Digitalis does not contain gallic acid, gallotannic acid or tannins like those found in oak bark, pecan nut, red rose, matè or wild cherry.

While the iron-greening factor is completely absorbed by hide-powder, it is equally capable of passing through animal membrane; which contradictory behaviors at once raise that continually recurring enigmatic question—What is a tannin?

To avoid adding to the existing confusion, it is suggested that, until more is known of this anomalous constituent of digitalis, the same be referred to as the iron-greening factor.

THE QUANTITATIVE DETERMINATION OF CAMPHOR IN PHARMACEUTICAL PREPARATIONS.

BY H. VIETH AND E. A. BILHUBER.

Though camphor is used to a considerable extent in the field of medicine there is no dependable method recorded for its quantitative determination in the small amounts in which it occurs in pharmaceutical preparations.

The usual method employed is based upon the degree of rotation of a camphor solution as determined by means of the polariscope. This method, given in the Pharmacopœia, can only be used for the natural dextro-rotatory camphor. Furthermore this method for the determination of camphor is not often practical for the analysis of pharmaceuticals, principally because relatively large amounts of camphor are required while the usual preparations contain but very small quantities. All the added ingredients and inerts that far outweigh the camphor present in most such compounded products detract from the accuracy of the polarization or from the simplicity of its application. The usual camphor preparations, tablets or pills, contain but from 0.05 to 0.1 Gm. camphor and at least 1.0 gram of camphor; that is, 10 cc. of a 10% solution absolutely free from foreign matter, is necessary for an exact polarization determination. More dilute solutions than given above permit too great possibilities of error in the readings. Therefore, this method may well be used for the determination of camphor in the official Spiritus Camphorae but is, in general, impractical for other preparations.

Other methods have been proposed, but have given unsatisfactory results. Thus Fuller gives a method in which he converts the camphor into its oxime with hydroxylamine and then titrates. Gildermeister proposed to determine camphor by oxidation with permanganate. Not only is this method not quantitative, but it requires larger amounts of camphor.

The natural procedure for the determination of camphor in small quantities in pharmaceutical preparations would be to isolate the pure camphor and weigh it as such. In the development of such a method it was found that the rapid volatilization of camphor had to be controlled.

Preliminary trials were made on the rate of evaporation of camphor and it was found that the pure powder loses about 10% in weight daily when exposed to the usual room temperature. It must therefore be weighed in a closed vessel. A solution of 0.5 Gm. camphor in 30 cc. chloroform contained only 0.26 Gm. after it had stood 48 hours in an open vessel at room temperature. Only the slightest trace of

camphor remained upon very careful evaporation of such a solution on the water-bath. Pure ether is the most practical solvent. The presence of oxidizing agents in the ether is shown by the yellow discoloration obtained when shaken with potassium iodide and if present are removed by washing alternately with water and hydrosulphite until the addition of the potassium iodide no longer produces the yellow color. In order to avoid loss through volatilization the ether solution of camphor was placed in a narrow-necked flask and then partially evaporated on a water-bath. Without further application of heat, the remainder of the ether was evaporated in a partial vacuum of about 110 mm. This occurs at so low a temperature that practically no camphor is lost. Care must be taken that no stream of air flows over the camphor. Check results of numerous trials proved that quite accurate determinations of camphor in solution could be obtained by this method. As an example a solution of 0.1 Gm. camphor in 30 cc. purified ether was placed in a 50-cc. narrow-necked flask, evaporated to about one-fifth its original volume on the water-bath and then to dryness under reduced pressure. The weight of camphor found varied from 0.099 to 0.097+ Gm.

The separation of the camphor from other ingredients contained in the usual pharmaceutical preparations or prescription mixtures followed the ordinary chemical methods using differences in solubility in the various media. An example may be in place. A powder consisting of gum arabic and milk sugar with 10% camphor was first ground with a little water and then extracted three times with ether. This solution was washed several times with water, dried over sodium sulphate and the pure camphor-ether solution evaporated as described above.

Camphor in a glyco-gelatin (gellets) base was hard to extract as the camphor was found to be so firmly held in this mass that it could only be extracted with difficulty by its usual solvents. It was to be presumed that only the camphor would be extracted by the ether, but this is not the case, for a considerable quantity of glycerin was found to have been carried into the solution with the camphor. The method found to be most simple and accurate was to digest the gellets in pepsin-hydrochloric acid. For one gellet, said to contain 0.1 Gm. camphor, 20 cc. of 1% hydrochloric acid with 1.2% pepsin—equivalent to about 10 times the strength of the stomach juices—were used. After digesting one hour at 40° C., the camphor was found to be suspended in the liquid in a state of fine subdivision and was readily extracted with ether in either the Soxhlet or by shaking with the solvent. The camphor is not determined by evaporation and weighing as such in accordance with the method developed. A series of analyses of gellets gave an average of 0.102 Gm. camphor as against the theoretical content of 0.1 Gm. The difference between the highest and lowest results was only a few milligrams.

CONCLUSIONS.

The present given methods for the quantitative determination of camphor in pharmaceutical preparations are often impractical and not necessarily accurate.

The method of weighing camphor direct after extraction and evaporation of its ether solution under partial vacuum as described in this paper is practical, rapid and exact.

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