

Effects of Selected U.S.P. Talcs on Acetylsalicylic Acid Stability in Tablets

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Talc U.S.P. varies in chemical composition according to its source and method of preparation. The effects of four different U.S.P. talcs on the stability of aspirin tablets at elevated temperature and humidity were studied. Data obtained indicated that different talcs varied significantly in their effects on the stability of aspirin. Aspirin stability was improved by acid washing the talcs. Selected talcs were analyzed and experiments conducted in an attempt to identify the factors adversely influencing aspirin stability.

AS DEFINED in the U.S.P. XVI (1) "Talc is a native, hydrous magnesium silicate, sometimes containing a small proportion of aluminum silicate." Chemically, talc is a hydrated magnesium silicate having the general formula, $3\text{MgO} \cdot 4\text{SiO}_2 \cdot \text{H}_2\text{O}$, in which layers of brucite are between silicon-oxygen layers with each layer being somewhat modified by isomorphous replacement. Talc is formed by the breaking down of tremolite, instatite, and other magnesium minerals (2). Purified talc is made by boiling very finely powdered talc with water containing about 2% hydrochloric acid, allowing the insoluble material to subside, decanting the supernatant liquid, and repeating the process with a weaker hydrochloric acid solution. The talc that has been freed of iron and other soluble impurities is thoroughly washed with water and dried at 110° (3).

Impurities which are reported to be present in talc are calcium carbonate, calcium silicate, and iron oxide (4). These impurities result in modification of the physical characteristics of the talc. When the calcium content is high and in the form of calcium silicate or crystalline calcium carbonate, the powdered material is abrasive. The presence of iron (either as ferric oxide or a complex magnesium ferric silicate) tends to make the talc grayish in appearance.

Talc is widely used in the pharmaceutical industry as a tablet lubricant and, as such, may influence tablet stability. The rate of aspirin decomposition in tablet formulations containing aspirin, phenacetin, and caffeine has been reported to be minimized when talc is used as the lubricant (5, 6). Since talc is a natural product, it does not have constant composition, but varies depending upon its origin and method of prep-

aration. Analyses of talcs usually show variations in composition (7).

This investigation was undertaken to determine whether different U.S.P. talcs would vary in their effects on the stability of aspirin. The data obtained indicated that the stability of aspirin did vary with different talcs and an attempt was made to determine whether additional acid washing of talc would result in better aspirin stability. Selected talcs were analyzed and experiments conducted to identify the factors in talc adversely influencing aspirin stability.

EXPERIMENTAL

Materials Used.—Commercially available 20-mesh aspirin crystals of U.S.P. grade and commercially available U.S.P. talcs were used throughout this experiment. The talcs were designated talc *A*, *B*, *C*, and *D*. Other chemicals used were U.S.P. grade of calcium carbonate, C.P. grade of aluminum silicate, pharmaceutical grade of red iron oxide, and purified calcium silicate.

Acid Washing of Talcs.—Talcs *A*, *B*, *C*, and *D* were acid washed by the following procedure: 50 Gm. of talc was placed in 200 ml. of 10% hydrochloric acid and boiled for 10 minutes. The talc was filtered with suction through a sintered-glass filter and washed thoroughly with distilled water until the filtrate had the same pH as the washing solution. The talc was then dried in a vacuum desiccator over concentrated sulfuric acid.

pH Measurements.—The pH of a 2% suspension of talc in distilled water was measured with a Beckman model H2 pH meter.

Chemical Analyses of Talc.—Using standard methods of chemical analysis, talcs *A*, *C*, and acid washed talc *C* were assayed for the following in the order listed: loss on ignition, SiO_2 , Fe_2O_3 , Al_2O_3 , CaO , and MgO . The anhydrous sodium carbonate fusion method was utilized to decompose the sample. Silica was volatilized by the hydrofluoric acid method and calculated by weight differences.

Gravimetric methods were employed for the determination of iron, aluminum, calcium, and magnesium. After preliminary separation of iron and aluminum as hydroxides, iron was precipitated from an acidic solution with cupferron, then ignited, and weighed as ferric oxide. Aluminum was precipitated with ammonium hydroxide, ignited, and weighed as aluminum oxide. Calcium was separated from mag-

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TABLE I.—STABILITY OF ASPIRIN IN TABLETS CONTAINING SELECTED TALCS

pH of talc →	Talc A 7.6	Talc B 7.7	Talc C 9.6	Talc D 9.2
Free Salicylic Acid in mg./Tablet at 40° C. and 90% Relative Humidity				
Time, wk.				
Original	<0.10	<0.10	<0.10	<0.10
1	0.13	0.30	0.93	0.28
2	0.23	0.69	2.61	0.57
4	0.41	1.07	5.85	1.12
8	0.32	2.05	13.00	1.46
12	0.80	3.35	25.80	2.96

nesium by a double precipitation with ammonium oxalate, then ignited, and weighed as calcium oxide. Finally, the magnesium was precipitated by the addition of ammonium phosphate, ignited to the pyrophosphate, weighed, and calculated as the oxide.

Preparation of Tablets.—Three series of aspirin tablets were prepared. Formulations of the first series contained talcs A, B, C, and D as commercially received. Formulations of the second series contained acid washed talcs A, B, C, and D, and formulations of the third series contained talc A plus known amounts of various talc impurities. Formulations of all three series contained in each tablet 325 mg. of aspirin and 13.5 mg. of talc. Formulations of the third series contained in addition 0.71 mg. per tablet of one of the following: aluminum silicate ($3\text{Al}_2\text{O}_3 \cdot 4\text{SiO}_2 \cdot \text{H}_2\text{O}$), red iron oxide (Fe_2O_3), calcium silicate (CaSiO_3), and calcium carbonate. Each ingredient was vacuum dried over concentrated sulfuric acid for not less than 16 hours prior to use and thereafter handled in a room in which the relative humidity did not exceed 19%. Tablets were compressed on a Colton single-punch machine using $\frac{3}{8}$ -in. standard cup punches and die. Compressed tablets had a hardness of 3.0 to 4.0 Kg. measured with a Pfizer hardness tester and contained less than 0.2% moisture measured with a Cenco infrared moisture balance with a 125-watt infrared bulb at 90 volts for 10 minutes.

Accelerated Stability Conditions.—Tablets were placed in a desiccator and stored at 40° and approximately 90% relative humidity. The humidity in the desiccator was controlled by a saturated solution of monobasic ammonium phosphate in which an excess of salt was present to insure saturation. The relative humidity above a saturated solution of monobasic ammonium phosphate at 37.7° is 91.1% (8).

Free Salicylic Acid Assay.—Aspirin stability in tablets was evaluated in terms of free salicylic acid content. Twenty tablets were weighed, the average tablet weight determined, and the tablets ground to a fine powder. Approximately one tablet weight was accurately weighed and transferred to a glass-stoppered centrifuge tube and 25 ml. of benzene added. The tube was shaken on a mechanical shaker for 2 minutes and centrifuged for approximately 3 minutes. Five milliliters of clear benzene solution was transferred to a second glass-stoppered centrifuge tube and 10 ml. of ferric ammonium sulfate

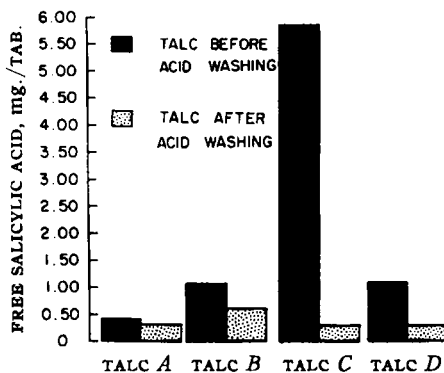


Fig. 1.—Effect of acid washed talcs on aspirin stability after 4 weeks at 40°C. and 90% relative humidity.

solution (0.1% ferric ammonium sulfate adjusted to pH 2.45 with sulfuric acid) was added. The tube was then shaken on a mechanical shaker for 30 seconds and centrifuged for 2 minutes. The benzene layer was aspirated off and the aqueous portion was read on an Evelyn photoelectric colorimeter using a 515-m μ filter. The instrument was adjusted to 100% transmittance with the reagent blank.

RESULTS AND DISCUSSION

The data from Table I indicate that different talcs vary significantly in their effects on the stability of aspirin. After 12 weeks at 40° and 90% relative humidity, tablets containing talcs A, B, C, and D had 0.80, 3.35, 25.80, and 2.96 mg. of free salicylic acid per tablet, respectively. Arranging the talcs in decreasing order of aspirin stability we have talc A, D, B, and C. It will also be noted that the pH of the talcs varied from 7.6 to 9.6. By arranging the pH of the talcs in the same order of decreasing aspirin stability, we have 7.6, 9.2, 7.7, and 9.6. The pH of talc, therefore, did not appear to be directly related to aspirin stability.

Figure 1 illustrates the effects of acid washed talcs on aspirin stability. After 4 weeks at 40° and 90% relative humidity, aspirin tablets contained the following concentrations of free salicylic acid in milligrams per tablet: talc A 0.41; acid washed talc A

TABLE II.—CHEMICAL ANALYSES OF VARIOUS TALCS, %

	SiO ₂ %	MgO %	CaO %	Al ₂ O ₃ %	Fe ₂ O ₃ %	Free Moisture %	Loss on Ignition %
Talc A	61.89	30.90	0.36	0.54	0.31	<0.2	0.53
Talc C	48.20	32.10	4.36	3.71	1.07	<0.2	6.44
Acid washed talc C	52.63	30.50	0.36	4.00	1.18	<0.2	1.38

TABLE III.—STABILITY OF ASPIRIN IN TABLETS CONTAINING TALC A AND VARIOUS IMPURITIES

Time, wk.	Free Salicylic Acid in mg./Tablet at 40°C. and 90% Relative Humidity				
	Talc A	Talc A + Red Iron Oxide	Talc A + Calcium Silicate	Talc A + Aluminum Silicate	Talc A + Calcium Carbonate
Original	<0.10	<0.10	0.12	<0.10	<0.10
1	<0.10	0.13	1.11	0.11	2.61
2	0.19	0.25	1.85	0.19	4.66
4	0.22	0.33	3.20	0.23	8.01

0.30; talc B 1.07, acid washed talc B 0.60; talc C 5.85, acid washed talc C 0.30; talc D 1.12, acid washed talc D 0.30. Therefore, aspirin stability was improved by acid washing the talcs.

The data in Table II present the chemical analyses of talcs A, C, and acid washed talc C which were assayed for SiO₂, Al₂O₃, CaO, and MgO to determine whether talcs which varied in their effects upon the stability of aspirin would also vary in their chemical composition. Talcs A and C were selected for analyses because they represented the talcs which were affected the least and the most, respectively, by acid washing. Acid washed talc C, which had previously been shown to have good aspirin stability, had relatively high concentrations of Fe₂O₃ and Al₂O₃. This suggests that aluminum or iron in talc does not adversely influence aspirin stability. Talc C, which was associated with poor aspirin stability, had a loss on ignition of 6.44% which exceeds the U.S.P. limit of 5%. The loss on ignition did not represent free moisture. Talc C also had a relatively high concentration of CaO which would reflect a calcium carbonate or calcium silicate impurity. A calcium carbonate impurity would also contribute to a high loss on ignition. By acid washing talc C, the loss on ignition and CaO content were reduced and aspirin stability significantly improved. A high loss on ignition and CaO content, therefore, may be indicative of impurities in talc which adversely influence aspirin stability.

The effect that impurities in talc have on aspirin stability is shown in Table III. A different aspirin lot was used in this phase of the experiment which may explain the low free salicylic acid levels obtained. It will be noted that after 4 weeks at 40° and 90% relative humidity, aspirin tablets containing talc A had 0.22 mg. of free salicylic acid per tablet. The series of tablets also prepared with talc A, but with added aluminum silicate, red iron oxide, calcium silicate, or calcium carbonate, had free salicylic acid values of 0.23, 0.33, 3.20, and 8.01 mg. per tablet, respectively. Aspirin stability, therefore, is adversely influenced by the presence of calcium carbonate or calcium silicate and not significantly in-

fluenced by the presence of aluminum silicate or red iron oxide. This is in agreement with the conclusions from the analyses of selected talcs in which aspirin decomposition was associated with the calcium content and not associated with aluminum or iron.

SUMMARY AND CONCLUSIONS

The effects of different U.S.P. talcs on the stability of aspirin tablets have been investigated. From the results obtained the following conclusions can be drawn.

Different U.S.P. talcs varied significantly in their effect on the rate of aspirin decomposition.

The stability of aspirin was improved by acid washing the talcs.

The pH of talc did not appear to be directly related to aspirin stability.

When using commercially available talcs, a high-calcium content and high loss on ignition were associated with increased aspirin decomposition. The aluminum and iron content were not associated with aspirin decomposition.

Aspirin stability in tablets was adversely affected by the presence in talc of added calcium silicate and calcium carbonate and not affected by aluminum silicate or red iron oxide.

As a result of this investigation, the authors are of the opinion that variations in talc could alter the stability of other pharmaceuticals containing or utilizing talc in their preparation.

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