

CORRECTABLE PHARMACEUTICAL AND CHEMICAL
INCOMPATIBILITIES.*

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The problem which gives the prescription pharmacist the greatest concern and the subject which enters into all branches of pharmaceutical learning, is *Incompatibility* involving more particularly the pharmaceutical and chemical types. The degree of permissible deviation from the prescription proper, is a matter of considerable controversy with many pharmacists, due largely to an inferiority complex, a lack of sufficient therapeutic knowledge or an unwarranted fear that any modification of the prescription would either change it medicinally or that such a change would meet with disfavor on the part of the physician.

No calling of any consequence was ever practiced by "rule of thumb." Both pharmacy and medicine are extremely broad in their application, and just as the physician's selections of remedies must be varied with the patient's needs, so the pharmacist must adjust his training to the peculiarities of the prescription.

Obviously, no agent should be used which increases the danger, changes the appearance, permanency, uniformity of dose or intended effectiveness which would in any manner, or in any material degree, alter the medicinal effect from that originally intended by the physician. *Correctives* then, in this sense, should be employed in the minimum quantities and only those *Changes* resorted to under this order of things which would be important therapeutically and acceptable to the physician, realizing that in every case the finished product must represent the original intent of the physician in its fullest measure. This thought is always an element of the greatest importance.

It is a matter of record that opinions of pharmacists are sought more and more by the members of the medical profession. Experience teaches them to respect the training and ability of the men who carry on the ethical practices of our profession. Confidence and recognition for the pharmaceutical profession must be established, if pharmacists are to fulfil in the greatest measure the type of service that is expected of them—in the face of certain interests that have unfortunately swept the country, and who by their persistency have crushed out a large part of pharmacy's rightful practice and flooded the country with high-priced specialties. Notwithstanding this vigorous campaign, the courage of pharmacists is demonstrated by progress and the study of incompatibilities presents a phase of pharmaceutical and medical research.

It is of fundamental importance that pharmacists strive for professional recognition and advancement.

The incompatibilities presented are studies of some of the more common problems which frequently confront the pharmacist. It is not intended that these prescriptions with the accompanying remarks convey anything particularly unusual to the prescription pharmacist, but they have proved satisfactory over a long period of years.

PHARMACEUTICAL AND CHEMICAL INCOMPATIBILITIES.

Rj 1	Acetylsalicylic Acid	10
	Potassium Citrate	10
	Syrup	} of each
	Water q. s.	

* Section on Practical Pharmacy and Dispensing, A. Ph. A., Portland meeting, 1935.

This is a typical example of the every-day prescription in a drug store when for the purpose of convenience the physician desires to present the medication in liquid form.

Acetyl Salicylic Acid being only partially soluble in this proportion, even in the presence of the potassium citrate, which contributes to its solubility, separates from the main body of the liquid and is partially deposited and suspended on the surface. The rapidity with which this separation takes place does not permit of a uniform dose even when the mixture is thoroughly shaken and, therefore, it becomes necessary to add an agent of suspension for the purpose of increasing the viscosity and thereby preventing the easy separation of this insoluble material. The substance best adapted to this prescription is tragacanth; 5 grains will accomplish the object desired, holding the insoluble Acetyl Salicylic Acid in a highly uniform degree of suspension until a dose can be poured.

℞ 2	Fluidextract of Iris	5
	Aromatic Elixir <i>q. s.</i>	60

This prescription clearly demonstrates a type of pharmaceutical incompatibility resulting from a change in menstrua. The resinous character of iris requires approximately 80% of alcohol. This is also true for drugs like buchu. When galenical preparations of this kind are brought in contact with vehicles such as Elixir of Pepsin Compound and Aromatic Elixir which are relatively low in alcoholic content a lowering of alcoholic percentage takes place with resulting precipitation. The correction is by addition of sufficient alcohol to prevent this precipitation. When two or more galenicals are present, one with a high alcohol content and another with a relatively low content, obviously, there cannot result a thoroughly clear liquid since an intermediate alcohol content must prevail, that is, an average between that of each of the preparations present. The correction was made with 4 drachms of alcohol.

℞ 3	Bismuth Subnitrate	8
	Phenyl Salicylate	4
	Syrup } of each <i>q. s.</i>	60
	Water }	

This prescription carries two insoluble substances—bismuth subnitrate and phenyl salicylate. While bismuth subnitrate is an impalpable powder, phenyl salicylate is a crystalline body requiring careful treatment in a mixture of this kind. The *modus operandi* is to reduce the phenyl salicylate to a fine powder in a mortar and mix thoroughly with the bismuth subnitrate. To this the syrup is added gradually and finally the water. Heat should never be employed in a preparation of this kind, since it fuses the phenyl salicylate and permits it to recrystallize in the mixture.

Both bismuth subnitrate and phenyl salicylate separate rapidly from this mixture and as a consequence must receive proper attention. The correction is made with 5 grains of tragacanth which is mixed intimately with the powders before the addition of the Syrup. Its presence increases the viscosity of the preparation preventing the ready separation of the insoluble bodies.

℞ 4	Citrated Caffeine	0.03
	Acetyl Salicylic Acid	4.0
	Phenacetine	2.0
	Elixir Pepsin Compound <i>q. s.</i>	60.0

This prescription presents another type requiring a suspension agent. Here again tragacanth is the preferred substance; however, owing to the alcoholic content of the Elixir of Pepsin Compound, 7 grains of tragacanth are required to accomplish the object desired.

℞ 5	Adrenalin Chloride Sol.	4.0
	Menthol } of each	0.03
	Camphor }	
	Olive Oil <i>q. s.</i>	30.0

Owing to the aqueous nature of solution of adrenalin chloride, it is immiscible with the menthol, camphor, olive oil. Correction is made by obtaining permission from the physician to use the practical equivalent in an oil solution, namely, adrenalin inhalant, ℞ 6. The same prin-

ciple is portrayed in prescription 6, wherein through ignorance of solubility the physician has prescribed ephedrine sulphate in place of ephedrine alkaloid.

℞ 6	Ephedrine Sulphate	0.30
	Menthol	} of each
	Camphor	
	Olive Oil	
	Liquid Petrolatum	
		0.015
		30.0

The correction is in obtaining the permission of the physician to substitute ephedrine alkaloid in an equal amount for the ephedrine sulphate thus providing for a relatively clear preparation.

℞ 7	Spirit Nitrous Ether	15.0
	Potassium Citrate	30.0
	Water <i>q. s.</i>	60.0

Potassium citrate is very soluble in water and nearly insoluble in alcohol. When a nearly saturated solution in water is prepared, as in this instance, this solution becomes immiscible with the Spirit of Nitrous Ether, which is alcoholic, and the two substances are noticeably separated and mix with difficulty. The speed with which the separation takes place prevents the giving of a uniform dose. The correction is in the dilution of the prescription to twice its quantity with water and doubling the dose. Potassium citrate is not thrown out of solution for the reason that the affinity of the water for this substance is greater than for the alcohol.

℞ 8	Solution Aluminum Acetate	12
	Hydrous Wool Fat	5
	Petrolatum <i>q. s.</i>	30

In the foregoing an ointment is wanted and the physician expects, owing to the properties claimed for wool fat, that the 12 cc. of solution of aluminum acetate will be picked up with the 5 Gm. of wool fat. This is erroneous since the hydrous wool fat will not take care of that quantity of fluid. The correction is in substituting 5 Gm. of Aquafor for an equal weight of petrolatum.

℞ 9	Zinc Sulphate	0.03
	Water	2.0
	Sol. Adrenalin Chloride	3.0
	Petrolatum, white	

This prescription is intended for an eye ointment. The 3 mg. of zinc sulphate are dissolved in water, solution of adrenal in chloride added and this added to 25 Gm. of white petrolatum. The ointment as prepared would appear to be free from criticism, but upon standing a short time separates water, due to the immiscibility of this quantity of aqueous material with Petrolatum.

The correction is in substituting 5 Gm. of Aquafor for an equal weight of white petrolatum.

℞ 10	Fluidextract Buchu	10
	Aromatic Elixir	50

Opportunity is taken to show the application of the Elixir Iso-Alcoholic advocated by Dr. Bernard Fantus, of the University of Illinois College of Medicine. Fluidextract of Buchu is shown with aromatic elixir resulting in the profuse separation of the resinous constituents of the drug.

Buchu is also shown with Elixir Iso-Alcoholic which results in a beautifully clear liquid. Elixir Iso-Alcoholic means of the same strength. In other words Fluidextract of Buchu has an alcoholic strength of 80%. To be essentially miscible with it, Elixir Iso-Alcoholic should be of the same strength. In making this Elixir an elixir of low alcoholic content is employed, 5%, and a high one of 90%. These two preparations are used in various proportions to obtain an alcoholic preparation of the desired strength.

℞ 11	Spirit Nitrous Ether	8.0
	Potassium Iodide	2.5
	Syrup	
	Water <i>q. s.</i>	30.0

Most specimens of Spirit of Nitrous Ether present an acid reaction due either to errors in manufacture or the breaking down of ethyl nitrite through long standing. It is a well-known fact that nitrous acid is incompatible with iodides, and since Spirit of Nitrous Ether is a solution of ethyl nitrite, a reaction naturally follows with liberation of iodine turning the prescription a bright red.

The correction is in neutralizing the free acid in the spirit of nitrous ether before adding it to the other ingredients, preferably with some agent like potassium bicarbonate. Prescriptions thus prepared have kept for several years without liberation of iodine.

℞ 12	Potassium Iodide	5.0
	Sodium Nitrite	2.0
	Syrup of Squill	15.0
	Water <i>q. s.</i>	120.0

This prescription presents the same type of incompatibility as No. 11 in a little different way. Sodium nitrite is used in the presence of potassium iodide and syrup of squill which is acid. Acetic acid breaks down the sodium nitrite forming nitrous acid which is incompatible with potassium iodide, liberating free iodine.

The correction is in obtaining the physician's permission to use an equivalent amount of another preparation of squill which is free from acid, preferably an equivalent amount therapeutically of the fluidextract which is free from acid.

℞ 13	Compound Solution Iodine	10
	Elixir Iron Quinine and Strychnine N. F. <i>q. s.</i>	120

This prescription presents another chemical incompatibility resulting in the precipitation of the alkaloids of quinine and strychnine.

The correction is in raising the alcoholic content of the preparation to a point where the quantities of these substances present will be soluble. This is accomplished with 8 cc. of alcohol substituted for an equivalent amount of the Elixir of Iron Quinine and Strychnine before the addition of the Lugol's Solution.

℞ 14	Codeine Sulphate	0.6
	Potassium Bromide	40.0
	Syrup	
	Water of each <i>q. s.</i>	120.0

The codeine previously dissolved in a part of the water is added to a solution of potassium bromide in the balance of syrup and water with the almost immediate formation of a white precipitation of codeine alkaloid. The corrective measure is to replace 10 cc. of the water with alcohol and add the solution of codeine sulphate to this mixture. The alcohol acts dissolving upon the codeine alkaloid and prevents its precipitation. A prescription of this kind as corrected is acceptable to the physician and safe for use by the patient.

℞ 15	Strychnine Sulphate	0.020
	Potassium Iodide	5.0
	Syrup	15.0
	Water <i>q. s.</i>	120.0

To strengthen the reaction 10 times this quantity of strychnine was used.

This presents the same problem as given in the preceding prescription, but owing to the small dose of strychnine, it is somewhat more treacherous. Strychnine is deposited as a white crystal and as such is difficult to detect. The corrective measure is as before, namely, alcohol in sufficient amount, approximately 6 cc., which acts dissolvingly upon the alkaloid keeping it safely in solution. For purposes of exhibit the quantity of strychnine is increased 10 times.

℞ 16	Tincture Digitalis	10.0
	Morphine Sulphate	0.5
	Liquor Potassium Arsenite	12.0
	Peppermint Water <i>q. s.</i>	120.0

The incompatibles are morphine sulphate and the potassium arsenite solution which is decidedly alkaline. Since there is insufficient alcohol present to keep the precipitated morphine in solution, more alcohol must be added; 12 cc. are necessary.

℞ 17	Soluble Ferric Phosphate	12.0
	Acid Phosphoric	8.0
	Strychnine Sulphate	0.030
	Elix Aromatic	
	Cinnamon Water of each <i>q. s.</i>	120.0

Sodium citrate in ferric phosphate is the substance which makes ferric phosphate soluble. In the presence of phosphoric acid, the sodium citrate is converted into sodium phosphate resulting in the precipitation of ferric phosphate. To prevent the precipitation it is necessary to add 3 drachms of sodium citrate to the three drachms of ferric phosphate solution, or use 10% solution of meta-phosphoric acid in a mortar and dissolve—add the remainder of water and finally the phosphoric acid—a clear solution results.

℞ 18	Betanaphthol	0.60
	Balsam Peru	8.0
	Acid Salicylic	2.0
	Olive Oil	45.0
	Lime Water <i>q. s.</i>	120.0

Since both an acid and alkali are present some trouble should be expected. When the lime water is added to the olive oil a small amount of calcium oleate is formed which in turn emulsifies the balance of the olive oil. To this mixture, the betanaphthol dissolved in a small amount of alcohol is added, then the Balsam of Peru, warmed and added very gradually under shaking or mixing in a mortar and, lastly, the salicylic acid also dissolved in a small amount of alcohol. As soon as the salicylic acid is added, calcium salicylate is formed which releases the calcium from the calcium oleate thus destroying the insoluble soap, which in turn removes the agent of emulsification, and the preparation becomes an unsightly mixture.

To correct, it is necessary to consult the physician and obtain his permission to eliminate either the salicylic acid or the lime water. If the lime water is eliminated an ordinary emulsion with acaecia can be easily prepared resulting in the same type of mixture. The Balsam of Peru is somewhat troublesome, but can be properly handled through careful emulsification in the mixture.

℞ 19	Crude Coal Tar	6.0
	Solution Aluminum Subacetate	12.0
	Petrolatum <i>q. s.</i>	60.0

Crude coal tar and solution of aluminum subacetate are not thoroughly picked up by the petrolatum. The crude coal tar remains stringy and the solution of aluminum subacetate separates in drops.

To correct, it is necessary to substitute 10 drachms of Aquafor for an equal amount of petrolatum when a smooth and homogeneous ointment is produced.

℞ 20	Mercurochrome	1
	Water	10
	Petrolatum	20

The physician has intended the petrolatum to pick up the water, necessary for solution of Mercurochrome. This, however is not accomplished. The pharmacist has one of two suggestions to offer to the physician:

1. To substitute a part (10 Gm.) of the petrolatum with wool fat.
2. To substitute 5 Gm. of petrolatum with an equal weight of Aquafor.

Owing to the simplicity of handling, the latter method is shown here in the exhibit—(at the meeting).