A PHARMACEUTICAL STUDY OF ACETYLSALICYLIC ACID.

BY HARRIET V. SNIDOW AND H. A. LANGENHAN.

No. 2*—Incompatibility.

Two thousand prescriptions, collected from eighty drug stores throughout Seattle, were classified: One hundred and forty or seven per cent contained acetylsalicylic acid. Of the one hundred and forty, seventy-seven, or fifty-five per cent, designated acetylsalicylic acid; forty-nine, or thirty-five per cent, designated Aspirin and fourteen, or ten per cent, called for Empirin. The one hundred and forty prescriptions contained forty-eight different medicinal substances, and represented many different combinations. The following table offers a survey of the ingredients, the number of times each appeared, and the number of combinations containing each substance. Acetylsalicylic acid of course appears in each prescription.

Ingredients prescribed with acetylsalicylic acid.	No. of times prescribed.	Combinations.	Ingredients prescribed with acetylsalicylic acid.	No. of times prescribed.	Combinations.
1. Acetanilid	4		26. Extract of Cannabis	1	
2. Aloin	2		27. Extract of Cascara Sagrada	3	
3. Ammonol	2		28. Extract of Nux Vomica	1	
4. Antipyrine	2		29. Euquinine	2	
5. Asafœtida	1		30. Heroine Hydrobromide	1	
6. Atropine Sulphate	1		31. Hexamethylenamine	5	
7. Benzyl Succinate	1		32. Magnesium Oxide	1	
8. Bismuth Subnitrate	2		33. Morphine Sulphate	4	3
9. Caffeine	2		34. Oxyl Iodide	2	
10. Caffeine Citrate	58	24	35. Phenacetin	53	20
11. Calcidin	3		36. Pilocarpine Hydrochloride	1	
12. Calomel	4	3	37. Potassium Citrate	1	
13. Camphor	7	5	38. Powder of Ipecac and Opium	6	
14. Camphor Monobromated	12	7	39. Quinine Sulphate	10	9
15. Carbo Ligni	1		40. Saccharum Lactis	5	
16. Caripeptic and Charcoal	1		41. Salol	16	14
17. Carmine	1		42. Sodium Bicarbonate	11	7
18. Cascara (powd.)	1		43. Sodium Bromide	1	
19. Cincophen	1		44. Sodium Citrate	1	
20. Cocoa	1		45. Sodium Salicylate	1	
21. Codeine	5		46. Strychnine Sulphate	1	
22. Codeine Phosphate	1		47. Tincture of Belladonna	1	
23. Codeine Sulphate	45	20	48. Veronal	4	1
24. Extract Aconite	2				
25. Extract of Belladonna	5	3			

It is worth while calling attention to the fact that caffeine citrate appears 58 times. Inasmuch as acids are considered incompatible (see survey under acids) this combination may be questioned. Phenacetin appears 53 times and as far as has been ascertained is compatible with acetylsalicylic acid. Codeine appears 45 times, and whereas no reports have appeared, relative to this substance being incompatible, tablets of acetylsalicylic acid five grains to codeine sulphate one-fourth grain, containing a small amount of starch and talcum that had been prepared in the laboratory, showed signs of decomposition after several weeks. A

* For No. 1, "Historical," see JOURNAL A. PH. A., v. 14, p. 125 (1925).

strong odor of acetic acid or more like the anhydride was given off and a coating of needle-like crystals appeared on the tablet.

Among the prescriptions analyzed a few combinations appeared repeatedly and are herewith appended:

Aspirin		Acetylsalicylic Acid	
Phenacetin	5 prescrip's	Sodium Bicarbonate	5 prescrip's
Acetylsalicylic Acid		Acetylsalicylic Acid	
Phenacetin		Codeine Sulphate	6 prescrip's
Codeine Sulphate	3 prescrip's	Acetylsalicylic Acid	
Acetylsalicylic Acid		Caffeine Citrate	4 prescrip's
Phenacetin		Acetylsalicylic Acid	
Codeine Sulphate		Veronal	
Caffeine Citrate	11 prescrip's	Codeine Sulphate	4 prescrip's
Acetylsalicylic Acid		Acetylsalicylic Acid	
Phenacetin		Caffeine Citrate	
Caffeine Citrate	15 prescrip's	Camphor Monobromate	5 prescrip's

The doses of the single ingredients varied in practically every prescription.

Before attempting a laboratory investigation of the possible incompatible combinations, a survey of all work already done was deemed feasible. Information was obtained from textbooks and journal literature, properly arranged and summarized. The summary is herewith appended:

According to Haynes,[1] acetylsalicylic acid is largely used as a substitute for the salicylates—the pure acid having no action on the stomach, decomposition into salicylates and acetates taking place in the intestines. It is said that the desirability of acetylsalicylic acid lies in the ester combination as compared with salicylic acid or salicylates. Hence the presence of free acid, or decomposed ester, is objectionable. That acetylsalicylic acid is easily decomposed by other substances, thus eliminating some of the desired properties, is quite apparent from the study of the various combinations in which it is dispensed.

WATER.

Water appears to be one of the principal substances that bring about decomposition. Even small quantities in apparently dry mixtures cause hydrolysis. Vanderkleed and Ewe[2] as well as Haynes believe that the presence of small amounts of free salicylic acid in compressed tablets may be due to contact with water during the process of manufacture, Vanderkleed and Ewe even stating that acetylsalicylic acid cannot be put through the processes necessary in making compressed tablets without slight decomposition. Ahrens[3] during the course of his work, centering about the melting point of acetylsalicylic acid, determined that it absorbs 1.7629 per cent of its weight from surrounding moisture. A report by Tsakalotos and Horsch[4] furnishes the information that at room temperature acetylsalicylic acid in the proportion of one part to five parts of pure water is almost completely decomposed in 100 days, the reaction being very complicated. The presence of hydrochloric or sulphuric acid increases the rate of hydrolysis, the hydrochloric producing the greater acceleration. Citric and acetic acids were found to increase the rate of decomposition for the first seven days and after that time to decrease it due to reverse reaction.

CITRATES.

Leech,[5] in his investigations on the hydrolysis of acetylsalicylic acid, employed sodium citrate. He used 18 grams of acetylsalicylic acid and 72 grams of citrate in 240 cc. of water. At the end of four days the acid was broken down to the extent of 50 per cent; after nine days to 75 per cent; and almost completely hydrolyzed at the end of seventeen days. This would tend to disprove the claim that acetylsalicylic acid may be dispensed in sodium citrate solution without decomposition. Heavy metals, present due to manufacturing conditions, act as catalytic agents in aiding decomposition, according to Merrill.[6] Acetylsalicylic acid apparently goes into solution when mixed with aqueous alkali acetate or citrate solutions. This according to Tattam[7] is due to a double decomposition, the acetylsalicylic acid combining with the alkali liberating the equivalent amount of acetic and citric acids. He further adds that, from a therapeutical standpoint, the incompatibility is probably not serious.

COLOR REACTION.

The conventional procedure for determining the presence of free salicylic acid or a salicylate in acetylsalicylic acid mixtures is to apply the ferric alum test. The indication is a purplish color. The absence of this color was interpreted as "no free acid or salicylate" until it was recalled that some substances "masked" the test. This interference as applied to acetylsalicylic acid has been investigated to some extent. Gehe and Co.[8] find that borax, sodium phosphate, tartaric acid, citric acid, and other oxyacids render the test as given by the German Pharmacopœia unsatisfactory. Smith[9] reports that strong organic acids, tartaric and more particularly citric, are used to mask the color reaction between ferric chloride and salicylic acid, one per cent of citric acid being sufficient to mask about 0.2 per cent of free salicylic acid. Therefore, he concludes that all tablets which after being powdered give no violet coloration with ferric chloride should be viewed with suspicion. The salicylic and acetylsalicylic acids may be removed from the tablet by extraction with a mixture of ether and petroleum ether, in which the tartaric and citric acids are insoluble. The statement is made by Ruddiman[10] that the violet color may not show at first because citrates and citric acid interfere, but after standing for a time the color will develop. A report[11] read at the 1924 meeting of the Scientific Section of the American Drug Manufacturers' Association states that no incompatibility exists between acetylsalicylic acid and cinnamic acid, and that there is no indication of any with oxalic acid. Oxalic acid was found to interfere with the sensitiveness of the ferric alum test. A ratio of five grains of acetylsalicylic acid to one-tenth grain of oxalic acid did not seem to give this interference. The following represent a few references to acetylsalicylic acid prescriptions, mostly in an acid vehicle, and comments on these combinations:

Prac. Drug., v. 32, p. 165 (1914).
Pac. Drug. Rev., v. 28, April, p. 12 (1916).
Ibid, v. 29, Oct., p. 22 (1917).
"Incompatibilities in Prescriptions, Ruddiman," Ed. 4, p. 163 (1917).
Pac. Drug Rev., v. 30, May and June, p. 28 (1918).
Prac. Drug., v. 37, p. 38 (1919).
Drug. Circ., v. 68, p. 150 (1924).

SODIUM BICARBONATE.

Acetylsalicylic acid is said to be incompatible with alkalies and their carbonates producing acetates and salicylates.[12] In 1903 Rosseau[13] reported that a mixture consisting of acetylsalicylic acid, sodium bicarbonate and exalgin within a few days became converted into a semifluid black mass, liberating acetic acid. The cause was traced to the action of the bicarbonate on the acetylsalicylic ester, the statement being made that the acetyl radical of the acetylsalicylic acid is easily removed by alkalies. In a reply to a query[14] as to the reaction taking place when acetylsalicylic acid and sodium bicarbonate are mixed in solution the following appears: "The aspirin is decomposed by sodium bicarbonate with the production of acetic acid and salicylic acid or sodium salicylate and the evolution of carbonic acid gas." According to Gerngrosz and Kersasp,[15] if 60 grams of acetylsalicylic acid are mixed with 27 grams of sodium bicarbonate and 120 cc. of water, and the filtrate evaporated, sodium acetylsalicylate will be formed. This salt is said by Bouvet[16] to be very hygroscopic and to hydrolyze rapidly in contact with water into sodium salicylate and acetic acid. In answer to a query[17] as to whether in a given prescription acetylsalicylic acid should be suspended or dissolved by the addition of sodium bicarbonate, this reply was given: "Since aspirin is prescribed on the assumption that it passed through the acid stomach secretions intact, and is not decomposed until it reaches the alkaline intestinal secretion, it would be incorrect to prescribe an alkali with acetylsalicylic acid, and still more so to make such an addition to merely produce a clear mixture. The aspirin should be finely powdered and suspended in the vehicle." A comment[18] on a simple mixture of acetylsalicylic acid and sodium bicarbonate, to be capsulated, states that if the powders are dry they should keep well the required time (about four days) and expresses a preference for granular sodium bicarbonate. Another prescription,[19] similar but containing in addition extract of cascara sagrada, brings the comment that decomposition will be in proportion to the amount of moisture present. A little moisture will decompose a small amount of acetylsalicylic acid into acetic and salicylic acids, these acids will start a reaction with the bicarbonate which will liberate more moisture and the reaction will thus proceed, forming a pasty residue,[20] the decomposition products being, not poisonous, but troublesome. According to U. S. Patent No. 1,404,673, Jan. 24,[21] "aspirin is dissolved in a saturated solution of sodium bicarbonate containing aromatic elixir and glycerol."

MAGNESIUM OXIDE, HYDROXIDE AND CARBONATE.

The patented process of Gerngrosz and Kast[22] for preparing magnesium acetylsalicylate consists in adding to an aqueous suspension of acetylsalicylic acid the oxide, hydroxide or carbonate of magnesium in calculated proportions, stirring or shaking the reacting mixture, cooling if necessary, and evaporating the aqueous solution of the salt *in vacuo*. This salt is water-soluble.[23] An unsigned article[24] states that acetylsalicylic acid and salol should not be combined with magnesium oxide in prescriptions, since in the presence of moisture magnesium acetylsalicylate would be formed and this, if moisture enough were present, would decompose yielding magnesium salicylate. The salol is also said to be decomposed. A. Wohlk[25] recommends a tablet mixture consisting of 18 grams of acetylsalicylic acid and 2.5 grams of light magnesia. The combination is supposed to eliminate any

undesirable secondary effects of the acetylsalicylic acid without altering its specific action and is said to be very popular in Denmark. Salicon,[26] claimed to be "an improved aspirin," was found to contain approximately 3.2 grains of acetylsalicylic acid, 2.2 grains of magnesium carbonate and some starch.

AMMONIUM CARBONATE.

Information was sought concerning prescriptions containing acetylsalicylic acid and ammonium carbonate, or aromatic spirits of ammonia, the vehicle in each case being liquid. One[27] reply tells us that the acetic and salicylic acids formed by the decomposition of acetylsalicylic acid attack the ammonium carbonate, forming to some extent the corresponding salts of ammonium and giving off carbon dioxide gas. Another reply[28] states, "As aspirin is an acid and aromatic spirit of ammonia contains a carbonate the gas produced is carbon dioxide." The third combination contained syrup of orange. The "querist" was told to prepare a shake mixture by triturating the acetylsalicylic acid in a mortar with the aromatic spirit of ammonia and syrup of orange and then to make up to volume by adding water slowly with trituration.[29] Tragacanth was suggested as a suspending agent.

HEXAMETHYLENAMINE.

In 1909 and 1910 queries concerning prescriptions containing acetylsalicylic acid and hexamethylenamine brought the information that in powder mixtures[30] the dampness is probably due to a reaction between the acetylsalicylic acid and hexamethylenamine. In solution[31] there is mutual decomposition yielding, in the case of acetylsalicylic acid, salicylic and acetic acids. An article [32] of a later date gives the decomposition products of the hexamethylenamine as being ammonia and formaldehyde. Robinson[33] states that he has seen capsules containing acetylsalicylic acid and hexamethylenamine dispensed hundreds of times without any trouble. An article by Linton[34] gives the information that powders of the two which were dispensed were afterwards returned in a decidedly moist condition; that this dampness occurred in a mixture of the two powders regardless of whether they were mixed with titration or by simply turning them over with a spatula, whether they were put up in capsules, plain powder papers or waxed powder papers. Diluents and drying agents with the exception of a large amount of althæa did not prevent the formation of a sticky mass. According to Ruddiman,[35] hexamethylenamine and acetylsalicylic acid when triturated together give a slightly damp powder, which becomes sticky on standing a short time and finally is almost liquid. A greenish yellow color is acquired by the mass and an odor of formaldehyde is noticeable. Hexapyrin[36] is said to be hexamethylentetramine acetylsalicylate.

QUININE AND SALTS OF QUININE.

One of the common combinations reported as being incompatible is that of quinine sulphate and acetylsalicylic acid. A mixture of these two, according to the literature, first becomes sticky, then cakes and contracts. The color change consists of a gradual darkening from a faint yellow to a brown-red. A strong odor of acetic acid is obtained. Scoville[37] was possibly the first to report on this combination. He assumed that the water of crystallization of the quinine sulphate hydrolyzed the acetylsalicylic acid; that the resulting acids acted slowly upon the qui-

nine forming some liquid quinotoxin; that this in turn formed a eutectic mixture with salicylic acid. Heat would hasten the liquefaction. This explanation was apparently accepted as is evidenced by its appearance in textbook[38] and journal[39] literature of a later date. Robinson[40] makes the following statement: "For some time the pharmaceutical journals carried the information that quinine was incompatible with aspirin, because a very dangerous, poisonous compound, quinotoxin, was formed, from which many deaths resulted. I put no credence in those reports at that time, and I do not now. As far as I know, the two chemicals are perfectly compatible. I have prescribed them and have seen them prescribed without any bad results." Sollmann[41] in an article entitled "The Quinotoxin Myth" agrees with Robinson as far as the absence of the formation of poisonous compounds in this mixture is concerned. He suggests that the incompatibility lies in the decomposition of the acetylsalicylic acid and subsequent liberation of salicylic acid which is objectionable. Ganassini[42] reported that quinine and acetylsalicylic acid ("as found from experiments *in vitro* and on rabbits") may be associated since the formation of quinotoxin was not discovered. Quinotoxin is formed, he reports, only with impure acetylsalicylic acid, by the action of acetyl chloride. In 1924 Ruddiman and Lawnwermeyer[43] conducted a series of experiments, the results of which were summarized as follows:

"1. Mixtures of aspirin with quinine sulphate or quinine bisulphate do not change much in appearance in six months.

2. A mixture of aspirin with quinine alkaloid will change much more quickly than with the sulphate.

3. Aspirin seems to increase the toxicity of quinine a little.

4. The old mixture of quinine and aspirin which has changed to a brown-red mass is no more toxic than the fresh mixture."

Frogs were used in determining the toxicity of the quinine-aspirin mixtures above. Further experimentation, using warm-blooded animals, was believed necessary.

In 1859, Miller and Rhode[44] obtained products from quinine and cinchonine which they called quinotoxin and cinchotoxin. As the names indicate they believed the products to be toxic. Sollmann's[41] article bears the following conclusion: "There is no occasion to fear toxic effects from the transformation of quinin into 'quinotoxin' (more properly, quinicin). This substance is not especially toxic and it could not be formed in significant quantities, if at all, in the body. It may be formed in prescriptions containing quinine and organic acids, but this would proceed slowly, and the quinicin would undergo further transformation into inactive products. Such solutions are perfectly proper if used within a few days. They should not be used after prolonged standing, when they have become discolored and precipitated; not because they have become toxic, but because they are inactive." B. F. Howard and O. Chick[45] in discussing the sterilization of acid quinine solutions state that it is not clear from the evidence available whether quinicine and cinchonicine are poisonous or not but that large quantities of cinchona febrifuge, containing high percentages of these bodies, are administered in India without, apparently, any evil results. In an unsigned article[46] it is reported that slightly dissociated acids such as acetylsalicylic, citric, malic, acetic, or tartaric, act as catalytic agents in the formation of quinotoxin from

quinine, this conversion being practically quantitative at from 98 to 102° C.

The fact that acetylsalicylic acid and quinine or a salt of quinine are dispensed in combination is brought forth by a study of the literature on the so-called "New Remedies." Based upon the information available the following proprietary products contain acetylsalicylic acid and quinine or a quinine salt.

1. Apochin.—*Pharm. Era*, v. 59, p. 143 (1924).
2. Captol.—*Jour. de pharmacie et chimie;* through Y. B. (1916).
3. Denesin tablets.—*Pharm. Ztg.;* through YEAR BOOK (1920).
4. Togal.—*Apoth. Ztg.*, v. 31, p. 290 (1916); through *Chemical Abstracts* (1917).
5. In addition to these a report on quinine acetosalicylsulphate offers material for a new line of thought. Dott[47] finds that, when acetylsalicylic acid (4 mols) is allowed to react with quinine sulphate (1 mol), there is formed a definite compound melting at 96° C. One part dissolves in 50 parts of water which is a greater solubility than that exhibited by either of its components. The salt is capable of combining with 9 mols of water, but Dott suggests that 4 mols of water be taken as the standard because the product readily loses water down to this point. The chemical formula is given as

$$B.2H_2SO_4.4C_9H_8O_4.4H_2O \qquad B = C_{20}H_{24}N_2O_2$$

A mixture of euquinine and acetylsalicylic acid, after standing a few days, was found to have formed a slightly damp, shrunken mass.[48]

ANTIPYRINE.

An unsigned article[49] bears the information that in such a mixture "the acetic ester" will be split off and "keep the powder moist." Ruddiman[50] reports that a sticky mass is formed, having a yellowish color. The mass becomes darker and forms a hard crystalline solid which gives a deep violet with ferric chloride. The statement relative to the formation of a mass is in direct contradiction to the statement in Incompatibilities.[51] Acetopyrine[52] is reported as being a new specialty composed of antipyrine and acetylsalicylic acid.

POTASSIUM IODIDE.

Duncan[53] reports that at first HI is formed which ultimately liberates free iodine under the influence of light and air. Ruddiman[54] finds that cachets containing such a mixture may become blue, the explanation of the presence of free iodine being the same as given above. He also states that the change occurs more quickly in a moist atmosphere. Robinson[55] believes such a decomposition to be purely theoretical. Aspriodine[56] is reported as being a combination consisting of iodine 41.47 per cent and acetylsalicylic acid 58.53 per cent.

MISCELLANEOUS.

Other substances reported[57] as being incompatible with acetylsalicylic acid are borax, phenol, lead acetate, and sodium phosphate.

PRELIMINARY LABORATORY EXPERIMENTATION.

In order to place the results on a comparable basis, the mixtures used were made up of the average U. S. P. doses of the medicinal agent with five grains of acetylsalicylic acid. The ratio of these ingredients in the prescriptions analyzed

varied much and a study of each ratio was impossible in the limited time available. The ingredients* were mixed and placed in clear glass vials, stoppered with corks. As prescribed the mixtures were dispensed in capsules or papers, hence again a slight difference as compared with the original prescription occurs.

The observations made are herewith recorded. No attempt is made to interpret these, but the continuation of this work will undoubtedly prove of value towards attempting an explanation.

Hexamethylenamine
Acetylsalicylic Acid

Jan. 26. Damp powder, packed when triturated.

Feb. 10. Acetic acid odor evolved; semi-solid mass in vial.

Feb. 23. Yellow tint noticeable; odor of formaldehyde strong.

Quinine Sulphate
Acetylsalicylic Acid

Jan. 26. Powder damp enough to pack slightly.

Feb. 10. No change.

May 26. Acetic acid odor evolved.

Salol
Acetylsalicylic Acid
Euquinine

Jan. 26. Sticky damp mass formed.

Feb. 10. Strong acetic acid odor evolved.

May 26. The powder in that portion of the vial toward the light had assumed a yellowish tint which deepened to reddish brown. The powder protected from the direct rays of light was not changed in color.

Quinine Sulphate
Salol
Citrated Caffeine
Acetylsalicylic Acid

Jan. 26. Powder packed but very slightly.

May 26. Decided acetic acid odor.

June 1. The powder exposed to the light had assumed a faint yellow tint.

Phenacetin
Euquinine
Acetylsalicylic Acid

Jan. 26. Damp powder; packed when triturated.

Jan. 31. Powder solidified forming a cylindrical cake which could be removed as such; odor of acetic acid evolved, mass yellow in color.

Phenacetin
Powdered Extract of Nux Vomica
Caffeine
Acetylsalicylic Acid

Jan. 26. Powder packed when triturated.

Feb. 10. Acetic acid odor evolved.

Sodium Bicarbonate
Acetylsalicylic Acid

Jan. 26. The powder formed was but slightly damp.

Exalgine
Sodium Bicarbonate
Acetylsalicylic Acid

Jan. 26. Powder packed readily.

Jan. 31. Odor of acetic acid evolved.

Feb. 10. Powder very soft and damp.

Antipyrine
Acetylsalicylic Acid

Jan. 26. Powder packed tightly upon trituration.

Jan. 31. Strong odor of acetic acid evolved.

Magnesium Oxide
Salol
Acetylsalicylic Acid

Jan. 27. Powders showed no dampness.

Feb. 10. Powders packed in vial.

Magnesium Oxide
Acetylsalicylic Acid

Jan. 26. No dampness.

Feb. 10. Slightly damp and with pressure packed in the vial.

Sodium Citrate
Acetylsalicylic Acid

Jan. 26. No dampness.

Jan. 31. Powders packed in the vial.

May 26. Very strong odor of acetic acid evolved.

Potassium Acetate
Acetylsalicylic Acid

Jan. 26. Powders packed upon trituration.

Jan. 31. Faint odor of acetic acid.

Sodium Phosphate
Acetylsalicylic Acid

Jan. 26. Powders became damp and packed upon trituration.

Jan. 31. Faint odor of acetic acid.

Feb. 10. Mass solidified in a cylindrical mass which could be removed from the vial as such.

March 16. Partial liquefaction had occurred.

May 26. Strong acetic acid odor.

* The ingredients are printed in bold face.

Borax

Acetylsalicylic Acid

Jan. 29. No packing upon trituration.

Jan. 31. Powders packed and faint acetic acid odor evolved.

May 26. Strong acetic acid odor.

Lead Acetate

Acetylsalicylic Acid

Jan. 29. Immediate odor of acetic acid; no dampness.

Jan. 31. Dampness had developed and the powders packed; strong odor of acetic acid.

Phenol

Acetylsalicylic Acid

Jan. 26. Powders became quite damp and packed tightly.

Acetanilide

Acetylsalicylic Acid

Jan. 26. Powders slightly damp and packed on trituration.

The addition of ferric alum test solution to an aqueous mixture of each of these combinations gave the characteristic salicylate color test which is not given with undecomposed acetylsalicylic acid. As stated before, the presence of citrate or acetate masked this test, hence it did not respond in the combinations containing those radicals. Furthermore it was noted that solutions or mixtures neutral to litmus did not respond but upon acidulation the violet color appeared. All combinations are being kept under observation and an attempt to determine both a qualitative and quantitative decomposition will be made. It will be noted that these preliminary experiments, in most instances, agree with the results already reported. Repeated attempts have been made to separate the products of decomposition, but so far the results are unsatisfactory, mainly because duplicate results are difficult to obtain. The mixtures are being kept at room temperature under ordinary conditions with the hope that after three months have lapsed (*i. e.*, the summer intermission) decomposition will have reached a stage wherein isolation of these products will become feasible.

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4. *Bull. soc. chim.*, v. 15, pp. 743–7 (1914); *Ibid*, v. 17, pp. 401–6 (1915).
5. *Jour. A. M. A.*, v. 78, p. 275 (1922).
6. JOUR. A. PH. A., v. 10, p. 186 (1921).
7. *Austral. J. Pharm.*, v. 4, p. 23 (1923); through "British Y. B.," p. 385 (1923).
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9. *Analyst*, v. 45, p. 412 (1920); through *Chem. Absts.*, v. 15, p. 410 (1921).
10. JOUR. A. PH. A., v. 11, pp. 796–8 (1922).
11. *Am. J. Pharm.*, v. 96, pp. 592–3 (1924).
12. *Pharm. Post*, v. 45, p. 728 (1912).
13. *L'Union Pharm.*, v. 43, p. 456 (1902); through "British Y. B.," p. 264 (1903).
14. *Pharm. Era*, v. 43, p. 680 (1910).
15. *Am. Chem.*, v. 406, pp. 241–260 (1914).
16. *Bull. Soc. Pharmacol.*, v. 24, pp. 86–90 (1917); through YEAR BOOK, v. 6, p. 400 (1917).
17. *Chem. & Drug.*, v. 88, p. 487 (1916); through "British Y. B.," p. 312 (1916).
18. *Drug. Circ.*, v. 65, p. 137 (1921).
19. *Drug. Circ.*, v. 68, p. 193 (1924).
20. *Kommentar zum Deut. Arzneib.*, v. 5, p. 69 (1911).
21. *Chem. Abst.*, p. 1130 (1921).
22. *Apoth. Ztg.*, v. 30, pp. 647–48 (1915); through YEAR BOOK, v. 4, p. 316 (1915).
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25. *Archiv. Pharm. og Chemi.*, Apr. (1924); through *Pract. Drug.*, v. 42, p. 34, Sept. (1924).
26. *Jour. A. M. A.*, v. 76, p. 397 (1921).
27. *Bull. of Pharm.*, v. 29, p. 95 (1915).
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29. *Chem. & Drug.*, v. 98, p. 35 (1923).
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31. *Pharm. Era*, v. 43, p. 680 (1910).
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36. *Pharm. Weekbl.*, v. 54, p. 155 (1919); through Y. B., v. 8, p. 136 (1919).
37. *Bull. of Pharm.*, v. 28, p. 527 (1914); *Ibid*, v. 29, p. 174 (1915).
38. "Incompat. in Prescriptions," Ruddiman, Ed. 4, p. 163 (1917); "U. S. Dispensatory," Ed. 20, p. 19 (1918).
39. "Even when death is not caused by this mixture, rash or other distressing symptoms have frequently followed the using of the two common drugs at the same time," *Drug. Circ.*, v. 68, p. 152 (1924); "In quinine aspirin powders that have been kept some time dangerous quantities of quinotoxin may have been formed," *Pharm. Jour.*, v. 97, p. 27 (1916); through "Digest of Comments," (1916).
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COLLEGE OF PHARMACY,
UNIVERSITY OF WASHINGTON,
SEATTLE, WASH.

A NEW EMULSIFYING AGENT FOR VOLATILE OILS.*

BY CHARLES H. LAWALL.

Several years ago while working with a commercial volatile oil emulsion, the ingredients of which were identified as having been used for producing a permanent degree of emulsification were so unusual in their character, that after the particular piece of research was completed, some experiments were performed with the substances in question. These experiments led to a recognition of the fact that a mixture of 20% of powdered egg albumin and 80% of powdered cream of tartar is an emulsifying agent with a selective power of sub-dividing or emulsifying volatile oils rather than fixed oils.

One of the particular points of interest in connection with this rather empiric combination is the fact that it can be used in very much smaller quantities than emulsifying agents usually are capable of serving. This can be best illustrated by giving a typical formula for such an emulsion with working directions.

To emulsify volatile oils heavier than water, such as oil of sassafras, wintergreen or clove, place 100 cubic centimeters of the oil in a bottle of a capacity of 200 cubic centimeters. Add one gram of the emulsifying mixture, consisting, as stated, of 20% egg albumin and 80% cream of tartar and agitate well. Then add

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