A Pharmacologic Study of Devil's Club Root (*Fatsia Horrida*)*

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The treatment of diabetes by insulin injections has many obvious disadvantages. In order to obviate these factors many investigations have been made with oral preparations (1). Much controversy exists over the efficacy of these products (2). Recently, interest has been shown in the effects of aqueous extracts of Devil's Club Root (*Fatsia Horrida*). This report presents observations on the blood sugar metabolism of rabbits treated with these extracts.

TABLE I.—GLUCOSE VALUE (MG. PER 100 ML. OF BLOOD) FROM UNMEDICATED RABBITS

Rabbit	Weight of Rabbit	Number of Readings	Low Reading	High Reading	Average	Average Deviations
A	4 lbs. 4 oz.	6	105.2	123.6	114.3	6.7
B	4 lbs. 8 oz.	6	98.5	132.4	116.5	7.2
C	6 lbs. 10 oz.	5	93.5	134.2	116.0	9.6
D	7 lbs. 4 oz.	7	90.7	129.9	113.7	7.9
E	8 lbs.	7	99.6	145.6	122.6	15.5

TABLE II.—GLUCOSE VALUES (MG. PER 100 ML. BLOOD) OBTAINED FROM RABBITS MEDICATED WITH DEVIL'S CLUB ROOT EXTRACT

Rabbit	Hours of Starvation	Extract[a] 1 Cc. = 3 Gm. of Drug	Dose per Lb. of Body Weight	Blood Sugar Value before Medication	Blood Sugar Values after Medication (Time in Hours) ½	1	1½	2	3	4	5	6
	15	No. 2	0.14 cc.	107.4	...	131.6	...	99.0	120.0	119.3	...	...
A	15	No. 3	0.14 cc.	117.2	...	94.5	...	104.7	117.9	118.6	...	...
	24	No. 3	0.07 cc.	105.2	...	95.8	...	123.6	118.6	...	...	...
	15	No. 2	0.14 cc.	118.6	...	114.6	...	100.5	115.3	117.3	...	...
B	15	No. 3	0.14 cc.	132.4	...	103.5	...	109.0	123.6	113.9	...	...
	24	No. 3	0.07 cc.	98.5	...	107.4	...	117.2	110.9	...	...	...
	15	No. 2	0.14 cc.	116.0[b]	...	101.0	...	98.0	103.5	109.0	...	...
C	15	No. 3	0.14 cc.	120.7	...	108.5	...	106.8	103.5	105.2	...	...
	24	No. 3	0.14 cc.	93.5	...	95.8	...	115.3	109.7	...	...	...
D	16	No. 1	0.06 cc.	119.3	138.7	138.7	124.3	123.6	...	...	...	...
	16	No. 1	0.14 cc.	113.7[b]	...	...	147.1	...	173.8	...	147.1	145.7
E	16	No. 1	0.06 cc.	116.6	125.2	147.8	114.6	127.5	...	...	...	...
	16	No. 1	0.14 cc.	122.6[b]	...	...	141.6	...	126.5	...	113.2	127.5

[a] Three different extracts were prepared.

[b] The blood sugar values before medication were not taken. The figures are the averages obtained from Table I.

EXPERIMENTAL

The dried root bark was ground to a coarse powder and extracted according to the method of Large and Brocklesby (3). The powder was boiled 3 times with twice its volume of water and the extract filtered off. Tannins were removed with neutral lead acetate and excess lead by means of H_2S. The precipitated tannins were separated by means of a Sharple's supercentrifuge. The excess H_2S was removed by boiling and the extract finally evaporated, so that the number of cc. of final volume was $^1/_3$ the number of grams of the original bark. The extract was made slightly alkaline with magnesium oxide, filtered and stored for use. This type of extract was used throughout the investigation. The extract was then administered in varying doses to rabbits. In order to ensure complete administration of the doses, they were passed directly into the stomach by means of a catheter.

Normal rabbits weighing $4^1/_4$ to 8 lbs. were used. Blood was taken from the marginal ear vein and tested for glucose content by Benedict's modification of the Folin-Wu micro method (4). Normal blood sugar values for each rabbit are shown in Table I. It is to be noted that in all cases the blood sugar value never fell below 90 mg. of glucose per 100 ml. of blood, and the general average of the group was about 115 mg./100 ml.

Medication was started after having established these normals. The rabbits were starved for 15 to 24 hours before administration of the extract and blood sugar determinations were made at various

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intervals following ingestion. The results obtained are shown in Table II.

SUMMARY

1. Rabbit *A* showed a lowest blood sugar value of 94.5 mg./100 ml. and a highest value of 131.6 mg./100 ml., using 2 different doses and two different extracts. These figures are within the range of normal blood sugar values for *A* as indicated in Table I.

2. Similarly the lowest and highest values obtained for rabbits *B*, *C* and *E* also fall within the normal values for each.

3. Rabbit *D*, although showing values greater than the normal, did not give any below the normal.

CONCLUSION

These observations seem to indicate that oral administrations of our aqueous extracts of Devil's Club Root have no hypoglycemic effect upon the blood of rabbits which have been starved for 15 to 24 hours.

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The Constitution of Celastrol —Part II

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A preliminary report on the constitution of celastrol, a pigment obtained from *Celastrus scandens*, was given in a previous paper (1). Celastrol crystallizes from organic solvents in the form of ruby-red cubes. The following derivatives were reported: methyl celastrol (orange needles), acetyl celastrol (yellow), methyl acetyl celastrol (yellow) and acetyl methyl celastrol (yellow). Of the derivatives prepared, the methylated compound (prepared by methylation with diazomethane) was the only one to be obtained in a good crystalline form. Its methoxyl content was 9.01 (av.) which indicated the introduction of one methoxyl group. The molecular weight by the Rast method was 347. Celastrol and methyl celastrol gave a green color with ferric chloride whereas the acetylated derivatives did not. Celastrol appeared to be reversibly reduced at 190° C. with Raney's nickel. Ultimate analysis of celastrol indicated the formula $C_{23}H_{36}O_3$. It will be shown in this paper that this formula is not correct because not all the solvent of crystallization could be removed by drying at 100° C. over phosphorus pentoxide in a vacuum. Ultimate analysis of the acetate indicated the formula $C_{26}H_{34}O_5$.

Subsequent investigations on the constitution of celastrol indicate that no carboxyl groups are present in the molecule. In addition to the introduction of one methoxyl group, it will be shown that two acetyl groups can be introduced, thus accounting for the presence of three oxygens. One or both of the acetyl groups must be hydrolyzed very rapidly because alcoholic alkali causes an immediate development of a deep red color. It appears that a second methoxyl group can be introduced into the molecule by means of dimethyl sulfate and alkali. This dimethoxyl compound is yellow in color. Catalytic reduction of celastrol and methyl celastrol with platinum black at 40-lbs.

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