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# The Studies of Durian Rind Extracts II : Evaluation of Tablets as an Aqueous Binder Properties(ศึกษาการใช้สารสกัดจากเปลือกทุเรียนเพื่อเป็นสารยึดเกาะ...

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ORIGINAL ARTICLE

# The Studies of Durian Rind Extracts as an Aqueous Binder II : Evaluation of Tablets Properties

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## Abstract

Durian rind extracts, $D_1$ and $D_2$ were evaluated for their binding properties as comparing with commonly used binders such as PVP K 30, corn starch, Starch 1500(R), gelatin and Methocel E15LV(R). They were employed at 1, 2 and 4% base on dry basis for both paracetamol and pyridoxine hydrochloride tablets using solution method. The important physical properties of tablets, for example, tablet hardness, friability, disintegration, dissolution and binder index were evaluated for their binding properties inaddition to granules properties as indicated in the previous study.

The results emphasized that both $D_1$ and $D_2$ showed accomplished binding properties in tablets as well as in granules as comparing with other binders. For paracetamol tablets, $D_1$ and $D_2$ gave more satisfy tablet strength, friability and binder index than corn starch and Starch 1500(R). Inaddition, $D_1$ and $D_2$ also revealed good results for pyridoxine hydrochloride tablets. The binder index of $D_2$ was obviously higher than corn starch and Starch 1500(R) but lower than PVP K 30 Methocel E15LV(R) and gelatin. Furthermore, $D_1$ gave stronger tablet than PVP K 30 and gelatin at concentration greater than 1%. Generally, it was noticed that $D_1$ produced tablets with slightly better properties than $D_2$. (Th.J.Pharm. Sci., Vol.15 No.3, 173-186 (1990))

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## A. INTRODUCTION

Durian rind extracts, $D_1$ and $D_2$ showed promising binding properties in granules as comparing with commonly used binders such as PVP K 30, corn starch, Starch 1500 (R), gelatin and Methocel E15LV(R). The binding properties of $D_1$ and $D_2$ such as granule size and size distribution, granule friability and flowability, these properties by general are superior to corn starch and Starch 1500(R) but inferior to PVP K 30, Methocel E15LV(R) and gelatin for both paracetamol and pyridoxine hydrochloride granules (1). However, binding properties in tablet need to be evaluated along with these granules properties. The reason might be due to interaction between granules could occur during compression and could effect binding properties of binders. In addition, some parameters of tablet properties could be employed to calculate binding index which is very important as indication of tablet binding property (2).

## B. EXPERIMENTAL

### Materials

Reagents used were ; paracetamol powder (China National Chemicals), pyridoxine hydrochloride (BASF, Germany), Lactose hydrous (Wyndale, New Zealand), PVP K 30 (BASF, Germany), corn starch (Pharmaceutical Sciences, Bangkok, Thailand), Starch 1500(R) (Colorcon Inc., U.S.A), gelatin (Pharmaceutical Science, Bangkok, Thailand), Methocel E15LV(R) (Premium grade, Colorcon Inc., U.S.A.), durian rind extracts $D_1$ (alcohol extraction), $D_2$ (acid alcohol extraction) (Biochemistry Lab, Chulalongkorn University, Bangkok, Thailand). All others reagents used were commercial grade and used without further purification.

## Methods

### Tablet Preparation

A batch of 500 g were prepared according to the formulation present in Tables 1 and 2. Active ingredient and lactose were dried mixed for 5 minutes in a cube mixer at a rotation speed of 30 rpm. Then the mixtures were gradually and uniformly moistened with binder solution in the planetary mixer at a fixed speed of NO 1. Mixing continued for 5 min and the wet mass was granulated by oscillating granulator through a 16 mesh sieve, the wet granules were dried in a hot air oven for 5 hours at 50°C and then resieved through a 20 mesh sieve. All binders solutions employed were fleshly prepared with sufficient purified water at the concentration of 1,2 and 4% dry weight of the formula.

Each batch of granules was mixed with 2% w/w of magnesium stearate in cube mixer for 5 minutes at a rotation speed of 30 rpm. The paracetamol granules were compressed into 500 mg tablets using 11 mm diameter round flat faced punch at the compression pressure of 3,000 pounds. Pyridoxine hydrochloride granules were compressed into 300 mg tablets using 9 mm diameter round flat faced punch at compression pressure of 2,400 pounds on instrumented single punch machine. The prepared tablets were kept in the desiccator until used.

**Table 1 Formulation of Paracetamol Tablet Used in This Study**

| Ingredients | % dry weight per tablet | | |
|---|---|---|---|
| | A | B | C |
| Paracetamol | 60 | 60 | 60 |
| Lactose | 37 | 36 | 34 |
| Binder* | 1 | 2 | 4 |
| Magnesium Stearate | 2 | 2 | 2 |

* Binders are $D_1$, $D_2$, PVP K 30, corn starch, Starch 1500(R), gelatin and Methocel E15LV(R) Batch size : 500 g

**Table 2 Formulation of Pyridoxine Hydrochloride Tablet Used in This Study**

| Ingredients | % dry weight per tablet | | |
|---|---|---|---|
| | A | B | C |
| Pyridoxine Hydrochloride | 60 | 60 | 60 |
| Lactose | 37 | 36 | 34 |
| Binder* | 1 | 2 | 4 |
| Magnesium Stearate | 2 | 2 | 2 |

* Binders are $D_1$, $D_2$, PVP K 30, corn starch, Starch 1500(R), gelatin and Methocel E15LV(R) Batch size : 500 g

**Tablet Evaluation**

Tablets prepared with various binders and $D_1$, $D_2$ were evaluated as follows:

**1. Weight Variation** For the test, twenty tablets were individually weighed and the average weight was calculated (USPXXII).

**2. Tablet Hardness** The hardness was measured using the Schleuniger-2E hardness tester and the mean of ten determinations was calculated.

**3. Tablet Thickness** The thickness was measured by using micrometer. The mean was averaged From ten determinations

**4. Tablet Friability** Twenty tablets or not less than 6 g were weighed and subjected in Roche friabilator rotated at 25 rpm for 4 minutes. The tablets were reweighed and friability was calculated as percent weight loss.

**5. Binder Index Determination**

The binder index for an overall binder activity evaluation, presented by El-Gindy et al (2), is calculated by following equation:

$$\theta_b \text{ index} = \frac{\sigma_o \cdot P}{T50\% \cdot F} \qquad (1)$$

where $\theta_b$ index is the binder index ($MN/m^2.min$), $\sigma_o$ is tensile strength ($MN/m^2$), P is porosity in percentage, T50% is median dissolution time (minutes), F is friability in percentage.

*5.1 Tablet Tensile Strength ( $\sigma_o$ )*

The tensile strength was determined by the diameteral compression test. The tablets were compressed diametrically on a modified Heberlein Hardnessd Tester. In order to minimize the shear and compressive stress below the loading area, the platen width is limitted to 1/10 of the diameter of the tablet (3-5). The motor was operated to apply an increasing force to the tablet at constant rate. When the tablet failed, the tester stopped automatically. The force reading were converted to tensile strength in the manner of Fell and Newton (6). The Tensile strength ($\sigma_o$ ) is given by :

$$\sigma_o = \frac{2F}{\pi Dt} \qquad (2)$$

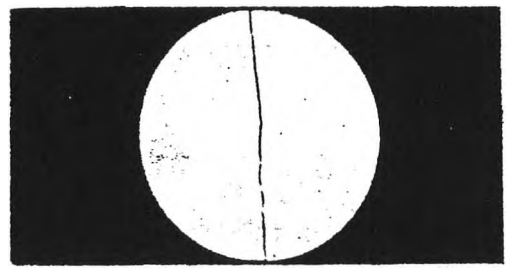
where $\sigma_o$ is tablet tensile strength ($MN/m^2$), F is the force applied diametrically at fracture (Newton), D and t are diameter and thickness of the tablet (mm), respectively.

The mode of failure was determined visually by checking the shape of the fragments after fracture. If the compact splits into two equal halved, tensile strength has recorded (Figure 1). All tensile strength reported are base on 10 determinations.

### *5.2 Tablet Porosity*

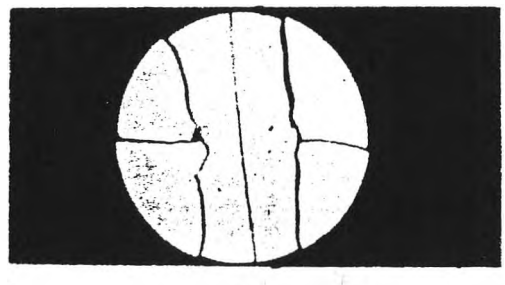
The total porosity of the tablets were determined using the method introduced by Seager et al (7) and calculated from the following equation :

$$\text{Porosity} = 1 - \frac{\text{Apparent Density}}{\text{True Density}} \qquad (3)$$



A

B



C

**Figure 1** Fractured Tablet after Diametral Compression (A) Accepted Normal Tensile Strength (B) Rejected Shear and Compression Failure (C) Rejected Tensile Failure.

The true density of the tablets was detemined by compressing the granules to their minimum volumes using 11 mm punch at 7,000 pounds and 9 mm punch at 4,000 pounds for paracetamol and pyridoxine hydrochloride, respectively. This mass was approximately taken to have zero porosity and the true density was obtained by dividing the compact weight by its volume.

The apparent density was determined similarly by dividing the tablet weight by the volume calculated from the tablet dimension measured using a micrometer.

**6. Disintegration** Disintegration time was determined according to USP XXII method (8). The average was calculated from six determinations.

**7. Dissolution Time** Dissolution time was determined using apparatus according to USP XXII. The average was calculated from three determinations

*7.1 Paracetamol Tablet :* The dissolution rate of single tablet was measured in 900 ml of phosphate buffer pH 5.8 at 37 ± 0.5 °C as the dissolution medium. A tablet was placed on the vessel and the paddle was rotated at 50 rpm. Sample of 5 ml were withdrawn periodically at 10, 20, 30, 60, 180, 240, 300 and 360 minutes interval. The volume taken was substituted by an equal volume of prewarm buffer. After suitable diluted with phosphate buffer, the sample was then assayed spectrophotometrically by measuring the absorbance at 249 nm and the concentration was calculated from standard curve. The medium dissolution time (T50%) was determined from dissolution profile.

*7.2 Pyridoxine Hydrochloride Tablet :* The dissolution rate of single tablet was determined in 900 ml of diluted hydrochloric acid (1 in 100) at 37 ± 0.5°C as the dissolution medium. The basket containing a tablet was placed on the vessel and rotated at 100 rpm. Sample of 5 ml were withdrawn periodically at 2, 5, 10, 15, 20, 30, 40 and 60 minutes interval. The volume taken was substituted by an equal of prewarm diluted hydrochloric acid. After suitable dilution with diluted hydrochloric acid, the sample was then assay spectrophotometrically by measuring the absorbance at 290 nm and the concentration was calculated from standard. The medium dissolution time (T50%) was determined from dissolution profile.

## Results

The physical properties of paracetamol and pyridoxine hydrochloride tablets prepared with $D_1$, $D_2$ and various binders are summarized in Tables 3-4. These data showed that both drugs were uniform in weight and thickness. For tablet hardness, it was found that the increase in binder concentration caused increase in hardness values for both drugs as indicated in Tables 3-4 and Figures 2-3. For paracetamol, the ranks of hardness decrease as follow, at 1% level : Methocel E15LV$^{(R)}$ ≃ PVP K 30 > gelatin > $D_1$ ≃ $D_2$ ≃ Starch 1500 $^{(R)}$ ≃ corn starch. At 2% level : Methocel E15LV $^{(R)}$ ≥ PVP K 30 ≥ gelation ≥ $D_1$ ≃ $D_2$ ≥ corn starch ≃ Starch 1500 $^{(R)}$ . In the case of 4% level ;Methocel E15LV $^{(R)}$ ≥ PVP K 30>$D_1$ ≃ gelatin ≃ $D_2$ ≃ Starch 1500 $^{(R)}$ ≃ corn starch. Comparative data showed that tablets made with Methocel E 15LV $^{(R)}$ were strongest. On the other hand, corn starch exhibited the weakest table except at 2% level. $D_1$ possessed slightly harder tablet than $D_2$. As was expected, capping was occurred during tabletting blank granules. Consequently, no evaluated data was obtained.

In the case of pyridoxine hydrochloride tablets. The hardness values could be ordered as follow, at 1% level : Methocel E15LV$^{(R)}$ > gelatin ≃ PVP K 30 > $D_2$ ≃ $D_1$ ≃ Starch 1500 $^{(R)}$ ≃ corn starch > Blank. At 2% level : $D_1$ ≃ Methocel E15LV $^{(R)}$> gelation ≃ PVP K 30 ≃ starch 1500$^{(R)}$ > $D_2$ ≃ corn starch > Blank. In the case of 4% level : Methocel E15LV $^{(R)}$ > $D_1$ ≥ gelatin ≃ PVP K 30 ≃ Starch 1500 $^{(R)}$ ≃ $D_2$ ≃ corn starchs > Blank. As was expected, tablets formulated with Methocel E15LV$^{(R)}$ also strongest, nevertheless, blank tablets were the weakest. At 1% level, both $D_1$ and $D_2$ had comparable tablet hardness but at higher level, $D_1$ imparted greater hardness than $D_2$.

The results of tablet friability of paracetamol and pyridoxine hydrochloride which presented in Tables 3-4 clearly revealed that tablet friability for both drugs decreased with increasing binder concentration. Friability values for both drugs will be employed for binder index determination.

**Table 3** Physical Properties of Paracetamol Tablets Prepared with Various Binders and Concentrations by Solution Incorporation Method.

| Binders | % (W/W) | Physical Properties of Tablets | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | # Weight Variation (mg, ± SD) | ## Thick ness (mm, ± SD) | ## Hard ness (kp, ± SD) | ### Friabi lity (%) | Tensile Strength (MN x 10/m²) | Poro sity (%) | #### Disinte gration (min, ± SD) | T50% (min) | ## Content Uniformity (%) | Binder Index (MNx10²/ m².min) |
| | 1 | 508.20(1.83) | 4.25(0.01) | 5.35(0.38) | 1.41 | 6.30 | 4.02 | 60.25(4.49) | 140.90 | 99.79(0.77) | 1.27 |
| $D_1$ | 2 | 496.60(2.25) | 4.23(0.00) | 7.12(0.56) | 0.71 | 7.70 | 4.05 | 62.51(3.55) | 203.70 | 101.29(1.19) | 2.28 |
| | 4 | 500.70(2.08) | 4.23(0.01) | 8.30(0.45) | 0.50 | 8.80 | 4.99 | 63.40(2.67) | 271.40 | 99.43(1.05) | 3.24 |
| | 1 | 498.60(1.71) | 4.24(0.03) | 5.25(0.51) | 1.59 | 6.60 | 4.71 | 63.12(3.10) | 226.00 | 100.93(1.43) | 0.87 |
| $D_2$ | 2 | 501.70(0.01) | 4.24(0.01) | 6.74(0.41) | 0.84 | 7.73 | 4.26 | 64.40(3.92) | 260.90 | 101.14(1.99) | 1.66 |
| | 4 | 494.80(1.99) | 4.23(0.01) | 7.56(0.67) | 0.52 | 8.00 | 4.73 | 65.01(3.10) | 281.90 | 100.05(1.66) | 2.58 |
| | 1 | 503.90(1.21) | 4.23(0.01) | 8.15(0.80) | 0.91 | 7.90 | 4.25 | 52.21(2.45) | 80.80 | 99.20(1.05) | 5.64 |
| PVP K 30 | 2 | 494.00(2.33) | 4.22(0.01) | 9.76(0.71) | 0.34 | 9.20 | 6.16 | 55.08(1.58) | 104.60 | 100.45(0.94) | 15.94 |
| | 4 | 490.00(1.90) | 4.22(0.01) | 11.15(0.82) | 0.24 | 9.70 | 5.53 | 58.55(3.12) | 145.10 | 98.20(1.13) | 14.57 |
| | 1 | 498.20(1.37) | 4.25(0.02) | 4.80(0.38) | c | 4.70 | - | 67.79(3.57) | 180.90 | 100.90(0.86) | - |
| Corn | 2 | 495.50(1.24) | 4.22(0.01) | 6.06(0.57) | 1.34 | 5.90 | 3.77 | 70.55(1.88) | 270.70 | 102.41(1.62) | 0.61 |
| Starch | 4 | 491.20(2.31) | 4.22(0.01) | 7.53(0.53) | 0.85 | 7.40 | 4.25 | 79.31(1.98) | 294.40 | 99.78(2.01) | 1.26 |
| | 1 | 503.20(1.14) | 4.23(0.01) | 4.83(1.00) | c | 6.20 | - | 62.10(2.78) | 177.50 | 99.59(0.50) | - |
| Starch | 2 | 497.10(2.03) | 4.22(0.03) | 5.64(0.98) | 1.17 | 6.80 | 3.33 | 65.74(2.36) | 237.20 | 100.10(0.61) | 0.88 |
| 1500(R) | 4 | 497.20(2.20) | 4.22(0.00) | 7.80(0.29) | 0.72 | 8.00 | 4.74 | 69.10(2.14) | 274.90 | 102.30(1.99) | 1.92 |
| | 1 | 497.20(1.82) | 4.24(0.01) | 6.55(0.59) | 2.67 | 6.70 | 4.25 | 47.30(2.38) | 107.43 | 98.99(1.90) | 0.99 |
| Gelatin | 2 | 504.70(1.71) | 4.24(0.01) | 7.75(0.61) | 1.09 | 7.80 | 4.01 | 53.45(1.67) | 147.90 | 101.34(1.58) | 1.94 |
| | 4 | 495.20(2.14) | 4.23(0.01) | 7.77(0.54) | 0.80 | 8.80 | 4.95 | 55.57(1.56) | 167.40 | 100.20(1.57) | 3.25 |
| | 1 | 499.10(2.22) | 4.21(0.01) | 8.28(0.74) | 1.03 | 7.40 | 4.04 | 47.00(1.95) | 97.70 | 99.90(1.01) | 2.97 |
| Methocel | 2 | 495.50(2.35) | 4.21(0.01) | 10.47(1.12) | 0.47 | 7.80 | 5.45 | 60.02(3.15) | 131.20 | 100.50(0.97) | 6.89 |
| E15LV(R) | 4 | 501.20(2.35) | 4.21(0.01) | 11.74(1.05) | 0.39 | 10.60 | 5.82 | 62.24(2.77) | 164.60 | 101.20(1.37) | 9.61 |
| Blank | | - | - | - | - | - | - | - | - | - | - |

c capping.
\- no data was obtained.
\# averaged from twenty determinations.
\# # averaged from ten determinations.
\# # # averaged from two determinations.
\# # # # averaged from six determinations.

**Table 4** Physical Properties of Pyridoxine Hydrochloride Tablets Prepared with Various Binders and Concentrations by Solution Incorporation method.

| Binders | % (W/W) | Physical Properties of Tablets | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | # Weight Variation (mg, ± SD) | ## Thick ness (mm, ± SD) | ## Hard ness (kp, ± SD) | ### Friabi lity (%) | ### Tensile Strength (MN x 10/m²) | Poro sity (%) | #### Disinte gration (min, ± SD) | T50% (min) | ## Content Uniformity (%) | Binder Index (MNx10²/ m².min) |
| $D_1$ | 1 | 298.10(1.69) | 3.10(0.02) | 6.55(0.30) | 0.77 | 8.60 | 3.89 | 7.81(0.30) | 18.70 | 99.02(1.11) | 23.33 |
| | 2 | 298.40(1.32) | 3.11(0.02) | 9.28(0.29) | 0.64 | 11.80 | 3.87 | 8.75(0.38) | 20.00 | 100.16(0.93) | 35.68 |
| | 4 | 301.40(1.05) | 3.11(0.01) | 9.50(0.43) | 0.56 | 12.30 | 3.90 | 10.75(0.09) | 23.00 | 99.54(1.07) | 37.24 |
| $D_2$ | 1 | 310.30(2.50) | 3.20(0.04) | 6.77(0.39) | 0.84 | 8.70 | 4.24 | 7.36(0.50) | 13.50 | 98.90(0.47) | 32.53 |
| | 2 | 302.50(2.31) | 3.12(0.04) | 7.00(0.38) | 0.71 | 10.60 | 4.30 | 8.10(0.12) | 15.10 | 99.95(0.44) | 42.51 |
| | 4 | 297.90(1.87) | 3.07(0.02) | 7.70(0.38) | 0.59 | 11.30 | 4.95 | 10.67(0.15) | 15.10 | 99.95(0.44) | 62.78 |
| PVP K 30 | 1 | 304.70(1.64) | 3.11(0.01) | 7.89(0.63) | 0.69 | 10.00 | 5.96 | 5.98(0.30) | 9.50 | 99.50(0.88) | 90.92 |
| | 2 | 299.90(2.05) | 3.10(0.01) | 7.93(0.20) | 0.59 | 11.20 | 5.59 | 6.14(0.13) | 10.00 | 99.11(0.58) | 106.12 |
| | 4 | 290.10(1.69) | 3.08(0.03) | 8.50(0.25) | 0.31 | 11.40 | 6.62 | 6.20(0.15) | 10.00 | 100.04(1.01) | 243.45 |
| Corn Starch | 1 | 308.40(1.81) | 3.11(0.02) | 6.24(0.34) | 0.84 | 10.60 | 3.90 | 6.01(0.32) | 20.27 | 99.24(0.92) | 24.28 |
| | 2 | 292.90(1.60) | 3.10(0.19) | 6.95(0.51) | 0.75 | 11.10 | 4.59 | 6.05(0.44) | 23.00 | 99.20(1.02) | 29.54 |
| | 4 | 299.60(1.88) | 3.12(0.11) | 7.91(0.15) | 0.69 | 11.30 | 4.95 | 6.92(0.18) | 23.00 | 100.04(1.10) | 31.69 |
| Starch 1500(R) | 1 | 308.70(1.44) | 3.11(0.03) | 6.24(0.42) | 0.81 | 10.30 | 4.24 | 6.71(0.53) | 18.90 | 99.48(0.66) | 28.53 |
| | 2 | 291.70(1.69) | 3.09(0.04) | 7.82(0.10) | 0.72 | 11.00 | 5.96 | 8.34(0.10) | 21.10 | 99.59(1.23) | 43.15 |
| | 4 | 294.90(2.26) | 3.10(0.03) | 8.29(0.18) | 0.63 | 11.50 | 5.63 | 8.59(0.10) | 25.90 | 99.89(0.79) | 39.68 |
| Gelatin | 1 | 295.00(2.21) | 3.10(0.07) | 7.81(0.60) | 0.68 | 10.80 | 4.27 | 5.08(0.31) | 7.60 | 100.02(1.07) | 89.92 |
| | 2 | 297.80(1.30) | 3.10(0.02) | 8.02(0.53) | 0.55 | 12.00 | 4.95 | 5.25(0.55) | 9.70 | 99.90(0.69) | 111.34 |
| | 4 | 298.10(1.90) | 3.12(0.06) | 8.96(0.47) | 0.33 | 12.70 | 4.56 | 6.09(0.68) | 10.50 | 99.21(1.15) | 167.13 |
| Methocel E15LV(R) | 1 | 292.50(2.37) | 3.11(0.02) | 8.89(0.27) | 0.77 | 11.50 | 4.25 | 6.25(0.28) | 10.00 | 100.28(0.48) | 63.47 |
| | 2 | 293.50(2.05) | 3.13(0.02) | 9.08(0.36) | 0.64 | 11.80 | 4.23 | 6.92(0.19) | 11.00 | 99.49(1.55) | 70.26 |
| | 4 | 301.60(1.21) | 3.12(0.16) | 10.61(0.49) | 0.35 | 13.80 | 4.61 | 8.58(0.48) | 11.10 | 99.33(0.77) | 156.65 |
| Blank | | 302.40(1.12) | 3.34(0.03) | 3.58(0.69) | 1.93 | 1.90 | 4.29 | 4.50(0.84) | 21.10 | 99.88(1.82) | 5.12 |

\# averaged from twenty determinations.
\## averaged from ten determinations.
\### averaged from two determinations.
\#### averaged from six determinations.

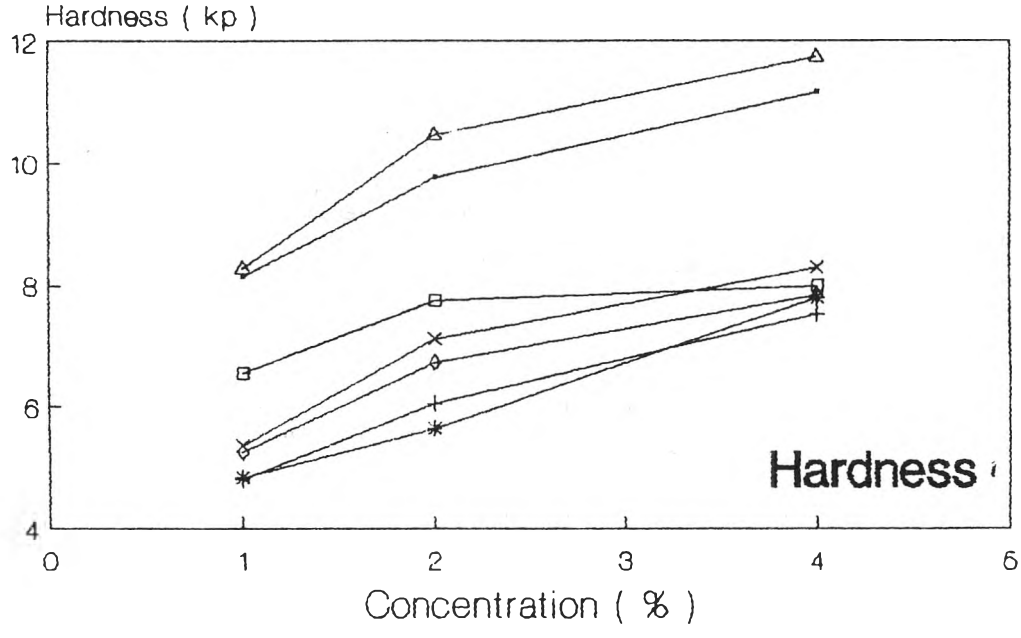



**Figure 2** Effect of Binder Types and Concentrations on Hardness of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : x $D_1$, ◇ $D_2$, • PVP K 30, + Corn starch, * Starch 1500$^{(R)}$, □ Gelatin, Δ Methocel E15LV$^{(R)}$).

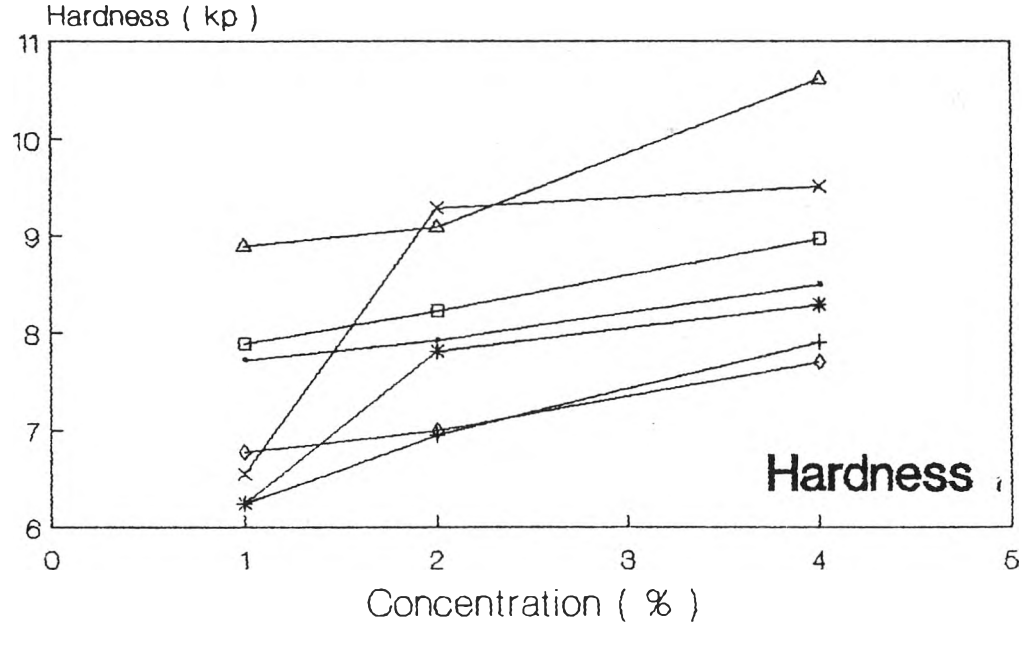



**Figure 3** Effect of Binder Types and Concentrations on Hardness of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method (Key : x $D_1$, ◇ $D_2$, • PVP K 30, + Corn starch, * Starch 1500$^{(R)}$, □ Gelatin, Δ Methocel E15LV$^{(R)}$).

Tablet tensile strength of paracetamol and pyridoxine hydrochloride are also reported in Tables 3-4. They slightly increased with the increasing of binder concentration. This behavior are in agreement to the result of tablet hardness. For all cases the tensile strength of paracetamol tablet ranged from 4.7 to 10.6 MN x $m^{-2}$ x 10. The tendency of high tensile strength was found on the tablet prepared with Methocel E15LV and PVP K 30. On the other hand, corn starch showed the lowest value. $D_1$ and $D_2$ were slightly difference in tensile strength. In the case of pyridoxine hydrochloride, the range of tensile strength were between 8.6 to 13.8 MN x $m^{-2}$ x 10. Methocel E15L V$^{(R)}$, however, gave the maximum tensile strength.

For paracetamol, present tablet porosity were between 3.32 and 5.82%. At 1% level, lamination was occurred for the tablets prepared with corn starch and Starch 1500$^{(R)}$ at highest compression pressure to obtain zero porosity thus no data were resulted. In addition at higher binder concentration, both corn starch and Starch 1500$^{(R)}$ showed lower porosity values than other tablets in this study. On the other hand, the high porous tablets were given by PVP K 30. The results of porosity value were between 3.87 and 6.62%. It was noticed that tablets produced by PVP K 30 and $D_1$ were the two highest and lowest porosity values, respectively.

As was expected the disintegration time of tablets for both drugs increased with increasing in binder concentration. For paracetamol, significantly prolonged disintegration time as binder concentration increased was noticed in all cases. It was found that $D_2$ disintegrated more rapid than $D_1$. The quicker disintegrated formulation did not mean better efficacy or better formulation. In this study, the longer disintegrated formulation usually mean better binding properties. However, disintegration time alone could not be employed to evaluate binder efficacy, another important factors should also be considered, such as hardness, friability and dissolution. In the case of pyridoxine hydrochloride disintegration values were unsignificantly influenced with the increase in binder concentration. In addition, it was clearly seen that pyridoxine hydrochloride disintegrated quicker than paracetamol tablets.

For dissolution properties, it obviously indicated that binder concentration can affect dissolution in the same maner as disintegration time. The same as in disintegration studies, the prolong dissolution rate usually mean better binder efficacy. The dissolution rate of paracetamol tablets were decreased with the increase in binder concentration. The quickest dissolution rate was given by PVP K 30 (Table 3). While $D_1$ tended to dissolved better than $D_2$. In the case of pyridoxine hydrochloride, it was found that dissolution rates were less affected by increasing binder concentration. As was mentioned previously, individual parameter such as hardness, friability, porosity, disintegration time and dissolution could be employed to determine binding property at some certain conditions. However, the parameter usually used to compare and determine overall binding property of tablets prepared with various binding agents is binder index. Binder index composed of the following parameters, they are tensile strength, porosity, median dissolution time and friability of the tablet.

According to the results of binder index, they tended to increase as the binder concentration increased for both drugs as given in Tables 3-4 and Figures 4-5. For paracetamol tablet, consideration for all concentration studies, PVP K 30 showed the greatest binder index whereas corn starch gave the lowest value. It could be noticed that $D_1$ had higher binder index than $D_2$. Both $D_1$ and $D_2$ had greater binder index than corn starch and Starch 1500$^{(R)}$ at all concentration employed.

In the case of pyridoxine hydrochloride the binder index values of tablet prepared with various binders were very high and all values were in acceptable limit. Binder index of pyridoxine hydrochloride tablets seemed to be many times higher than paracetamol tablets. This indicated that pyridoxine hydrochloride had better binding property than paracetamol. It also noted that the highest and lowest binder index were tablet produced with PVP K 30 and corn starch (except at 2%), respectively. However, $D_2$, showed higher binder index than $D_1$. Inaddition, blank tablet for both drugs were typically the least binder index values.

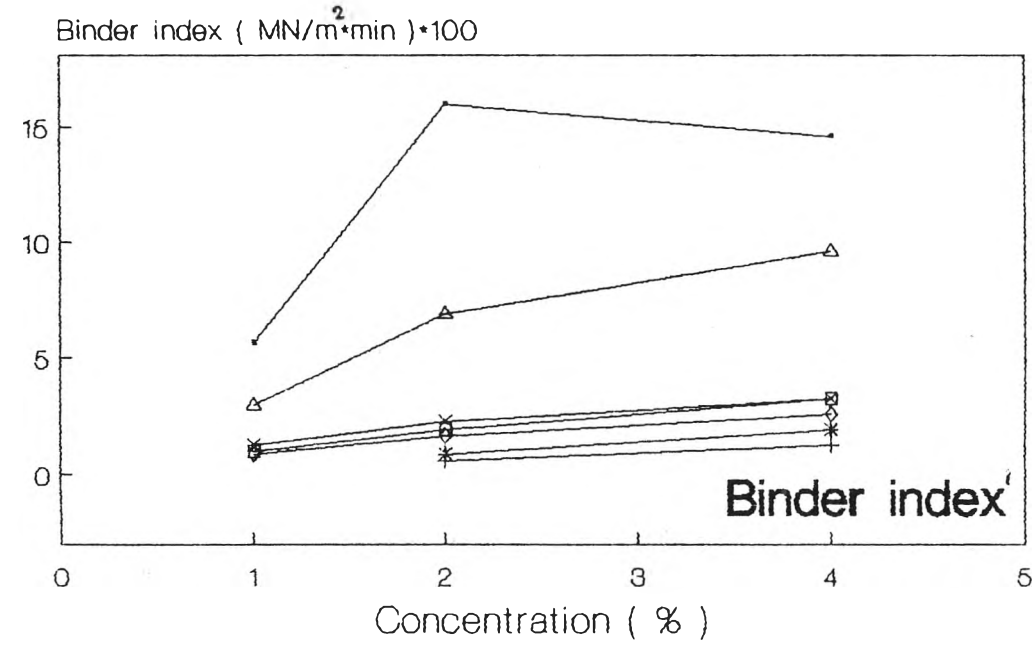



**Figure 4** Effect of Binders Types and Concentrations on Binder Index of Paracetamol Tablets Prepared by Solution Incorporation Method. (Key : x $D_1$, ◇ $D_2$, • PVP K 30, + Corn starch, * Starch 1500(R), □ Gelatin, Δ Methocel E15LV(R)).

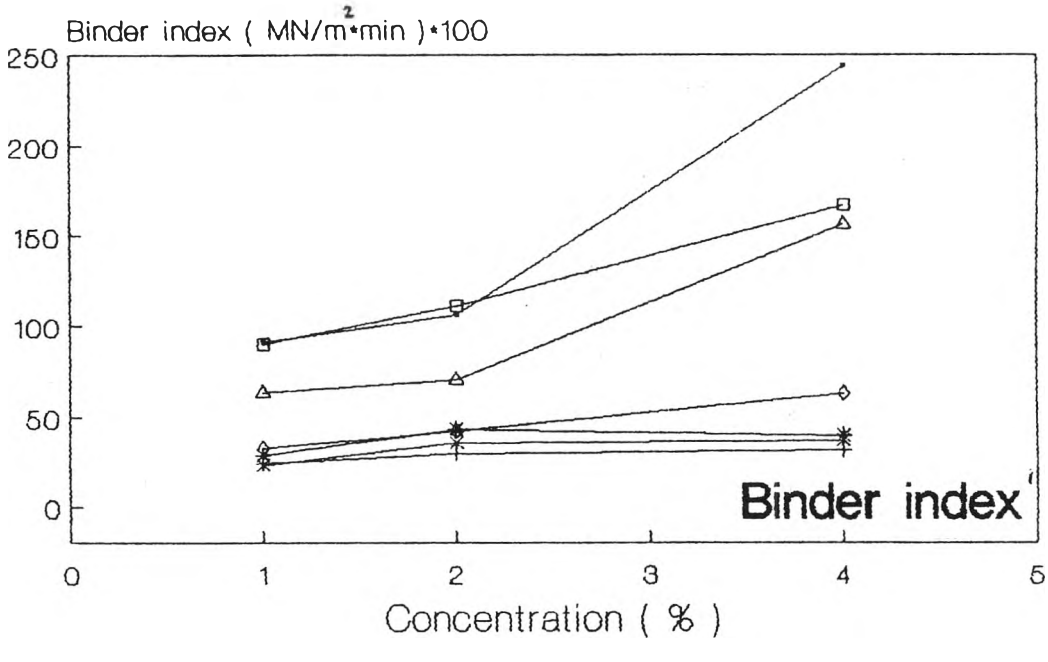



**Figure 5** Effect of Binders Types and Concentrations on Binder Index of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method. (Key : x $D_1$, ◇ $D_2$, • PVP K 30, + Corn starch, * Starch 1500(R), □ Gelatin, Δ Methocel E15LV(R)).

## THE PHYSICAL PROPERTIES OF TABLETS

All tablets prepared with various binders in this study showed good weight variation owing to the free-flowing of granules. As a result, uniformity of tablet thickness was observed with standard deviation of less than 0.06.

The tablet hardness is mainly influenced with the amount of the binder utilized (Tables 3-4 and Figures 2-3). It clearly increased proportional to the binder concentration. This may be attributed to the stronger bond formation and increasing in crystalline bridge between the particles.

For paracetamol tablets, at all binder concentrations used, Methocel E15LV(R) gave the hardest tablets whearas corn starch gave the weakest. The results are corresponding to the knowledge that cellulose groups usually form hard tablet but starch forms soft and brittle tablet (9). The comparative hardness values were found from the tablet prepared with $D_1$ and $D_2$.

The tendency of capping occurred as compressing paracetamol blank tablets. More recent research has attributed capping in paracetamol to a low degree of plastic deformation and bonding during compressional proccess (10-11). Carless et al (12) showed that capping of paracetamol tablet could be eliminated by using approprite binders. The authors explained that employing the binders resulted in both an increase in residual die wall pressure and a decrease in elastic recovery. Therefore the lack of binder in blank tablets may cause capping due to the reason mention above. Consideration with pyridoxine hydrochloride tablets (Table 4), Methocel E15LV(R) also imparted the strongest tablets whereas blank tablets were the weakest. Above 1% binder concentration, obviously higher in hardness value was found for $D_1$ than $D_2$.

As regarding to the results of friability (Tables 3-4), it is noticed that friability decreased with increasing binder concentration. The increase in binder concentration caused tablet hardness to increase and may be the explanation of less friability. In the case of paracetamol tablets, PVP K 30 possessed the least friability value. Capping was seen for the tablet prepared with corn starch and Starch 1500 (R) at 1% level. This could be remarked that the amount of binder used may not sufficient to impart binding properties for the tablet to withstand the abrasive test. At 1% level, only PVP K 30 showed friability value in acceptable limit (< 1%). In the case of 2%, PVP K 30, Methocel E15LV (R) $D_1$ and $D_2$, gave friability value of less than 1%. Furthermore, at above 2% concentration none of tablet friability was excess acceptable limit. For $D_1$ and $D_2$, the friability values were comparable and within the limit as binder concentration greater than 1%. When pyridoxine hydrochloride was used, the friability values of all tablet were in acceptable range (<1%). The less friable tablets were given by PVP K 30 and gelatin.

The tensile strength of tablet is an important measurement for characterizing the interaction between solid particles. Hiestand et al (3) explained that the higher the true areas of particles contacted, the stronger the interaction occurred. Tables 3-4 indicated that tensile strength was increased as binder concentration increased. The reason may be explained in the same manner of tablet hardness. Consideration with paracetamol tablets, PVP K 30 and Methocel E15LV (R) gave high tensile strength values whearas corn starch represented low value. In the case of pyridoxine hydrochloride the high tensile strength was also found in Methocel E15LV(R). According to tablet prepared from both drugs, the different in tensile strength between $D_1$ and $D_2$ was not distinguished.

In this study, relationship between porosity of tablets and binder concentration are not clearly seen (Tables 3-4). They slightly inconsistency changed with altering binder concentration. The porosity values of paracetamol tablets and pyridoxine tablets were ranging between 3.77-6.16 % and 3.90-6.62%, respectively. It was interesting that PVP K 30 produced the tablet with more porous than other binders. Lamination was occurred on the paracetamol tablets prepared with 1% corn starch and Starch 1500 (R) at high compressional pressure to obtain approximately zero porosity. This behavior could be attributed to the weaker bond formation of such binders.

The influence of binder concentration on tablet disintegration and dissolution were proposed in many reports (13-19). It was found that they were increased with increasing of binder concentration. The presence of binders in tablet formulation would be expected to reduce size, number and alter the shapes of capillary space between the particles which are contributing to the transport of water. They, therefore, affected the penetration of water in tablet which is necessary for the process of disintegration and dissolution (20). This effect are magnified as concentration of binding agent increased. Furthermore, the increase in tablet hardness also hinder the water penetration. However, in this study, slow disintegration and dissolution did not mean poor tablet properties. In contrast, the retardation in both properties may indicated good binding property and can be used to elucidate binder efficacy. For paracetamol tablet, neither of tablets disintegrated within the USP limit. It mainly due to the absence of disintegrant in the formulation and poor water solubility of paracetamol. At the same binder concentration employed, PVP K 30, Methocel E15LV(R) and gelatin showed faster tablet dissolution than other binders. This may be owing to their good

water solubility and absorbing ability. Therefore, they enhanced tablet dissolution greater than corn starch and Starch 1500(R) which are less water soluble. Although $D_1$ and $D_2$ could dissolve and hydrate in the presence of water but they probably from viscous barrier against the penetration of water. As a result, in both cases slow dissolution were noticeable. Consideration with pyridoxine hydrochloride, all tablets show good disintegration and dissolution because of water solubility of active drug. Pyridoxine hydrochloride tablet produced with gelatin, PVP K 30, Methocel E15 LV (R), $D_1$ and $D_2$ gave faster dissolution rate than corn starch and Starch 1500(R). This may be attributed to the reason metioned above and the effect of viscous barrier from $D_1$ and $D_2$ could be overcomed by good water solubility of drug.

According to Tables 3-4, binder index was increased as binder concentration increased. In the case of paracetamol at all level of binder concentration utilized the binder index generally decreased as follow, PVP K 30 > Methocel E15LV (R) > $D_1$ > $D_2$ > Starch 1500(R) > corn starch. For pyridoxine hydrochloride : PVP K 30 > gelatin > Methocel E15LV(R) > $D_2$ > Starch 1500 (R) > $D_1$. It is noticed that binder index of paracetamol tablets significantly appeared to be less than pyridoxine hydrochloride tablets owing to their poor dissolution.

## CONCLUSION

It was recognized that durian rind extracts : $D_1$ and $D_2$ possessed binding properties superior to corn starch and Starch 500(R) but inferior to PVP K 30, Methocel E15LV(R) and gelatin for paracetamol and pyridoxine hydrochloride tablets, respectively. The significant physical properties of granules (1) and tablets e.g. granule size and size distribution, granule friability, flowability, hardness, friability, disintegration, dissolution and binder index were used to assess their binding properties.

The results emphasized that both $D_1$ and $D_2$ showed accomplished binding properties as comparing with other binders in this study. For paracetamol tablets, $D_1$ and $D_2$ gave more satisfy tablet strength, friability value and binder index than corn starch and Starch 1500(R).

In addition, $D_1$ and $D_2$ also revealed good results for pyridoxine hydrochloride tablets. The binder index of $D_2$ was obviously higher than corn starch and Starch 1500(R) but lower than PVP K 30, Methocel E15LV(R) and gelatin. Furthermore, $D_1$ gave more stronger tablet than PVP K 30 and gelatin at concentration greater than 1%. Generally, it was noticed that $D_1$ produced tablets with slightly better properties than $D_2$.

Ultimately, both durian rind extracts can be employed as binding agents in wet granulation process for tablet preparation containing either slightly water soluble or water soluble active drug, The effective concentrations were greater than 1% for paracetamol and at all concentration studied for pyridoxine hydrochloride, respectively.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# ศึกษาการใช้สารสกัดจากเปลือกทุเรียนเพื่อเป็นสารยึดเกาะโดยใช้น้ำเป็นกระสาย II : การประเมินคุณสมบัติของเม็ดยา

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## บทคัดย่อ

การประเมินคุณสมบัติช่วยยึดเกาะของสารสกัดจากเปลือกทุเรียน $D_1$ และ $D_2$ เปรียบเทียบกับสารช่วยยึดเกาะอื่นที่ใช้กันแพร่หลาย เช่น PVP K 30, corn starch, Starch 1500 (R), gelatin และ Methocel E15LV(R) สารช่วยยึดเกาะที่ใช้ในการศึกษาจะนำมาเตรียมยาเม็ด paracetamol และ pyridoxine hydrochloride ในระดับความเข้มข้น 1, 2 และ 4% ของน้ำหนักแห้งด้วยวิธี solution incorporation คุณสมบัติช่วยยึดเกาะของสารช่วยยึดเกาะจะประเมินจากคุณสมบัติทางกายภาพที่สำคัญของเม็ดยา เช่น ความแข็งของเม็ดยา ความกร่อน การแตกกระจายตัว การละลาย และค่าดัชนียึดเกาะโดยเพิ่มเติมจากคุณสมบัติของ แกรนูลที่ได้จากการศึกษาครั้งก่อน

จากผลการทดลองแสดงว่าทั้ง $D_1$ และ $D_2$ มีคุณสมบัติการยึดเกาะที่ดีในเม็ดยาพอๆ กับในแกรนูลเมื่อเปรียบเทียบกับสารยึดเกาะอื่นๆ สำหรับยาเม็ดที่เตรียมจาก paracetamol ทั้ง $D_1$ และ $D_2$ ให้ความแข็งแรงของเม็ดยา ความกร่อน และค่าดัชนียึดเกาะเป็นที่น่าพอใจกว่าเมื่อเทียบกับ corn starch และ Starch 1500 (R) สำหรับยาเม็ดที่เตรียมจาก pyridoxine hydrochloride ก็ให้ผลดีเช่นเดียวกันโดยค่าดัชนียึดเกาะของ $D_2$ จะสูงกว่า corn starch และ Starch 1500(R) แต่จะด้อยกว่า PVP K 30 และ gelation ที่ความเข้มข้นมากกว่า 1% $D_1$ จะให้เม็ดยาที่ยึดเกาะดีกว่า $D_2$ เล็กน้อย (ไทยเภสัชสารปีที่ 15(3) : หน้า 173-186 (2533))

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