13±0.07 N)

#### **Underground part**

E. longifolia: PP(74.36±0.17 N)

Stem

*C. verum*: SP(57.01±0.16 N), SG(55.41±0.3 N), PP(85.64±0.50 N) and

GT(43.80±0.22 N)

*C. sappan*: SG(50.86±0.27 N), PP(75.14±0.51 N) and GT(45.78±0.06 N) *D. scandens*: SP(71.66±0.54 N), PP(51.93±0.58 N) and GT(54.77±0.54 N)

Three types of herbal tablet formulations from stem had the hardness exceeding 40 N, while there were no tablet produced from leaf had the average hardness of more than 40 N. Each type of binder provides tablet with different hardness and disintegration property. The formulations with hardness of more than 40 N were evaluated for quality control in the next step.



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Plant		SP			SG	17		PP			GT	
Types	Hard	Weight	DT	Hard	Weight	DT	Hard	Weight	DT	Hard	Weight	DT
	ness (N)	(g)	(min)	ness (N)	(g)	(min)	ness (N)	(g)	(min)	ness (N)	( <b>g</b> )	(min)
Fruit		6	7 /			3)						
P. emblica	13.00	0.5076	-	22.48	0.5033	- 4	29.99	0.5033	-	11.02	0.5195	_
	$\pm 0.08$	$\pm 0.01$	0.01	$\pm 0.16$	$\pm 0.01$	3	$\pm 0.20$	$\pm 0.01$		$\pm 0.06$	$\pm 0.00$	0.54
S. trilobatum	4/./4	0.4216	0.91	18.82	0.39/4	197	27.80	0.4089		44.13	0.4016	0.54
<b>—</b> 1.1.1	±0.14	±0.00*	±0.29	$\pm 0.03$	±0.01*	6'3	$\pm 0.05$	±0.00*	3721	$\pm 0.07$	±0.00*	±0.05
T. chebula	24.62	0.5085	-	31.16	0.4933		34.24	0.5106		22.81	0.5134	_
D .	$\pm 0.10$	$\pm 0.00$		$\pm 0.10$	$\pm 0.00$		$\pm 0.1/$	$\pm 0.01$		$\pm 0.12$	$\pm 0.00$	
P. nigrum	15.12	0.5126		10.37	0.4871		17.54	0.4987		11.36	0.5241	_
	±0.12	±0.01		±0.07	$\pm 0.00$		±0.17	±0.00	$\bigcirc$	±0.07	±0.00	
M. citrifolia	5.85	0.4744	- \	8.03	0.5043	(7)	4.09	0.5045		6.02	0.5045	—
	±0.44	$\pm 0.00$		±0.10	±0.00		$\pm 0.06$	$\pm 0.00$		±0.04	±0.01	
Underground part						ふうと						
Z. officinale	12.99	0.5211		7.46	0.5002		38.08	0.5154	—	16.74	0.5054	_
	±0.12	$\pm 0.01$		$\pm 0.07$	$\pm 0.00$		±0.18	±0.01		±0.10	$\pm 0.00$	
C. longa	26.65	0.4872	-	25.57	0.5059		20.39	0.5069	_	28.73	0.5168	_
-	$\pm 0.14$	$\pm 0.01$		±0.18	±0.00		±0.14	$\pm 0.00$		±0.11	$\pm 0.00$	
A. calamus	13.30	0.4958	-	12.3	0.4852		10.69	0.5144	_	20.28	0.4946	_
	±0.24	$\pm 0.01$		$\pm 0.09$	$\pm 0.00$		$\pm 0.08$	$\pm 0.00$		$\pm 0.20$	$\pm 0.00$	
E. longifolia	26.98	0.4095		19.51	0.3899	_	74.36	0.5163	9.53	32.37	0.4177	—
	$\pm 0.09$	±0.00*		$\pm 0.10$	$\pm 0.00*$		±0.17	$\pm 0.00$	±0.04	±0.24	$\pm 0.01*$	
G. glabra	26.32	0.5010	151	24.62	0.5028		13.01	0.4895	() - r	28.25	0.5252	_
-	±0.27	±0.00		±0.22	$\pm 0.00$		±0.19	±0.01		±0.26	±0.01	
	С	opyri	ght <sup>@</sup>	b	y Ch	iang	Mai	Uni	vers	ity		
	Α		ri	gł	n t s		es	e r	v e			

 Table 4.6 Hardness, weight and disintegration time of herbal tablets prepared using different binders compressed at 15,000 N (n = 6)

`````````````````````````````````								0 0,1				
Plant		SP	9	/ <	SG		>	PP			GT	
Types	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf												
C. angustifolia	11.33 ±0.14	0.4915 ±0.01	7	11.94 ±0.26	0.4901 ±0.00		7.68 ±0.12	0.5124 ±0.00	Sint I	9.89 ±0.13	$0.5160 \pm 0.00$	_
A. paniculata	34.30 +0.20	0.4971 +0.01	) _	32.41 +0.17	0.4907 +0.00	S-	38.74 +0.15	0.5131 +0.01	507	27.80 +0.12	0.5102 +0.00	-
C. asiatica	32.56 +0.36	0.4979	ł	31.20	0.5070 +0.01	( - <sub>)</sub> ,	17.18	0.4979	7-	17.10 + 0.07	0.5103	_
P. indica	13.51	0.5111	3-	19.95	0.4156	A	22.04	0.5056	8-//	22.11	0.4049	_
C. hystrix	$\pm 0.17$ 13.34 $\pm 0.07$	$\pm 0.01$ 0.4926 $\pm 0.00$	7.	$\pm 0.07$ 5.33 $\pm 0.06$	$\pm 0.01^{+}$ 0.4817 $\pm 0.00^{-}$		$\pm 0.03$ 25.65 $\pm 0.19$	$\pm 0.02$ 0.4881 $\pm 0.01$	×	±0.03 23.48 ±0.15	$\pm 0.00^{+}$ 0.5119 $\pm 0.01^{-}$	_
Stem							~					
T. crispa	26.98 ±0.17	0.5233 ±0.01		32.25 ±0.07	0.5117 ±0.01	NTT VI	35.03 ±0.36	0.5158 ±0.01	_	21.88 ±0.17	0.5171 ±0.01	_
C. verum	57.01 ±0.16	0.5025 ±0.00	5.03 ±0.03	55.41 ±0.3	$0.5141 \pm 0.01$	$4.42 \pm 0.54$	85.64 ±0.50	0.5030 ±0.01	2.17 ±0.11	43.80 ±0.22	0.5096 ±0.01	$6.56 \pm 1.02$
C. sappan	24.49 ±0.06	0.4163 ±0.01*	3	$50.86 \pm 0.27$	$0.4108 \pm 0.01*$	$0.56 \pm 0.03$	75.14 ±0.51	0.5241 ±0.00	$2.55 \pm 0.40$	45.78 ±0.06	0.3918 ±0.00*	$0.53 \pm 0.01$
D. scandens	71.66 ±0.54	0.4924 ±0.02	5.28 ±0.15	35.22 ±0.15	0.4097 ±0.00*	8-18	51.93 ±0.58	0.4504 ±0.03	5.44 ±0.56	54.77 ±0.54	0.4036 ±0.01*	4.44 ±0.57

**Table 4.6** Hardness, weight and disintegration time of herbal tablets prepared using different binders compressed at 15,000 N (n = 6)

(cont.)

\* Tablets formulation was prepared as a 400 mg/tablet because granules had low bulk density, ersity

All values are expressed as mean  $\pm$  SD, DT: Disintegration time

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**4.5.2 Development Phase II** Effect of binders at a compression force of 20,000 N

The basic formulation from phase I that had the hardness of more than 20 N, but less than 40 N (Table 4.6) was compressed at a compression force of 20,000 N. The results were shown in Table 4.7.

Formulation		
	Amount per tablet (mg)	λ
Herbal powder	449.50	
Binder	33.00	
Talcum	15.00	
Magnesium stearate	2.50	7
Compression force	20,000 N	

n 117/

The effect of increase in compression force from 15,000 N to 20,000 N on the hardness was slight for most herbal powder. Only one herbal powder that achieved the hardness of more than 40 N was:

#### Leaf

A. paniculata: SP(42.22±2.19 N), SG(44.54±1.49 N) and PP(49.25±2.06 N)

(Table 4.7)

It can be considered that modification of the formulation was necessary to conduct in order to improve the tablet hardness.

ts r



Plant		SP			SG	N/A		РР			GT	
Types	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit						<u> </u>						
P. emblica	_	f.		25.03 ±0.14	0.5044 ±0.01	-	32.67 ±4.47	$0.5051 \pm 0.01$	-	-	_	_
S. trilobatum	_	-53		- 8	- @	(7)	_	-		-	_	_
T. chebula	28.95 ±1.87	$0.5148 \pm 0.00$		32.90 ±2.46	0.5231 ±0.01		36.90 ±2.43	0.4999 ±0.01	<u> </u>	28.66 ±2.07	$0.5085 \pm 0.01$	_
P. nigrum	_	t (	2-1	_	- (	- /		7	5	_	_	_
M. citrifolia	_			-	-					_	_	_
Underground part					4	1 32 E		A				
Z. officinale	_	-	- (	7	_ 01		21.65 ±3.11	0.5075 ±0.01	_	-	_	_
C. longa	23.73 ±0.96	0.4973 ±0.01	-	30.00 ±2.47	$0.5080 \pm 0.00$	NIV	18.85 ±2.03	$0.5066 \pm 0.00$	_	35.77 ±2.45	0.5080 ±0.01	_
A. calamus	_	_	_		_		-	_	_	25.83 ±0.85	0.5193 ±0.00	_
E. longifolia	6	28	nêi	-	กลิท	-	<u>Š</u> ei	Re	2		-	—
G. glabra	29.03 ±2.80	0.5118 ±0.01	IĐ	27.28 ±1.64	0.5132 ±0.67		ດູູ	100	ΟΠ	26.18 ±2.39	0.5177 ±0.01	_
		opyr	ight <sup>®</sup>		y Ch	iang	Ma	i Uni	ivers	ity		
	Α		ri	i g l	h t s	s r	es	s e r	VE			

 Table 4.7 Hardness, weight and disintegration time of herbal tablets prepared using different binders compressed at 20,000 N (n = 6)

							0 0,1				
Plant		SP	/ <	SG		>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf											
C. angustifolia	_	502 -	- \	<u> </u>	R.	-	-	502	-	-	_
A. paniculata	42.22	0.5115 6.13	44.54	0.5074	5.26	49.25	0.5127	42.52		_	_
	$\pm 2.19$	$\pm 0.00$ $\pm 1.75$	$\pm 1.49$	$\pm 0.00$	±0.08	$\pm 2.06$	$\pm 0.01$	±9.36			
C. asiatica	21.40	0.4944 –	32.23	0.5153	J - w	/ /	-	×-	_	_	_
	±3.12	$\pm 0.02$	$\pm 2.63$	$\pm 0.02$				6			
P. indica	—	+	-	-	-7	33.03	0.5101		27.88	0.4193	—
						±0.99	$\pm 0.00$	_ / / /	$\pm 0.56$	$\pm 0.01*$	
C. hystrix	_		-	- [ [	741	25.93	0.4852	· / <del>-</del>	21.40	0.4959	_
					20 6	±1.15	$\pm 0.00$		$\pm 1.70$	±0.00	
Stem						ć					
T. crispa	31.78	0.5159 –	35.05	0.5238	-	37.07	0.5212	_	28.92	0.5213	_
-	±3.57	±0.00	±2.37	±0.01	NTN	±2.69	±0.01		$\pm 2.86$	$\pm 0.01$	
C. verum	_		-		INT .	_	-	_	_	_	_
C. sappan	—		-	_	_	_	—	-		—	-
D. scandens	0	JANSI		1570	<b>2F1</b>	d t	168	l () - L k	11	_	_

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**Table 4.7** Hardness, weight and disintegration time of herbal tablets prepared using different binders compressed at 20,000 N (n = 6)

a

(cont.)

\* Tablets formulation was prepared as a 400 mg/tablet because granules had low bulk density, nang Mar

All values are expressed as mean  $\pm$  SD, DT: Disintegration time

**4.5.3 Development Phase III** Effect of adding microcrystalline cellulose at a concentration of 20%

The formulations that had hardness below 40 N from development phase II were improved by adding microcrystalline cellulose (MCC) to a concentration of 20% of the formulation. Microcrystalline cellulose (Avicel PH101<sup>®</sup>) was used as a filler and binder because of its unique compressibility and creates tablets that are very hard and yet disintegrate rapidly. Then, the formulation was compressed at 15,000 N.

#### Formulation

	Amount per tablet (mg)
Herbal powder	329.50
Binder	53.00
Microcrystaline cellulose (MCC)	100.00
Talcum	15.00
Magnesium stearate	2.50
Compression force	15,000 N

Formulations that had the hardness of more than 40 N (Table 4.8) were

#### Fruit

*T. chebula*: PP(42.72±7.29 N)

#### Leaf

*P. indica*: SP(45.15±3.49 N), SG(43.18±3.07 N), PP(44.38±3.57 N) and

GT(45.00±2.59 N)

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It can be obviously seen from Table 4.8 that addition of MCC at a concentration of 20% of the formulation led to the increase in tablet hardness of some formulations. The remaining formulations were compressed at 20,000 N.

 Table 4.8
 Hardness, weight and disintegration time of herbal tablets prepared using different binders and 20% MCC compressed at 15,000 N (n = 6)

Plant		SP	/ -	SG	NY C	>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit											
P. emblica	_	502	33.41 ±1.95	$0.5079 \pm 0.00$	12	37.95 ±2.36	$0.5102 \pm 0.00$		-	_	_
S. trilobatum	_	- 500 -			S.F	7	-	20A)	-	_	_
T. chebula	_		37.80	0.5105	/ - ) <sub>#</sub>	42.72	0.5079	9.52	_	_	_
	15 57	0.5105	±0.97	$\pm 0.00$		±7.29	$\pm 0.01$	±0.87	12 17	0 5150	
P. nigrum	15.57	0.5105 -	14.97	0.5133		13.33	0.5042	ハブ	13.1/	0.5150	-
M situifalia	$\pm 1.05$	$\pm 0.00$	$\pm 1.5 /$	$\pm 0.00$		$\pm 1.00$	$\pm 0.01$		$\pm 1.53$	$\pm 0.00$	
м. сипуона	8.05 ±0.07	0.3027 - +0.00	9.70 ±0.08	0.3038	122 F	10.43	0.3033		10.03	0.491/ ±0.01	—
Underground part	±0.97	±0.00	10.90	10.00		12.40	10.00		±0.09	<u>0.01</u>	
Z. officinale	25.05	0 5147 -	24.95	0 5094	= _ 1	31.80	0.5092	_	25 17	0 5053	_
21 0))/01/01/0	+3.43	+0.01	+3.24	+0.01	NIV	+2.59	+0.01		+2.81	+0.00	
C. longa	17.50	0.5082 -	25.00	0.5123		12.37	0.5074	_	28.12	0.5091	_
	±1.27	$\pm 0.00$	±3.08	$\pm 0.00$		$\pm 2.38$	±0.00		$\pm 2.58$	$\pm 0.00$	
A. calamus	33.37	0.5131 -	31.70	0.5024	_	31.27	0.5064	-0	29.45	0.5024	_
	±1.87	±0.00	±1.36	±0.00	CIO	±1.42	$\pm 0.00$		±3.15	±0.01	
E. longifolia	9	GUDI	ULI			<u>η</u> Ο		0.11	HJ	-	-
G. glabra	17.57	0.4983	26.75	0.5094	iang	17.18	0.4930	vers	13.57±	0.4826	_
	±2.12	$\pm 0.00$	±2.19	±0.01	0	$\pm 2.38$	$\pm 0.00$		0.01	$\pm 0.00$	
	Α	II ri	g	h t s		es	er	Ve			

978181 Table 4.8 Hardness, weight and disintegration time of herbal tablets prepared using different binders and 20% MCC compressed at

15,000 N (r	n = 6) (cont.)			RI	10						
Plant		SP	1 <	SG	N/S	>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min	Hard ) ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf											
C. angustifolia	15.45 ±3.13	0.4977 – ±0.01	12.43 ±2.00	0.4961 ±0.00	n h	11.70 ±2.67	0.5017 ±0.01 ∽		13.57 ±2.22	0.4864 ±0.01	_
A. paniculata	-			E	-\$ <u>1</u> -	)-	-/ '	207	-	_	-
C. asiatica	15.98 ±2.07	$0.4972 - \pm 0.00$	$26.08 \pm 2.90$	0.5045 ±0.01		16.12 ±3.27	0.4896 ±0.00	7-	21.58 ±3.18	0.5138 ±0.00	—
P. indica	45.15 ±3.49	$\begin{array}{ccc} 0.5236 & 0.58 \\ \pm 0.01 & \pm 0.34 \end{array}$	$43.18 \pm 3.07$	0.5172 ±0.00	1.18 ±0.03	44.38 ±3.57	0.4867 ±0.02	1.49 ±0.09	45.00 ±2.59	0.5137 ±.0.01	0.50 ±0.01
C. hystrix	$33.38 \pm 2.60$	0.5080 - ±0.01 -	35.58 ±3.13	$0.5115 \pm 0.00$	336	39.17 ±2.35	0.4997 ±0.01		37.18 ±2.05	0.5123 ±0.00	-
Stem						Ć					
T. crispa	33.13 ±2.11	0.5015 ±0.01	38.26 ±3.20	$0.5016 \pm 0.00$	NĪV	38.32 ±1.85	0.5114 ±0.01	_	31.54 ±3.33	0.5129 ±0.00	_
C. verum	-		-			_	-	-	-	_	—
C. sappan	ā	2.2	-	5.0	-	5	S	-7.		—	_
D. scandens	<b>Ğ</b>	Jalla	<b>NU.</b>	1.2-11	<b>U</b> -10		601	0-1 r	١IJ	-	_
All values are expressed	d as moon	SD DT: Digint	arotion tim		iana	Mai					

All values are expressed as mean  $\pm$  SD, DT: Disintegration time

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**4.5.4 Development Phase IV** Effect of adding microcrystalline cellulose at a concentration of 20% in combination with a compression force of 20,000 N

#### Formulation

An An	nount per tablet (mg)
Herbal powder	329.50
Binder	53.00
Microcrystaline cellulose (MCC)	100.00
Talcum	15.00
Magnesium stearate	2.50
Contraction of the second	
Compression force	20,000 N

The formulations from development phase III that had the hardness of more than 20 N, but less than 40 N (Table 4.8) was compressed at 20,000 N. The results are shown in Table 4.9. Formulations that had the tablet hardness of more than 40 N were as follows:

#### Fruit

P. emblica: PP(42.17±3.12 N)

#### Underground part

*Z. officinale*: PP(44.33±2.59 N)

- C. longa: GT(45.40±1.96 N)
- G. glabra: SG(44.33±2.51 N)

#### Leaf

C. asiatica: SG(43.63±2.18 N)

*C. hystrix*: SP(43.03±5.67 N), SG(43.67±1.22 N), PP(41.93±2.96 N) and GT(51.50±3.13 N) Stem

*T. crispa*: SP(41.09±2.75 N), SG(41.50±1.91 N), PP(45.45±2.48 N) and GT(41.79±3.61 N)

A lot of formulation showed acceptable hardness in this stage with the combination of adding MCC and compression at a high compression force of 20,000 N. The remaining formulations were further improved by adding a higher concentration of either binder or MCC into the formulations in the following stages.



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 Table 4.9
 Hardness, weight and disintegration time of herbal tablets prepared using different binders and 20% MCC compressed at 20,000 N (n = 6)

Plant		SP	/ -	SG		>	PP	, i		GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit					×						
P. emblica	_	502	37.32 ±1.56	0.5012 ±0.00	(?)	42.17 ±3.12	0.5016 ±0.00 =	6.42 ±2.26	-	_	_
S. trilobatum	_		_ C	E.	-St	$\overline{)}$	-	202	-	_	_
T. chebula	_	TQ-	_	-	- 7		-	X-	_	_	_
P. nigrum	_	- 3-	-	-			- 5	5 -/	_	_	_
M. citrifolia	_	- 7	-	-		-	A		_	_	_
Underground part			× ,			Ċ					
Z. officinale	30.90 ±1.04	0.5120 - ±0.00 -	33.97 ±1.25	$0.4770 \pm 0.00$	NĪV	44.33 ±2.59	0.5113 ±0.01	10.52 ±0.06	32.30 ±1.94	$0.5067 \pm 0.00$	-
C. longa	-		35.57 ±2.54	0.5114 ±0.00	111	_	-	_	45.40 ±1.96	0.5164 ±0.00	8.59 ±0.38
A. calamus	35.80 ±2.30	0.5038 - ±0.00	35.33 ±4.11	$0.4879 \pm 0.00$	-	37.45 ±2.39	0.5019 ±0.01	เกิง	38.87 ±2.67	$0.5038 \pm 0.00$	-
E. longifolia	<u>_</u>	UGIIDI	JL			ດບ	100		нJ	-	-
G. glabra	-C	opyright	44.33 ±2.51	0.5189 ±0.01	19.35 ±0.96	Mai	Un	ivers	ity	-	—
	A	ri	g	h t s	i r	es	e r	V E	e d		

GT SP SG PP Plant **Types** Hard Weight DT Weight DT Weight Weight DT Hard Hard DT Hard (min) (g) (min) ness (g) **(g)** (min) **(g)** (min) ness ness ness (N) (N) **(N)** (N) Leaf C. angustifolia 20.48 0.4933 18.48 0.4974 13.38 0.5143 0.5002 15.00 \_  $\pm 2.12$ ±0.00 ±0.30 ±0.00 ±1.22 ±0.01  $\pm 0.00$  $\pm 0.55$ A. paniculata F C. asiatica 34.65 0.5123 43.63 0.4967 12.10 24.67 0.5110 34.63 0.5066 ±0.06 ±1.74 ±0.01  $\pm 3.50$ ±0.01  $\pm 2.18$  $\pm 0.00$  $\pm 1.51$  $\pm 0.00$ P. indica \_ \_ D \_ C. hystrix 4.46 7.01 4.02 43.03 0.5092 5.55 43.67 0.5142 41.93 0.4868 51.50 0.5169 ±0.35 ±0.46  $\pm 5.67$  $\pm 0.00$ ±0.54 ±1.22  $\pm 0.00$  $\pm 2.96$ ±0.01  $\pm 3.13$  $\pm 0.00$ ±0.46 Stem 10.10 T. crispa 41.50 0.5181 11.55 45.45 0.5092 20.55 9.56 41.09 0.5078 41.79 0.5019 ±2.75  $\pm 0.00$ ±0.54 ±1.91  $\pm 0.01$ ±0.52  $\pm 2.48$ ±0.01 ±0.51 ±3.61 ±0.36  $\pm 0.00$ C. verum \_ \_ \_ \_ C. sappan D. scandens All values are expressed as mean  $\pm$  SD, DT: Disintegration time

Table 4.9 Hardness, weight and disintegration time of herbal tablets prepared using different binders and 20% MCC compressed at

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 $<sup>20,000 \</sup>text{ N} (n = 6) (\text{cont.})$ 

#### 4.5.5 Development Phase V Effect of adding binder at a higher concentration

Adding binder at a higher concentration to a formulation could not be done directly by increasing the concentration of a binder in a granulating fluid, because the binding solution at a concentration of 10% is usually highly viscous. An indirect method by increasing the concentration of binder in this stage was performed by doing granulation twice. The granules prepared from the first granulation after drying were comminuted and subjected to the process of wet granulation again. The tablet hardness values of the formulation are shown in table 4.10.

#### Formulation

STR 7	Amount per tablet (mg)
Herbal powder	302.50
Binder	80.00
Microcrystaline cellulose (MCC)	100.00
Talcum	15.00
Magnesium stearate	2.50
	A

**Compression force** 

15,000 N

Formulations that had the hardness of more than 40 N could not be successfully obtained (Table 4.10).

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 Table 4.10
 Hardness, weight and disintegration time of herbal tablets prepared using different binders by double wet granulation with

20% MCC	and comp	pressed at 15,000 N	(n = 6)	RÍ	N/A		64				
Plant		SP	/ -	SG		>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit											
P. emblica	—	-582	_ \	6	A	-	-	Siz	-	_	_
S. trilobatum	_	- 500 -	_ C	- te	S.F	7	-	50A	-	-	-
T. chebula	_	t Q -	_	- /	- ) <sub>#</sub>	) +	-/	7-	-	_	_
P. nigrum	21.87	0.5125 -	21.93	0.5088	-7	18.67	0.5008	5-//	21.40	0.5047	-
M. citrifolia	$\pm 2.05$ 19.47 $\pm 2.19$	$\pm 0.00$ 0.5089 - $\pm 0.01$	$\pm 1.76$ 17.78 $\pm 1.17$	$\pm 0.00$ 0.4974 $\pm 0.01$		$\pm 1.48$ 20.20 $\pm 2.99$	$\pm 0.00 \\ 0.5110 \\ \pm 0.00$		$\pm 0.48$ 20.03 $\pm 1.74$	$\pm 0.01$ 0.4975 $\pm 0.00$	-
Underground part						Ċ					
Z. officinale	_		14	1/-11	NĪN	ER		_	_	_	_
C. longa	_				<u>11</u>	_	_	_	_	_	_
A. calamus	34.45	0.5100 -	32.58	0.5097	-	31.11	0.5119	-?.	30.78	0.5006	_
E. longifolia	±2.13 -	001051	±1.30	±0.00	13	=5.19	±0.00	JŪli	±0.91	±0.00 —	_
G. glabra	-C	opyright	9 - b	y €h	iang	Ma	i Un	ivers	it∀	_	_
	Α	ll ri	g	n t s	i r	e s	s e r	'V E	e d		

PP GT Plant SP SG Types Hard Weight DT Hard Weight DT Hard Weight DT Hard Weight DT (g) (min) (min) ness (g) **(g)** (min) ness **(g)** (min) ness ness (N) (N) **(N)** (N) Leaf C. angustifolia 24.07 0.5085 21.13 0.4989 20.53 0.5124 23.60 0.4932 ±1.33 ±2.54 ±0.00  $\pm 0.00$  $\pm 1.11$ ±0.00 ±1.89  $\pm 0.00$ A. paniculata C. asiatica P. indica C. hystrix Stem T. crispa C. verum C. sappan D. scandens All values are expressed as mean  $\pm$  SD, DT: Disintegration time All rights r **e** s e r C

20% MCC and compressed at 15,000 N (n = 6) (cont.)



**4.5.6 Development Phase VI** Effect of adding binder at a higher concentration in combination with a compression force of 20,000 N

The formulations from the development phase V that had the hardness of more than 20 N but less than 40 N as shown in Table 4.10 were subjected to double wet granulation (the first batch of granules obtained were comminuted and reprocessed by wet granulation again) and compressed at 20,000 N. The summary of the formulation and the compaction condition was as follows:

#### Formulation

Amo	ount per tablet (mg)
Herbal powder	302.50
Binder	80.00
Microcrystaline cellulose (MCC)	100.00
Talcum	15.00
Magnesium stearate	2.50
Compression force	20,000 N

From the results of development phases V and VI, addition of binder at a higher concentration into a formulation was not considered as an efficient method for improving the hardness of the herbal tablets (Table 4.11).

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 Table 4.11
 Hardness, weight and disintegration time of herbal tablets prepared using different binders by double wet granulation with

Plant		SP		SG			PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit				50							
P. emblica	_	582	_	<u>}</u>	A	-	-	565	-	_	_
S. trilobatum	_	-909 -	_ 6	- Ly	SF.	7	-	500	-	_	_
T. chebula	_	t Q -	_	-	- )#	) -	-/	X-	_	_	_
P. nigrum	27.70	0.4990 –	27.05	0.5130	-7		- (	5-//	27.20	0.5056	_
	$\pm 2.37$	$\pm 0.00$	±3.23	$\pm 0.00$				Y //	±1.42	±0.00	
M. citrifolia	—			-	1206	24.17	0.5089	/=	23.83	0.4940	-
Underground part						1.70	±0.00		<u> </u>	-0.00	
Z. officinale	_			17-11	NĪN	ER		-	_	_	_
C. longa	-				<u>11</u>	_	-	-	_	_	_
A. calamus	37.10	0.4979 -	34.68	0.5017	-	36.58	0.5095	-7	34.67	0.5155	_
E. longifolia	±2.77		±3.15	±0.01	<b>PB</b>	±2.24	±0.00	<b>JOII</b>	±1.80 -	±0.01 _	_
G. glabra	-C	opyright <sup>(</sup>	0 - b	y €h	iang	Ma	i Un	ivers	it∀	_	_

 Table 4.11
 Hardness, weight and disintegration time of herbal tablets prepared using different binders by double wet granulation with

Plant		SP	9	<	SG	Y	$\geq$	PP			GT	
Types	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf												
C. angustifolia	25.15 ±0.65	0.5035 ±0.00	-	24.32 ±2.87	0.5090 ±0.01		24.45 ±1.63	0.5071 ±0.01		25.50 ±1.66	0.4906 ±0.00	_
A. paniculata	_	1408	-		E.		)-		202-	-	_	_
C. asiatica	—	-C	-	_	-	-	/	7	7-	_	_	_
P. indica	_		-	-	-	7		- 0	7	_	_	_
C. hystrix	_		1	-	-	30 6	) -	A	/-	—	_	_
Stem				7			2					
T. crispa	—	_		<u>A</u>		VĪV	EKP	/-	_	_	_	_
C. verum	—	_	-	Ŧ		1	-	-	_	-	_	—
C. sappan	6,	an	ຂົ້າ	1140	8-n	-	ă ci i	Rei	2		-	_
D. scandens	Q (	Jan	DL		JI	010		0_0	UII	ΗU	_	_
All values are expressed as	s mean ±	SD, DT: D	isintegra	ation time	<del>, Chi</del>	ang	Mai	Uni	vers	ity		
-	Α		r i	gh	ts	ľ	e s	e r	v e	d		

20% MCC and compressed at 20,000 N (n = 6) (cont.)

#### 4.5.7 Development Phase VII Effect of adding MCC at a concentration of 50%

The formulations of which the hardness values were less than 40 N from the development phase IV were further developed by increasing the concentration of MCC from 20% to 50%.

Formulation	54	
	Amount per tablet (mg)	30
Herbal powder	179.50	
Binder	53.00	$\mathbf{D}$
Microcrystaline cellulose (MCC)	250.00	
Talcum	15.00	372
Magnesium stearate	2.50	205
		005
Compression force	15,000 N	A

The results in Table 4.12 revealed that the tablet hardness values of the following formulations were greater than 40 N.

#### Fruit

M. citrifolia: SG(43.50±3.44 N) and PP(53.85±4.13 N)

A large number of formulations showed a significant increase in hardness with the values nearly met the acceptance criterion of 40 N. The remaining formulations were further investigated under the compression force of 20,000 N.

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 Table 4.12 Hardness, weight and disintegration time of herbal tablets using different binders with 50% MCC compressed at 15,000 N (n = 6)

Plant		SP		SG	NY C	>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Fruit											
P. emblica	_	502	_ /	<u>s</u>	2	_	-	502	-	_	_
S. trilobatum	_		_ <	E.	S.Z	7	-	2021	-	_	_
T. chebula	_	t Q -	_	- /	/ - <u>}</u>		-/	X	_	_	_
P. nigrum	38.20	0.5063 –	37.78	0.5090	27	32.17	0.5103	5 -//	28.37	0.5124	_
0	±2.73	$\pm 0.00$	±1.80	±0.00		±2.76	±0.01		±1.53	±0.01	
M. citrifolia	38.08	0.5019 –	43.50	0.5022	5.48	53.85	0.5029	15.47	32.23	0.4932	_
	±2.46	±0.01	±3.44	±0.00	±0.57	±4.13	±0.01	±0.60	±0.00	±0.00	
Underground part						C C	$\mathcal{Y}$				
Z. officinale	_			11-11	NĪŃ	EK	_	_	_	_	_
C. longa	_		-	_	112	_	_	—	_	_	_
A. calamus	38.49 +2.12	0.5071 -	39.45 +3.46	0.5092 + 0.01		39.18±	0.5154 + 0.00	1.	37.56 +1.15	0.5117 + 0.00	-
E. longifolia	-0	GUIDI	JE		1.D	αIJ	102	JOLI	HJ.	_	_
G. glabra	-C	opyright <sup>@</sup>	9-b	y Eh	iang	Mai	Un	ivers	ity	_	_
	Α	l ri	g	nts	ľ	e s	eı	Y E	d		



Plant		SP			SG	Y	$\succ$	PP			GT	
Types	Hard ness (N)	Weight (g) (r	DT I nin)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf												
C. angustifolia	36.30 ±2.72	$0.5007 \pm 0.00$	- :	34.47 ±2.31	$0.5055 \pm 0.01$	(2)	34.38 ±1.94	0.5103 ±0.01		30.48 ±2.34	$0.4976 \pm 0.00$	-
A. paniculata	_	-7082	-		Eu	\$ <u>7</u>	)-	-   '	2021	-	_	_
C. asiatica	_	- C	ł	-	- <	) - J	/	1	7-	_	_	_
P. indica	_	+ =	-	-	-			- 5	57	_	_	_
C. hystrix	_	- 7	7	-	-	32	) -	A		_	_	_
Stem				>			Ċ					
T. crispa	_	-		4A	<u>]                                     </u>	VĪV	ERP	_	_	-	—	_
C. verum	—	_	-	-		<u>, 1</u>	-	-	_	_	_	_
C. sappan	ā		5	-	-	-	5	S	.7.	-1	_	_
D. scandens	đ	Jan	<b>5</b> U	h.I	1 <b>-</b> 2-11	<u>9-10</u>	JUI	6-01	Ú-L ľ	ηIJ	_	_
All values are expressed a	s mean ±	SD, DT: Dis	sintegrati	on tim	e Chi	ang	Mai	Uni	vers	ity		
	Α		rig		n t s	ľ	es	e r	v e			

**4.5.8 Development Phase VIII** Effect of adding MCC at a concentration of 50% together with a compression force of 20,000 N

The formulations which had unacceptable hardness from the development phase VII were further studied using a compression force of 20,000 N.

#### Formulation

R D D	Amount per tablet (mg)	
Herbal powder	179.50	
Binder	53.00	3
Microcrystaline cellulose (MCC)	250.00	2
Talcum	15.00	
Magnesium stearate	2.50	502
Compression force	20,000 N	2021

It was shown in Table 4.13 that almost all the remaining formulations from the development phase VIII had the hardness of more than 40 N as follows. **Fruit** 

*P. nigrum*: SP(43.67±1.11 N), SG(42.15±4.16 N) and PP(45.37±1.42 N) Underground part

*A. calamus*: SP(43.18±1.35 N), SG(45.35±1.86 N), PP(45.65±2.33 N) and GT(41.83±1.42 N)

Leaf

C. angustifolia: SP(50.08±2.29 N), SG(46.20±3.65 N), PP(47.79±3.56 N) and

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GT(41.58±1.97 N)

Only the formulation of *P. nigrum* using gelatin solution as a binder had the average hardness slightly lower than 40 N ( $38.13\pm2.61$  N). MCC proved to be the effective filler to enhance the tablet hardness although the high compression force was required to meet the qualified hardness.

SP PP GT SG Plant Types Hard Weight DT Hard Weight DT Weight DT Hard Weight DT Hard (min) ness (g) (min) ness (g) **(g)** (min) ness **(g)** (min) ness (N) (N) (N) (N) Fruit P. emblica S. trilobatum T. chebula P. nigrum 3.30 42.15 0.5155 2.08 0.5111 7.42 38.13 0.5115 43.67 0.5093 45.37 ±0.11 ±0.06 ±1.11  $\pm 0.00$ ±4.16  $\pm 0.00$ ±1.44 ±0.01 ±0.46 ±2.61  $\pm 0.00$ M. citrifolia \_ **Underground part** Z. officinale C. longa 8.11 0.5166 7.19 0.5026 8.32 7.05 A. calamus 43.18 0.5042 45.35 45.65 41.83 0.4913 ±0.39 ±0.42 ±0.06 ±0.01 ±0.15 ±1.42  $\pm 0.01$ ±1.35  $\pm 0.00$ ±1.86  $\pm 2.33$  $\pm 0.00$ E. longifolia \_ hiang Mai Universit<del>y</del> G. glabra

Table 4.13 Hardness, weight and disintegration time of herbal tablets using different binders with 50% MCC compressed at 20,000 N

(n = 6)



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Plant		SP	9	/ <	SG	y =	>	PP			GT	
Types	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf												
C. angustifolia	$50.08 \pm 2.29$	$0.5065 \pm 0.00$	> 1 hour	46.20 ±3.65	0.5146 ±0.00	>1 hour	47.79 ±3.56	0.5232 ±0.00	> 1 hour	41.58 ±1.97	$0.4995 \pm 0.00$	> 1 hour
A. paniculata	_	-2050	-		Ey	\$7-	)-	- / '	202-1	-	_	_
C. asiatica	_	-0	ł	_	- / /	) - y	/	7	7-	_	_	_
P. indica	-	+ 7	- /	-	-	A	A	- 5	57	_	_	_
C. hystrix	_	-	The second	-	-	336	-	A		_	_	_
Stem				<u>}</u>			_Ć					
T. crispa	_	_	-	14A	JT	NĪV	ER		_	_	_	_
C. verum	—	_	-	-			-	_	_	_	—	_
C. sappan	ā		ล้.	-		-	5	S	-7.	-	_	_
D. scandens	<b>Č</b>	Jan	βl	JH.	1 <b>.</b> ]-U	<b>8</b> -16	d	301	Ú-LI	١IJ	_	_
All values are expressed a	is mean =	± SD, DT: I	Disintegr	ation tim	e Chi	iang	Mai	Uni	ivers	ity		
	Α		r i	g h	n t s	ľ	es		v e			

#### 4.5.9 Development Phase IX Effect of adding superdisintegrant

From disintegration results (Table 4.6-4.13), all formulations except C. angustifolia leaf tablet showed the disintegration time of less than the defined standard values (not more than 30 minutes). The superdisintegrant i.e. croscarmellose sodium (CS) at a concentration of 3% was added to improve disintegrating property. The formulation was as follows:

#### Formulation

6		Amount per tab	let (mg)
	C. angustifolia leaf powder	179.50	
5	Binder	53.00	No.
	Microcrystaline cellulose (MCC)	235.00	205
	Croscarmellose sodium (CS)	15.00	308
	Talcum	15.00	X
	Magnesium stearate	2.50	8
			$\sim$ //
mp	ression force	20.000 N	J

#### Co

It was shown in Table 4.14 that the formulation of C. angustifolia leaf tablet using SP or SG as a binder had the disintegration time of less than 30 minutes. The tablet hardness values were more than 40 N;

SP(44.85±5.89) and SG(50.55±1.63)

After the acceptable formulations were established, the scale-up batch (100 g) was produced. The tabletting machine was set to run continuously. The acquired tablets were investigated for the finished product quality control.

Table 4.14 Hardness, weight and disintegration time of *C. angustifolia* tablets using different binders with 47% MCC and

Plant		SP	/ ·	SG	密 E	>	PP			GT	
Types	Hard ness (N)	Weight DT (g) (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)	Hard ness (N)	Weight (g)	DT (min)
Leaf				RA							
C. angustifolia	44.85	0.5033 22.02	50.55	0.4975	24.45	42.67	0.5054	> 30	54.08	0.4927	> 30
	$\pm 5.89$	$\pm 0.01$ $\pm 0.76$	±1.63	$\pm 0.00$	±1.15	±4.40	±0.02 ∘	<b>min</b>	±3.30	±0.01	min

3% CS compressed at 20,000 N (n = 6)

All values are expressed as mean  $\pm$  SD, DT: Disintegration time



#### 4.6 Quality control of herbal tablet formulation

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The thickness and diameter of each herbal tablet was within the range of  $\pm 5\%$  of the mean value. Weight variation of herbal tablets was within the acceptable range of 475.00-525.00 mg (479.70-512.00 mg) for the formulations designded to have a tablet weight of 500 mg and was within the range of 380.00-420.00 mg (0.3953-0.4039 g) for the formulations designd to have a tablet weight of 400 mg which indicated the consistency of the amount of active compounds in herbal tablets. The hardness of the tablets was more than 40 N (40.19-85.92 N) while the friability was lower than 1% (-0.25-0.64%) and the disintegration time was less than 30 minutes (0.44-26.36 min)(Table 4.15). These findings indicated that herbal tablet formulations obtained in this study have a high potential for production in the pharmaceutical industry.

In conclusion, the most appropriate herbal tablet formulation of each plant considered based on the tablet hardness and disintegration time was suggested in Table 4.16.

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 Table 4.15
 Quality control of herbal tablet formulations

Plant	Diameter	Thickness	Weight	Hardness	Friability	Disintegration
Types	(mm)	( <b>mm</b> )	(g)	(N)	(%)	time (min)
<u>Fruit</u>						
P. emblica						
PP +MCC 20%+20,000 N	12.93±0.02	3.14±0.07	$0.4980 \pm 0.02$	46.67±4.47	$-0.05\pm0.01$	6.25±0.36
S. trilobatum						
SP+15,000 N	12.93±0.01	3.97±0.04	0.5120±0.01	65.63±2.80	$-0.08\pm0.02$	$1.38\pm0.10$
GT+15,000 N	12.94±0.01	$4.03 \pm 0.05$	0.4995±0.01	57.00±2.60	0.04±0.01	$2.47 \pm 0.09$
T. chebula	502			20	λ.	
PP+MCC 20%+15,000 N	12.92±0.01	3.16±0.04	0.4943±0.01	40.19±5.43	$0.19 \pm 0.07$	10.36±0.65
P. nigrum				4	. //	
SP+MCC 50%+20,000 N	$12.90 \pm 0.02$	$3.35 \pm 0.02$	$0.5003 \pm 0.01$	37.58±6.24	$-0.03\pm0.01$	$3.00 \pm 0.42$
SG+MCC 50%+20,000 N	$12.90 \pm 0.01$	$3.40 \pm 0.04$	0.4995±0.01	$38.65 \pm 5.43$	$-0.05\pm0.01$	$2.20\pm0.25$
PP+MCC 50%+20,000 N	12.87±0.01	3.48±0.04	$0.5061 \pm 0.02$	50.17±4.87	$-0.09\pm0.02$	8.01±0.61
M. citrifolia						
SG+MCC 50%+15,000 N	12.94±0.01	3.53±0.04	0.4917±0.01	$36.55 \pm 2.12$	$0.29 \pm 0.06$	5.21±1.16
PP+MCC 50%+15,000 N	12.88±0.01	$3.56 \pm 0.05$	0.5009±0.01	45.95±7.37	0.21±0.03	15.54±0.06
		MALI	INIVE			

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 Table 4.15 Quality control of herbal tablet formulations(cont.)

Plant Types	Diameter (mm)	Thickness (mm)	Weight (g)	Hardness (N)	Friability (%)	Disintegration time (min)
Underground part						
Z. officinale						
PP+MCC 20%+20,000 N	12.88±0.02	3.31±0.06	0.4920±0.02	53.32±6.49	$-0.04 \pm 0.00$	$20.18 \pm 1.5$
C. longa						
GT+MCC 20%+20,000 N	12.88±0.01	$3.32 \pm 0.02$	$0.4979 \pm 0.01$	47.15±2.32	-0.09±0.01	9.26±0.10
A. calamus	582			5	2	
SP+MCC 50%+20,000 N	12.90±0.02	3.31±0.45	0.5034±0.01	37.90±4.13	crack	_
SG+MCC 50%+20,000 N	12.92±0.01	$3.52 \pm 0.01$	0.5010±0.01	42.73±3.09	$0.02 \pm 0.00$	7.32±0.46
PP+MCC 50%+20,000 N	12.90±0.01	$3.65 \pm 0.04$	0.4990±0.01	43.37±4.50	$0.64 \pm 0.08$	6.29±0.12
GT+MCC 50%+20,000 N	12.90±0.01	$3.62 \pm 0.03$	$0.5060 \pm 0.01$	33.32±3.67	crack	_
E. longifolia						
PP+15,000 N	12.89±0.01	3.82±0.04	0.5018±0.02	50.83±3.25	$-0.09\pm0.02$	9.16±0.57
G. glabra				A		
SG+MCC 20%+20,000 N	12.89±0.02	3.42±0.07	0.5011±0.02	41.08±7.85	$-0.06 \pm 0.01$	19.55±0.68
		MAIN	JNIVE	251		

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 Table 4.15 Quality control of herbal tablet formulations(cont.)

Plant Types	Diameter (mm)	Thickness (mm)	Weight (g)	Hardness (N)	Friability (%)	Disintegration time (min)	
Leaf							
C. angustifolia							
SP+MCC 47%+CS 3%	$12.87 \pm 0.01$	3.29±0.03	$0.4884 \pm 0.01$	48.38±7.17	0.13±0.02	$21.26 \pm 1.04$	
SG+MCC 47%+CS 3%	12.86±0.01	3.44±0.04	0.5031±0.01	51.20±3.20	$0.09 \pm 0.03$	$26.36 \pm 1.80$	
A. paniculata	308		3	30	R		
SP+20,000 N	12.94±0.01	3.45±0.02	0.4915±0.02	44.33±3.75	0.12±0.01	9.02±0.41	
SG+20,000 N	12.96±0.01	$3.42 \pm 0.03$	$0.4842 \pm 0.01$	42.70±8.02	$0.16\pm0.02$	$8.54{\pm}1.04$	
C. asiatica				· · · ·			
SG+MCC 20%+20,000 N	$12.90 \pm 0.01$	$3.30 \pm 0.03$	0.4909±0.01	43.58±7.14	$0.10 \pm 0.02$	$13.48 \pm 1.54$	
P. indica				6			
SP+MCC 20%+15,000 N	12.99±0.00	$3.78 \pm 0.03$	0.5006±0.01	32.35±4.53	$0.09 \pm 0.02$	3.43±0.59	
SG+MCC 20%+15,000 N	12.97±0.01	3.73±0.05	$0.5020 \pm 0.02$	36.93±4.08	$-0.01\pm0.00$	3.13±0.20	
PP+MCC 20%+15,000 N	12.93±0.01	$3.54 \pm 0.05$	$0.4797 \pm 0.08$	38.78±3.76	$-0.01\pm0.00$	6.43±0.66	
GT+MCC 20%+15,000 N	12.94±0.01	3.90±0.05	$0.5079 \pm 0.02$	43.03±5.58	$-0.11 \pm 0.03$	$5.38 \pm 0.46$	
C. hystrix				SY'			
SP+MCC 20%+20,000 N	12.96±0.01	3.68±0.06	0.5107±0.01	42.87±5.55	$-0.07\pm0.10$	6.44±0.73	
SG+MCC 20%+20,000 N	12.95±0.00	3.76±0.03	$0.5096 \pm 0.01$	49.18±4.07	$-0.03\pm0.02$	$5.43 \pm 0.46$	
PP+MCC 20%+20,000 N	$12.95 \pm 0.01$	3.63±0.05	$0.4971 \pm 0.01$	52.12±3.24	$-0.14 \pm 0.04$	$11.48 \pm 0.65$	
GT+MCC 20%+20,000 N	12.95±0.01	$3.66 \pm 0.05$	$0.5019 \pm 0.02$	44.65±5.25	$-0.03\pm0.00$	10.19±0.90	

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 Table 4.15
 Quality control of herbal tablet formulations(cont.)

Plant Types	Diameter (mm)	Diameter Thickness (mm) (mm)		Hardness (N)	Friability (%)	Disintegration time (min)	
Stem		. ,				. ,	
T. crispa			易				
SP+MCC 20%+20,000 N	$12.95 \pm 0.01$	3.53±0.04	0.5008±0.01	42.55±5.16	$0.07 \pm 0.02$	8.23±0.11	
SG+MCC 20%+20,000 N	12.95±0.01	3.37±0.06	0.4973±0.01	41.87±5.76	$0.25 \pm 0.05$	9.41±0.35	
PP+MCC 20%+20,000 N	12.95±0.01	3.59±0.06	$0.5095 \pm 0.01$	47.18±8.02	0.11±0.03	17.40±0.46	
GT+MCC 20%+20,000 N	12.95±0.01	3.53±0.08	0.5043±0.01	38.60±3.88	0.13±0.02	12.05±1.16	
C. verum	500			50			
SP+15,000 N	12.92±0.02	$3.54 \pm 0.05$	0.5043±0.01	34.95±5.15	crack	_	
SG+15,000 N	12.92±0.01	3.92±0.06	0.5119±0.01	34.52±4.78	$0.07 \pm 0.06$	$3.55 \pm 0.42$	
PP+15,000 N	$12.90 \pm 0.02$	3.78±0.07	$0.5060 \pm 0.01$	46.78±6.83	$-0.03 \pm 0.00$	4.17±0.28	
GT+15,000 N	12.92±0.02	3.72±0.07	0.5021±0.01	54.30±4.28	$0.05 \pm 0.01$	9.43±0.48	
C. sappan							
SG+15,000 N(400 mg)	12.89±0.01	3.28±0.04	0.4039±0.01	55.02±3.81	$0.12 \pm 0.05$	$0.44 \pm 0.30$	
PP+15,000 N	12.90±0.01	3.99±0.10	0.4929±0.02	41.43±7.58	$-0.25\pm0.04$	3.35±0.51	
GT+15,000 N(400 mg)	12.88±0.01	3.29±0.04	0.4065±0.01	50.80±6.34	$0.12 \pm 0.01$	$0.54 \pm 0.32$	
D. scandens		YAT T	HITTE				
SP+15,000 N	12.91±0.01	3.87±0.07	$0.5067 \pm 0.01$	67.42±6.53	$0.03 \pm 0.02$	8.32±0.43	
PP+15,000 N(400 mg)	$12.92 \pm 0.01$	3.19±0.08	0.3953±0.02	48.43±6.66	$-0.04\pm0.01$	$12.44 \pm 2.33$	
GT+15,000 N	$12.90 \pm 0.02$	$3.74 \pm 0.06$	$0.4900 \pm 0.01$	85.92±7.34	$0.10 \pm 0.05$	8.31±0.98	

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Plant Types	Formulation (Amount per tablet)						
	Herbal powder (mg)	Binder (mg)	MCC (mg)	CS (mg)	Talcum (mg)	Mg Stearate (mg)	pression Force (N)
Fruit					4		
P. emblica	342.50	40 mg of PP	100.00	2	15.00	2.5	20,000
S. trilobatum	432.50	50 mg of SP	3)	-	15.00	2.5	15,000
T. chebula	332.50	50 mg of PP	100.00	-	15.00	2.5	15,000
P. nigrum	182.50	50 mg of PP	250.00	)	15.00	2.5	20,000
M. citrifolia	182.50	50 mg of PP	250.00		15.00	2.5	15,000
Underground pa	art		\$ 23				
Z. officinale	342.50	40 mg of PP	100.00	-	15.00	2.5	20,000
C. longa	322.50	60 mg of GT	100.00		15.00	2.5	20,000
A. calamus	182.50	50 mg of PP	250.00	้อ้า	15.00	2.5	20,000
E. longifolia	432.50	50 mg of PP	ians		15.00	2.5	15,000
G. glabra	332.50	50 mg of SG	100.00	r e	15.00 S e	2.5	20,000

 
 Table 4.16
 Optimal herbal tablet formulations that passed quality control
 evaluation

Plant Types	Formulation (Amount per tablet)							
	Herbal powder (mg)	Binder (mg)	MCC (mg)	CS (mg)	Talcum (mg)	Mg Stearate (mg)	pression Force (N)	
Leaf		R			4			
C. angustifolia	172.50	60 mg of SP	235.00	15.00	15.00	2.5	20,000	
A. paniculata	432.50	50 mg of SG	3)	-	15.00	2.5	20,000	
C. asiatica	312.50	70 mg of SG	100.00	-	15.00	2.5	20,000	
P. indica	302.50	80 mg of GT	100.00		15.00	2.5	15,000	
C. hystrix	302.50	80 mg of SG	100.00		15.00	2.5	20,000	
Stem			\$ 22					
T. crispa	322.50	60 mg of SP	100.00	-	15.00	2.5	20,000	
C. verum	442.50	40 mg of PP	NI	V <u>E</u>	15.00	2.5	15,000	
C. sappan	342.50	40 mg of SG	-	a	15.00	2.5	15,000	
D. scandens	452.50	30 mg			15.00	2.5	15,000	

 
 Table 4.16
 Optimal herbal tablet formulations that passed quality control
 evaluation (cont.)

Α

The appearance of the optimal herbal tablet formulations that passed the quality control evaluation were shown in Fig 4.27-4.30. Herbal tablets manufactured from a single stroke tableting machine by continuous compression showed good



appearance. The formulations containing high concentration of MCC were lighter in color but seemed to have less homogeneity in color.

Fig 4.27 Appearance of the most appropriate herbal tablet formulations from fruit powder:
(a) *P. emblica* PP+MCC 20%+20,000 N
(b) *S. trilobatum* SP+15,000 N
(c) *T. chebula* PP+MCC 20%+15,000 N
(d) *P. nigrum* PP+MCC 50%+20,000 N
(e) *M. citrifolia* PP+MCC 50%+15,000 N



Fig 4.28 Appearance of the most appropriate herbal tablet formulations from





Fig 4.29 Appearance of the most appropriate herbal tablet formulations from





**Fig 4.30** Appearance of the most appropriate herbal tablet formulations from stem powder:

- (a) *T. crispa* SP+MCC 20%+20,000 N
- (b) *C. verum* PP+15,000 N
- (c) C. sappan SG+15,000 N
- (d) D. scandens GT+15,000 N

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