

dissolve essential oils, camphor, menthol and the like and still mix with water. Acetone mixes with water and has been used successfully in external remedies such as liniments and pain killers where the odor has been masked by the presence of highly aromatic oils. But there is a prejudice against its use in any remedy which might be capable of internal use owing to its supposed toxicity. From experiments recently conducted and still incomplete it would appear that the toxicity of acetone has been exaggerated, and that the reports of its toxicity may have been due to the fact that it is found in the excretions accompanying certain diseases, rather than to any actual proof of deleterious effects caused by ingestion.

The evolution of substitutes has proceeded apace. Most of the new products proposed have been discarded, because they do not measure up to the requirements. Several derivatives of glycerin appear to answer some or all of the necessary conditions such as solvent power, miscibility with water and lack of pungency, odor and toxicity. Special mention should be made of those wherein one or more of the glycerin hydroxyls have been esterified by certain inorganic acids especially the halogen acids, and by certain organic acids of the acetic series. Some of the most promising are those obtained by introducing a side chain group into the glycerin molecule, the side chain being a halogen derivative of a lower organic acid of the acetic series.

It has been asked whether the results of these researches have any practical application or value. It can be answered that they certainly have. We have on our shelves samples of several different types of liquid medicines and toilet preparations, ranging all the way from simply tonic formulas and blood purifiers where the alcohol previously functionated from 8-20 percent, to bay rums, hair tonics, mouth washes, etc., in which it was formerly necessary to use from 35-75 percent alcohol, all of which are non-alcoholic. Non-alcoholic formulas are already on the market and some manufacturers are in a position to switch to a non-alcoholic basis at their pleasure.

Many interesting side problems have arisen during the progress of the work, especially those concerned with the therapeutic efficiency of the mixture, made up with the new solvents and preservatives. Several of these problems are now being worked out in the physiological and pharmacological laboratory, supplemented by actual clinical observations. Enough has been accomplished to demonstrate the real importance of the work and its economic significances to the manufacturer of medicines.

PHARMACOPOEIAL NOTES.*

BY JOHN K. THUM,¹ PH. M.

Without a doubt pharmacists have always appreciated and realized the importance of alcohol and the large part it plays in their vocation, but it remained for the exigencies of the Great War to make them focus their attention on it and give the matter of alcohol more serious consideration. Thoughtful pharmacists are beginning to think that the thing to do under present circumstances is experimentation with the end in view of curtailing the use and importance of alcohol

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in pharmacy. Our experience leads us to believe that quite a few preparations in the United States Pharmacopoeia could be made with less alcohol. Undoubtedly work along this line by the pharmacists of the country would be timely in view of the near approach of the Pharmacopoeial Convention; and as a stimulus to such work on the part of others we offer the result of using less alcohol in the manufacture of several much-used pharmacopoeial preparations:

Aromatic Elixir.—In the course of a year we use many liters of this admirable vehicle. We have revised the formula as follows and find that it is satisfactory in every way.

Compound Spirit of Orange.....	10.00	mils.
Alcohol.....	110.00	"
Syrup.....	375.00	"
Purified Talc.....	25.00	Gm.
Distilled Water, a sufficient quantity to make.....	1000.00	mils.

Add the alcohol to the compound spirit of orange, then to this mixture slowly add the syrup in several portions, shaking well after each addition, and then add enough distilled water to make one thousand mils. Lastly add the purified talc and agitate frequently during twenty-four hours, at the end of which time filter through a wetted filter, returning the first portions of the filtrate until it passes through clear. As the Pharmacopoeia calls for 238 mils of alcohol, to say nothing of requiring that the filter be washed with a mixture of one volume of alcohol and three of water, it is easily seen that in the manufacture of appreciable quantities there is quite a saving of alcohol in using this revised formula.

Compound Tincture of Gentian.—Here we have a preparation that is classed as being a bitter tonic, useful in atony of the stomach, but in reality generally employed as a vehicle, usually used as such in the prescribing of drugs that may have a tendency to cause gastric disturbance. In the giving of mixed treatment to patients, having a specific disease, we use much of it in our institution and, naturally, any diminution in its alcoholic content would result in quite a saving. By "mixed treatment" is meant a mixture containing mercury and potassium iodide. For decades this combination has been given with the compound syrup of sarsaparilla as a vehicle, but we have learned that the compound tincture of gentian is ideal in mitigating and preventing nausea and other gastric disturbances.

The Pharmacopoeia directs that the menstruum for extracting the drugs that enter into this tincture should consist of a mixture of 100 mils of glycerin, 500 mils of alcohol, and 400 mils of water. The glycerin is added for the purpose of preventing or diminishing precipitation, which it fails utterly in accomplishing; it has been our experience that notwithstanding the presence of glycerin precipitation commences as soon as the tincture is finished. In this connection it would be well to advise that the glycerin be omitted, and the finished preparation be allowed to stand ten days and then filtered. We have found that it is possible to thoroughly exhaust the drugs by percolating them with a menstruum consisting of 400 mils of alcohol and 600 mils of distilled water. As the extractive matter is readily soluble in this menstruum, packing the drugs lightly possesses some advantage in that much of the inert matter that causes the usual precipitation is retained in the marc.

Tincture of Cinchona and Compound Tincture of Cinchona.—These two tinctures have always been very popular, both as a stomachic and tonic, and also as a vehicle for giving other bitter medicines such as nux vomica, etc. There is no question in my mind that cinchona can be just as easily exhausted with 50 percent alcohol as it can be with strengths ranging from 67.5 to 70 percent alcohol. Assay of tinctures made with a menstruum containing 50 percent of alcohol showed conformity to the required alkaloidal standard. We would recommend, however, that the time for maceration be increased from 24 to 48 hours.

Tincture of Aloes.—Besides the drug, aloes, this preparation contains licorice root. Aloes is very soluble in water; the Pharmacopoeia states that from 50 to 60 percent should be soluble in cold water; the extractive of licorice is also very soluble in cold water and the Pharmacopoeia recognizes this fact in its directions for making the fluidextract. There is, therefore, no reason why the amount of alcohol in making the tincture should not be reduced to a minimum. At present the official directions for preparing the tincture require that the drugs be macerated with diluted alcohol. We have obtained a tincture that keeps very well by macerating the drugs with a menstruum of 1 part of alcohol and 3 parts of distilled water. Comparison of this preparation with one made according to the present pharmacopoeial requirements shows no shortcomings.

Tincture of Strophanthus.—Now that the Pharmacopoeia permits the percolation of this drug with purified petroleum benzin, to rid it of the oil, there is no reason why the ground seed should not be extracted with a hydroalcoholic menstruum instead of pure alcohol. The U. S. P. VIII called for a menstruum of 650 parts of alcohol and 350 parts of water, and the resulting tincture is a most unsightly preparation. Removal of the oil first, however, and subsequent percolation give a tincture of fairly good appearance. We have found that it is possible to obtain even a better result by increasing the alcoholic content of the menstruum to 750 parts of alcohol and 250 parts of distilled water. This menstruum thoroughly exhausts the drug and results in a tincture containing all the characteristic activity of the strophanthus seed. It has a brownish yellow color which gives it a distinctive appearance, and its stability is everything that could be desired by the careful pharmacist.

Tincture of Hyoscyamus.—The United States Pharmacopoeia states that this tincture should be prepared by percolation with diluted alcohol. The British Pharmacopoeia requires 70 percent alcohol and the French Codex likewise. While it is true that extraction with 70 percent makes a very fine looking tincture, it is a needless waste of alcohol, as extraction with the official diluted alcohol answers just as well. Some experiments were made by extracting the drug with 35 and 40 percent alcohol. Neither of the preparations made with this strength alcohol showed up well pharmaceutically and the weaker strength did not assay up to U. S. P. requirements. Within a week both preparations had thrown down quite a lot of precipitate. On subsequent filtration they showed up better with appearances in favor of the one made with 40 percent alcohol. This preparation assayed up to pharmacopoeial requirements.

Tincture of Physostigma.—U. S. P. IX states that in making the tincture the drug should be extracted with alcohol. How it reconciles this requirement with

the pharmacopoeial requirement that in the manufacture of the Extract of Physostigma a mixture of 3 volumes of alcohol and 1 volume of water should be used as the menstruum, it is hard to say. We find that a menstruum of 3 volumes of alcohol and 1 volume of water answers admirably in making the tincture. That the drug is completely exhausted is shown by the fact that the last 50 mils of the percolate gave no precipitate with Mayer's Reagent. The finished tincture conformed to the required alkaloidal standard.

UROROSEIN.*

BY J. ATLEE DEAN.

Indican (indoxyl-potassium-sulphate) is not the only product of intestinal putrefaction of proteins. Urorosein is of equal or even greater significance. The reporting of no excess of indican without testing for urorosein is not only a serious omission in a complete urine analysis, but misleads because it suggests no intestinal intoxication.

For some years clinicians have been paying more and more attention to the presence of ethereal salts in the urine (indicative of putrefactive decomposition of the proteins in the intestine). These salts are esters of phenol, indol, and skatol. Indican is perhaps the most widely known and easily recognized. It is readily oxidized to indigo blue, and can be shaken out with chloroform in which substance the indigo is soluble. Indican is not the only product of the decomposition of aromatic amino acids. Another equally or even more important, cromogen, can be isolated in the same manner; it is, however, insoluble in chloroform and soluble in amyl alcohol. The color of this solution is red, and indicates the presence of another ethereal salt. It has been given the name, urorosein. It is probable that urorosein is in reality indole acetic acid; that skatol is formed from urorosein, and may be one step in the formation of indole from tryptophane.

The purpose of this paper is not to study the complex chemical problems presented by these products of intestinal putrefaction; its only object is to point out the necessity of making a test for urorosein, in each specimen, at the same time that an examination for indican is made.

When we consider that our limited knowledge of these substances points to a chemical and physiological similarity with histidine, adrenaline, and the active principles of ergot, the probability develops that these ethereal salts are responsible for the production of high blood pressure, and the resulting sequelae. Having observed the importance of these substances, it matters little whether one or more are reported, provided they occurred in equal or proportionate quantities. However, a slight excess of indican is frequently encountered and an enormous excess of urorosein, or *vice versa*. In fact, in hundreds of analyses, of which we have records, no excess of indican is observed, while urorosein is present in large excess. We often observe that after a patient, who has an excessive amount of indican, is placed on a meat-free diet, the indican disappears and the urorosein remains excessive. This suggests the possibility that other proteins than found in meats, when present in the intestines in large amount, produce urorosein.

It is to be hoped that the observations set forth here will impress the laboratory worker with the importance of making tests for urorosein, regardless of whether indican is present or not. Only then will the true extent of intestinal toxemia be fully realized.

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