

Toxicity of Extracts of Derris Root for Mice.

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Several authors^{1,2} have shown that the toxicity of derris for mammals does not necessarily parallel its rotenone content or its content of other known active compounds or fractions. It is conceivable that this is due to the presence in the root of an as yet unidentified fraction. During efforts to clarify this situation we have made certain observations on the toxicity of several derris extracts, which data we feel are worthy of reporting, although they do not answer the main question.

Experimental. A sample of finely ground derris root containing 4.6% rotenone and 14.0% total chloroform extractives was used. The different fractions were prepared by extraction with organic solvents in a Soxhlet, or by shaking a suspension with water.³ The extracts from the organic solvents were deposited on talc by evaporation of the solvent, but the colloidal water extract was used as such. The two samples of talc, of different particulate size, were prepared by fractionation in an air classifier. The rotenone, chloroform extractive, and red color values (rotenone plus deguelin),⁴ together with a description of all samples, are given in Table I.

The acute oral L.D.₅₀ toxicities of the sample of derris and its several fractions were determined on white mice of mixed sexes, weighing from 16 to 22 g. The materials were used in water suspension. After preliminary trials 20 or more mice were used at each of from 3- to 5-dose levels, and the L.D.₅₀ was determined from the charted results. The

animals were kept under observation for 5 days or longer after administration of the materials.

Discussion of Results. These studies (Table I) show that, with the specimen of derris used, all materials highly toxic to mice were removed by complete extraction with chloroform. This chloroform extract when deposited on talc did not have as great toxicity as it did in the original form in whole derris, probably because of the absence of certain dispersing agents which are present in the root, and which cause colloidal suspensions of the toxicants to be formed when the root is administered alone. This dispersing action is demonstrated by the ease with which colloidal water extracts can be prepared from the root. The water extract was shown to be relatively highly toxic, although water recovers only 30% of the rotenone-deguelin content as determined by the red color test. The marc, still containing 70% of these materials, was only slightly more toxic. The toxicity of the petroleum ether extract and the marc from this extraction was related to the amount of insecticidal substances present as estimated by the red color test. Further extraction with cyclohexane of the marc from the petroleum ether extraction reduced the toxicity to a very low value. Most of the remaining material is probably retained in unbroken plant cells.

Comparison of the same toxic material (petroleum ether extract) deposited on two different samples of talc shows that the more finely divided sample had the higher toxicity. Lightbody and Mathews⁵ previously have reported finely powdered rotenone to be more toxic for rats than the crystalline form. We have not been able thus far to isolate an active alkaloid or glycoside from any of the

¹ Mathews, J. A., and Lightboy, H. D., *Ind. Eng. Chem.*, 1936, **28**, 812.

² Ambrose, A. M., and Haag, H. B., *Ind. Eng. Chem.*, 1936, **28**, 815.

³ Goodhue, L. D., and Haller, H. L., *J. Econ. Entomol.*, 1939, **32**, 877.

⁴ Goodhue, L. D., *J. Assn. Off. Agri. Chem.*, 1936, **19**, 118.

⁵ Lightboy, H. D., and Mathews, J. A., *Ind. Eng. Chem.*, 1935, **28**, 809.

TABLE I.
Acute Oral Toxicity for White Mice of Derris Root and Various Extracts of It.

Sample	Rotenone, %	Total Chloroform Extractives, %	Red color % of total	L.D. ₅₀ white mice, mg/kg
1. Powdered derris root	4.6	14.0	100.00	350
2. Marc, after extraction of No. 1 with water			70.5	470
3. Marc, after extracting No. 1 with petroleum ether 20 hr	2.44	6.8	50.7	570
4. Water extract of No. 1			31.0	600
5. Petroleum ether extract of No. 1 on tale having mean diameter of 1 μ	2.20	7.2	56.0	600
6. Petroleum ether extract of No. 1 on tale having mean diameter of 2 μ	2.20	7.2	55.0	700
7. Total chloroform extract of No. 1 on 2 μ tale	4.6	14.0		700
8. Chloroform extract of No. 3 on 2 μ tale	2.4	6.8	44.0	1,100
9. Marc after extracting No. 3 with water			40.5	3,000
10. Marc from complete extraction of No. 1 with chloroform	0	0	0.0	>3,600*
11. Marc from No. 3 extracted 20 hr with cyclohexane	1.5	4.5	20.0	>1,200†
12. Tale control, 2 μ				>4,200*

* No fatalities. † 10% fatalities.

fractions, or from whole derris.

Summary. From studies dealing with the acute toxicity of derris and several extracts thereof for mice, it appears that this toxicity is due to the insecticidally active materials represented by the rotenone content, total chloroform extractives content, and red color

index. No single one of these three determinations, however, seemed uniformly to indicate the relative toxicity of the various fractions studied. Materials not extractable with chloroform were found to be practically non-toxic. Thus far no active alkaloid or glycoside has been isolated from derris.

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Changes in the Adrenals Following Prolonged Treatment with Methyl-Testosterone.

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The fact that adrenal cortical tumors are often accompanied by clinical signs of "virilism" called attention, at an early date, to possible relationships between the adrenal cortex and the production of testicular or "testoid" hormones. It has been found that the zona reticularis or "x-zone" of the adrenal cortex in the mouse undergoes rapid involu-

tion under the influence of testoid hormones.¹⁻³ In other species, however, this is not the case. For instance in the rat testosterone and its propionate fail to elicit specific changes in the reticularis although they decrease the weight of the organ due to a slight involution of the cortex as a whole.^{4,5} It has been espe-

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¹ Howard, E., *Am. J. Physiol.*, 1940, **129**, P 297.

² Burrows, H., *J. Path. and Bact.*, 1936, **43**, 121.

³ Starkey, W. F., and Schmidt, E. C. H., Jr., *Endocrinology*, 1938, **23**, 339.

⁴ McEuen, C. S., Selye, H., and Collip, J. B., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 390.

⁵ Selye, H., *Canad. M. Assn. J.*, 1940, **42**, 113.