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The efficiency of powdered corncob as a tablet disintegrating agent was compared to that of a number of wood products and to starch, the most popular agent used today. Corncob appeared to be superior in its disintegrating effectiveness.

The optimum particle size, at which powdered corncob produced its best disintegrating activity, was found to be about No. 40 mesh size U.S.P. The tablet disintegrating action of corncob and starch in tablets containing some partially or fully insoluble materials such as acetysalicylic acid, calcium carbonate, and sulfadiazine was tested. Corncob proved to be superior to starch in all these tests. The three layers of corncob were separated and tested individually for their tablet disintegrating action. The pith portion showed superior results over the other two layers. The possible role of starch and/or cellulose in the tablet disintegrating activity of corncob was examined. Cellulose and starch appeared to potentiate the disintegrating effectiveness of one another. The mechanism through which corncob is thought to produce its disintegration action was studied. It was concluded that corncob produced its effect through an "absorb moisture and swell" type of action.

A STUDY OF POWDERED CORNCOB AS A DISINTEGRATING AGENT IN COMPRESSED TABLETS

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TAGHI FAKOUHI

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APPROVED:

[redacted]

Professor of Pharmacy, School of Pharmacy

In Charge of Major

[redacted]

Dean of School of Pharmacy

[redacted]

Chairman of School Graduate Committee

[redacted]

Dean of Graduate School

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STATEMENT OF PROBLEM

Tablets are solid dosage forms made by compression in a tablet machine. The effectiveness of tablets is dependent, among other things, upon their rapid disintegration when they come into contact with gastric juice to release their active medicaments. In order to achieve rapid tablet disintegration, a substance called a disintegrating agent is added to the compressed tablet granulation.

The purpose of this paper is to investigate the effectiveness of powdered corncob as a tablet disintegrating agent.

A STUDY OF POWDERED CORNCOB AS A TABLET DISINTEGRATING AGENT IN COMPRESSED TABLETS

INTRODUCTION

Historical

The word "tablet", probably first used in 1608, was applied to a type of troche which contained sugar (23, p. 366). The term "compressed tablet" was originated by the Wyeth Brothers of the United States in 1877 (21, p. 938).

The invention of a tablet machine by William Brochedon of England in 1843 resulted in modern compressed tablets as we know them today (20, p. 822). Tablet machines have developed progressively since the invention by Brochedon. Today, electrically operated rotary machines are capable of producing thousands of tablets per hour.

Although compressed tablets date back to 1877 in the United States, it was not until 1916 that tablets were officially recognized by USP IX* (25, p. 56). The main reason for this delay of recognition was the inability of tablets to disintegrate in a desirable length of time. The use of starch as a tablet disintegrating agent by Charles Rilgere was the reason for the acceptance of tablets as a dosage form in the U.S.P. (20, p. 816). Today, over

* U.S.P.: Pharmacopeia of the United States, Ninth Revision.

two hundred tablets are recognized in the U.S.P. XVI and N.F. XI*, thus reflecting the increasing popularity of tablets as a dosage form (1, p. 1-531)(8, p. 1-1148).

Advantages and Disadvantages of Tablets

The extreme popularity of tablets indicates that they are practical, efficient and ideal dosage forms for administration of orally active therapeutic agents. The accuracy of dosage, ease of administration, elegance of appearance, ease of manufacturing, practicability and stability are the outstanding advantages of tablets (25, p. 63).

There are only minor disadvantages to this form of medication, the most frequent of which is the psychological difficulty encountered by some individuals in swallowing the tablets.

Ingredients in Tablets and Their Purposes

Compressed medicinal tablets are composed of two general types of ingredients: the medicament and the excipient. The medicament is the portion of the tablet with the therapeutic value for which the tablet is used. The excipient is an inert ingredient or ingredients that gives the tablet suitable form and consistency. It may be composed of one or a combination of the following: diluent, binder, disintegrator, lubricant, absorbent, coloring agent and flavoring agent.

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*N.F. XI: The National Formulary, Eleventh Addition, 1960.

Diluents are inert substances added to the active ingredients to increase the bulk of the tablet to a convenient size. Kaolin, lactose, sodium chloride, starch, sucrose, calcium carbonate and calcium phosphate are among the more commonly used diluents (25, p. 67).

Binders, sometimes known as adhesives, are intended to hold the tablet together. The most widely used binders, in order of decreasing adhesiveness, are: glucose, acacia mucilage, gelatin syrup, starch mucilage, water and alcohol (17, p. 94). According to Scoville, binders can be either powders or liquids, but they are considerably more effective when they are used in the liquid form (17, p. 94).

A disintegrator has been defined by Scoville as a substance or combination of substances used in a tablet to break them apart, upon contact with moisture, into small particles so that a prompt medicinal action is obtained (17, p. 95). Tablet disintegrating agents will be more thoroughly discussed later in the text of this paper.

Lubricants, another class of excipients, fulfill two purposes when added to tablet granulations. They improve the flow properties of the granules and keep the granules from adhering to the surfaces of the punches and dies of the tablet machine (15, p. 61). The following are examples of lubricating agents: magnesium stearate, starch, calcium stearate, sodium chloride, boric acid (powder), paraffin waxes and cocoa butter (25, p. 68)(23, p. 375).

Studies on the application of lubricants indicate that they have an optimum action when used in the form of a fine powder or spray to coat the outer surface of the tablet granulation (35, p. 410).

Absorbents are inert substances incorporated to absorb liquid medications such as tinctures, fluid extracts and oils. The most commonly used absorbing agents are lactose, starch and magnesium carbonate (21, p. 938).

Colors and flavors are often used to give a desirable color or impart a desirable taste to the tablets. By increasing the aesthetic value of the tablet, these agents may have an important psychological effect on some patients (25, p. 64). Furthermore, characteristic colors are helpful in tablet identification.

TABLET DISINTEGRATION

Tablet Disintegrating Agents

As previously defined, tablet disintegrators are substances or mixtures of substances added to tablets to cause them to break apart after administration. There are three known methods responsible for tablet disintegration. These are: (a) the addition of a peroxide, such as sodium carbonate peroxide, that will react with the medium forming oxygen and thus breaking the tablet; (b) the addition of small amounts of acids and carbonates or bicarbonates, such as calcium carbonate with citric acid, which, when wetted, will produce carbon dioxide upon reaction and disintegrate the tablet; and (c) the inclusion of a gum or carbohydrate, such as gum tragacanth or starch, that will absorb water and swell (14, p. 157). The mechanism of action of the "absorb moisture and swell" type of disintegrating agents is by absorption and swelling when in contact with water, thus resulting in the rupturing of the tablets in which they are incorporated (9, p. 520). However, this popular belief is of doubtful validity. In fact, the action appears to be mainly capillary penetration of water into the tablets (11, p. 16)(22, p. 443).

Most common disintegrating agents are of the "absorb moisture and swell" type (9, p. 520). A list of these agents should begin with starch, one of the most popular tablet disintegrating agents from its first use in 1887. Even today, starch is considered the best disintegrating agent and is the one agent most commonly used by tablet manufacturers (17, p. 95). Some of the other agents in this group are bentonite, agar, alginic acid, pectin, gelatin, methylcellulose, Veegum HV®, and the new disintegrating agents, powdered orange pulp and powdered sponge. These new additions to the disintegrator family have shown outstanding results and are spoken of very favorably in the literature (18, p. 350)(10, p. 364).

Dried citrus pulp is prepared by washing off the natural waste products from concentrated juice until all the soluble material is removed. The pulp is dried and passed through a sieve until reduced to powdered form (18, p. 350). Preparation of powdered sponge involves, first, the washing of the sponge to dispose of the foreign matter, followed by drying and grinding the sponge to a suitable particle size (10, p. 363). Gross and Becker have compared dried sponge and citrus pulp with twenty-two disintegrating agents (14, p. 158). They found that these agents compare favorably with currently used disintegrating agents. The powdered sponge is reported to be the better of the two agents (14, p. 160).

Factors Affecting Tablet Disintegration

Disintegration time is a function of many factors -- hardness of tablets, weight of the tablets, method of granulation of the powders, size of granules, method of manufacturing and humidity.

Hardness is one of the most important variables to be considered. (18, p. 350)(2, p. 505). According to most authorities, the tablet should be hard enough to reach its destination in as good a condition as when it is made (17, p. 85)(7, p. 637).

Tablet weight is a second variable to consider. Preliminary work by the author indicated that a direct relationship exists between tablet disintegration and weight of the tablet being tested. For instance, two groups of tablets with identical active constituents, hardness and disintegrating agents were compared for disintegration times. The only variable was that one group of tablets was heavier than the other, resulting in a considerably longer time required for the disintegration of the heavier tablets.

The particle size of the granulated material is another important factor influencing the relative hardness of the tablets, and, indirectly, the tablet disintegration time. Preliminary studies indicated that tablets with too many large granules tended to be too soft and frequently broke down during the processes of handling, shipping and storage. Tablets with excessive amounts of fine granules tended to be too hard and to have longer disintegration time. According to Silver and Clarkson, 10-20% fine particles (No. 60 mesh size U.S.P. and smaller), and 80-90% granules (No. 14 mesh size U.S.P. and smaller), will produce uniform tablets in weight and hardness, yet maintain a smooth appearance (30, p. 4). They considered this to be due to consistency in the filling of spaces between granules by the fine particles.

Particle size is critically important in relation to tablet disintegrating agents. It is generally assumed that there is an optimum particle size for each disintegrating agent. Optimum particle size for powdered sponge and dried citric pulp is reported to be No. 40 mesh size U.S.P. (18, p. 383).

The characteristics of the particular tablet machine constitute still another variable to be considered in the manufacturing of tablets. Burlinson states that tablet disintegration time is a function of the degree and speed of compression (7, p. 637). According to Moskalyk et al, a source of difficulty during manufacturing of tablets is the setting of the machine, and, consequently, the irregular filling of the dies due to lack of uniform free-flowing granulation (27, p. 651). Raff considers some manufacturing difficulties to be caused by incomplete filling of the dies due to internal flow, thus resulting in a separation of particles in the hopper (29, p. 290). This, in turn, leads to a lack of "fines" in the later stages of tablet compression.

After tablets are produced, the only significant variable is aging. Burlinson and Pickering studied the effects of aging on tablet disintegration rate and moisture content over a period of four years (7, p. 634). They found that the changes in disintegration time were not very significant and were probably due to changes in the moisture content. Other investigators have found that aging, as a rule, has little or no effect on hardening or disintegration time if the tablets are properly formulated (9, p. 554)(19, p. 451).

EXPERIMENTAL

Billups and Cooper introduced wood flour and powdered wood bark as possible tablet disintegrating agents (4, p. 280). In an attempt to continue their work, the present research was originally directed toward testing a large number of wood products for their tablet disintegrating effects. It was found during this part of the research that powdered corncob, one of the agents included in the preliminary study, produced significantly more rapid tablet disintegration. Since an extensive study of each of these agents was not possible, research was then devoted to powdered corncob.

The research was divided into two parts: comparative disintegration tests of wood products and other tablet disintegrating agents, and studies of powdered corncob as a disintegrating agent.

A Comparative Study of Wood Products as Tablet Disintegrating Agents

All drugs and chemicals used in this study were of U.S.P. or N.F. quality (1, p. 1-531)(8, p. 1-1148). All sieves and mesh numbers conformed to the U.S.P. equivalent series (8, p. 932).

The first factor to be considered was the proper selection of disintegrating agents. This selection was based on the possible effectiveness of these agents, availability and cost.

Powdered corncob was chosen because of its availability and low cost. Powdered corncob is considered a waste product of corn. It is used only in small quantities to feed cattle, fertilize land and act as a fuel in remote farming areas (32, p. 9). The corncob used in this study was obtained through the courtesy of the Department of Farm Crops, Oregon State University. Both field corncob and popcorncob were used in the preliminary tests and, since there was an indication that field corncob was slightly better as a disintegrating agent than popcorncob, and because this agent was readily available, it was used throughout this study.

Lactose, a substance with no apparent tablet disintegrating property, was used as a control. Lactose is regarded as a good diluent or inert base for many tablet preparations (14, p. 158). Therefore, it was used in tablets as a diluent throughout this work, unless otherwise specified.

Starch was chosen because it is used extensively in the tablet industry. Many authorities still consider this classical agent as the best tablet disintegrating agent in use today (17, p. 95)(26, p. 376). Since there is no significant difference in tablet disintegration time between varieties of starch (corn, potato, etc.), cornstarch was the variety used in this study because of its availability (7, p. 632).

Powdered Redwood bark was the next agent used. This agent is the powdered bark of a coniferous timber tree (Sequoia sempervirens) of California, found only on the Coast Range (33, p. 2810).

Powdered Douglas fir bark was another substance included for evaluation of its tablet disintegrating properties. Commercial samples of powdered Douglas fir bark, Silvacon® 383G, 495, and 515, supplied by The Silvatek Products Division of the Weyerhauser Timber Company of Longview, Washington, were used in this study. According to the 1958 annual report of the Weyerhauser Company, the three basic types of Silvacon® are pliable, spongy flakes, tough needle-like fibers and fine amorphous powders (34, p. 2).

Billups and Cooper used only one type of Silvacon®, (383G), in their study (4, p. 280). All three forms of Silvacon® were used in this research.

Methylcellulose, a methyl ether of cellulose, was included for comparison with the rest of the wood products (8, p. 431). It is interesting to note that methylcellulose has been extensively used in many research projects concerning tablet disintegration and has always given unfavorable results (4, p. 32)(14, p. 159).

Wood flour was used in this study to compare with the other wood products. This agent has been reported to be highly hydrophilic, and is classified as an "absorb moisture and swell" type of tablet disintegrating agent (4, p. 280). Wood flour is powdered inner wood from Douglas fir (Pseudotsuga taxifolia), a tall evergreen tree of the western United States, often known in the lumber trade as red fir or Oregon pine (33, p. 777). It was obtained through the courtesy of the Forest Products Research Laboratories in Corvallis, Oregon.

Method of Manufacturing of the Tablets

Basically, there are three methods for manufacturing compressed tablets. These methods are direct compression, dry granulation and wet granulation (25, p. 69).

Direct compression is the term applied to the process of manufacturing compressed tablets with little or no preliminary treatment (e. g. lubrication) needed before feeding the material into the tablet machine (25, p. 69). Ammonium chloride, sodium chloride, sodium bromide and sodium bicarbonate are examples of this group of materials. Husa has indicated that most of these materials are self-lubricating (9, p. 70).

The dry granulation or slugging process is the second method of manufacturing of compressed tablets. This method is carried out in two steps. First, the fine powders are precompressed into "slugs" or large tablets, in a heavy-duty tablet machine. The "slugs" are then reduced to proper granule size with a Fitzmill

Comminuting Machine or other suitable device. These granules are then ready for compression in the tablet machine (9, p. 72).

The third and most widely used method of manufacturing compressed tablets is the process of wet granulation (25, p. 70). In this process the fine powders are converted into granule form by special treatment. A detailed discussion of this process will be given, since this method was used to manufacture all the tablets in this research. Twenty-five pounds of lactose, the diluent, was placed in a large container and, with constant stirring, Syrup U.S.P. XVI was added until a gummy mass was produced. This mass was broken down into small particles and spread out on trays in an air oven at 45° C. for 48 hours to dry. The granulation was then passed through a No. 60 sieve to separate the fine particles from the granules. The fine particles, designated as fines, consist of particles of mesh size No. 60 and smaller. The granules were retained in the sieve. The ratio of fines to granules is selected by some authors as 10-20% fines and 80-90% granules (30, p. 40). However, in this study, quantities of disintegrating agents as high as 25% were used and since disintegrating agents are considered as fines, a 30% fine and 70% granule ratio was used. Prior to mixing fines and granules, the disintegrating agents and lubricating agents were added to the fines. The lubricating agent in this study was 1% magnesium stearate. The granules and mixture of fines were then carefully mixed together. This was done by spreading the granules and fines over a large sheet of paper and mixing intimately with the use of a spatula and a wooden paddle. The uniformly mixed granulation was kept in an oven at 40° C. for 24 hours to reduce the moisture content of the preparation. Following this period, the material was immediately fed into a Stokes Model B-2 rotary tablet machine. Since random sampling of a large number of commercial tablets showed that 500 mg. is a convenient and commonly used tablet weight, all the tablets in this research were kept constant at 500 mg. The prepared tablets were tested for weight variation with an Exact Weight Shadow-graph (The Exact Weight Scale Co., Columbus, Ohio). An Exact Weight Shadow-graph is a highly sensitive instrument and average weight variation of tablets was kept well within the ± 5% limit allowed by U.S.P. XVI (8, p. 942).

A Strong Cobb (Strong Cobb Co., Inc., Cleveland, Ohio) tablet hardness tester was employed to determine the average hardness for each tablet. Whenever possible, the tablet machine was adjusted to fixed pressure to produce tablet hardnesses of 7 and 10 Strong Cobb units*. Most commercial tablets are manufactured and marketed

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*A Strong Cobb unit is an arbitrary unit which is approximately equal to a pressure of 1.6 kg. exerted against the tablets (7, p. 85) at a hardness of 6-7 Strong Cobb units. However, if a hardness of 6-7 is used, some tablets tend to become too soft, resulting in much variation among disintegration times. Using a hardness of 10 Strong Cobb units would tend to create tablets with more uniformity in hardness and less variation among disintegration times.

Tablet Disintegration Test

The purpose of a tablet disintegration test is to ensure the breakup of a tablet. Apparatus and methods used in disintegration tests have been discussed by many workers (12, p. 1070)(31, p. 73)(5, p. 492)(3, p. 251).

The official disintegrating test apparatus specified in the U.S.P. XVI consists of a basket-rack assembly, a suitable vessel for the immersion fluid, a thermostatic arrangement for heating the fluid between 35° and 39° C. and a device for raising and lowering the basket in the immersion fluid at a constant frequency of 28 to 32 cycles per minute through a distance of not less than 5 and not more than 6 cm. The U.S.P. further specifies that the volume of the fluid in the vessel is such that at the highest point of upward stroke the wire mesh remains at least 2.5 cm. below the surface of the water and descends to not less than 2.5 cm. from the bottom of the vessel on the downward stroke (8, p. 934).

The basket-rack assembly consists of 6 open-ended glass tubes, each 7.75 to 25 cm. long and having an inside diameter of 21.5 mm. The tubes are held in vertical position by two plastic plates. A No. 10 mesh size U.S.P. screen is screwed to the lower plate.

O'Brien, Pacenti and Duescher have suggested the use of small clear plastic disks designed to ride above the tablets, as a means of improving the results obtained in the official disintegration test for tablets (28, p. 126). According to these authors, by using the aforementioned plastic disks, the falsely prolonged disintegration times due to soft gummy residues are eliminated.

A Gershberg-Stoll type disintegration apparatus, which complies with all the specifications set forth by U.S.P. XVI, was used in this research (8, p. 934). However, the plastic disks required by the U.S.P. XVI, were only applied when there was specific need for their use. Distilled water was compared with simulated gastric juice* and since there was no significant difference in disintegration times produced by the two media, distilled water was used as the disintegrating solution (16, p. 284).

*Simulated gastric juice (fluid): A combination of sodium chloride and pepsin in hydrochloric acid and distilled water (8, p. 1072).

All batches of compressed tablets were tested according to the official tablet disintegration tests in U.S.P. XVI after manufacturing. The results of these tests are reported in Table I and figure 1. As may be seen from the data, there is considerable variation in disintegration time among the various agents. Powdered corncob has the shortest disintegration time of all the agents tested.

Corncob as a Tablet Disintegrating Agent

The second phase of this study concerned the disintegrating action of powdered corncob. However, before any extensive investigation of powdered corncob could be undertaken, the results of the previous disintegration tests on tablets containing powdered corncob had to be confirmed. Accordingly, a second lactose granulation was prepared, using powdered corncob as the tablet disintegrating agent, in order to test the reproducibility of the first test. Five batches of tablets containing 5, 7.5, 10, 15 and 20 per cent powdered corncob disintegrating agent were manufactured in the same manner as those prepared earlier and were subjected to the U.S.P. tablet disintegration test (8, p. 934). The results of these tests are reported in Table II. A comparison of these results to those of earlier tests is shown in Table III and figure 2. Starch and lactose are included in the comparison to

TABLE I

A COMPARATIVE STUDY OF SELECTED TABLET DISINTEGRATING AGENTS

Tablet disintegrating agent	Appearance of tablets	Comments on the manufacturing of tablets	Disintegration Time (Ave. in secs. for 12 tablets) Per cent disintegrating agent 5	10	25
Corncob (Powdered)	tan, grainy	tablets good. No difficulty in mfg.	339	100	115
Lactose (Control)	white	tablets good. No difficulty in mfg.	1195	1195	1195
Methylcellulose	white	tablets good. Glossy appearance	962	1622	4500
Redwood bark	red	tablets good, but excessive pressure nec. for smooth tab.	493	475	682
Silvacon® 383G	brown	tablets good. Slightly soft at 25% dis. agt.	1073	1397	4554
Silvacon® 495	brown	excessive pressure nec. to manufacture tablet	702	998	1609
Silvacon® 515	brown	tablets fair, but excessive pressure nec. for tab. mfg.	949	1187	2550
Starch (Corn)	white	tablets good	613	495	305
Wood flour	tan	tablets with 25% disintegrating agt. too soft	1203	890	---

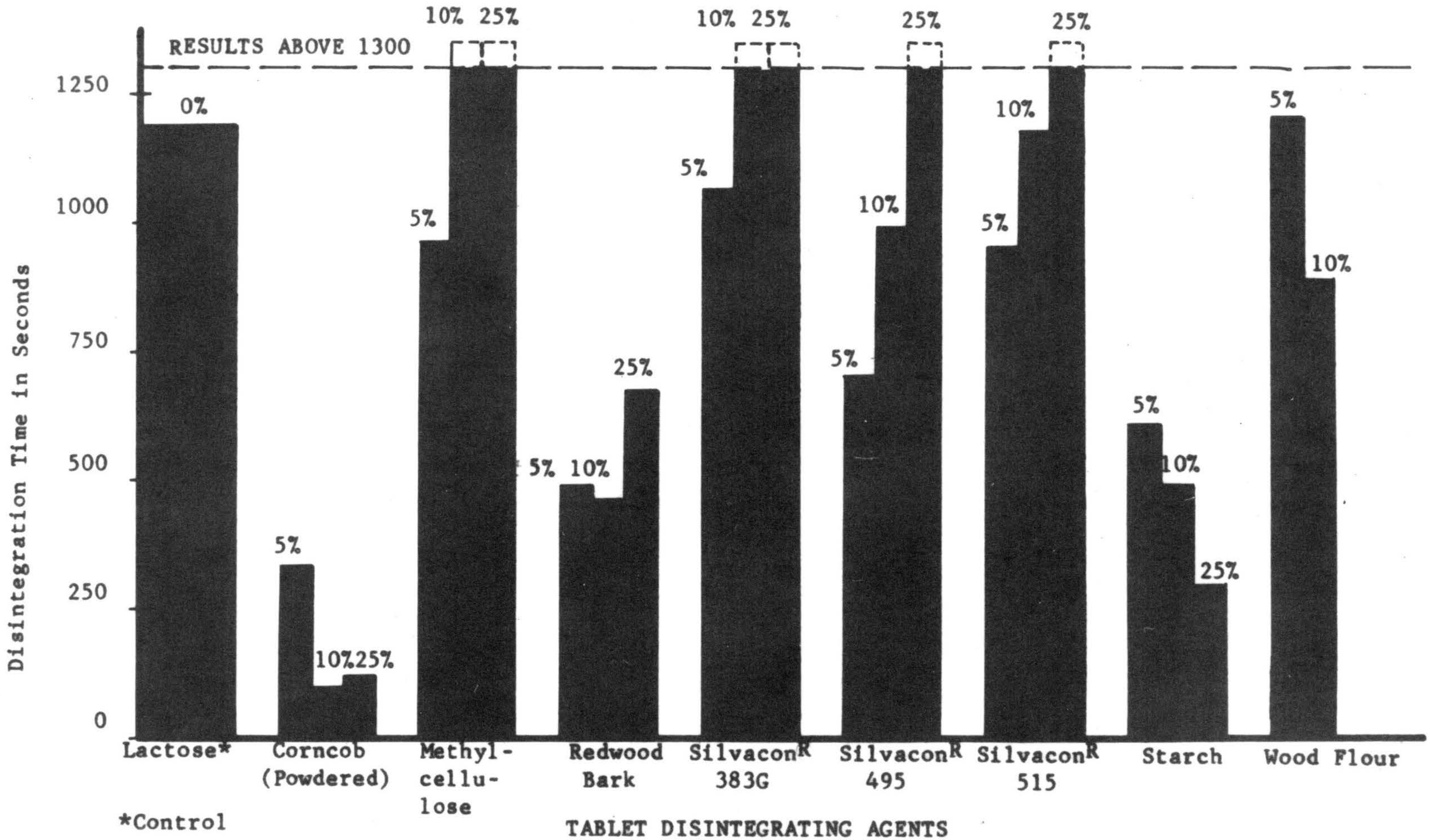

Figure 1. Disintegration Times of Tablets Containing Various Disintegrating Agents.

TABLE II

DISINTEGRATING ACTION OF POWDERED CORNCOB (TEST TWO) IN LACTOSE TABLETS

Powdered Corncob %	Disintegration Time (Ave. 12 tabs. in secs.) Hardness 10
5	350
7.5	223
10	135
12.5	285
15	428
20	541

TABLE III

COMPARISON OF POWDERED CORNCOB (VALUES FOR TWO INDEPENDENT TESTS) AND STARCH AS DISINTEGRATING AGENTS IN LACTOSE TABLETS

	Disintegration Time (Ave. 12 tabs. in secs.) Hardness 10			
Per cent Disintegrant Used	Powdered Corncob Test 1	Powdered Corncob Test 2	Starch	Lactose*
5	339	350	613	>1000
7.5	210	223	512	>1000
10	100	135	495	>1000
12.5	249	285	311	>1000
15	413	428	270	>1000
20	522	541	338	>1000

*Control

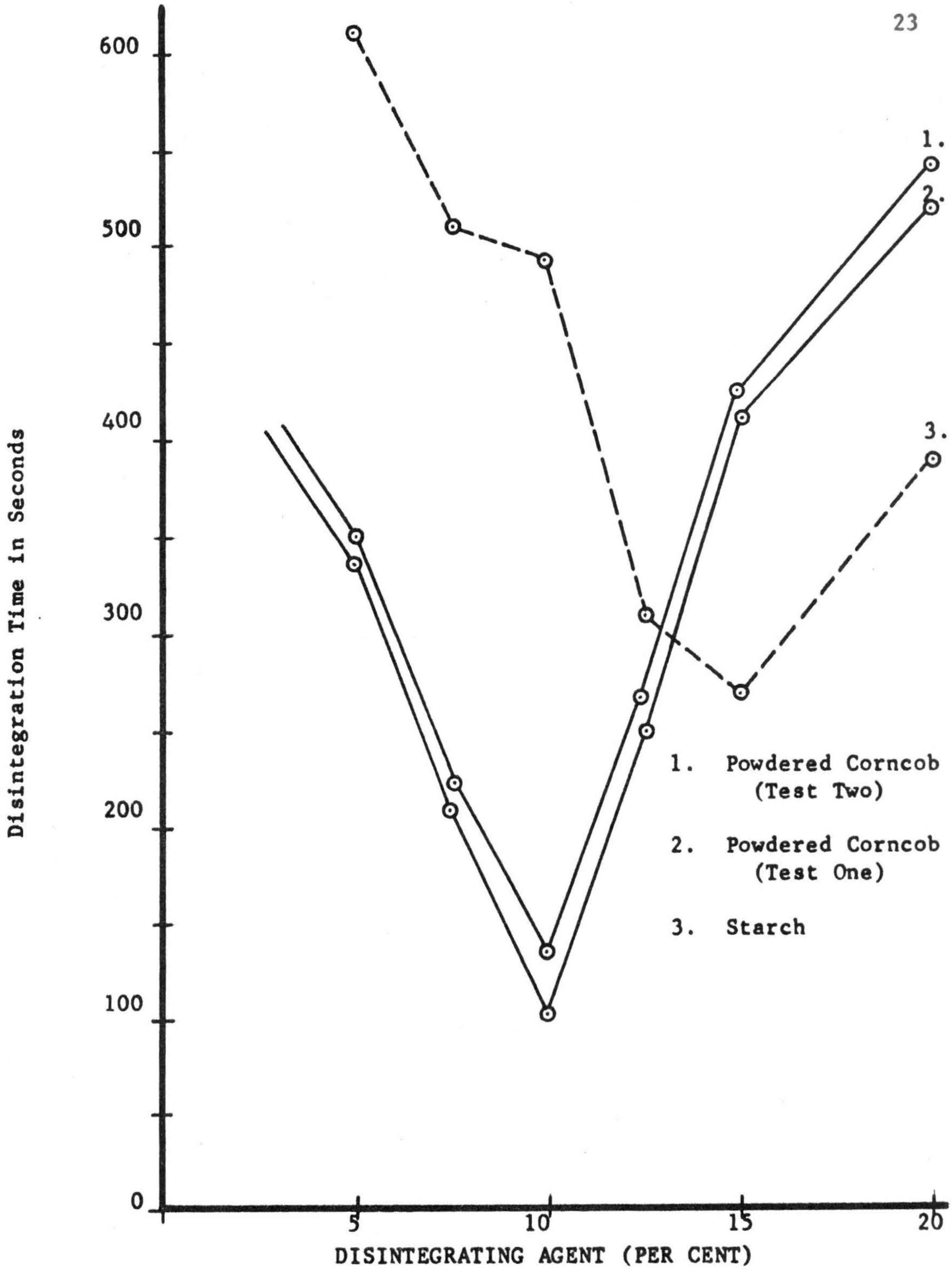

Figure 2. Comparison of Corncob and Starch as Disintegrating Agents in Lactose Tablets.

indicate the efficiency of powdered corncob as a tablet disintegrating agent. From these data, no significant difference was indicated between the two tests employing powdered corncob but significant differences were noted between powdered corncob and lactose and starch. Thus, it was concluded that reproducible results could be obtained with powdered corncob as a tablet disintegrating agent.

Once the reproducibility of the tests had been established, a series of tests was conducted to determine the physical characteristics of the powdered corncob which would produce the optimum results when incorporated into tablets. The importance of proper particle size cannot be overly stressed and it was this physical property that was first to be determined. According to Forlano and Chavkin every agent has an optimum particle size at which it produces its best effect as a disintegrating agent (13, p. 69). Since powdered corncob is a new agent in tablet studies, it was essential to find its optimum particle size. Up to this point in the research, No. 40 mesh size U.S.P. particle size had been used. This particle size was arbitrarily chosen since this is the particle size most commonly used for tablet disintegrating agents of the "absorb moisture and swell" type. Although No. 40 mesh size U.S.P. is thought to be the most effective particle size, it was necessary to confirm this fact. This was accomplished using lactose granulation with 10% powdered corncob in Nos. 60, 40, 20 and 14 mesh sizes U.S.P. Each one of the four particle sizes was incorporated into tablets. All these tablets were readily compressed except the No. 14 mesh size U.S.P. The tablets in this latter batch were too soft due to the large particle size of the powdered corncob and were easily broken before they could be subjected to the disintegrating test. Results of these tests are reported in Table IV. It could be seen from the data of Table IV that No. 40 mesh size U.S.P. produced the most outstanding results. For this reason, No. 40 mesh size U.S.P. was used throughout the remainder of this research.

The second test was undertaken to check the variability of different varieties of corncob as disintegrating agents. Powdered field corncob and powdered popcorncob were the varieties used for this study. Using No. 40 mesh size U.S.P., both varieties were included in tablet formulations as tablet disintegrating agents. The tablets were subjected to the U.S.P. tablet disintegration tests. The results of these tests are reported in Table V. Although the results are by no means conclusive, it may be seen that field corncob is slightly superior to popcorncob. For this reason, and because of the availability of field corncob, it was chosen as the variety used in further tests.

TABLE IV

EFFECT OF PARTICLE SIZE OF POWDERED CORNCOB
ON TABLET DISINTEGRATION TIME

Particle size (USP mesh No.)	Time required to disintegrate (Ave. in secs. for 12 tablets)
No. 60	410
No. 40	95
No. 20	530
No. 14*	---

* Difficulties encountered in manufacture of tablets.

TABLE V

DISINTEGRATION ACTIVITY OF POPCORNCOB VS. FIELD CORNCOB

Per cent disintegrant used	Time required to disintegrate (Ave. in secs. for 12 tablets)	
	Popcorncob	Field corncob
5 per cent	396	345
10 per cent	228	117
25 per cent	295	235

The effects of tablet hardness and tablet disintegration medium (water or gastric juice) on the tablet disintegration times were also determined. These tests, similar to those reported in the literature by Burlinson and Pickering (7, p. 634) for other agents, indicated that tablet hardness is directly proportional to tablet disintegrating time of powdered corncob. Preliminary experiments indicated that comparable results were obtained for distilled water and artificial gastric juice when used as disintegration media for tablets containing powdered corncob. Therefore, distilled water was used as the disintegration medium throughout the remainder of this work.

<u>Disintegrating Effects of Powdered Corncob in Tablets Containing Various Active Constituents</u>

Thus far, powdered corncob had shown favorable results when used as a disintegrating agent. Although these results have appeared significant in lactose tablets, it remained to be determined if the same results would be obtained in tablets containing active ingredients. Because lactose is water soluble, it can affect the disintegration time of the tablets in which it is incorporated. A solution to this problem would be to use powdered corncob with active constituents which are partially or completely insoluble in the disintegration medium. Three such agents --

acetysalicylic acid, calcium carbonate and sulfadiazine were chosen. Lactose was used as the control. Three batches of each active constituent were used. Ten per cent powdered corncob, 10% starch, and 10% lactose, respectively, were incorporated into the three active constituents. The methods for granulation of acetylsalicylic acid, calcium carbonate and sulfadiazine powders and manufacturing of the granulation into finished tablets were conducted in the manners as those outlined earlier in this paper. All tablets were subjected to U.S.P. tablet disintegration tests immediately following manufacturing. The results of these tests are reported in Table VI and figure 3. From these data, powdered corncob appeared to be superior to starch, the classical disintegrating agent, in all tablets tested.

Disintegrating Effects of Different Parts of Corncob: Chaff, Middle Section and Pith

The physical appearance of corncob reveals that it is composed of three distinctive parts: the inner area or pith, the middle section -- the woody substance, and the outer layer or the chaff. Burke, after separating the three layers of corncob, analyzed each layer both quantitatively and qualitatively (6, p. 5). His findings indicated that the two major constituents of corncob are starch and cellulose. Although each of the three sections of

TABLE VI

COMPARISON OF POWDERED CORNCOB AND STARCH AS DISINTEGRATING AGENTS IN TABLETS CONTAINING ACETYLSALICYLIC ACID, CALCIUM CARBONATE OR SULFADIAZINE

Active Medicament	Disintegration Time (Ave. 12 tabs in secs.). Tablet hardness 6.5 Strong Cobb units			Disintegration Time (Ave. 12 tabs in secs.). Tablet hardness 10 Strong Cobb units		
	Cornstarch	Corncob (Powdered)	Lactose (control)	Cornstarch	Corncob (Powdered)	Lactose (control)
Acetylsalicylic Acid	600	406	>7200	3600	1560	>7200
Calcium Carbonate	1800	420	>7200	>7200	1200	>7200
Sulfadiazine	2500	410	>7200	6000	1680	>7200
Lactose*	300	95	1000	117	495	1195

*Control

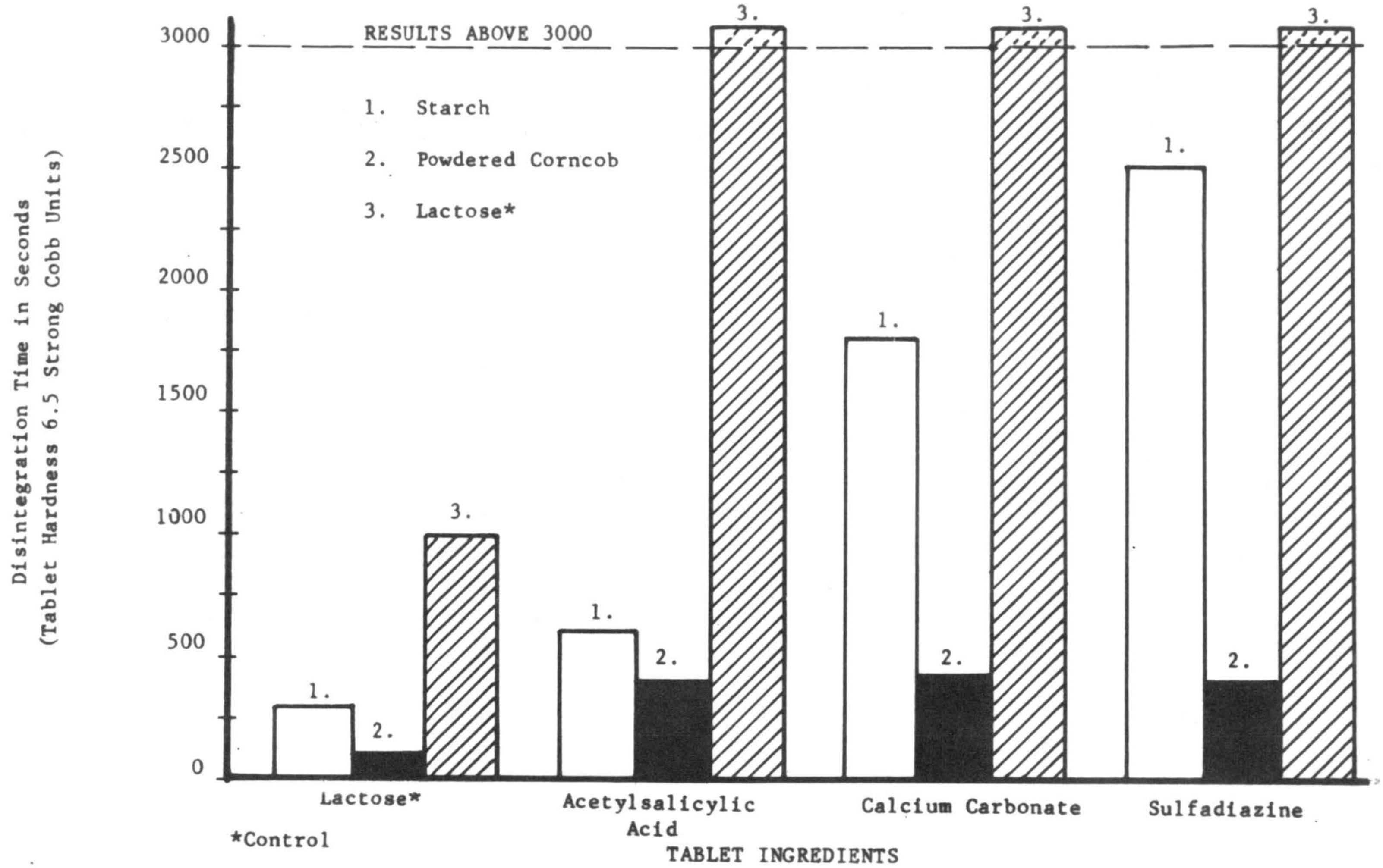

Figure 3. Comparison of Corncob and Starch as Disintegrating Agents in Tablets Containing Acetylsalicylic Acid, Calcium Carbonate or Sulfadiazine.

corncob (chaff, woody substance and pith) contain cellulose and starch, there is a variation in the quantity of these two ingredients in each part (See Tables VII, VIII). Starch and/or cellulose may be responsible for the effectiveness of corncob as a tablet disintegrating agent. Thus, a quantitative variation of starch and/or cellulose in different parts of the corncobs may result in different disintegrating times when these parts are incorporated independently into tablets instead of the whole powdered corncob. Accordingly, each of the three parts of corncob was separated by physical means. The chaff was scraped off with a grater, the pith was bored out by an electric drill, and the remainder of the corncob was ground in a Wiley Mill (A B B E Engineering Co., New York, N. Y.) to be used as the woody substance. Each of the separated parts was ground to a fine powder and passed through a No. 40 mesh size U.S.P. sieve. The fine powders were then incorporated into lactose granulations and manufactured into finished tablets. The finished tablets were subjected to tablet hardness and U.S.P. tablet disintegration tests, the results of which are reported in Table IX. As can be seen from the data in Table IX, there are pronounced differences among the tablet disintegration times. The three parts of corncob in order of decreasing disintegrating action are pith,

TABLE VII

CELLULOSE CONTENT OF CORNCOB AND PARTS*

	As Analyzed %	Moisture Free %
Entire Corncob+	25.12	26.37
Chaff	26.39	28.28
Woody part	25.89	27.30
Pith	33.45	35.85

TABLE VIII

STARCH CONTENT OF CORNCOB AND PARTS*

	Sugar as Dextrose gms	Calc. to Starch %
Entire Corncob+	0.3794	34.15
Chaff	0.3868	34.80
Woody part	0.3828	34.45
Pith	0.3366	30.29

+ The entire corncob is composed of:

	Ave. %
Chaff	24.97
Woody part	73.36
Pith	1.67
	100.00

*Burke, George W. Some analytical data on corncob. (6, p. 3)

TABLE IX

TABLET DISINTEGRATING ACTIVITY OF CORNCOB AND ITS PARTS

Part(s) Used	Disintegration Time (Ave. 12 tabs. in secs.) Hardness 6.5 Strong Cobb units	Hardness 10 Strong Cobb units
Entire Corncob	95	145
Chaff	291	577
Wood part	56	248
Pith	10	87

TABLE X

TABLET DISINTEGRATION STUDY OF CELLULOSE VS. STARCH

Disintegrant	Disintegration Time (Ave. 12 tabs. in secs.) Hardness 6.5 Strong Cobb units	Hardness 10 Strong Cobb units
Cellulose	123	245
Cornstarch	300	495
1:1 Parts of Cellulose + starch	86	110

wood-like middle section and chaff. These results raised the question as to whether the disintegrating action of powdered corncob, or its parts, were due solely to the activity of its starch content. It was evident that cellulose must have had an active part, since the pith, with the lowest starch content and the highest cellulose content of all parts, showed the best tablet disintegration time by a large margin.

<u>The Role of Cellulose* in the Disintegrating Activity of Powdered Corncob</u>

Cellulose has not been reported as a disintegrating agent. However, the results of the previous tests have led to the belief that this agent is partially or fully responsible for the disintegrating activity of corncob. In order to clarify this further, three batches of lactose tablets containing cellulose, starch and a combination of cellulose and starch were manufactured. Ten per cent starch and 10% cellulose, respectively, were added to the first two batches. In the third batch, a 10% mixture of equal parts of cellulose and starch was incorporated. All tablets were manufactured according to the procedure outlined earlier in this report and were immediately subjected to the U.S.P. tablet disintegration test. The results are reported in Table X, and indicate

*Cellulose was obtained from Stanley Drug Products, Inc., Portland, Oregon. This product is marketed as Stanocel®.

that cellulose has better disintegrating action than starch. The combination of equal parts of cornstarch and cellulose, in turn, is superior to either one of the separate agents. This may indicate that starch and cellulose, in addition to serving as disintegrants *per se*, exhibit a potentiating effect on the disintegrating action of each other. Crisafi and Becker noticed the same potentiating effect of starch on the disintegrating action of powdered sponge (10, p. 365). The potentiating effect of cellulose and starch could be a reasonable explanation for the improved tablet disintegrating activity of powdered corncob.

Mechanism of Disintegrating Action of Powdered Corncob

The mechanism through which powdered corncob, starch, or cellulose accomplish their disintegrating action is most likely the same. These agents swell when in contact with water and as a result are capable of rupturing tablets in which they are incorporated. Since absorption is an important factor in this action, tests were conducted on powdered corncob, starch, cellulose, a combination of equal parts of starch and cellulose, and lactose (control) to determine the comparative absorptive qualities of these agents. One-gram samples of the materials were first dried to constant weight at 120° C. and then placed in a humidity chamber for a

TABLE XI

ABSORPTIVE PROPERTIES OF VARIOUS DISINTEGRATING AGENTS

Relative Humidity %	Moisture absorbed by selected agents after 24 hours				
	Cellulose %	Corncob (Powdered) %	Starch %	1:1 Cellulose & Starch %	Lactose* %
50	3.7	5.8	6.5	5.2	3.1
60	3.9	6.8	6.9	6.2	3.2
70	6.6	10.8	9.6	9.2	4.4
80	7.8	13.6	13.4	11.3	4.7
90	10.2	19.5	19.3	16.5	6.1
98	17.5	51.3	47.2	38.8	6.6

*Control

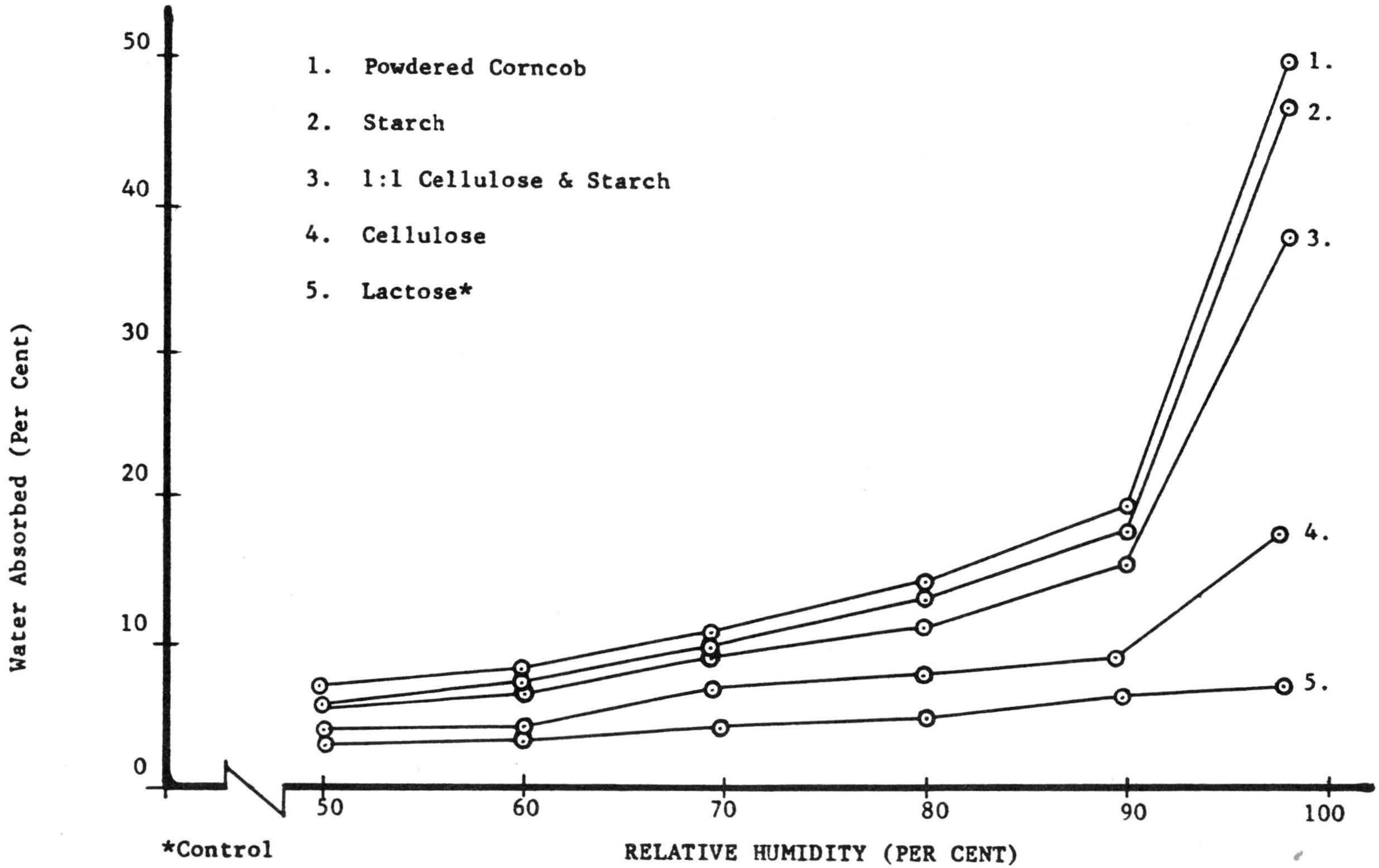

Figure 4. Absorptive Properties of Various Disintegrating Agents

twenty-four hour period. A Vapor-Temp (BLUE M Electric Co., Blue Island, Ill.) humidity chamber was used. The weight gain was calculated by reweighing each sample after the twenty-four hour interval. Results of these tests are reported in Table XI and figure 4. The weight gain is recorded in Table XI as per cent of sample weight. These results indicated that a slight negative correlation existed between water absorption and tablet disintegration time. Generally, the disintegrating agents which absorbed the most water were those which, when incorporated into tablets, required the shortest times for tablet disintegration.

SUMMARY AND CONCLUSION

The purpose of this paper was to investigate the tablet disintegrating activity of powdered corncob. The research program was divided into two parts, first, a comparative study of a number of wood products including corncob and, second, a number of more specific tests concerning physical properties related to tablet disintegrating action of the powdered corncob. The results of the first part of the research indicated that powdered corncob was superior to starch, one of the best disintegrating agents to date, and to other wood products as well. The results of the disintegrating action of powdered corncob proved to be reproducible.

The optimum particle size, at which powdered corncob produced the highest disintegrating activity, was about No. 40 mesh size U.S.P. This correlates with the optimum particle size of other new disintegrating agents such as powdered sponge and powdered orange pulps.

Two varities of corncob, field corncob and popcorncob, were tested. The results indicate that field corncob is slightly superior to popcorncob as a tablet disintegrating agent.

Disintegrating action of powdered corncob was tested in both partially and completely insoluble material -- acetylsalicylic acid, calcium carbonate and sulfadiazine. Powdered corncob produced superior results over starch as a tablet disintegrating agent in tablets containing all three above mentioned materials.

The three physically distinctive layers of corncob -- chaff, woody substance, and pith -- were separated and incorporated in lactose tablets as disintegrating agents. Significant differences were seen among the disintegration times produced by the three layers of corncob. The pith showed superiority over the other two parts.

Starch and cellulose are the two main constituents of corncob. A series of tests was conducted to study the separate and combination effect of these agents on the disintegration of tablets. The combination of cellulose and starch indicated better results than the separate action of either agent alone.

The mechanism through which powdered corncob, starch and cellulose accomplish their disintegrating actions is most likely the same. These agents swell when in contact with water and will rupture the tablets in which they are incorporated. Because absorption is a major factor in this action, tests were conducted on the comparative water absorption rate of these agents. A slight negative correlation existed between water absorption and tablet disintegration time. Thus, the disintegrating agents which absorbed the most water were in general those which, when incorporated into tablets, required the shortest times for tablet disintegration.

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