

Study on Korean Acid Clay as the Tablet Disintegrator

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國產酸性白土의 錠劑崩壞劑로서의 開發에 關한 研究

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國產酸性白土를 錠劑의 崩解劑로 開發하고자 從來 崩解劑로 使用해 오든 corn starch, calcium methylcellulose, kaolin, calcium silicate 및 pectin과 國產酸性白土를 崩解劑로하고 錠劑의 主藥成分 으로서는 不溶性인 Ca-PAS KP II 를 擇하였다. 以上の 各 崩解劑의 一 錠當 含量을 0%에서 25%까지 7種으로 달리하고 이것을 各各 使用 하여 만든 顆粒의 粒子度도 各各 4種類로 分類하였다. 여기에 滑澤劑 로서 0.5% mg-stearate⁹⁾를 共通으로 添加하였다.

以上을 各各 同一한 條件下에서 打錠하여 數種의 錠劑를 만들었다.

이들 錠劑에 對하여 硬度 및 崩解度試驗을 하여 比較檢討한 結果 다 음과 같은 結論을 얻었다.

1. Corn starch는 優秀한 崩解劑이나 그 添加量이 8%以上이 될때 는 打錠時 壓力을 받지 않아 錠劑 崩解劑로서 使用할 수 없었다.

2. Ca-Mc는 崩解劑로서 添加量이 8%以上 일때에도 使用可能 하였 으나 15%以上 일때는 打錠時 壓力이 弱해졌다.

3. Kaolin은 崩解劑로서 不適當 하다고 思慮되었다.

4. Ca-silicate도 崩解劑로서 適當하였으나 pectin은 가장 不適當 하였다.

5. 酸性白土는 錠劑崩解劑로서 打錠時 25% 添加時에도 壓力을 잘 받아 錠劑의 硬度를 維持할수 있었을 뿐만 아니라 崩解度도 良好한 成績을 나타내어 가장 優秀한 崩解劑임을 確認하였다.

6. 一般적으로 打錠에 使用되는 顆粒의 size가 적을수록 崩解時間 은 짧았으며 錠劑의 硬度가 높을수록 崩解時間은 길었다. 그러나 正 確한 比例性은 찾기 힘들었다.

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The acid clay is produced as natural products in many places inland of Korea. It is refined and used for widely not only as the absorbent, deodorizer and decolourator in most chemical engineering fields but also medical purpose as gastric absorbent and antidiarrheics.

It is scentless and yellowish-white powder containing a small amount of iron, magnesium and calcium. It has been not tried yet to use as tablet disintegrator.

Tablet disintegration time is one of the important factor which is effect to the principle pharmacological action in tablets medication and tablet disintegrator is the main factor for the tablet disintegration time, that is the why tablet disintegration time is limited accurate in every pharmacopoeia.

Nowadays the most commonly used disintegrators for tablets are starch, calcium methyl cellulose(ca-mc), calcium phosphate, kaolin, pectin and calcium silicates(ca-sil) etc. Among those, the starch is the most popular material but it is almost limited to use the amount because of practical difficulties of tableting.

There are several reports in this field about tablet disintegrators using some kind of clay but not Korean acid clay.

In this view of point to develop a new another suitable and costless material as tablet disintegrator, Korean acid clay was studied on here as the tablet disintegrator which is not been studied before.

Gross and Becker⁴⁾ studied and reported on bentonite used as tablet disintegrator until 17% of tablet weight but found not good results of effects as tablet disintegrator. Firouzbadian Ward and et al.⁵⁾ reported the Mg-Al-silicate was the excellent one as disintegrator. Feinstein and Birtukyccu⁸⁾ reported the results of study that the disintegration time was delayed when increased the amount of disintegrator which is used in common.

Kee-neng Wau and et. al.⁹⁾ reported about montmorillonite what is one of the sort of clay, and found as one of the excellent tablet disintegrator.

Here Korean acid clay was studies as water insoluble calcium p-aminosalicylate tablet disintegrator comparing with the other materials as corn starch, ca-mc, pectin, ca-silicate and kaolin, and got quite interest and useful results.

Experimental and Methods

Test materials

All the materials were used here dried at 50°C in 24 hours before preparing granules according to the procedure Banker has been employed.

The materials which used here are follow,

Acid clay,	screened 24 mesh, Dongbo chemical Co, Korea.
Corn starch,	U. S. P XVII and KP II(Korean Pharmacopoeia II)
Ca-mc,	Food additive Official Formulary, Japan II

Kaolin,	U. S. P. XVII
Ca-silicate,	Harwick Stand Chem. Co.
Pectin,	N. F. XI

and testing tablet is calcium p-aminosalicylate KPII which is subjected as a water insoluble main ingredient.

Preparing tablets

By wet granulation, mixed 50kg ca-PAS with each test materials as disintegrator each percentages of 0.5, 1, 2, 4, 8, 15 and 25 separate.

Daugh mixer has been used for mixing, and prepared granules through oscillating granulator. 15% of corn starch paste has been employed as binder.

The wet granules were dried at 60°C and sieved separate in each group of size as follow,

1. 16-24 mesh
2. 24-30 mesh
3. 30-40 mesh
4. 50-60 mesh

Those granules were obtained 10kg each and mixed with 0.5% of magnesium stearate on those granules as lubricant and tabletted in stocks rotary tablet press machine as follow,

punch,	concave punch
tablet weight,	550mg
pressure,	1.5ton
speed,	3,500tab/hr
filling,	9mm

as the same ca-PAS was tableted without any disintegrator with same each group of size of granules as blank test tablet separate. The total testing tablets batch numbers which are combination of different granule sizes and percentages of testing disintegrator were 172 group.

Tablet hardness test

Tablet hardness were checked by Erweka hardness tester and taken the average value of six times of calculation of each batch of tablet, the results show in table 1,2,3 and 4.

Disintegration test

U. S. P tablet disintegration test method has been employed and taken the average value. The results also show in table 1,2,3 and 4.

Results and discussion

In this experimental test the results of disintegration time and hardness show in table 1, 2, 3 and 4.

Table 1. The Disintegration Time and Hardness of Tablets Containing Various Concentrations of Disintegrating Agents (Prepared from 16-20 mesh Granulations)

Disintegrating Agent	Tests	Concn. of Disintegrating Agent %							
		0	0.5	1	2	4	8	15	25
Corn Starch	Disintegration time Sec	1860	1445	1370	762	145	54	50	26
	Hardness kg	8.50	8.00	7.50	8.20	7.50	6.50	4.25	2.50
Ca-MC	Disintegration time Sec	1860	1830	1260	1080	840	360	60	30
	Hardness kg	8.50	8.75	8.20	8.00	8.50	7.50	6.50	4.25
Kaolin	Disintegration time Sec	1860	1820	1020	815	600	410	180	120
	Hardness kg	8.50	8.50	7.00	7.75	5.75	5.50	6.50	3.50
Ca-Silicate	Disintegration time Sec	1860	1810	970	780	540	330	120	62
	Hardness kg	8.50	8.75	8.50	7.50	7.75	7.50	7.75	6.00
Pectin	Disintegration time Sec	1860	1365	1120	810	1115	1350	2600	3690
	Hardness kg	8.50	7.75	8.75	8.00	7.75	6.25	7.00	4.00
Acid clay	Disintegration time Sec	1860	1410	1020	840	380	255	120	60
	Hardness kg	8.50	8.00	8.50	8.25	7.75	7.25	6.00	4.50

Table 2. The Disintegration Time and Hardness of Tablets Containing Various Concentrations of Disintegrating Agents(Prepared from 24-30mesh Granulations)

Disintegrating Agent	Tests	Concn. of Disintegrating Agent %							
		0	0.5	1	2	4	8	15	25
Corn Starch	Disintegration time Sec	1176	1380	1175	610	196	98	53	25
	Hardness kg	8.25	8.50	8.00	8.50	8.30	6.70	3.75	0.25
Ca-MC	Disintegration time Sec	1776	1747	1202	1030	802	343	37	28
	Hardness kg	8.25	8.90	8.75	8.50	8.00	8.75	8.75	4.50
Kaolin	Disintegration time Sec	1776	1734	972	778	572	391	172	114
	Hardness kg	8.25	8.25	8.00	7.50	6.00	7.25	5.00	4.50
Ca-Silicate	Disintegration time sec	1776	1725	925	744	516	314	114	59
	Hardness kg	8.25	8.50	8.75	7.75	7.50	7.75	7.25	5.25
Pectin	Disintegration time Sec.	1776	1308	1068	772	1061	1288	2480	3521
	Hardness kg	8.25	8.75	8.25	8.00	7.50	8.75	5.75	3.00
Acid clay	Disintegration time Sec	1776	1202	970	626	280	188	88	44
	Hardness kg	8.25	7.75	8.50	7.75	8.00	7.00	6.25	5.00

Generally disintegration time of tablets were comparatively shortened when the concentration of disintegrator was increased and size of granule was getting smaller(Fig 1, 2, 3, 4 and 6).

In corn starch as disintegrator, it was difficult to check the hardness too soft to test when added more than 15%, and it started capping on tablet when added more than 8%.

Exceptionally disintegration times was prolonged when the pectin was increased more than 4% in granules(Fig 5).

Table 3. The Disintegration Time and Hardness of Tablets Containing Various Concentrations of Disintegrating Agents(Prepared from 30-40 mesh Granulations)

Disintegrating Agent	Tests	Concn. of Disintegrating Agent %							
		0	0.5	1	2	4	8	15	25
Corn Starch	Disintegration time Sec	1580	1229	1045	544	174	87	47	22
	Hardness kg	8.50	9.00	8.25	8.75	7.75	6.75		
Ca-MC	Disintegration time Sec	1580	1555	1120	915	715	305	51	25
	Hardness kg	8.50	8.25	8.25	8.75	8.25	8.00	6.00	4.75
Kaolin	Disintegration time Sec.	1580	1545	864	693	508	348	153	101
	Hardness kg	8.50	7.75	8.50	7.75	6.25	7.50	5.25	4.75
Ca-Silicate	Disintegration time Sec	1580	1535	823	662	459	279	101	52
	Hardness kg	8.50	8.00	8.25	8.00	7.75	8.00	7.50	5.50
Pectin	Disintegration time Sec	1580	1162	950	687	945	1145	2217	3139
	Hardness kg	8.50	8.25	7.75	8.25	7.75	8.50	6.00	3.25
Acid clay	Disintegration time Sec	1580	980	863	556	249	167	78	39
	Hardness kg	8.50	8.50	8.75	8.00	8.25	8.75	6.50	5.25

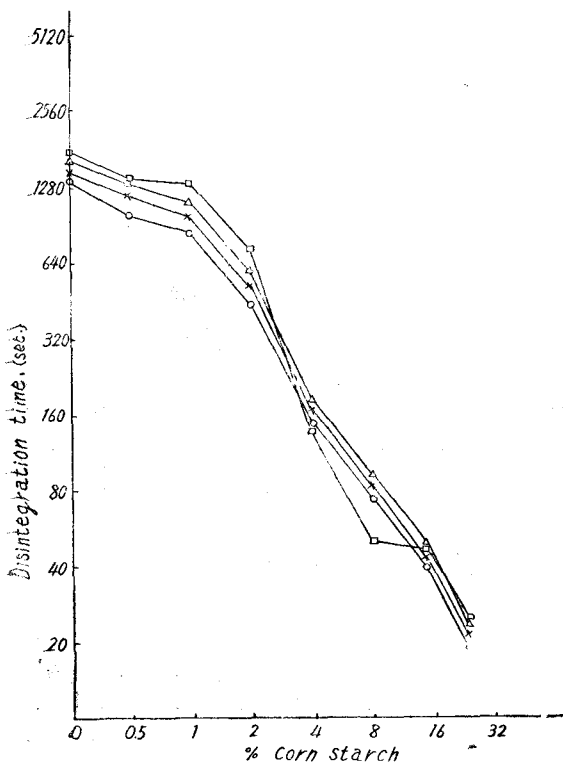


Fig. 1. Keg: □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

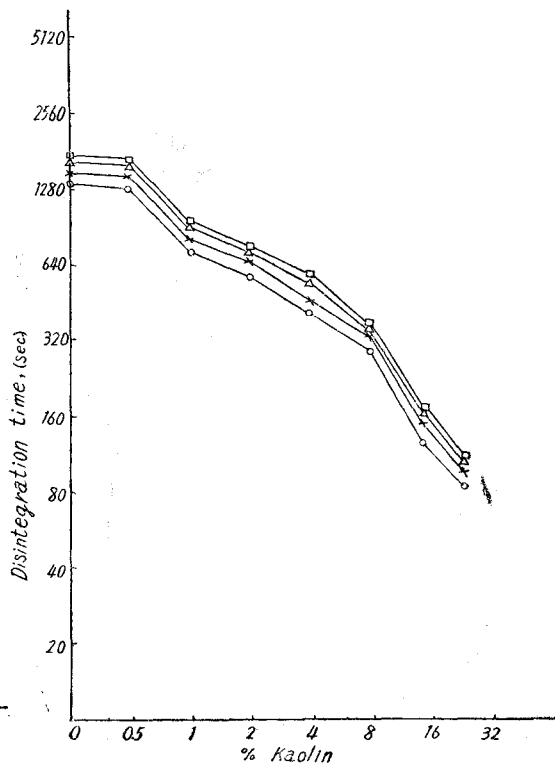


Fig. 2. Keg: □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

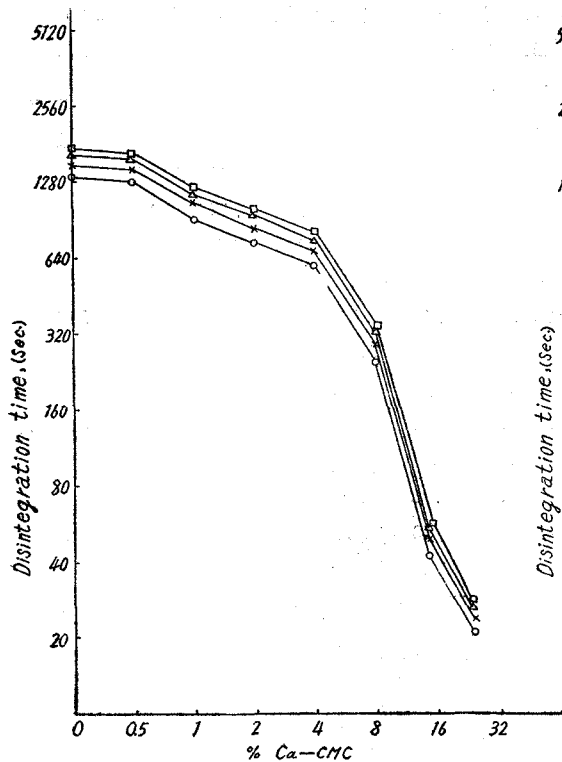


Fig. 3. Key : □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

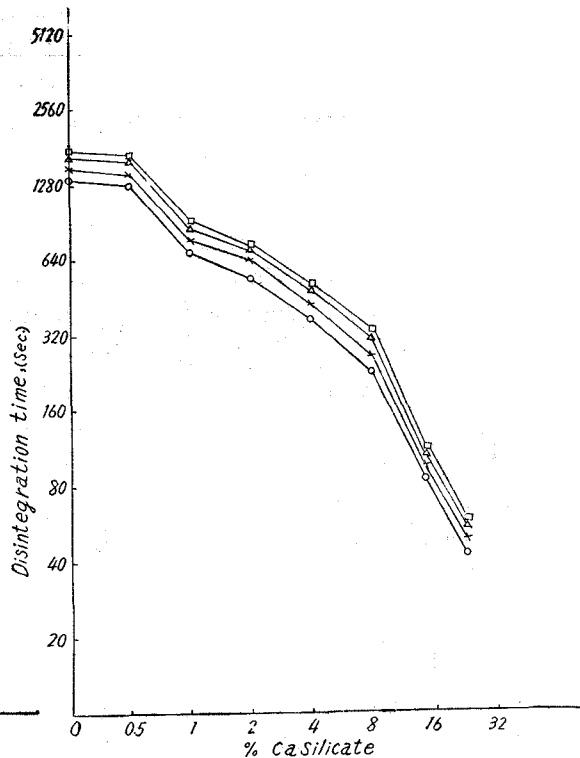


Fig. 4. Key : □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

Table 4. The Disintegration Time and Hardness of Tablets Containing Various Concentrations of Disintegrating Agents(Prepared from 50-60 mesh Granulations)

Disintegrating Agent	Tests	Concn. of Disintegrating Agent %							
		0	1.5	1	2	4	8	15	25
Corn Starch	Disintegration time Sec	1372	1064	907	473	151	761	41	19
	Hardness kg	8.25	8.75	8.00	8.75	8.50	6.00		
Ca-MC	Disintegration time Sec	1372	1350	972	795	621	265	44	22
	Hardness kg	8.25	8.00	8.00	8.75	8.25	8.00	6.50	5.50
Kaolin	Disintegration time Sec	1372	1341	750	602	442	362	133	88
	Hardness kg	8.25	7.50	8.25	7.75	7.25	7.50	5.75	5.50
Ca-Silicate	Disintegration time Sec	1372	1331	715	575	398	342	88	45
	Hardness kg	0.25	7.75	8.00	8.00	7.50	8.00	8.00	5.75
Pectin	Disintegration time Sec	1372	1010	825	596	821	994	1924	2723
	Hardness kg	8.25	8.00	7.50	8.25	7.75	8.50	6.50	3.75
Acid clay	Disintegration time Sec	1372	852	750	483	216	145	68	34
	Hardness kg	8.25	8.75	8.75	8.00	8.25	8.75	7.00	6.00

Ca-mc as tablet disintegrator, the hardness and disintegration time of tablets show in Fig 2. It also appeared the hardness was become soft when added more than 15%.

Kaolin as the disintegrator, the hardness was decreased more then other materials and very soft when added more than 4%(Fig 3).

Ca-silicate as the disintegrator, the hardness of tablet was decreased when the percentages of ca-silicate were increased, but these were comparatively harder than the others(Fig 4).

Acid clay as disintegrator, the hardness was become decreased when addition of acid clay was increased but it could still have enough hardness(more than 5.0kg) even added 25%(Fig 6).

Generally for tableting the same size on this study the size of granule is used with 24-30 meshes practically. The Fig.7 shows the comparing results of the hardness and disintegration time of the testing tablets in each different percentages but same granule size of 24-30 meshes, in corn starch was not shapped enough as tablet when the percentage was more than 8% and the corelation spot diagram of hardness and disintegration time of these tested tablets is made as Fig.8.

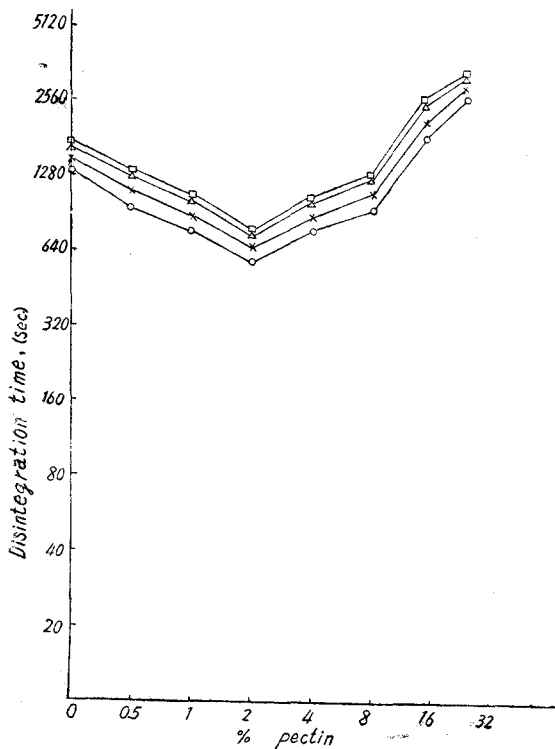


Fig. 5. Key : □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

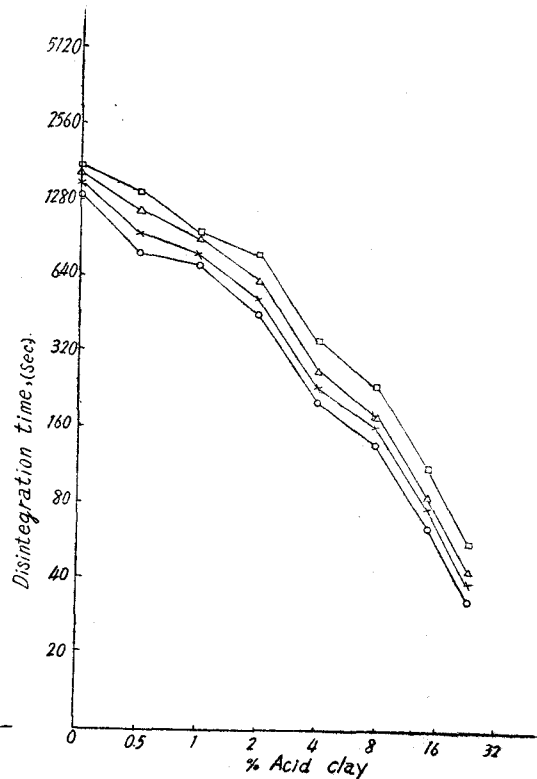


Fig. 6. Key : □ 16-20 mesh
 △ 24-30 mesh
 × 30-40 mesh
 ○ 50-60 mesh

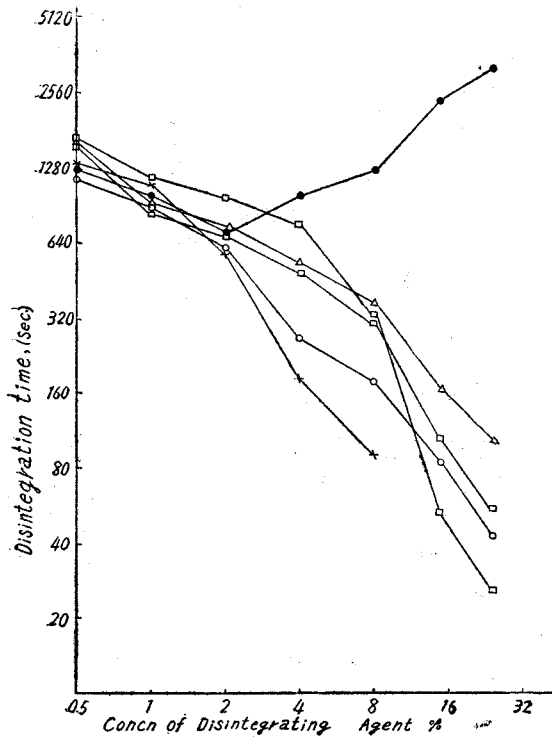
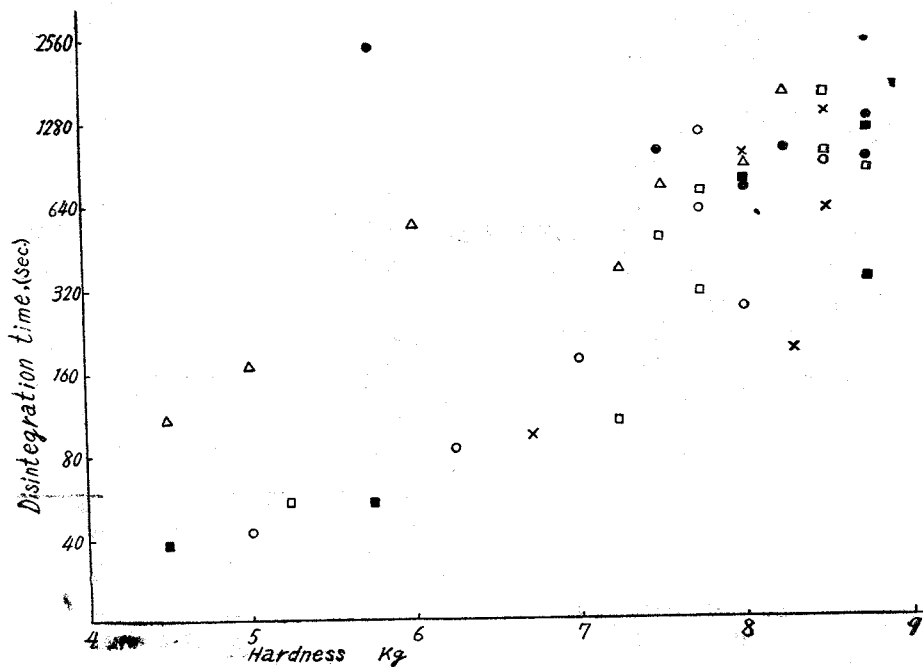


Fig. 7. Disintegration time of PAS-Ca tablets Containing Starch, Ca-CMC, Acid clay, Ca-silicate, Kaolin, & Pectin as disintegrating Agents (Prepared from 24-30 mesh granulations). Key: X Starch, ■ Ca MC, ○ Acid clay, □ Ca-silicate, △ Kaolin, ● Pectin.

Fig. 8. Corelation Spot Diagram on Hardness and Disintegration time of Tablets prepared from 24-30 mesh granulations. Key: X Stach, ■ Ca-Mc, ○ Aci-d clay, □ Ca-silicate, △ Kaolin, ● Pectin.



It shows disintegration time of tablets was delayed when the hardness was increased in most of tablets but it was difficult to find out some accurate relation between them.

According to the results of this study, it is summarized as follow,

1. Though it is an excellent disintegrator, corn starch cannot be recommended when it is added more than 8% of the weight of tablet because the hardness of tablet was very low and it happened capping at tableting.

2. Ca-mc and ca-silicate can be used as the tablet disintegrator, but the hardness was become low when added more than 15%.

3. It might not be recommended kaolin and pectin as a suitable tablet disintegrators. The disintegration time of tablets prepared by kaolin and pectin were too long and the hardness was contrastly higher compared with others when added more than 8% to the tablet.

4. When the hardness of tablet is getting harder, generally the disintegration time of tablet was delayed and the granular size is getting smaller the disintegration time of tablet was become shorter.

5. Acid clay was the most excellent disintegrator among those studied in this paper. Even it is added until 25%, the hardness of tablet was harder than the others though the disintegration time was not much varied than the others.

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