PRESCRIPTION CLINIC.*

SHOWING SOME INCOMPATIBLE AND SOME UNUSUAL PRESCRIPTIONS.

BY CHARLES H. LAWALL AND IVOR GRIFFITH.

(1)	Sodium Borate	1 1/2 drachms
	Acid Salicylic	1 drachm
	Glycerin	10 fluidrachms
	Syrup to make	4 fluidounces

No matter how this prescription is compounded a chemical change is bound to occur between the sodium borate and the glycerin with the formation of boric acid and sodium metaborate, both of which would be soluble in the menstruum of glycerin and syrup. This reaction is stated to be progressive but is hastened when heat is used in the manipulation.

The thoughtless way of compounding this prescription would be to triturate the solids with the glycerin and add the syrup and dispense the mixture with a "shake well" label disregarding the floating needles of undissolved acid. Two ways of compounding this prescription suggest themselves to us:

In the first, salicylic acid is dissolved in a very small volume of alcohol and the borax is dissolved in the warmed glycerin. The two solutions are mixed and the syrup then added. A perfectly clear solution results.

The other method is to dissolve the salicylic acid in 5 fluidrachms of the glycerin, heated on a water bath and the borax in the rest of the glycerin, also heated. These two solutions are mixed and enough syrup added to measure 4 fluidounces. Both methods produce apparently permanent solutions.

(2)	Quinine Bisulphate	2
	Phenol	1
	Glycerin	4
	Distilled Water	60

Compounded in any manner, strictly according to this formula, a crystalline precipitate is bound to occur after the product has stood a while. This precipitate or rather tufted masses of crystals, on examination, proved to be alkaloidal quinine.

The addition of an excess of an acid which gives soluble salts of quinine, prevents the formation of this precipitate. Lactic acid which lately has been frequently and successfully used in the treatment of seborrhoea seems the logical one to use. Addition of this acid inhibits the production of a precipitate, and while no trial was made with the substitution of dilute alcohol for the distilled water, such a change, it would seem, would also prevent this precipitation.

(3)	Sodium Nitrite	20 grains
	Sodium Citrate	
	Sodium Bromide ..... of each	2 drachms
	Compound Digestive Elixir ..... to make	3 fluidounces

* Presented before Section on Practical Pharmacy and Dispensing, Indianapolis meeting, 1917. Most of the prescriptions were further discussed by the authors, and also by E. A. Ruddiman, W. H. Glover, C. P. Wimmer, L. C. Hopp, Carl Whorton, Louis Saalbach, Frank Schachleiter and R. W. Terry.

Every combination was tried in order to hasten the reaction which occurs in the compounding of this prescription. Effervescence does not totally cease for from 36 to 48 hours. Tests of the mixture after it had stood several days proved the presence of a nitrate, non volatile and volatile nitrites and the turbidity of the product was due to the salting out of the digestive ferments in the elixir.

There is no way, within our ken, of overcoming the incompatibility of this prescription.

(4)	Sodium Salicylate	2 drachms
	Hexam	1 drachm
	Spirit of Nitrous Ether	2 fluidrachms
	Water to make	2 fluidounces

When this prescription is filled, contrary to expectation, it develops a peculiar brownish black coloration which deepens perceptibly on standing. If the spirit is decidedly acid one may look for crystals of salicylic acid in the mixture. This could probably be overcome by neutralizing the spirit. Another possibility is that nitrosalicylic acid may be formed in the mixture. The hexamethylenamine is apparently unaltered unless such a change will occur after the mixture has stood a while. We have not been able to determine the cause of this development of color.

(5)	Theobromine and Sodium Salicylate	2
	Sodium Iodide	4
	Corrosive Mercuric Chloride	065
	Distilled Water	60

Snap judgment in this particular case is liable to lead one astray. The sodiomercuric iodide formed in the prescription, presumably should, like Mayer's reagent precipitate alkaloids. We are taught however that the dimethylxanthine group, consisting of caffeine, theobromine, and others, are not precipitated by this reagent. Acting on this presumption we accordingly fill this prescription and send it out a clear transparent solution. It is brought back in a day with a white precipitate. This precipitate contains theobromine and mercury. Caffeine citrate in the same combination gives no precipitate. Perhaps we have discovered a new differentiating test between caffeine and theobromine, we shall pursue this subject further but give the example as a warning.

(6)	Quinine Sulphate	1
	Potassium Acetate	6
	Aromatic Sulphuric Acid	sufficient
	Syrup of Lemon to make	90

The potassium acetate is quickly dissolved in one-half of the syrup. The quinine sulphate, with the aid of a few drops of the acid is dissolved in the rest of the syrup and the two solutions are mixed. The result is a heavy, bulky precipitate of quinine acetate.

This prescription was compounded in this way, in a certain drug store, and the patient returned it with a request that it be transferred to an ointment box, so that it could be administered with less trouble.

Using simple elixir in place of syrup of lemon modifies the difficulty somewhat, although it does not correct it altogether.

(7) Thymol Iodide..... 1/2 drachm
Wool Fat..... 1/2 ounce
Cottonseed Oil..... to make 6 fluidounces

This is a favorite prescription with an eminent Philadelphia physician. He reports several "messes" as the result of careless and thoughtless filling of this recipe. The proper way and a way that is always productive of perfect admixture is to dissolve the thymol iodide in part of the oil and the melted wool fat in another portion. When the latter is cool the two solutions are mixed and the preparation thoroughly shaken. It does not produce a perfect solution.

(8) Strychnine Sulphate..... 1/2 grain
Tincture of Digitalis.....
Tincture of Strophanthus..... of each 1/2 fluidounce

A turbidity at first, and afterwards a precipitate appears on compounding this prescription. Using a fat-free tincture of digitalis avoids this complication to a certain extent.

(9) Glycerin.....
Solution of Hydrogen Dioxide.... of each 2 fluidounces

It was recently stated in one of the drug journals that this combination on standing a few days, developed oxalic acid, that is, the glycerin was oxidized by the dioxide. As a matter of fact the solution which was on exhibition was made some five or six months ago and when tested recently showed no evidence whatever of oxalic acid. Assay developed the fact that the peroxide in the solution still retained its full volume of available oxygen. This is another evidence of what is too often seen in the way of criticism. The graphitic cellulose method of criticising prescriptions is a very unsafe way to attain accurate results.

(10) Sodium Bromide..... 4 drachms
Elixir of Pepsin and Rennin Compound
to make..... 2 fluidounces

After standing a few hours a peculiar turbidity manifested itself in the solution, later depositing as a slimy, gelatinous precipitate. This was probably the rennin and pepsin with impurities salted out by the sodium bromide. The addition of an acid did nothing to prevent this precipitation. As a matter of fact the addition of an excess of ammonia water was the only way whereby the precipitate could be redissolved; and this being destructive of the enzymic action would be impermissible.

It is only the unsightly appearance of the product of the prescription that calls for comment, since it can well be dispensed as it is with a "shake-well" label.

(11) Acetphenetidin..... 10 grains
Quinine Sulphate..... 20 grains
Aromatic Sulphuric Acid sufficient
Syrup of Citric Acid or,
Aromatic Elixir to make 2 fluidounces

There is no incompatibility in this prescription. Notice however is to be taken of the fact that the marked fluorescence which is usually exhibited in this acid solution of the quinine salt is practically absent here. For some peculiar reason acetphenetidin prevents the occurrence of this phenomenon.

(12)	Aspirin		1 drachm
	Potassium Iodide		1 drachm
	Glycerin		4 fluidrachms
	Anise Water	to make	4 fluidounces

As one would suspect there is a fairly quick dissociation of the acid radicals of the aspirin in the product of this prescription due of course to hydrolysis. The aspirin loses its identity breaking up into acetic and salicylic acids, the presence of both of which was proven. The fine display of crystals exhibited in the one product as well as the grape-like form of precipitate shown in the other bottle are salicylic acid. Acetic acid and free iodine are present in the supernatant fluid.

(13)	Potassium Permanganate		20 grains
	Phenol		20 grains
	Glycerin		4 drachms
	Distilled Water	to make	2 fluidounces

Potassium permanganate in the presence of glycerin is immediately reduced to the black oxide of manganese and oxygen is liberated. This nascent oxygen will bring about a change in the composition of the glycerin and the phenol. This change, however, is probably very slow and need not be considered since there is no way of filling this prescription without bringing about the chemical change mentioned. It presents a clear case of an incorrigible incompatibility.

(14)	Quinine Sulphate		15 grains
	Sodium Benzoate		2 drachms
	Distilled Water	to make	3 fluidounces

In the consideration of the proper means of filling this prescription, the use of an acid to assist in the solution of the alkaloidal salt is prohibited since such an addition would only create a new difficulty, that is, the releasing of the insoluble benzoic acid from its combination.

In attempting to fill the prescription we dissolve the benzoate in one fluidounce of water and the quinine salt as nearly as possible in the rest of the water. The two portions were then mixed. The result was the precipitation of the very bright crystal masses of quinine benzoate. The filled prescription reminds one very much of the old time miniature snow storm scene enclosed in a sealed glass bulb that aroused our curiosity in our younger days.

(15)	Sodium Benzoate		3 drachms
	Solution of Calcium Hydroxide	to make	4 fluidounces

Precipitation of the slightly soluble calcium benzoate occurs here and is intensified somewhat the longer the bottle is allowed to stand. There is no way of overcoming this without an impermissible change in the formula. It can be dispensed with a "shake-well" label.

(16)	Strontium Bromide		
	Potassium Citrate	of each	2 drachms
	Distilled Water	to make	2 fluidounces

Quite a peculiar phenomenon occurs here. Dissolving the strontium bromide in a fluidounce of the water and the potassium salt in the rest of the water, then mixing the two solutions produces a precipitate which soon disappears. Shaking the bottle brings it back immediately and on standing a while the prescription looks

more like milk of magnesia than anything else. The insoluble precipitate of course is strontium citrate.

(17)	Menthol	8 grains
	Quinine Sulphate	20 grains
	Phenol	24 grains
	Ichthyol	$2^1/_2$ drachms
	Hydrous Wool Fat	4 drachms
	Castor Oil	10 fluidrachms

This prescription is reported to have given various results in the hands of different compounders and one will not be surprised at this. As the formula stands we can conceive of no way of making a permanently presentable and smooth product.

Substituting 15 grains of alkaloidal quinine for the salt and melting this with the menthol, phenol and ichthyol and incorporating this mixture with the solution of anhydrous (not the hydrous) wool fat in the warmed castor oil gives a permanently presentable and non-granular creamy liquid.

DISCUSSION OF OTHER PRESCRIPTION AND MANUFACTURING PROBLEMS.

The spare moments of the Section on Practical Pharmacy and Dispensing were given over to discussions relating to practical pharmacy:

ENTERIC PILL COATING AND CAPSULES.

W. L. SCOVILLE: An enteric coating for pills must be insoluble in the stomach and soluble in the intestines. Salol would be the ideal coating for this purpose, if it could be applied in an amorphous condition, but as the solvent gets in between the crystals of the salol there is no certainty that the pill will pass the stomach intact.

WILLIAM GRAY: We have never found a better coating than salol, but as Professor Scoville states this is not always satisfactory.

W. L. SCOVILLE: I carried on quite a series of experiments on gelatine capsules treated with formaldehyde several years ago. I found this: that if you take a one percent solution of formaldehyde, and dip the capsules, let them stay in this solution for not more than thirty seconds, take them right out and drain them and dry them, you have a condition that after about two weeks the gelatine has an enteric property; that is, it is insoluble in acid but is soluble in five-tenths percent solution of sodium carbonate. All experiments were carried out at a temperature of 37.5° C., at which they will dissolve readily in an alkaline solution. It looked very promising. I kept them for a year or two years. I tested them every three months, and while they dissolved up nicely in alkali, they refused to go to pieces in acid. They would swell but they would not dissolve. After a year and a half I began to find that the solubility in the alkali was decreasing. In other words, the process seemed to be progressive. The reaction, whatever it is, whether it is physical or chemical, in gelatine, goes on; keeps on increasing. At first it is very weak, and the capsules were not fit to be used for two weeks. Then they were all right for a year. We have used that process at the laboratory for experimental purposes—that is, where we could control it ourselves for enteric experiments.

By the way, Mr. Gray just asked me about using ipecac internally. I would like to state that if he wants to put ipecac in capsules and treat them that way, do not use them for a month, and then see that they are all used within a year, you will then get as good results as you can with anything. In hospital work that is thoroughly practical, but not for commercial work; it is unsafe to place a product of this kind on the market that is only good for a limited time.

PHARMACOPOEIAL AND NATIONAL FORMULARY PREPARATIONS.

R. W. TERRY: About a year ago I prepared some Compound Tincture of Cudbear; recently I had occasion to use some and found the caramel had separated out.

W. H. GLOVER: My experience with caramel of the market is unsatisfactory, hence I prepare it myself and do not experience the trouble indicated by Mr. Terry.

LOUIS SAALBACH: Much of the commercial caramel is not made from sugar but starch. (See p. 495 Vol. III and p. 1510 Vol. IV, JOURNAL A. PH. A.—Editor.)

CHARLES H. LAWALL: I use sodium carbonate in making caramel from glucose.

C. M. SNOW: We have had some trouble in the manufacture of Liquid Petroxolin, but we overcame the trouble by proper heating in a water-bath instead of on a water-bath.

W. H. GLOVER: In making Iodine Petroxolin formerly I found that after standing there would be a separation. I overcame this by using Russian oil.

C. P. WIMMER: Soft Soap, as now made is no longer green, and we have had some difficulty in making a satisfactory product by using the present formula.

LOUIS SAALBACH: I heard of an experience with soft soap which may be of interest. In making it according to the formula and following the directions as printed: "Dissolve 86 Gm. of potassium hydroxide in 100 mils of water in a capacious dish by the aid of heat. Immediately add 430 Gm. of cottonseed oil to the solution, and stir the mixture actively for a few moments. Then reapply the heat and, at first evidence of froth from boiling pour in 50 mils of alcohol, stir actively until the froth suddenly rises;" the mixture took fire and burned the operator who had followed these directions. My experience with this formula is not satisfactory. (Similar expressions came from W. H. Glover, C. P. Wimmer and C. M. Snow.)

C. L. EDDY: The Compound Solution of Phosphates formula calls for more than 1000 mils.

C. M. SNOW: This evidently is an error in the formula and the volume of water should be reduced.

(A discussion of Elixir of Gentian concluded the session. The point discussed was relative to the amount of Compound Spirit of Cardamom in the preparation which nearly all considered excessive.)

CATALYSIS.

D. W. Horn, in the Transactions of the Wagner Free Institute of Philadelphia, Volume VIII, p. 97, states that "contact underlies chemistry." He continues in saying, "Bodies may influence each other at almost incredible distances, but this action is physical, not chemical. Briefly, no contact, no chemical action. In the time-honored generalizations, of chemistry, its 'fundamental laws,' the action of pure substances upon each other was considered without reference to the effects of adjacent bodies. In some few instances, however, the effects of adjacent bodies were so striking as to compel early attention. Until recent years the multiplication of such instances has been slow. Such action or influence of an adjacent body may be covered by the term 'catalysis,' introduced by Berzelius, the famous Swedish chemist, in 1834.

"In 1836, Berzelius compiled all cases known in which, by the presence of a foreign body, a chemical reaction is hastened without the foreign body itself being changed. These foreign bodies thus acting he called 'catalysts.' Historically, catalysis is not a new phenomenon. Processes of fermentation were known to the ancients, and these involve catalysts. In fermentation by yeast, the yeast plant produces the catalyst, or enzyme, as it is more frequently called. In sharp contrast with chemical reactions that, when not catalyzed, proceed at so slow a rate as to produce less than noticeable amounts of products, stand the reactions that are so rapid as to be practically instantaneous. Catalysis, of course, is not concerned with such reactions.

"It is not strictly true that a catalyst is found to be *unchanged* at the end of a catalyzed reaction. It is correct to say that the final products are the same, as they would have been had the catalyst been absent. The catalyst may be rather unmistakably changed, not in amount, but in physical state. Thus the crystalline manganese dioxide used to generate oxygen from potassium chlorate becomes a fine powder, and changes in physical state are known to occur in iron oxide and in platinum used as catalysts in other systems. The amount of the catalyst, no matter how small, seems to remain unchanged. Catalysts themselves may be accelerated or restrained in their rapidity of action. Two catalysts usually have a greater joint effect than either would have singly. 'Promoters' that increase the activity of catalysts are also known. Some substances so completely obstruct the action of catalysts that they have been called 'Poisons.' Enzymes and toxins have their poisons and antitoxins, and the analogy to them is quite close, even in the case of metallic catalysts. Some catalysts seem specific for a given reaction, but many are capable of manifold application, and no general method is known for guidance in selecting a catalyst for a given reaction."