from trimethylene bromide and potassium cyanide has been shown to be advantageous. This alcohol is suggested as a general solvent for making nitriles especially where there is danger of hydrolysis. Here again the yields are increased by the application of the collision method of study and mass action to the chemical equilibria involved.

7. It has been found that when γ-bromobutyronitrile is treated with one equivalent of aceto acetic ester two products result: one, γ-cyano-α-acetovalerianic ethyl ester, a combination of one molecule of each; the other, 1 : 7-dicyano-4-aceto-4-carboxethyl heptane, composed of one molecule of the ester and two of the nitrile. When 1.5 equivalents of aceto-acetic ester were used the latter was suppressed to one-ninth of the amount produced when one equivalent was used. This result was predicted from a consideration of the principle of mass action.

8. Two new substances, δ-cyano-α-acetovalerianic ethyl ester and 1,7-dicyano-4-aceto-4-carboxethyl heptane have been prepared and characterized.

9. δ-Acetovalerianic acid has been prepared in a pure state and in large quantities for the first time. Its ionization constant is $1.926 \pm 0.002 \times 10^{-5}$. The application of "calculated" Λ_0 proves this value to be accurate. Its correct capillary melting point is 36.5°.

10. The electrolytic conductance of the sodium salt of δ-acetovalerianic acid has been determined for a series of concentrations and the extrapolated Λ_0 value found to be 80.

11. The application of "calculated" Λ_0 to the existing conductance data of normal heptanoic acid shows that it is very inaccurate.

URBANA, ILL

[CONTRIBUTION FROM THE LABORATORIES OF THE INLAND REVENUE DEPARTMENT.]

THE MANGANESE CONTENT OF THE ASH OF CERTAIN DRUGS.

BY L. E. WESTMAN AND R. M. ROWAT.

Received December 18, 1917.

Although the significance of the presence of manganese in plants and its relation to plant metabolism is not yet clear, the quantity of manganese observed to be present in the barks of certain laxative drugs and in other portions of plants used for similar purposes, was considered by the authors to be worthy of general mention.

Hafner and Krist[1] have pointed out in a qualitative way that a large number of drug plants contain manganese. They were able to obtain positive tests for manganese on 164 drugs listed in the Austrian Pharmacopeia, and were led to this investigation by the occurrence of a greenish color in the ash of many drugs. This color is formed when the ash is

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[1] *Z. Osterr. Apoth. Ver.*, **45**, 387–399 (1907).

strongly heated in a muffle, from the manganite salts present and is certainly most marked in many instances, especially those where an extract of the drug has been evaporated and ashed. This is due to the fact that only a small fraction of the lime salts present in plants is extracted by methods of percolation, and in the relative absence of these salts the manganese that is extracted becomes observable in the ash.

The method adopted by these authors in their tests was as follows: 3 to 4 g. samples of the drug were ashed and the ash dissolved in 8 to 10 cc. of dilute nitric acid (free from hydrochloric acid), filtered if necessary, then heated, and after the addition of a small amount of brown, manganese-free lead peroxide, was brought to boiling. When manganese was present the liquid acquired a more or less intense purple-red color according to the amount. This reaction naturally fails in the presence of chlorides.

According to Pichard,[1] the seeds of plants are quite rich in manganese, and Jadin and Astruc[2] find that the aerial portions of plants contain more manganese than the subterranean. McHargue[3] tabulates 51 determinations made on nuts, shells, seeds, and seed coatings, obtaining for his two highest results 0.04% manganese in dried potato peelings, and 0.09% in dried turnip tops. Manganese has been shown by Headden[4] to be present in all samples of wheat examined in amounts from 0.004 to 0.007%.

Results and Discussion.

The results obtained are tabulated below and are calculated on the dry basis at 110°.

TABLE I.

Drug examined.	% manganese present.	
Rhamnus Frangula (or alder buckthorn bark)	0.0242 to 0.0674	±0.0003
Cinnamomum Cassia Cortex (or cassia bark)	0.0624	±0.0003
Rhamnus Purshiana (cascara sagrada)	0.0137 to 0.0223	±0.0003
Podophyllin (root)	0.0052	±0.0002
Senna (leaves)	0.0043	±0.0002
Rhubard (root)	0.0036	±0.0002
Rhamnus Californica (mature bark)	0.0033	±0.0002
Licorice (root)	0.0026	±0.0001
Jalap (root)	0.0024	±0.0001
Euonymus Atropurpureus (wahoo bark)	0.0021	±0.0001
Cassia pulp	0.0017	±0.0001
Aloes (barbadoes)	0.0006	±0.00005

From data available it would appear that both *Rhamnus Frangula* and cassia bark show a higher content of manganese than any other

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[1] P. Pichard, *Compt. rend.*, **126**, 1882 (1898).

[2] Jadin and Astruc, *Ibid.*, **156**, 2023 (1913).

[3] J. S. McHargue, THIS JOURNAL, **36**, 2532 (1914).

[4] W. P. Headden, *J. Agr. Res.*, **5**, No. 8, 349 (1915).

similar plant tissue previously examined. It was found that all samples of these barks did not show the same manganese content, and observed limits of the amounts present are given above. The lower numbers represent mature or thick bark while the higher numbers were obtained from thinner bark. It is quite possible that an examination of specially selected bark would widen this range, but the work reported was carried out on various samples and it is thought that it covers the range fairly well. Factors involving the change of manganese content with the season have not, however, been studied. In an attempt to locate the cells or region of the bark giving the highest content of manganese, both inside and outside scrapings were examined. It was found for *Rhamnus Purshiana* that the concentration of manganese in the inner third of the bark was about double that present in the outer third. This may indeed be generally true and would go to show that although manganese is present in the outer layers of the bark it really functions more particularly in the inner layers where plant metabolism is more actively going on. The accidental presence of definite amounts of manganese in these barks cannot be accepted as an explanation, while the conception that a definite concentration of manganese is a factor in the normal metabolism of any particular species, seems more probable. It is natural to expect that a plant using a higher concentration of manganese in certain working cells might leave behind in the older bark a higher uniform residue. In any case it seems evident that definite amounts of manganese may be found present in all or any of the different parts of plants.

Manganese Fraction Soluble in Water.

By methods of percolation, and by boiling the powdered barks in water, it was found that about one-quarter of the total manganese present may be extracted from members of the *Rhamnaceae* family by this means.

TABLE II.

Bark examined.	Total manganese in the bark.	Manganese extracted.[1]
Rhamnus Frangula	0.0242%	0.0058%
Rhamnus Purshiana	0.0137	0.0029
Rhamnus Californica	0.0033	0.0008

The numbers are based on dry samples as above and are the average results of several good duplicate determinations, showing the uniformity with which manganese is extracted from such materials. Manganese thus extracted does not appear to have the properties of inorganic manganese and is not removed from these solutions by ordinary means. This at once leads to a new method for distinguishing between these closely related species and it follows from this that the development of a "Manganese Number" for commercial extracts of such drugs would seem to be a quite

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[1] U. S. P. type process D, p. 176 (1910).

reasonable and practical method of procedure in their examination. It is our hope to develop such an application in the near future.

Method of Estimation.

The analytical work reported was accomplished by a simple application of the ammonium persulfate method for the determination of small amounts of manganese. The work was done in two ways, depending on the manganese found present by initial trials.

Wherever 10 g. samples are available, the following procedure may be recommended: If the presence of manganese is known to be of the order of 0.015% or higher, it is possible to titrate directly the permanganate formed with standard sodium arsenite solution. If the percentage is lower than this it is more feasible to compare the color developed with solutions of known permanganate content which have been carefully prepared and correspond with the unknown solution with regard to acidity and general ion concentration.

In cases of the first order of manganese content, 10 g. samples of the well-ground materials were ashed in platinum in a muffle and 20 cc. of pure concentrated sulfuric acid was added. The sample was then heated till the acid fumed freely in order to remove chlorides. It was then cooled and diluted with distilled water, washed out into a 500 cc. beaker and diluted to at least 300 cc. To this solution was added one cc. of a silver nitrate solution (5 g. in 100 cc.) and the whole warmed to about 80°. Approximately one g. of ammonium persulfate was gradually stirred into this solution which was then heated on the steam bath as long as the color of the permanganate deepened. By check analyses the reaction was found generally to be complete at the end of 30 minutes. The solution was, however, heated 45 minutes and allowed to cool. When cold it was rapidly titrated with sodium arsenite solution which had been standardized against known amounts of permanganate developed in the same way. Unless the dilution is sufficient a brown hydrated form of manganese will separate out after the addition of the ammonium persulfate. Where the percentage of manganese is as high as 0.06 a volume of 500 cc. is necessary when working on a 10 g. sample.

In cases where the manganese was of a lower order than 0.01% the color was developed as above from a 10 g. sample in a 200 cc. volumetric flask and compared by means of a colorimeter with standard solutions of permanganate.

Our thanks are due to Dr. J. M. Francis, of the Parke Davis Co., Detroit, Mich., for kindly supplying us with genuine samples of some of the above materials.

Summary.

1. The manganese content of certain laxative drugs has been measured along with allied species of plants.

2. It has been found that for the family *Rhamnaceae* the manganese is extracted in water proportionally to its total amount in the bark.

3. A practical use of this determination is suggested leading to the establishment of a "Manganese Number" for extracts of these drugs.

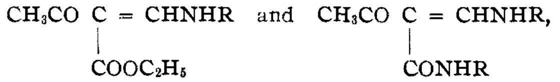
OTTAWA, CANADA.

ON THE REACTIONS OF THE FORMAMIDINES. VII. THE CONSTITUTION OF SOME PYRAZOLE DERIVATIVES.

BY F. B. DAINS AND ROLLA N. HARGER.

Received December 22, 1917.

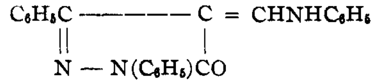
In some previous papers it has been shown that the substituted formamidines react with compounds containing methylene hydrogen, giving rise to complexes in which the hydrogen of the methylene group has been replaced with the grouping = CHNHR.[1] In the case of ethyl-acetoacetate, there are formed derivatives of the two types



$$\begin{array}{l} CH_3CO\ C = CHNHR \\ \qquad\quad | \\ \qquad COOC_2H_5 \end{array} \quad \text{and} \quad \begin{array}{l} CH_3CO\ C = CHNHR, \\ \qquad\quad | \\ \qquad CONHR \end{array}$$

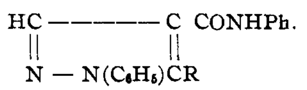
the latter resulting from the action of the amine set free in the first reaction with the carbethoxy group.

In a dissertation published in Freiburg in 1903, Ruggeburg investigated the action of phenylhydrazine on the anilide of anilino-methylene-benzoylacetic ester and obtained a pyrazole derivative to which he ascribed the formula



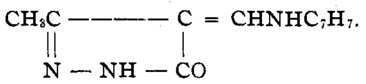
$$\begin{array}{lcl} C_6H_5C & \text{———} & C = CHNHC_6H_5, \\ \| & & | \\ N - N(C_6H_5)CO & & \end{array}$$

1,3-diphenyl-5-keto-4-anilino-methylene pyrazole. Later work[2] proved that phenylhydrazine reacted with the anilino-methylene derivatives of acetoacetic ester or of benzoylacetic ester yielding the anilide of 1-phenyl-5-methyl or phenyl-4-pyrazole carboxylic acid, a pyrazole rather than a pyrazolone ring being formed,



$$\begin{array}{lcl} HC & \text{———} & C\ CONHPh. \\ \| & & \| \\ N - N(C_6H_5)CR & & \end{array}$$

In the following year, a second dissertation by Jacob Gattermann formulated the reaction between hydrazine and the *p*-toluide of *p*-toluido-methylene-acetoacetic ester in the same fashion as did Ruggeburg, assuming that the product was 3-methyl-4-*p*-toluido-methylene-5-pyrazolone,



$$\begin{array}{lcl} CH_3C & \text{———} & C = CHNHC_7H_7. \\ \| & & | \\ N - NH - CO & & \end{array}$$

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[1] *Ber.*, 35, 2497 (1902); THIS JOURNAL, 31, 1148 (1909); 35, 959, 970 (1913); 38, 1510 (1916).

[2] *Ibid.*, 31, 1156 (1909).