The Thai Journal of Pharmaceutical Sciences

Volume 36
Issue 0 *supplement issue*

Article 36

1-1-2012

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KEYWORDS: Nava-Kote, Aromatic powder, Ya-hom, Dry granulation, Copovidone

INTRODUCTION

Tablets have long been accepted as the most convenient dosage forms to patients. Most tablets are manufactured by wet granulation, a popular manufacturing method which improves the flowability and compressibility of the drug powder. Direct compression is well known for providing the reduction of manufacturing process as well as the elimination of heat and moisture effect.[1] Currently, herbal compressed tablet dosage form has become more acceptable because of many benefits. However, some of the recipes contain high amount of essential oils and volatile substances which risk being lost by heat during drying of the wet granules. In addition, high relaxation of the plant-based materials makes most herbal medicines impossible to manufacture by direct compression. Ya-hom Nava-Kote is one of the traditional aromatic powders that are listed as National Herbal Medicine Products, a worthy collection of difference parts and more than thirty kinds of herbal plants with the indicative uses to relieve nausea, vomiting (stomach discomfort) and as blood circulation stimulant.[2] Since Nava-Kote recipe is traditionally produced by comminuting into very fine powder, therefore the product may exhibit poor flowability. Dry granulation is a particle-bonding or agglomeration process. The powder is first compressed to larger secondary particles by roller compaction or slugging.[3-4] The compressible excipients and dry binder are needed in dry granulation. The direct compression aids like microcrystalline cellulose (MCC), spray dried lactose and dicalcium phosphate are specially designed to overcome the problematical consolidation process of drug powder.[5] Copovidone, a copolymer of vinylpyrrolidone and vinyl acetate in a ratio of 6:4, is widely used in the pharmaceutical industry and has recently received greater attention. Chronic toxicity and carcinogenicity studies in Wistar rats and Beagle dogs revealed it to be a safe material.[6] The low toxicity via oral route is brought about by the very low absorption in the gastrointestinal tract.

The present study assesses the effects of direct compression filler (microcrystalline cellulose) and dry binder (copovidone) concentrations on the characteristics of Nava-Kote aromatic powder tablets manufactured by dry granulation method.

MATERIALS AND METHODS

Preparation of tablets : The experiments were established as shown in Table 1. All the excipients for dry granulation (slugging) were blended for 10 min. Lastly, 1% w/w of magnesium stearate was added and blended for 2 min. Slugs were compressed on a single punch tablet machine using flat surface punches of 15 mm diameter to obtain the hardness between 2-4 kP. Then the slugs were passed through oscillating granulator with the sieve opening of 16 mesh. The granules were again consecutively blended with 1% w/w of talcum, 0.125% w/w of Aerosil®200 and lastly, 1% w/w of magnesium stearate. Tablets (concaved, 10-mm diameter, 400 mg of weight) were compressed on a hydraulic press under three different compression forces, i.e., 1, 1.5 and 2 tons. After compaction the tablets were stored at least 24 hours in well closed containers at ambient temperature pending for evaluation.

Table 1 Tablet composition for slugging

Ingredients	Functions	Amount (%w/w)
Nava-Kote aromatic powder	Active drug	50, 60, 80-90
Avicel® PH 102 (Microcrystalline cellulose)	Direct compression filler	qs
Copovidone	Binder	5-15
Talcum	Antiadherant	1
Aerosil®200	Glidant	0.125
Magnesium stearate	Lubricant	1

Angle of repose : Angle of repose of each mixed granule was determined using funnel method. The mixed granule was poured through a funnel, and then the cone height (h) and the radius of the heap (r) were measured. The angle of repose was calculated.

Friability test : Ten tablets were randomly picked from each formula, and accurately weighed (W_1). They were placed inside the friabilator and operated for 4 min at a speed of 25 rpm. Then, the dust was removed carefully, and the tablets were re-weighed (W_2). The % friability was calculated from two weight values.

$$\% \text{ Friability} = [1 - (W_2 / W_1)] \times 100$$

Hardness test : Ten tablets from each formula were randomly sampled and determined as the crushing strength using Erweka hardness tester.

Disintegration time : The disintegration time required for six tablets of each formulation was determined using disintegration apparatus. Deionized water thermostatically maintained at 37±2 °C was used as the disintegration medium. Time taken for the last tablet or its fragment to pass through the mesh into the medium was recorded.

Statistical analysis: Statistical analysis was performed using the unpaired t-test, significant difference was set at $p < 0.05$.

RESULTS

Flowability of dry granules : The flowability of the dry granule is a crucial parameter for direct compression process. Nine formulas of the dry granules were prepared. The flowability of the granules produced as designed in Table 1 was poor according to the friction of such the fine fibrous herbal powder. Nevertheless, the formulas containing MCC were more readily to flow than those without MCC.

Tablet friability : All of the 9 formulas of Nava-Kote tablets were found to be perfectly robust after testing due to the high tablet binding property of both MCC and copovidone. Even though the low concentration of 5%w/w copovidone (with and without MCC), the tablets compressed with 1 ton of force resulted in the same minimal % friability compared to those from 10% w/w and 15% w/w of copovidone incorporated formulas.

Tablet hardness : The tablet hardness data of all formulas are shown in Table 2. Tablets composed of different levels of herbal powder ranging from 50% (A), 60% (B) and about 80-90% (C, formulas without MCC) were designed to investigate the binding property of the copovidone. Each formula was incorporated with different concentrations (5%, 10% and 15%) of copovidone (Kollidon® VA64) as dry binder. The granules were compressed at 1, 1.5 and 2 tons. As shown in Figure 1, the tablet hardness was concomitantly increased with the increase of copovidone concentrations in the similar fashion. The tablet hardness prepared from formulas containing 50% (A) and 60% herbal powder (B) ranged between 4.39 ± 0.69 – 8.66 ± 0.33 kP and 5.22 ± 0.14 – 7.92 ± 0.43 kP, respectively. The tablets hardness of the formula without MCC (C) resulted in the least tablet strength at 5% w/w and 10% w/w of copovidone. It was obvious that MCC in the formulas facilitated the tablet strength in combination with copovidone.

Table 2 Hardness of Nava-Kote tablets (n = 10) (kP, mean, (SD))

CP (ton)	50% Herbal powder (copovidone)			60% Herbal powder (copovidone)			~80-90% Herbal powder (copovidone)		
	(5%)	(10%)	(15%)	(5%)	(10%)	(15%)	(5%)	(10%)	(15%)
1.0	4.39 (0.69)	7.67 (0.52)	8.28 (0.47)	5.22 (0.14)	7.27 (0.40)	8.16 (0.60)	4.23 (0.18)	5.41 (0.34)	7.86 (0.52)
1.5	4.68 (0.46)	8.01 (0.49)	8.41 (0.30)	5.44 (0.13)	7.13 (0.32)	7.89 (0.36)	4.30 (0.67)	5.91 (0.20)	8.12 (0.38)
2.0	5.24 (0.43)	8.45 (0.46)	8.66 (0.33)	5.78 (0.30)	7.92 (0.43)	8.14 (0.34)	4.50 (0.19)	5.94 (0.16)	8.19 (0.25)

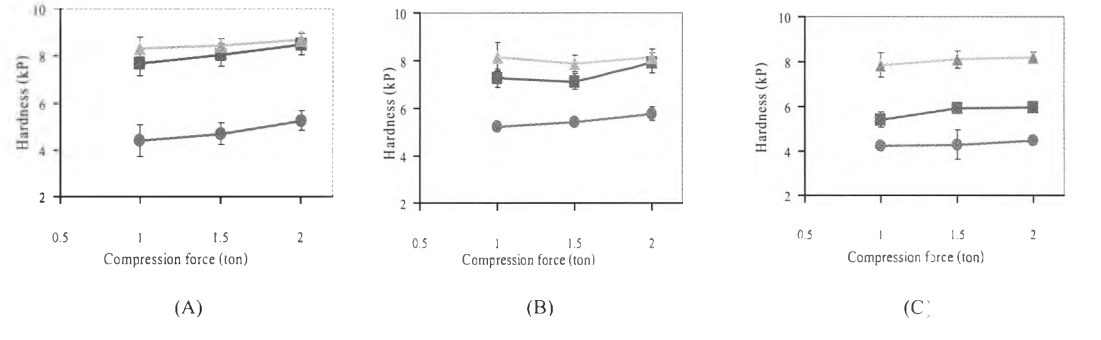

Figure 1 Hardness of Nava-Kote tablets compressed by different forces (n = 10) with various herbal powder compositions (A = 50%, B = 60%, C = 80-90% (without MCC), and various copovidone concentrations). ● = 5% w/w, ■ = 10% w/w, ▲= 15% w/w

The hardness of all tablets prepared from the highest concentration of copovidone ranged from 7.86 ± 0.52 – 8.66 ± 0.33 kP at all compression forces. It is interesting to note that 15% w/w of copovidone is high enough to create almost identical tablet hardness. No significant difference in hardness was found among the different compression forces and different levels of the herbal powder ($p<0.05$) at this concentration. This might be due to the low glass transition temperature property and the outperformance of high plasticity which can form the complete bonds during compression.

Tablet disintegration time: Figure 2 illustrates the disintegration times of all formulas. From the results it is obvious that higher amount of copovidone resulted in longer disintegrating time. From all compression forces, the tablets prepared from 50% and 60% herbal powder showed the disintegration times ranging from 3.84 ± 0.39 – 12.99 ± 1.46 min and 3.46 ± 0.8 – 7.46 ± 0.65 min, respectively. The tablets prepared from only herbal powder (without MCC) showed the disintegration times ranging from 7.52 ± 0.54 – 13.10 ± 0.46 min. The first two formulas composed of MCC at 45% and 35%, respectively, thus at the appropriate arrangement in the tablets occurred and MCC broke the tablets by water wicking and deformation recovery.[7] The formula without MCC disintegrated by the similar mechanism, that might be due to the relaxation of the compressed herbal powder itself after bonding by copovidone. Nonetheless, all the disintegration time values of the tablets produced with moderate to high amounts of dry binder passed the general finished products requirement for herbal tablets.

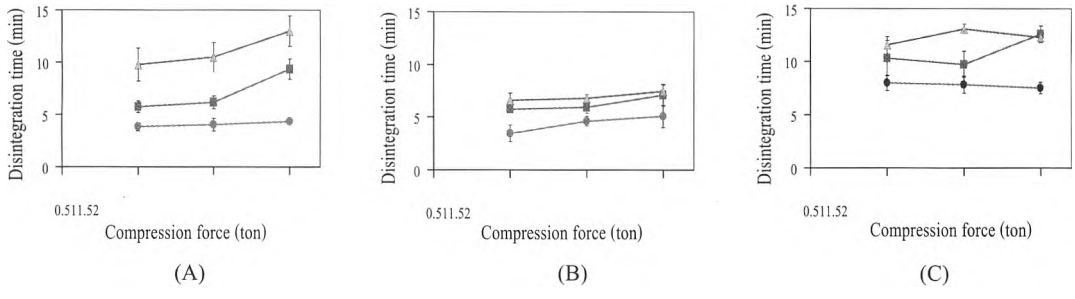

Figure 2 Disintegration time of Nava-Kote tablets compressed by different forces (n = 6) with various herbal powder compositions (A = 50%, B = 60%, C = 80-90% (without MCC), and various copovidone concentrations). ● = 5% w/w, ■ = 10% w/w, ▲= 15% w/w

DISCUSSION

The current study was designed to investigate the effects of MCC and copovidone Nava-Kote tablets produced by direct compression after dry granulation. All the formulas did not exhibit satisfactory flowability due to the friction of the bulky fibrous herbal powder. However, the granule flowability was simply improved by adding higher concentration of colloidal silicon dioxide up to 0.5% (data not shown). The friability of all tablets absolutely satisfied the tablet requirement. There was no weight loss after testing which reflected the good cohesion of the tablet ingredients.

To determine the effects of dry binders (MCC and copovidone), the disintegrant was not included in the study. Conversely, the unpredictable disintegrant property was included in the formulas containing MCC. Avicel® PH102 was selected to create mechanical strength owing to its excellent compactibility even at low compression force.[5] In addition, it possesses multiple functions depending upon the concentration used in the formula. Disintegration property is employed at the concentration of 5-15%. In this study, MCC was used up to 45%, thus it could act as both disintegrant and mechanical filler to the tablets. From the present data, it is considered that suitable tablets hardness could be produced by using 5% w/w of copovidone without MCC and loading the herbal powder up to 90%. In case that MCC is used, the concentration of copovidone might be reduced to less than 5% w/w depending on the tablets characteristics and the packages of the finished product desired.

CONCLUSION

Nava-Kote tablets are simply produced by direct compression after previously preparing into dry granules by slugging using a well-known, plastic, deformable material like microcrystalline cellulose in combination with a dry binder, copovidone. The data suggest that, Kollidon® VA64 is a good dry binder for dry granulation and direct compression. The further study is to optimize the concentrations of copovidone vs MCC, and the optimal amount of glidant to promote the better flowability of the dry granules.

ACKNOWLEDGMENTS

The authors wish to thank BASF (Thai) Limited for kindly providing copovidone (Kollidon® VA64).

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