THE PREPARATION OF TINCTURES BY THE DILUTION OF FLUIDEXTRACTS.*

BY EDWARD D. DAVY.

It is not uncommon, in fact it is a common practice among pharmacists to prepare tinctures needed from time to time by dilution of fluidextracts. In some cases this procedure is warranted, as may be seen by taking into consideration the percentage of alcohol in either preparation and also the solubility of the active agents in varying strengths of alcohol. When tinctures are needed for immediate use, or for those which have a limited demand in everyday practice, they are commonly made from the fluidextract without considering the result of such dilution. Fluidextracts are usually at hand, and dilution of them therefore is an easy method for making tinctures on short notice, but the resulting preparations of some of these are questionable. A few examples will suffice to make clear the result of this procedure.

Fluidextract of Aconite has an alcoholic menstruum composed of three volumes of alcohol and one of water, or 71% alcohol, while that of the tincture has seven volumes of alcohol and three of water, or 66.5% alcohol. The difference in alcoholic strength of the two menstrua is not so striking as in other cases and, since the activity of the preparation is dependent on the alkaloids present, the dilution of the standardized fluidextract may be used to advantage and in this case would not throw out of solution any of the active agents with so small a change in the alcoholic content.

In the preparation of Tincture of Cannabis from the fluidextract there could be no serious objection to the common practice of dilution, inasmuch as the alcoholic content in the two preparations is the same.

In preparations of Calumba the activity is due in part to a small alkaloidal content, also to gum and resin. The fluidextract U. S. P. VIII contains 66.5% and the tincture 57% alcohol. It will readily be seen why in this dilution, involving the solution of gum and resin, a precipitate forms so that the resulting preparation does not represent the extractive matter obtained in a tincture made by the usual method.

In the Fluidextract of Cinchona U. S. P. IX the menstruum contains hydrochloric acid, while that of the tincture has none. It would be manifestly unfair and unwise to make a tincture whose alkaloids should be as such in combination with their organic acids, from a solution the alkaloids of which are in the form of hydrochlorides. In the preparation of Fluidextract of Lobelia, acetic acid is used in the menstruum and since this tincture as well as that of cinchona are commonly used in compounding, the presence of acid might greatly impair the value of subsequent mixtures in which they were used.

In the Fluidextract of Belladonna the menstruum is 76% alcohol while that of the tincture is about 49% and the result of dilution is the formation of considerable precipitate which can be overcome only by making the dilution with approximately 76% alcohol. It is obvious that this method would work in most every case but the tincture would be unlike the *official* preparation.

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It has been a common practice, and still is to some extent, to prepare the tincture and also the infusion of Digitalis from the fluidextract regardless of the fact that all the recent investigations show digitalis preparations lose their efficiency to a greater or less extent with age. The medical profession in general is insisting on a fresh tincture and also the freshly prepared infusion, and the Revision Committee of the U. S. P. IX endorses the idea. This is shown by the absence of alcohol in the infusion which acted merely as a preservative and allowed for its keeping a greater length of time.

In the Fluidextract of Rhubarb the menstruum is 76% alcohol while that of the tincture is 49%, a difference of 27% in the two menstrua. The active constituents of rhubarb are largely resinous matters and cathartic acid. On diluting the fluidextract with a 49% alcohol and glycerin menstruum, considerable deposit forms in forty-eight hours which increases with time until its maximum is reached. Glycerin tends to prevent the precipitation but does not entirely overcome it.

In fluidextracts one cubic centimeter represents the extractive matter from one gramme of drug, but in very few cases do we actually get all of the extractive matter from the evaporated percolate in solution. The extractive being largely, if not wholly aqueous, is incorporated with the first percolate whereby its alcoholic strength is lowered and a deposit results. Fluidextracts if made by the same process will be quite uniform and they present the best means now available for administering drugs in concentrated form, but in no way do they represent other preparations when diluted.

Excluding the tinctures of Iodine and Ferric Chloride there are 20 official tinctures wholly or partly dependent on the alkaloidal content for their activity, while 32 are dependent on glucosides, resins, oils or acids. If one follows consistently the last named tinctures when made from fluidextracts, it will be found that in nearly all cases where the alcoholic content is made that of the Pharmacopoeia a decided precipitation occurs with the exception of those in which there is no change in menstrua. Squills present an exceptional case in that the tincture has a higher alcoholic content than the fluidextract but in this case a deposit results from a dilution. In all these cases it remains to be proven that the precipitated matter is inactive in those drugs dependent on gums, resins or glucosides for their activity.

It will be noted that in fluidextracts one has in many cases a product nearing saturation and a menstruum varying from 0% to 27% in alcohol from its corresponding tincture. The tincture in most cases represents only 10% of the drug thereby making the extraction more complete and retaining in solution all of the extractive since it is completely dissolved in the menstruum used. It is true that some tinctures under ordinary working conditions will precipitate on long standing due to evaporation or effect of light and heat, conditions over which we have no direct control, leading some to believe it to be due to the same cause in either case.

In conclusion it might be said that Pharmacy has been greatly drawn from its original course by too many "ready to use" preparations. It is the aim of everyone to bring it into a professional rather than wholly commercial light, and also to eliminate many so called "short cut" methods imposed on the profession, thereby taking the initiative from the individual. If any dilutions as above mentioned

are made the individual preparations should be thoroughly studied before making such dilutions, and a procedure other than this must be considered a very poor one to follow.

DISCUSSION.

CHARLES H. LAWALL: The evident care with which the statements were made in the paper and conclusions drawn appear to me to be very worthy of widespread publication to the pharmaceutical profession. This investigation goes to show that we are moving in circles, in a way. I do not mean to detract in any way from the value of the paper by that remark, but I am reminded of discussions on this subject in 1895. The conclusions reached at that time were practically the same as the conclusions reached in this paper. We believed then, and still believe, that the manufacture of pharmaceutical preparations requires a certain amount of attention, care and skill.

WILLIAM GRAY: In the first eight hundred mils of fluidextract percolate we may assume that it is saturated with the active constituents. When the last percolate is evaporated it becomes a more or less aqueous product. When this is mixed with the first percolate the strength of the alcohol is reduced and consequently there is a precipitation.

C. M. FORD: The manufacturers of fluidextracts age their preparations by allowing them to stand for some time, so that insoluble matter is precipitated.

R. W. TERRY: They obtain a preparation of better appearance but may not invariably represent the drug. The finished product, however, in most instances, is standardized.

HENRY P. HYNSON: I can go a little further back on this subject than Professor LaWall. I regard the paper of great importance because it touches upon a subject that is not yet settled. I want to ask him if he knows whether the propaganda started a few years ago, to have fifty percent extractions take the place of tinctures and fluidextracts, has made any progress.

CHARLES H. LAWALL: No, because after all it is a matter of educating the physician. If the physicians ever become acquainted with the value of fifty percent preparations and learn to prescribe them, then we should admit such preparations to the Pharmacopoeia.

R. W. TERRY: In the preparation of Tincture of Capsicum the effect of different strength alcohol is very nicely shown. If all the menstruum is not made up at one time and a further amount of menstruum is made up to finish the percolation, and there is even a slight variation in alcoholic strength, the percolate comes through cloudy or milky.

H. P. HYNSON: There does not seem to be any reason why we should have fluidextracts and tinctures of variable strength. I want to ask the Chairman of the Committee of Revision of the U. S. Pharmacopoeia if he does not think the propaganda for "50 percent tinctures" should be continued. I want to leave that thought with you.

A NOTE ON TINCTURE CINCHONA COMPOUND.*

BY F. W. NITARDY.

The U. S. P. directs Tincture Cinchona Compound to be made by percolating a definite amount of red cinchona, bitter orange peel and serpentaria with first a definite amount of hydro-alcoholic menstruum containing some glycerin, completing the percolation with a plain hydro-alcoholic menstruum and adjusting the tincture so that each 100 mils will assay 0.45 Gm. of cinchona alkaloids.

In the practical application of this formula, it has been found that the finished tincture will sometimes assay 50 percent or more above the specified strength (due to cinchona bark of high alkaloidal strength). The subsequent adjustment of this tincture to U. S. P. strength produces a product that contains less bitter orange peel, serpentaria, and glycerin than would be present if the cinchona used

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