

THE CORRECTION OF INCOMPATIBILITIES IN PRESCRIPTIONS. I.*

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In the present-day practice of pharmacy a real pharmacist finds many opportunities to be of service by avoiding or correcting incompatibilities in prescriptions. Every physician who has any originality or capacity for professional development will frequently prescribe new combinations of medicaments. In many cases such original prescriptions will not result in presentable preparations without the advice of the trained pharmacist.

Needless to say, the pharmacist should not make any important changes in a prescription without having first secured the consent of the physician. However, the pharmacist should establish his professional standing in such a manner that the physicians will not only welcome his advice on prescriptions but will bring their prescription problems to him to secure an opinion.

Now that professors of pharmacy are teaching their students to cooperate with physicians it would be logical for the medical faculties to train the future physicians to consult the pharmacist on all pharmaceutical questions. Some medical colleges are handling this problem in a commendable manner but in others there is considerable room for improvement. For example, in some medical schools the subject of incompatibilities is scarcely mentioned in the courses in materia medica and prescription writing. One reason given for this is that the medical professor thinks the medical graduates would be afraid to formulate a prescription if they knew they might run into such a thing as an incompatibility. Such teaching is not fair to the medical student; he should be taught that incompatibilities are frequently encountered and that such difficulties can be avoided or corrected by consultation with the pharmacist, who is a specialist in the field of drugs.

In some medical schools great stress is placed on prescribing one drug at a time, thus avoiding all incompatibilities. Such a policy is of doubtful validity. Although the combination of twenty or thirty ingredients in a single prescription may be very undesirable, the insistence of some medical men on giving only one drug is a resurrected principle of homeopathy and is just another manifestation of poorly conceived therapeutic nihilism. It is very evident that in many cases more than one drug is needed to produce a number of medicinal effects which may be desired, or one drug may be used to antagonize an undesirable effect of another drug without hindering the effect which is wanted. In the two following prescriptions, selected at random, it is impossible to suppose that any single ingredient would meet the needs as well as the formulated prescriptions.

℞ Zinci Sulfatis	gr. i
Sol. Adrenalin	℥ vi
Sodia Chloride	gr. iiiss
Sol. Acidi Borici Sat.	℥ i
<i>M. Sig.</i> Two drops in eyes.	

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℞ Tr. Opii Camph.	10
Bism. Subgallate	30
Tr. Catechu Co.	20
Po. Acacia	8
Syr. Auranti, q. s.	120
M. and Sig. ̄i q. 3 h.	

Regardless of the soundness of such a policy, every physician is free to prescribe one drug at a time if he chooses to do so. However, many individual drugs would be very unpalatable unless prescribed with some flavored vehicle. If this is done the question of incompatibility between the drug and the vehicle arises. Fantus and Dyniewicz (1) have recently discussed the incompatibilities of certain vehicles. Syrup of cherry and syrup of raspberry are incompatible with salts of silver, mercury, lead and quinine, owing to the presence of benzoic acid in the syrup as a preservative; these syrups are incompatible with alkaline substances on account of the resulting precipitation and color change. Other examples could be cited but it is evident that incompatibilities cannot be avoided even in one-drug therapy.

Correction of Incompatibilities.—Although incompatibilities may be a bugbear to the physician they should not be viewed in this light by the pharmacist. To the pharmaceutically trained man, an incompatibility should be looked upon as a problem to be solved and an opportunity for service.

The prescriptions which follow represent incompatibilities and dispensing problems which have recently been subjected to study and experimentation.

PREScription No. 1.

℞ Potassium Citrate	℥ iiiiss
Spirit of Nitrous Ether	f℥ iv
Simple Syrup	f℥ iv
Water, q. s.	f℥ ii

Prescriptions of this type have frequently been cited in the literature as examples of incompatibility. There is a cloudiness on mixing and subsequent separation into an upper layer consisting chiefly of alcohol and a lower layer which is mostly an aqueous solution of potassium citrate. It has been reported (2) that with the addition of half a drachm of water the above prescription can be dispensed as a clear, uniform preparation. In the present study this was found to be true under ordinary conditions of filling.

PREScription No. 2.

℞ Potassium Citrate	℥ ii
Spirit of Nitrous Ether	f℥ ss
Syrup of Orange	f℥ ss
Water, q. s.	f℥ ii

It has been stated (3) that in this prescription cloudiness and separation into layers can be prevented by replacing half of the water by glycerin. However, when this prescription was filled as written by students in the course in prescriptions at the University of Florida it was found that a clear solution with no layering was ob-

tained. Subsequent investigation showed that in mixing the ingredients in a graduate at room temperature as much as 3 drachms of potassium citrate consistently failed to cause separation into layers. However, the use of 3.25 drachms resulted in layering; this result is in accord with the findings in prescription No. 1, in which a slight dilution of the prescription containing 3.5 drachms of potassium citrate obviated the layering.

Further tests were carried out to determine the effect of glycerin, syrup of orange and temperature on the layering. Glycerin was found to be of no value in preventing layering, since replacement of half of the water by glycerin did not prevent separation when 3.25 drachms of potassium citrate was used. Syrup of orange increased the tendency toward separation; when the quantity of syrup of orange was doubled, layering was observed with as little as 2.5 drachms of potassium citrate, while a reduction of syrup of orange to three-fourths of the specified quantity resulted in a clear, uniform solution with as much as 3.5 drachms of potassium citrate. When the ingredients of prescription No. 2 were cooled to about seven degrees centigrade the resulting prescription was cloudy but there was no separation.

It was found that if the ingredients were mixed in a graduate a considerable proportion or perhaps almost all of the ethyl nitrite was forced out of solution and escaped as a gas. When the ingredients were mixed in a tightly closed container the ethyl nitrite proved to be a factor in the layering, since under these conditions 3 drachms of potassium citrate caused a layering which was not the case when the mixing was done in a graduate.

PRESCRIPTION No. 3.

℞ Sodium Nitrite
Sodium Iodide, *aa* gr. iiss
Make 20 such capsules.
Sig. One three times a day as directed.

In a discussion of this prescription it was stated (4) that free iodine is liberated and that the two salts cannot be dispensed in the same capsule. In our consideration of this prescription the question arose as to whether or not the liberation of iodine was due to reaction between the two salts. In order to settle the question a number of tests were carried out. When the prescription was filled as written the capsules turned yellow, absorbed water and disintegrated within a few days. The addition of an equal quantity of starch prevented disintegration but the capsules showed spots of discoloration in a short time. Sodium iodide alone in capsules turned dark, absorbed water and dissolved the capsule with greater rapidity than when the prescription was filled as written. Sodium nitrite alone in capsules gave no sign of deterioration in several weeks. An aqueous solution containing 25 grains each of sodium iodide and sodium nitrite to the fluidounce had not changed color after several weeks. These results clearly show that the deterioration of the capsules is due to the deliquescence and decomposition of sodium iodide rather than to any reaction between sodium iodide and sodium nitrite. In acid solution, the well-known reaction between iodides and nitrites would occur but this does not take place in absence of excess hydrogen ions.

PRESCRIPTION No. 4.

℞ Naphthaline	℥ ii
Benzoic Acid	℥ iii
Alcohol	℥ ii
Dil. HCl, <i>q. s.</i>	℥ iv

This prescription would not give a clear solution as written. However, by using some ether and more alcohol and replacing the diluted hydrochloric acid by an equivalent quantity of the concentrated acid, a clear solution was obtained. The procedure was as follows: Dissolve the naphthalene in one ounce of ether and add the benzoic acid dissolved in a portion of the alcohol; add alcohol to make three ounces; then add 25 cc. of concentrated hydrochloric acid and bring to volume with alcohol.

PRESCRIPTION No. 5.

℞ Quinine Sulph.	30
Syr. Glycyrrhiza, <i>q. s.</i>	120
<i>M. Sig.</i> Teaspoonful as directed.	

When the patient shook the bottle and took out the cork a large portion of the medicine foamed out of the bottle. The foaming was caused by use of a fermented syrup by the pharmacist. When the prescription was refilled using a freshly prepared syrup and the patient instructed to keep the medicine in a refrigerator, there was no further difficulty.

PRESCRIPTION No. 6.

℞ Potass. Brom.	15
Aq. Camph., <i>q. s.</i>	120
<i>M. Sig.</i> 8 cc. as directed.	

It was expected that this prescription would show precipitation of camphor but no precipitate was observed unless the camphor water was freshly made. Even then the precipitate was not appreciable but there was considerable precipitation if the proportion of potassium bromide was increased slightly. It would appear that camphor water loses an appreciable proportion of camphor under usual conditions of storage.

In connection with the three prescriptions which follow, the senior author sought the assistance and advice of his colleagues on the Committee on Pharmaceutical Dispensing¹ of the National Conference on Pharmaceutical Research and grateful acknowledgment is made of their interest and help.

PRESCRIPTION No. 7.

℞ Liq. Pot. Arsenitis	℥ i
F. E. Phytolaccæ	℥ iii
F. E. Echinacæ	℥ iii
Syrup Ferri Iodidi	℥ iii
Elixir I. Q. S., <i>q. s.</i>	℥ iii
<i>Sig.</i> ℥i T. I. D. A. C.	

There are a number of possible incompatibilities in this prescription, the worst

¹ The personnel of this committee is as follows: W. J. Husa (chairman), I. A. Becker, W. Gray, S. L. Hilton, J. L. Lascoff, L. D. Bracken, L. A. Seltzer, H. A. Whitney.

being the heavy, gray, gelatinous precipitate formed on direct mixing of syrup of ferrous iodide and solution of potassium arsenite. However, the latter incompatibility may be avoided by mixing the syrup of ferrous iodide with part of the elixir and then adding successively the solution of potassium arsenite, the fluid-extracts and the remainder of the elixir. This procedure gives a presentable mixture with no definite precipitate but only a slight turbidity which appears when the fluidextract of echinacea is added.

PRESCRIPTION No. 8.

℞ Ichthyol		10%
Pulv. Boric Acid		℥ ii
Pulv. Zinc Oxide		℥ ii
Acid Carbolic		1/2 of 1%
Liquid Petrolatum		℥ iv
<i>M. Fl. sol.</i>		

The physician insisted that this prescription be filled as written. Since ichthyol does not mix very well with liquid petrolatum and the powders will settle to the bottom, it seems impossible to obtain a really smooth mixture unless the physician consents to some change. The simplest change would be to use petrolatum in place of liquid petrolatum (5). If a liquid is insisted on the ichthyol might be incorporated with an ounce of liquid petroxolin and combined with a mixture of another ounce of liquid petroxolin with the zinc oxide, boric acid and phenol, after which two ounces of liquid petrolatum would be incorporated (5). A product of very good appearance which shows no separation was made by mixing a solution of the ichthyol in a very small quantity of water with a solution of ten grains of stearic acid in a very small quantity of hot water and adding the remainder of the ingredients (6).

PRESCRIPTION No. 9.

℞ Liquor Carb. Detergens		℥ ss
Glycerin		℥ ii
Spts. Vini Rect.		℥ i
Amyli		
Zinc Oxide,	<i>aa</i>	℥ iss
Aq. Calcis, <i>q. s.</i>	<i>ad</i>	℥ vi
<i>M. Sig. External use.</i>		

In prescriptions for lotions containing starch the question arises as to whether the physician wishes to have the starch suspended as such, so as to leave a powder on the skin when the vehicle evaporates, or whether he wishes to get a demulcent effect as might be obtained by boiling the starch with water. In connection with prescription No. 9, the opinion of leading dermatologists in various sections of the United States was secured. Most of the dermatologists were of the opinion that the purpose of the starch was not as a demulcent but as a powder on the skin after evaporation of the vehicle. However, some dermatologists held the opposite opinion and stated that it would be desirable to convert the starch to a mucilage or glycerite. In view of these conflicting opinions it is apparent that the best procedure is for the pharmacist to consult the physician and determine his exact intent. Some pharmacists avoid heat in all starch preparations unless it is specified. A good policy is for the physician to prescribe glycerite of starch when the demulcent effect is required.

REFERENCES.

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- (2) Nichols, A. B., and Nebinger, J. L., *Ibid.*, 13, 344 (1924).
- (3) Lascoff, J. L., *Ibid.*, 19, 851 (1930).
- (4) Hilton, S. L., *Ibid.*, 22, 128 (1933).
- (5) Gray, W., Communication to senior author.
- (6) Lascoff, J. L., Communication to senior author.

THE PRESIDENT OF THE FIRST CONVENTION, CALLED TO
FORMULATE THE UNITED STATES PHARMACOPŒIA; SAMUEL
LATHAM MITCHILL, AUGUST 20, 1764—SEPTEMBER 7, 1831;
PHYSICIAN, CHEMIST, AUTHOR, SENATOR,
REPRESENTATIVE AND PROMOTER
OF THE SCIENCES.*

BY LYMAN F. KEBLER.¹

Samuel Latham Mitchill is one of the most outstanding and influential, if not the most outstanding and influential person that ever occupied the presidency or any other position connected with any convention, or any other activity, dealing with the United States Pharmacopœia. I realize that this is a very broad statement but believe that what follows will fully substantiate the assertion. I have been rather surprised to find that so little is recorded in pharmaceutical literature and that so few persons in pharmacy, chemistry, botany or the cognate sciences seem to have the remotest knowledge of the activities of this super-man, in calling attention to the frauds and impositions practiced by drug dealers, in stimulating uniformity in the manufacture of medicines, in aiding unification in the writing of prescriptions and in taking a leading part in providing the early American drug standards. Even Professor LaWall does not refer to him in his comprehensive, "Four Thousand Years of Pharmacy." Brief references to certain of the above activities will be found in the "Life of Dr. Lyman Spalding," by his grandson, Dr. James A. Spalding, 1916.



SAMUEL LATHAM MITCHILL.

The part that Dr. Mitchill played in connection with the early pharmacopœial work in the United States, is briefly related in the 1820 or the first edition of the United States Pharmacopœia and much more briefly in the historical writeups

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