This differentiated the spots *E* and *F* due to bimolecular anthranols from the spots *D* and *H(1)* due to monomolecular anthraquinones. Hence it was clear that while benzene concentrate *G* contained chrysophanol, the spot *H(1)* most probably was due to rhein; the spot *H(2)*, however, did not correspond to any of the aglycones chromatographed.

Chromatography with a second solvent system: lower phase of water:acetone:benzene (2:1:4) gave the following R_f values: chrysophanol, 0.00; rhein, 0.74; benzene solution, 0.00; alcohol solution, (*1*) 0.74, (*2*) 0.89; *C* + *G*, 0.00; *D* + *H*, (*1*) 0.74 and (*2*) 0.89. All the spots were colored pink with 1 *N* sodium hydroxide.

In the above paragraph *H(1)* is evidently due to rhein as indicated by R_f values of rhein and *D* + *H* (*1*). Similarly, comparison of chrysophanol, benzene solution, and *C* + *G* indicated that the second aglycone was chrysophanol.

Identification of Sugars

The aqueous acidic layer (mentioned in *Identification of the New Aglycones*) was cooled, neutralized with sodium hydroxide pellets, and concentrated to dryness using high vacuum. The 1:3 filtered aqueous pyridine extract of the residue was used for spotting on Whatman No. 1 paper. For comparison, a glucose solution and a mixture of the two were spotted simultaneously.

The chromatograms were developed with *n*-butanol:glacial acetic acid:water (4:1:5), by radial chromatographic techniques, and sprayed with Partridge's reagent (5). The average of four R_f values were found to be—glucose, 0.32; aldose from the acid precipitate, 0.30; and a mixture of glucose and the aldose, 0.33. This clearly indicated that the sugar of the glycosides present in the acid precipitate was glucose.

DISCUSSION

In this study the drug was extracted with water instead of alcohol. This not only made the process more economical, but also permitted better separation of the acid precipitate. Since the glucosides present in the drug were thermolabile, all concentrations by heat even under reduced pressure were avoided, and a concentrated extract was obtained by following the procedure of repercolation.

Precipitation of the aqueous extract at different pH, from 1.0 to 7.0, showed that the highest yield of the so-called acid precipitate was obtained at pH 3. This precipitate showed the presence of a laxative principle when tested on albino mice. Tested similarly, the second fraction obtained from the filtrate on addition of calcium chloride and ammonium chloride at pH 7 was inactive, but the third fraction obtained on addition of sufficient alcohol to the mother liquor from the second fraction was again active. A detailed report on the biological assay of the different fraction will be published separately. The fraction II (*C*) contained sennoside A and B, the presence of which is already reported by Stoll (1).

The glucosides present in the acid precipitates could not be crystallized, but they have been shown to be different from sennosides A and B by chromatographic techniques. In addition, the new glycosides have been shown to be those of rhein and chrysophanic acid by cochromatography from two different solvent systems. The sugar part of the glycosides is glucose in both the cases.

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Two Disintegrating Agents *versus* Cornstarch for Compressed Tablets

By G. HECHT† and C. L. HUYCK‡

Cornstarch, Dry-Flo, and Solka-Floc BW 40, were tested for suitability as disintegrating agents. The Dry-Flo and the cornstarch proved favorable for the sodium bicarbonate and the acetylsalicylic acid tablets. It was noted that Solka-Floc BW 40 (due to its fibrous nature) helped to prevent capping of the tablets. Analysis of the disintegration tests of tablets containing Solka-Floc BW 40 and Dry-Flo were statistically different than cornstarch at the 1 per cent probability level.

Cornstarch has been used in compressed tablets as a disintegrant for decades and is still the disintegrant of choice. Dried corn or potato starch is sometimes used with the object of shortening the disintegration time of the tablet, when moisture is detrimental to the stability of the active ingredients (*i.e.*, in aspirin tablets), and in tablets containing medicinals that are incompatible with each other. Even though cornstarch is quite satisfactory, the search continues for faster and more efficient disintegrants. The quicker the release of the medicament after ingestion, the greater the efficiency of the tablet. In this study, two disintegrants are compared with cornstarch and the results are analyzed statistically.

Two compounds were chosen to be tested as tablet disintegrants: Solka Floc BW 40[1] (a purified wood cellulose) and Dry-Flo[2] (a starch ester containing a hydrophobic group). As a control disintegrant, 10% cornstarch was used.

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† Present address: Purdue University, Lafayette, Ind.
‡ Present address: Eaton Laboratories, Division of The Norwich Pharmacal Co., Norwich, N. Y.

[1] Solka-Floc BW 40, The Brown Co., Berlin, N. H.
[2] Dry-Flo, National Starch Products, Inc., 270 Madison Avenue, New York 16, N. Y.

EXPERIMENTAL

The disintegrants were tested with relatively soluble and insoluble medicinals. Sodium bicarbonate was selected as the soluble medicinal agent, while acetylsalicylic acid was selected as the insoluble medicinal. The tablets of sodium bicarbonate were tested for disintegration (1) in both simulated gastric juice U.S.P. and distilled water to determine the extent of disintegration caused by effervescence of the sodium bicarbonate.

As an aid to disintegration into fine particles one-half or 5% of the disintegrant was added to the medicament before granulation; the other 5% was added to the dry granulation before compression. Ten per cent acacia mucilage was used as a binder.

Granulation.—The sodium bicarbonate employed was furnished from one company and met the standards of the "United States Pharmacopeia XV" (1). Since 5% of the disintegrating agent was to be placed in the granulation, it was necessary to make three separate granulations. The proper weight of sodium bicarbonate for 1000 tablets was placed in a stainless steel container and mixed with 5% disintegrant. Each batch was mixed for 30 minutes in a small laboratory Hobart mixer. To insure a uniform hardness of granules, an attempt was made to keep the amount of acacia mucilage as equal as possible for each of the three batches. To achieve the proper consistency, an average 215 Gm. ± 8 Gm. of acacia mucilage was used. The three batches were then granulated and passed through a No. 10 screen on the Stokes oscillating granulator. The wet granules were spread uniformly on paper covered trays and air dried for 42 hours. The dry granules were then passed through a No. 16 screen. One per cent magnesium stearate, previously screened through a No. 80, along with 5% disintegrator was added to each granulation. Each batch was then mixed for 5 minutes in the Patterson–Kelly twin shell blender.

Compression.—The three batches were compressed into tablets on a Stokes model E single punch tableting machine at a speed of 80 tablets per minute using $^{13}/_{32}$-in. punches of standard concavity. The tablet weight was kept constant at 0.380 Gm., and the tablet hardness kept as nearly to 10 Kg. as possible by the Strong Cobb hardness tester. Sampling was done on a 10% time basis; *i.e.*, 13 minutes was required to compress 1000 tablets at a rate of 80 tablets per minute. Therefore, a sample of 10 tablets was taken every 80 seconds. As nearly constant as possible with all three granulations were the following: (*a*) hopper feed by the same hopper at the same initial feed level, (*b*) speed of the machine at 80 tablets per minute, (*c*) weight, size, and hardness of the tablets.

Difficulty in flow was encountered with Solka-Floc BW 40 granulation. A constant tablet weight and hardness was difficult to maintain with this granulation. Flow characteristics better than cornstarch were noted for Dry-Flo.

Disintegration.—The U.S.P. (1) apparatus and method was used to determine disintegration. Thirty tablets from each batch were tested in five trials using six tablets per trial. The average time per trial was calculated in seconds. The mean and mean deviation were calculated for the five trials, and from this the standard deviation for the population was calculated.

The disintegration time of 30 tablets of each of three granulations of sodium bicarbonate plus a disintegrant also was tested in distilled water at 37°. Table III represents the data compiled from this experiment.

In the second part of the experiment, disintegration time of tablets containing the relatively insoluble acetylsalicylic acid with each of the three disintegrants was compared. Five per cent disintegrant was incorporated before granulation, and 5% was incorporated with the granules after granulation and just before compression. Granulation was by the precompression method, using $^{5}/_{16}$-in. punches and die for the slugs. The slugs were passed through a No. 8 mesh screen on the Stokes oscillating granulator. This process was repeated in order to eliminate "fines." The final granulation was passed through a No. 16 mesh screen. The granules were then mixed with 5% disintegrant to be tested and 1% magnesium stearate was added as lubricant. The tablets were compressed on $^{13}/_{32}$-in. punches at a weight of 0.380 Gm. with a hardness of approximately 10 Kg. as measured by the Strong Cobb hardness tester.

TABLE I.—FORMULAS OF THE SODIUM BICARBONATE TABLETS CONTAINING CORNSTARCH, SOLKA-FLOC, AND DRY-FLO AS DISINTEGRANTS

	Solka-Floc		
	Starch	BW 40	Dry-Flo
Sodium bicarbonate	324.0	324.0	324.0
Cornstarch	32.4	..	..
Solka-Floc BW 40	..	32.4	..
Dry-Flo	..	..	32.4
Magnesium stearate	3.24	3.24	3.24
Acacia mucilage 10%	*q.s.*	*q.s.*	*q.s.*

TABLE II.—DISINTEGRATION TIME IN MINUTES OF SODIUM BICARBONATE TABLETS CONTAINING DRY-FLO, CORNSTARCH, AND SOLKA-FLOC AS DISINTEGRANTS IN SIMULATED GASTRIC JUICE

	Trials				
Disintegrant	1st	2nd	3rd	4th	5th
Dry-Flo	2.8	2.1	2.2	1.9	1.8
Cornstarch	2.7	2.1	2.8	4.8	4.0
Solka-Floc BW 40	11.6	11.3	10.3	15.6	17.3

DISCUSSION

Using equation $d = \Sigma(X_1 - \bar{X})/N$ for calculation of mean deviation in which $\Sigma(X_1 - \bar{X})$ is the sum

TABLE III.—DISINTEGRATION TIME IN MINUTES OF SODIUM BICARBONATE TABLETS CONTAINING DRY-FLO, CORNSTARCH, AND SOLKA-FLOC DISINTEGRANTS IN WATER

	Trials				
Disintegrant	1st	2nd	3rd	4th	5th
Dry-Flo	2.83	3.50	2.33	2.66	2.50
Cornstarch	6.66	5.50	5.66	7.00	7.16
Solka-Floc BW 40	28.00	29.33	28.83	28.83	29.66

TABLE IV.—FORMULAS FOR THE ACETYLSALICYLIC ACID TABLETS CONTAINING CORNSTARCH, SOLKA-FLOC, AND DRY-FLO AS DISINTEGRANTS

	Starch	Dry-Flo	Solka-Floc BW 40
Acetylsalicylic acid	324.0	324.0	324.0
Cornstarch	32.4	..	..
Dry-Flo	..	32.4	..
Solka-Floc BW 40	..	..	32.4
Magnesium stearate	3.24	3.24	3.24

With Dry-Flo, a starch ester containing hydrophobic groups, no lubricant was necessary because of the splendid flow characteristics of this compound. Solka-Floc BW 40 is a white, purified, wood cellulose of a purity of 99.5% and an average particle size of 90 μ. This grade of Solka-Floc exhibited poor flow characteristics, and a lubricant was necessary.

Tablets of acetylsalicylic acid containing Dry-Flo as the disintegrating agent had a mean disintegration of 38.99 minutes, compared to 47.57 minutes for cornstarch and 54.56 minutes for Solka-Floc BW 40.

TABLE V.—DISINTEGRATION TIME IN MINUTES OF ACETYLSALICYLIC ACID TABLETS CONTAINING DRY-FLO, CORNSTARCH, AND SOLKA-FLOC AS DISINTEGRANTS IN SIMULATED GASTRIC JUICE

Disintegrant	Trials 1st	2nd	3rd	4th	5th
Dry-Flo	35.16	38.16	40.66	37.66	40.33
Cornstarch	36.33	54.00	54.23	46.16	47.16
Solka-Floc BW 40	50.16	57.33	54.83	55.50	55.00

of the absolute deviations from the mean and $(N - 1)$ is the number of degrees of freedom for a small sample, then $s = (X_1 - \bar{X})^2/N - 1$ (2).

The results of the disintegration tests of the tablets were analyzed statistically by the students "t" test and were found to be statistically[3] different from cornstarch at the 1% probability level.

Tablets of sodium bicarbonate containing Dry-Flo as the disintegrating agent had a mean disintegration time in artificial gastric juice of 2.16 minutes, compared with 3.28 minutes for tablets containing cornstarch as the disintegrant and 13.22 minutes for tablets containing Solka-Floc BW 40 as the disintegrant. All disintegrants yielded tablets which were white and smooth in appearance.

The disintegration of the sodium bicarbonate tablets was tested in simulated gastric juice U.S.P. and in distilled water to determine how much of the disintegration was due to the decomposition of the sodium bicarbonate by the acid media. In distilled water the tablets containing the Dry-Flo disintegrated in 2.76 minutes or 27% longer than in simulated gastric juice U.S.P. Sodium bicarbonate tablets containing cornstarch disintegrated in water in 6.40 minutes or 94% longer than in simulated gastric juice and the tablets containing Solka-Floc BW 40 disintegrated in 28.92 minutes in water or 111% longer than in simulated gastric juice U.S.P.

[3] In the statistical study the authors acknowledge the help of Mr. George O'Bleness, Director of the Computer and Statistical Division, Eaton Laboratories, Division of The Norwich Pharmacal Co., Norwich, N. Y.

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Books

REVIEWS

Some General Problems of Paper Chromatography. Edited by I. M. HAIS and K. MACEK. Publishing House of the Czechoslovak Academy of Sciences, Prague, 1962. 220 pp. 17 × 35 cm.

A symposium was organized to cover the chemical structure of a substance and its behavior on a paper chromatogram and the mechanism of paper chromatography; the proceedings of the symposium are reported in this volume. A number of European scientists participated. Most of the papers and discussions have been translated from the original Czech, German, and Russian languages. The book should be of valuable assistance to pharmaceutical scientists who wish to explore the possibilities of utilizing more recent applications of paper chromatography in novel situations.

Specifications for Reagents Mentioned in the International Pharmacopoeia. World Health Organization, Geneva, 1963. U. S. agent: Columbia University Press, International Documents Service, 2960 Broadway, New York 27, N. Y. 267 pp. Price $6. French and Spanish editions in preparation.

A book of specifications for those reagents needed for testing the substances included in the "International Pharmacopeia" is presented. The volume covers about 400 reagents, ranging from the common mineral acids used in a multitude of tests to the complex organic compounds required for perhaps only one intricate assay, and represents a collaborate effort of pharmaceutical experts from all over the world. The specifications are designed to give the quality tests of the "International Pharmacopoeia" practical value by attempting to provide a worldwide reagent standard.