series. It has also been pointed out in this paper that the considerations of relative cost, definiteness of the end point and time necessary for making an assay are all in favor of the M. L. D. cat method.

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BIOLOGICAL LABORATORIES OF SHARP AND DOHME,
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THE CHEMICAL INVESTIGATION OF THE RESINS FROM DATURA METELLOIDES.*

BY CHARLES H. ROGERS.

Comparative amounts of alkaloids, glucosides, neutral principles and other medicinally active plant constituents have to a large degree been the bases upon which the value of vegetable drugs or drug preparations have been established. Tschirch and others have pointed out that vegetable drugs are far from simples as indicated by Galen, but rather that they are exceedingly complex. Pharmacological investigation has shown that the action of isolated principles does not always correspond with the action of the drug itself. Therefore, the pharmaceutical chemist and pharmacologist must pay more attention to the complex ingredients of drugs, or, as they are usually called, "extractives." The term "extractives" used in this connection refers to those supposedly inert materials that are soluble in the menstruum used to dissolve the more important constituents of the drug. Before it is possible to determine the part that these extractives play in the production of the total or composite action of drugs it is necessary to have a clearer chemical and pharmacological understanding of them *per se*. Not only is it of importance to understand their chemistry and pharmacology but it is also necessary that their physical constants in respect to temperature, their susceptibility to enzymic action, etc., must be studied.

It has been shown[1] that preparations made from digitalis which has been dried at a uniformly high temperature (70–90° C.) has an absorption value from 25 to 30 percent greater than preparations made from the commercially prepared article. Knowing that the active constituents of this drug are not vitally affected by ordinary temperatures, it is reasonable to conclude that the extractives have in some way been injured by careless manipulation, and, furthermore, that their alteration may have a decided deleterious effect on the rate of absorption of preparations made from the drug. These same conclusions may have a very important bearing on other vegetable drugs. With these fundamental facts in view, the chemical investigation of the resins (extractives) of *Datura metelloides* was undertaken.

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[1] E. L. Newcomb, *St. Paul Medical Journal*, August 1914.

Five hundred grammes of the No. 60 powdered leaves from *Datura metelloides*, 1913 crop, grown in the Medicinal Plant Garden of the University of Minnesota, were moistened with fifty percent alcohol and allowed to macerate for twelve hours. After having packed the moistened drug in a cylindrical percolator, menstruum was added until the liquid began to drop from the lower orifice. Percolation was then discontinued and the whole allowed to macerate for twenty-four hours. The drug was then exhausted of alkaloids as shown by Mayer's reagent. The percolate measured 3380 mils. Fifty percent alcohol was used in the extraction in order that the resins obtained for investigation might be those which would be present in an analogous tincture to that of the U. S. P. IX, *Tinctura Stramonii*.

To the acid tincture thus obtained freshly slaked lime was added until the solution was alkaline to litmus, filtered to remove excess of calcium hydroxide and also the precipitated gums, chlorophyll, etc., and acidulated with dilute sulphuric acid. Three hundred mils of this liquid at a time were placed in a still and the alcohol removed. This operation was conducted on a water bath and at a reduced pressure varying from 350 to 600 millimeters' vacuum. The purpose of reducing the temperature during the distillation of the alcohol was primarily in order that another line of investigation on the alkaloids of *Datura metelloides* might be carried on. This reduction of heat, however, would tend to the least alteration of the constants during extraction of the resin from the crude drug.

The deposited resins were collected, purified and dried in an electric oven for two days at a temperature of 50° C. The total resins from 500 Gm. of drug weighed 13.265 Gm., neutral to litmus, specific gravity, 1.1868 and in color, feel and odor resembled powdered aloes. The percent of soluble resins in the various solvents was then determined and is listed below:

Ether.	Alcohol.	Chloroform.	Ligroin.
35%	91%	82.5%	about 1%
Water.	**Methyl Alcohol.**		**Acetone.**
5.32%	86.14%		52.64%

The method employed by A. Tschirch for the proximate analysis of resinous substances was used to classify these particular resins. From previous analyses it has been found that resins are composed of a mixture of compounds and may be classified only by the particular kind of resin which predominates. Tschirch classifies them as ester-resins, acid-resins, resin-alcohols and resenes. The method employed dissolved the resin in ether, but due to only 35 percent of the resins under investigation being soluble in ether, they were dissolved in chloroform. This chloroformic solution was agitated successively with (1) a 1 percent solution of ammonium carbonate, (2) a 1 percent solution of monohydrated sodium carbonate, and (3) solutions of potassium hydroxide of one-tenth and one percent strength, respectively. These reagents dissolved the acid-resins, which were then precipitated from the alkaline liquids with dilute hydrochloric acid. Analysis showed the chloroform-soluble resins to be 33.33 percent acid-resins. These acid-resins or resinolic acids are composed of the characteristic free acids of the original resin and are usually substances of very complex constitution and possess a high molecular weight.

The residue contained the resin-esters, alcohol-resins and resenes. These were separated by saponification with alcoholic potash when the acid radicles of the esters formed soluble potassium salts. It was determined that 54.54 percent of the sample was composed of resin-esters. These esters, as a rule, yield aromatic acids upon saponification and hence are sometimes classed as aromatic balsams.

The resenes and alcohol-resins were then extracted by agitation with ether. This mixture was then boiled for two hours with acetyl chloride under a properly fitted-up reflux condenser, during which process the alcohol-resins were acetylated while the resenes were not affected. The latter were carefully weighed and found to constitute 9.66 percent of the total resin. The results, showing the composition of the chloroform-soluble portion of the original resin, are given below:

Acid-resins	33.33%
Ester-resins	54.54%
Resenes	9.66%
Alcohol-resins	1.84%
	99.37%

Tschirch distinguished two kinds of resin-alcohols., *viz.*, resinols and resinotannols. The members of the first group are colorless compounds giving no tannin reaction with iron salts, while those of the second group are colored and give a tannin reaction. The resin-alcohols investigated were light amber in color and gave no tannin reaction with a solution of ferric chloride.

Previous investigations have shown resenes to be oxygenated compounds, not acted upon by alkalies and possessing no characteristic chemical properties. They do not appear to be alcohols, esters, acids, ketones or aldehydes.

Combustions were made on two individual samples of the resins with the following results:

Sample.	Carbon.	Hydrogen.	Oxygen.
No. 1	69.4%	9.35%	21.25%
No. 2	68.5%	9.49%	22.01%
Average	68.95%	9.42%	21.63%

Empirical formula: $C_6H_{10}O$.

The analytical characters of the resin from the leaves of *Datura metelloides* are recorded below, also those for its alcohol-soluble, alcohol-insoluble and ether-insoluble portions:

CONSTANTS FOR DATURA METELLOIDES RESIN.

Resin	Saponification number.	Iodine value.	Acid number.	Ester number.	Ash.	Melting point.
Original resin	221.3	85.15	61.8	159.5	0.48	90° C.
Alcohol-soluble resin	168.4	99.86	47.04	121.36	0.23	110.5° C.
Alcohol-insoluble resin	286.2	99.53	39.5	246.7	0.65	above 217° C.
Ether-insoluble resin	315.9	97.88	141.06	174.84	0.14	149° C.

The saponification number (number of milligrammes of potassium hydroxide absorbed by one gramme of resin) was determined by boiling a definite weight of the resin with $\frac{N}{2}$ alcoholic potassium hydroxide V. S. for two hours under a reflux and titrating the excess of alkali with $\frac{N}{10}$ hydrochloric acid V. S.

The iodine value (number of grammes of iodine absorbed by 100 Gm. of resin) was estimated by the Hanus method. This method depends upon the fact that

unsaturated fatty acids, as well as their esters, absorb halogens to form mainly addition products. This constant, then, may indicate to what group of unsaturated acids the resin-acids belong. Compared with iodine values of other resins, it checks with that of Elemi resin[2] of the Bursera species, they being 85.15 and 85.1, respectively.

The acid number (expressed in terms of milligrammes of potassium hydroxide required to neutralize one gramme of resin) was obtained by boiling a definite weight of resin for five minutes under a reflux with 90 percent alcohol and titrating the liquid when cold with $\frac{N}{10}$ alcoholic potash V. S., phenolphthalein used as indicator. This constant expresses the amount of free acids present.

The ester number was obtained by subtracting the acid number for the resin from the saponification number and expresses the number of milligrammes of potassium hydroxide that would be required to combine with only the esters present in the resin.

The foregoing methods with their results afford indications of the nature of resinous substances in question, but their use in the positive identification of the various individual commercial resins is a matter of considerable difficulty even when only one resin is present, and in case of an admixture is often impossible. These constants vary and may even be entirely destroyed by aging, heating, etc. J. Lewkowitsch[3] has shown that the constants for various resins are absolutely destroyed by heating to 300° C. The saponification numbers, iodine values and acid numbers for the resins under examination checked after being heated to a temperature not exceeding 110° C. for two days. However, the constants for resins, including those obtained from *Datura metelloides*, may be recorded, but it is evident that any definite conclusions as to the value or purity of the resins should be drawn with the greatest care.

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A WOOL FAT (LANOLIN) SUBSTITUTE AND THE PREPARATION OF CETYLIC ALCOHOL.*

BY SOL. AXELRAD.

The question of substitutes for various materials has been one of prime importance during these war times, especially those substances and chemicals used in medicine and pharmacy. A year and a half ago the supply of wool fat was very limited and the price asked was four times more than that under normal conditions. A substitute called "Eucerin" imported from Germany was also scarce and the agency for this product had only four ounces left. It was claimed that "Eucerin" was made from the washings obtained in the manufacture of wool fat. The uses of lanolin are many, especially in pharmacy; as a vehicle for ointments, in the

[2] Schmidt and Urban, *J. Soc. Chem. Ind.*, 8, 308, 1889.

[3] *Analyst*, 26, 38, 1901.

* Contributed by the author to the JOURNAL A. PH. A., October 18, 1917.