RESEARCH PAPERS

A NOTE ON THE DETERMINATION OF ALKALOIDS BY EXCHANGE OF IONS

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Received March 3, 1950

D. van Os has given a survey of the various methods for the determination of alkaloids[1]. One of us (A. Jindra[2]) has described the first experiments in which the chromatographic method of ion-exchange in determining alkaloidal salts and some galenicals containing alkaloids was adopted. Further experiments on this subject have been carried out at this Institute in accordance with our view that the determination of the physiologically active base is to be considered the only precise method. The results achieved can be summarised as follows.

We aimed at working out suitable semimicro- and micro-methods for the determination of the alkaloidal salts and galenicals of the Czechoslovak Pharmacopœia I using anion-exchange resin. According to Kunin and Myers[3] the mechanism of reaction in the chromatographic column when applying resin Amberlite IR4B must be considered as anion exchange, having two phases. With most of the salts the reaction was quantitative and the results were entirely satisfactory where both the methods were adopted. As the weighed quantities of the samples were too small it became necessary to determine the content of the base electrometrically. The larger quantities of active constituent used in the semimicro-method enabled a more accurate reading of the 0·01N hydrochloric acid consumed to be made and therefore, the results on the whole were more accurate. On the other hand the equivalence point could also be determined correctly by the micro-method, as the rapid change in the concentration of hydrogen ions at the stage when the process was about to reach the equivalence point, was relatively greater and more expressive with regard to the small amounts of base than in the semimicro-method.

As the data in the literature on the application of the quinhydrone electrode in titrations of alkaloids differ, it was tested in experiments as indicative electrode in direct titrations of alkaloids, when the solutions are very dilute and the dissociation constants low. In general it can be said that this did not work well. The results were mostly lower and they were correct only for arecoline, papaverine and pilocarpine, i.e. for very weak bases. Stronger bases, as ephedrine and the tropeines, could not be titrated at all, which is to be expected since the quinhydrone electrode gives correct results only at *p*H8, in buffered solutions at *p*H9. The results thus obtained correspond on the whole to the opinion of Kolthoff[5] and the experiments of Wagener and Gile[6]. The glass electrode is very suitable and the results obtained by its application were correct, but the antimony electrode proved to be the best.

With certain alkaloids, however, the results obtained were not satisfactory when the standard method was applied hence the conditions of the experiment had to be changed.

Apomorphine, which turns blue in dilute ethyl alcoholic solutions owing to the presence of oxidation products, had to be titrated in an atmosphere of nitrogen.

Physostigmine showed higher results. In solutions it is unstable and its decomposition products are most probably the cause.

Lower results were obtained with ephedrine hydrochloride even under changed conditions of experiment. Probably the acid component, owing to the greater basicity of ephedrine, is much more bound than in the case of other alkaloids and the Amberlite IR4B is unable to separate both these components quantitatively. This proved to be still more evident with cotarnine hydrochloride, which is a salt of a strong quaternary base. The separation was incomplete and the results achieved were very low (approx. 50 per cent. of the theoretical results). It is quite probable that a suitable resin of stronger basic character will be found, which will enable these salts to be determined.

Standard methods were worked out for the following alkaloidal salts: — Arecoline hydrobromide, atropine sulphate, cocaine hydrochloride, codeine phosphate, homatropine hydrobromide, morphine hydrochloride, papaverine hydrochloride, pilocarpine hydrochloride, quinine hydrochloride, quinine sulphate, scopolamine hydrobromide, strychnine nitrate.

Methods were worked out for the determination of the alkaloidal drugs and galenicals of the Czechoslovak Pharmacopœia I. The material was sorted into several groups according to the character of the alkaloids contained therein. In most cases it was necessary to isolate the alkaloid to some extent before the actual process. In some cases this isolation was considerably simplified, in other cases no simplification of the official methods was achieved. But even in such cases some advantage in speeding up the process is found as much smaller quantities of sample and solvent are used.

In the course of the process the cause of the anomaly in the determination of tincture of nux vomica, which could be traced also with other galenicals as mentioned in the previous article, was cleared up. Some galenicals in rapid direct experiments, without the prior removal of accompanying substances, showed slightly higher results, some even multiple results. This is caused (a) by the presence of amines in the drugs, which pass with the alkaloids into the solution, and are titrated simultaneously (b) by the splitting of salts of alkalis contained in the drugs. Although this splitting due to the resin is small still it is noticeable and is more especially of consequence when smaller quantities of samples are used. In such cases the alkalinity of the eluate becomes greater, the smaller the weight of the sample and is, therefore, relatively greater than with larger quantities of sample. The galenicals contain not only neutral salts but especially easily hydrolysable ammonium salts, the splitting of which is facilitated by hydrolysis.

With cinchona bark and its galenicals (fluid extract and dry extract)

direct chromatography gives rather high results. A method for separating the accompanying substances has been worked out.

With ipecacuanha root and its galenicals (tincture) when chromatographing directly it must not be forgotten that inactive psychotrine is determined together with emetine and cephaëline; e.g. with the tincture the results were insignificantly higher, with the root the splitting of salts is evident from the unsatisfactory results (approx. 50 per cent. of the theoretical results). The method worked out will secure correct results.

For nux vomica seed and its galenicals (tincture and extract) a method for the determination of the alkaloids has been worked out.

For belladonna leaf and its galenicals (tincture and extract) the method worked out proves to be more advantageous than the officially adopted methods, chiefly because of its complete and rapid separation of chlorophyll and other accompanying substances.

Summary

Following on work previously published, methods depending on ion exchange by chromatography with Amberlite IR4B have been worked out for the determination of alkaloids in the alkaloidal salts, crude drugs and galenicals.

References

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