

	Alkanet.	"Syrian Alkanet."
Total ash.....	17.0 percent	11.7 percent
Acid-insoluble ash.....	8.0 percent	0.8 percent
The ash in both cases was high in carbonates		

From the above data it may be seen that the coloring extracts from both plants consist of at least two chemical individuals and that both extracts are very similar in nature. In view of the fact that in Syrian Alkanet the coloring extract was present in much larger amount than in the true alkanet, and possessed equivalent tinctorial strength, it would appear to be a valuable substitute for the latter.

THE ESTIMATION OF ALCOHOL.*

BY C. R. HARER.

While the estimation of alcohol in pharmaceutical preparations is not very complicated, it, nevertheless, presents many difficulties and affords opportunities for experiment and research.

Frothing, in numerous cases, is readily controlled by tannic acid; while in particular instances sulphuric or phosphoric acid, as advised by some writers may be preferable, I find tannic acid more generally practical, although the variation of its action with different drugs has not been determined. After the addition of tannic acid to fluidextracts of gelsemium, helonias and several other drugs, they must be heated very rapidly to boiling to control the frothing. The addition of tannic acid to fluidextracts of black haw, mango bark and several others increases the frothing instead of retarding it. The addition of tannic acid to preparations of cinchona produces an uncontrollable frothing when heated, while if heated slowly without tannic acid, the liquid will froth at first, but the foam will soon subside and regular boiling take place; the initial frothing may be almost instantly eliminated if the liquid is heated rapidly in such a way that the flame is thrown on the upper part of the distilling flask for a few seconds, when the liquid starts to boil.

The estimation of alcohol in fluidextract of sarsaparilla presents greater difficulties than many other preparations, and the following experiments were undertaken for the purpose of finding a convenient and rapid method for its determination: Mechanical methods (paraffin, fixed oils, etc.) to control the frothing were tried, but without success. Baryta water was then used to precipitate the saponins and resins, but this gave no satisfactory results. Several experiments were made by adding a suspension of aluminum hydroxide to the fluidextracts also by adding an aluminum salt to the fluidextract and subsequently precipitating the hydroxide with a caustic alkali. These experiments were failures. Next an addition of the official solution of lead subacetate was tried, but I found that a direct distillation of fluidextract of sarsaparilla with lead subacetate solution was impracticable because frothing was unavoidable and it was impossible to separate the aqueous alcoholic liquid quantitatively from the voluminous gelatinous precipitate by fil-

* Read before Scientific Section, A. Ph. A., Indianapolis meeting, 1917.

tration; however, the following method yielded satisfactory results: Fifty mils of the fluidextract was transferred to a 100-mil cylinder, 15 mils of solution of lead subacetate was added, and sufficient water to make 100 mils. The mixture was thoroughly shaken and 50 mils, equivalent to 25 mils of fluidextract, was filtered off. This was transferred to a distilling flask, sodium bicarbonate was added to an alkaline reaction, followed by a slight excess of tannic acid. Generally traces of acetic acid are present in the distillate, but in such small quantities as not to influence the results.

In order to ascertain whether or not the method gave accurate results, the following experiments were made: 200 mils of the fluidextract of sarsaparilla was evaporated to a syrupy consistency; this residue to which 50 mils of water was added twice, which each time was evaporated, was taken up in water and transferred to a 200-mil flask; 90 mils of 94% alcohol was added and enough water to make 200 mils. Two distillations were made with this dilution and 41.5 percent and 41.2 percent of alcohol was found. At the same time a volume of water approximately equal to that of aqueous solution of the residue was placed into a 200-mil flask, 90 mils of 94% alcohol was added and sufficient water to make 200 mils. The sp. gr. of this aqueous-alcoholic mixture showed that the liquid contained 42.3 percent of alcohol. When 25 mils of this aqueous-alcoholic solution, to which 50 mils of water and 3 mils of solution of lead subacetate had been added, followed by sodium bicarbonate to an alkaline reaction and then tannic acid to an acid reaction, was distilled, 41.3 percent and 41.4 percent of alcohol was found. In the latter distillation approximately the same conditions are given as in the distillation of the liquid which is obtained by treating the fluidextract of sarsaparilla with lead subacetate solution and filtering.

The estimation of alcohol in preparations containing volatile substances presents another interesting part of this kind of work. Volatile alkali can easily be eliminated by adding tannic acid or other suitable acids, preferably phosphoric acid, while volatile acids can be taken care of by adding a fixed alkali; substances, however, like camphor, volatile oils and chloroform can be removed only by special processes.

The U. S. P. directs that the sample containing volatile substances be distilled in the usual way, the distillate transferred to a separator and saturated with sodium chloride; 15 mils of petroleum ether are then added, the mixture is thoroughly shaken and allowed to separate. The salt solution containing the alcohol is then drawn into another separator and washed once with petroleum ether. The combined ethereal solutions are washed once with 10 mils of a saturated solution of sodium chloride, which is added to the aqueous solution. The combined aqueous liquids are then distilled and the alcohol estimated in the usual way.

For liquids containing chloroform, the U. S. P. method gives satisfactory results, as the following experiments show:

Sample No. 1.—Seven mils of chloroform was transferred to a 200-mil flask and sufficient diluted alcohol (about 45 percent) was added to make a total volume of 200 mils. Three determinations of alcohol of this sample by the U. S. P. process gave 44, 43.65 and 44 percent.

Sample No. 2.—Seven mils of water was transferred to another 200-mil flask and enough of the above hydro-alcoholic solution was added to obtain 200 mils. The sp. gr. of this sample indicated 45.55 percent of alcohol, while the determination of the alcohol by distillation gave 44.5 and 44.83 percent of alcohol.

While there is quite a difference of opinion as to the best method of estimating alcohol in liquids containing volatile oils, the U. S. P. method as previously stated and the N. F. IV process, which directs distilling the liquids, shaking the distillate with magnesium carbonate and filtering, are generally used. Very good results can be obtained in preparations containing a mixture of volatile oil and alcohol, or oils, alcohol and water without other extractive matter, such as spirit peppermint, spirit myrica, by eliminating the oil first, then distilling and taking the gravity of the distillate as the following experiments show; for these experiments a concentrated fluid of bay laurel was made containing about 20 percent of the combined oils pimento, myrica, and orange and 66.15 percent of absolute alcohol.

Experiment No. 1.—Twenty-five mls of the fluid was transferred to a separator containing 20 mls of saturated solution of sodium chloride and 20 mls of petroleum ether was added. The separator, containing the mixture, was thoroughly shaken and the liquids allowed to separate. The alcoholic liquid together with the salt which had separated from the solution when the fluid was added, was drawn into another separator and washed with a second portion of petroleum ether. It was then transferred to a distilling flask. The combined petroleum ether was washed with 10 mls of a saturated salt solution which was also transferred to a distilling flask and the combined aqueous-alcoholic liquids were distilled. The sp. gr. of the distillate indicated the presence of 56.9 percent alcohol, while a check experiment indicated 57.2 percent.

Experiment No. 2.—This experiment differs from the preceding only in that when the fluid was added to the 20 mls of salt solution, enough water was added to redissolve the salt which had separated. By this method 62.1 and 62 percent of alcohol was obtained. This seems to indicate that in the presence of excess of salt, some alcohol is carried mechanically into the petroleum ether with the oils.

Experiment No. 3.—Twenty-five mls of the fluid was transferred to a separator and saturated with sodium chloride and after the addition of 20 mls of petroleum ether the mixture was shaken. When the liquids had separated, the aqueous-alcoholic layer was drawn into another separator and washed with another portion of petroleum ether; the combined ethereal liquids were washed with 10 mls of saturated salt solution, which was added to first solution. The combined aqueous-alcoholic liquids were then distilled and the distillate was found to contain 64.6 percent of alcohol, while a check experiment indicated 64.7 percent.

Experiment No. 4.—Twenty-five mls of the fluid was transferred to a separator, 20 mls of saturated salt solution was added and enough water to dissolve the salt which had separated. After the addition of 20 mls of petroleum ether, the estimation was carried out in the usual way, with the exception that after the petroleum ether had been washed with 10 mls saturated salt solution, it was washed with two portions of 10 mls each of water. By this process 65 and 65.2 percent of alcohol was obtained.

Experiment No. 5.—This experiment was made by following the exact directions of the U. S. P., 65 and 65.3 percent of alcohol was found.

Experiment No. 6.—Twenty-five mls of the fluid was transferred to a distilling flask and after the addition of 50 mls of water, the mixture was distilled. The distillate was shaken with talcum and filtered. It contained 64.9 percent of alcohol and a check experiment gave 64.7 percent of alcohol.

Experiment No. 7.—As a last process Richter's modification (*Pharm. Zeit.*, 1914, page 431) of a process originated by Thorpe and Holmes (*Jour. Chem. Soc.*, XIX, page 259) was applied. This method is very simple and gives accurate results and is carried out as follows:

Thirty mls of the fluid is mixed with 30 mls of a 15% sodium chloride solution and 30 to 40 mls of petroleum ether boiling below 60° C. is added. The mixture is shaken well in a separator and then allowed to settle; when the lower layer has become clear, it is drawn off and, if necessary, filtered with a small amount of magnesium carbonate, 50 mls of the filtrate representing 25 mls of original sample is distilled. 65.8 and 66.1 percent of alcohol was obtained by this method, which percentage agrees closely with the theoretical amount.

The results appear tabulated as follows:

Process.....	1. Percent.	2. Percent.	3. Percent.	4. Percent.	5 U. S. P. Percent.	6. Percent.	7. Percent.
1st.....	56.9	62.1	64.6	65.2	65.3	64.9	65.8
2nd.....	57.2	62.0	64.7	65.0	65.0	64.7	66.1

The tabulation indicates that process VII yields the best results, while the U. S. P. and process IV yield very nearly the theoretical amount of the process alcohol present.

LABORATORIES OF SHARPE & DOHME.

THE REACTIONS OF GOLDFISH TO CERTAIN HABIT-FORMING DRUGS—THE USE OF THE GRADIENT TANK.

BY VICTOR E. SHELFORD.

The problem of the cause of the development of the drug habit, *i. e.*, of the peculiar effects of habit-forming drugs which cause the user to crave them, has been approached from several different angles, but none of them have afforded a solution. Attention appears to have been directed especially toward morphine and related compounds.¹ The theory that morphine causes the formation of oxymorphine, which produces an effect the opposite of morphine, has been exploded by the discovery that oxymorphine is not formed and that its effects are not the opposite of morphine. The idea that immunity is developed is rejected because of the fact that such immunity does not exist in animals which are habituated by the use of morphine. The increased capacity of the organism to destroy morphine is not an adequate explanation as morphine is very slowly destroyed.

Most of the work has been done on mammals, some on frogs, but I find almost nothing in the literature that shows the development of anything like a craving, taste, or preference for the substance in question, on the part of the lower vertebrates. In fact it is not easy to show that these animals are so affected. By chance the writer discovered that fishes are peculiarly affected by numerous organic substances in aqueous solution, when put under special experimental conditions. These conditions are established in a long, narrow tank, 122 cm. long, 15 cm. wide and 13 cm. deep (see Fig. 1-A), in which water containing a drug flows into one end and out at both top and bottom, at the middle, while water which contains none of the drug flows into the other end at the same rate. The two flows meet at the middle and with most substances there is a mixture of the two kinds of water which occupies the center third of the tank. In this mixture a fish moving from the pure water end toward the drug-containing end encounters a gradual rise in concentration of the drug. This region of change of concentration is called the gradient. The character of the gradient in these tanks has been fully determined, by taking samples, by measuring conductivity, and by the use of colored water. Usually a sample which contains none of the salt or any amount from the faintest traces up to the full concentration introduced, may be withdrawn (Fig. 1-B). Some substances diffuse almost through-

¹ Sollman Manual of Pharmacology, 1917.