

EVALUATION OF GROWTH PROMOTING EFFECT OF TOTAL RAUWOLFIA EXTRACT AND ITS ALKALOID RESERPINE

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This work was undertaken because of a large number of reports in literature which mention increase in the weight of patients suffering from diverse diseases like hypertension, psychoses and psychoneuroses and treated by crude Rauwolfia root or Reserpine (Achor et al., 1955; Bleuler et al., 1955; Tasher and Chermak, 1955; Wilkins, 1954 and Smith, 1955). This increase in weight has been explained on the basis of increase in appetite caused by the tranquilising action of the drug resulting in decrease in tension and anxiety, and better sleep and improved digestion. A few patients also developed oedema which was circumscribed in some cases and generalized in others. It was thought that water retention may be due to disturbance of electrolyte balance but Moyer (1954) and Moyer et al., (1955) found that sodium ion and potassium ion concentration in the plasma, as well as the excretion rates for these electrolytes, showed no change in patients to whom reserpine was given over a long period or in dogs which received intravenous injections. More recently Genest et al., (1955) reported increase in weight in patients suffering from psoriasis and constitutional leanness and treated by Rauwolfia preparations. This led us to think that this weight increase after use of Rauwolfia preparations may be a specific effect and not merely secondary to fluid retention or a tranquilising effect. It was considered that this effect may be mediated through some endocrine gland. Clinical and experimental work lent some support to the endocrinal nature of action of Rauwolfia but definite conclusions could not be drawn (Cronheim et al., 1955; Gaunt et al., 1955; Goodman et al., 1955 and Barraclough, 1955). In this study are reported to the effects of Rauwolfia extract or its alkaloid reserpine on weight in normal rats as well as on nitrogen balance, voluntary food and water uptake and urinary and faecal excretion.

METHODS AND MATERIAL

Young rats of 3-4 weeks of age weighing between 30 to 40 gm. were selected for the study. They were divided into three groups of fifteen rats each. The groups were so arranged that the total weight of each group was approximately the same. Each group was kept in a separate wire metabolic cage with fine mesh bottom to retain faeces. The urine was collected in glass jars containing toluene to prevent evaporation and decomposition and suffi-

cient sulphuric acid to acidify the urine. The animals were fed on a diet of the following composition and water was allowed ad libitum.

	Percent
Wheat flour	86
Bone meal	8
Skimmed milk	3
Yeast	1
Cod liver oil	1
Sodium chloride	1

The weights of the animals were recorded twice a week, and food consumption, water consumption, urine and faecal excretion were recorded daily for eight weeks.

Nitrogen balance studies were made during a four week period (4th to 7th week). Nitrogen estimations of Food, Urine and Faeces were done by the usual Kjeldahl procedure. Each animal in group A received approximately 100 $\mu\text{g./kg.}$ daily of reserpine and each animal in group B received approximately 300 $\mu\text{g./kg.}$ daily of total extract of Rauwolfia. Group C served as control. The drugs were thoroughly mixed with the weighed food powder which was later made into dough and baked into chapatis to minimise scattering. At the end of eight weeks the animals were autopsied and the weights of the different organs were recorded.

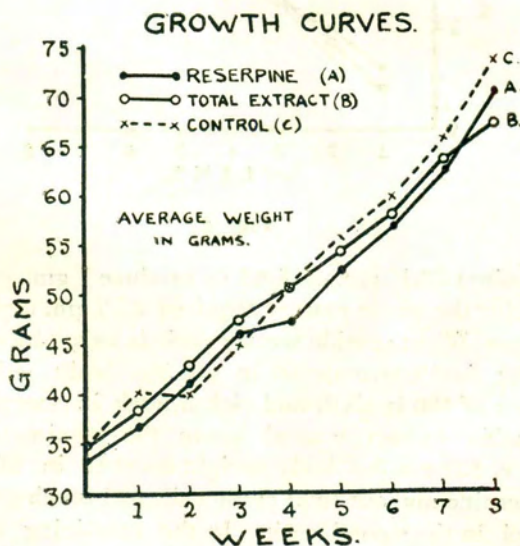


Fig. 1

RESULTS

Growth. As illustrated in figure 1 it was found that group A treated with reserpine had an average growth of 37.5 ± 5.1 gm., group B treated with total extract of Rauwolfia had an average growth of 35.6 ± 3.8 gm. and group C serving as control had an average growth of 40.0 ± 4.6 gm. over a period of eight weeks. These differences in growth are statistically insignificant.

Food Consumption and Faecal Excretion. Figure 2 shows cumulative kilograms of food eaten by each group over a period of eight weeks. The figures for the reserpine treated and the total extract treated groups are 3.3 kg. and 3.1 kg. respectively and for the control the figure is 3.5 kg. When the efficiency for food utilisation for adding weight is considered the reserpine

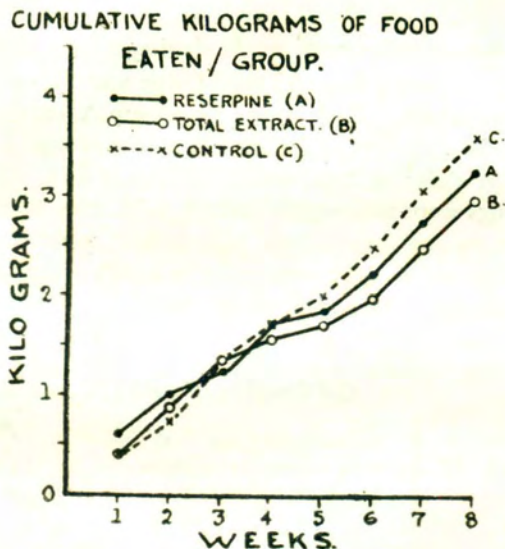


Fig. 2

treated rats required 88.1 gm. of food to produce 1 gm. gain in weight, the group treated with the whole extract required 87.6 gm. and the control group required 89.17 gm. When specific weekly periods were observed (Fig. 3) it was noticed that the food consumption in gm./kg. body weight declined to a minimum figures of 480 in sixth and eighth week in reserpine treated group. In total Rauwolfia extract treated group the maximum decline in food consumption, i. e. 325 gm./kg. body weight occurred in fifth week. Groups treated with reserpine and the total extract showed much greater consumption than the control in the second week. In the remaining seven week period total extract treated group had consistently less consumption of food than the control group. Reserpine treated group also showed less food consumption

throughout the remaining period except in third and seventh week when it showed slight increase over the control. Faecal excretion was more or less parallel to the food consumption.

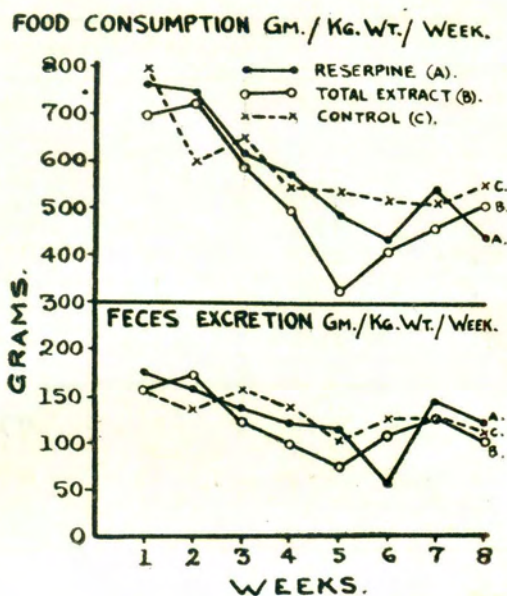


Fig. 3

Water Consumption and Water Excretion. When weekly averages in millilitres of water consumed per kilogram of body weight were plotted against time (Fig. 4) it was found that the reserpine treated group consumed the least quantity of water almost throughout the eight weeks observation period. The maximum decline in water consumption in reserpine treated group occurred in third, fourth and eighth week. The total extract treated group also had uniformly less consumption of water than the control group except in the fourth week when it slightly increased. The maximum decline in the water consumption in the total extract treated group, as also in the control, occurred in the eighth week. The cumulative consumption of water in litres over eight weeks in reserpine treated (A) and total extract treated (B) groups and in the control (C) were 11.4, 13.4 and 15.0 respectively. Out of this total water consumed the percentage excreted out as urine in groups A, B and C was 13.23, 24.6 and 25.4, respectively.

Nitrogen Balance. All the groups over four weeks of nitrogen determination have shown considerable positive nitrogen balance (Table 1.) The reserpine treated group showed the maximum retention of nitrogen (82.3 gm.) and the total extract treated group showed the least retention of nitrogen (68.5 gm.).

Drugs	Weeks	Weight in Nitrogen in gm.			
		Food	Urine	Faeces	Retention
A Reserpine	4	21.5	0.33	0.11	20.56
	5	20.8	0.89	0.12	19.79
	6	17.5	1.038	0.108	16.354
	7	28.7	0.98	0.11	25.61
	Total	88.5	3.738	0.48	82.314
B Total Extra- act of Rau- wolfia.	4	19.71	1.15	0.138	18.422
	5	14.65	1.58	0.179	12.891
	6	18.8 I	1.33	0.157	17.322
	7	21.6	1.52	0.163	19.917
	Total	74.77	5.58	0.637	68.552
Control	4	15.70	1.49	0.163	14.047
	5	26.32	1.66	0.192	24.468
	6	20.1	1.79	0.181	18.119
	7	26.32	1.97	0.230	24.120
	Total	88.44	6.91	0.766	80.754

Table 1 Showing the nitrogen balance over four week period for the treated and control group.

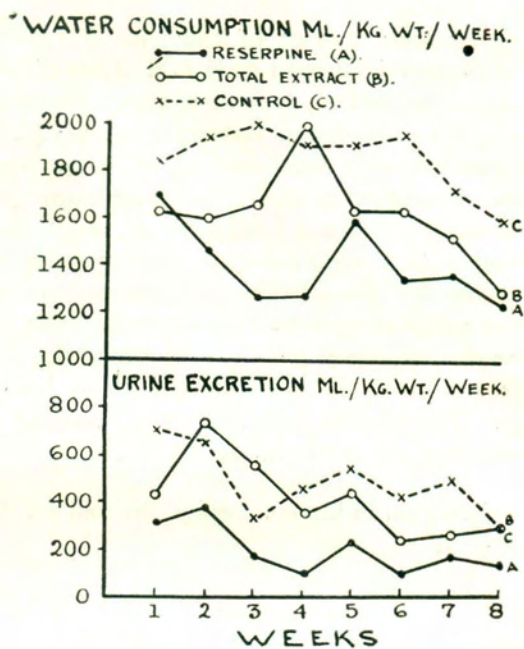


Fig. 4

	Reserpine.	Whole extract.	Control,
Weight gm. per rat	71	69.8	73.9
Body length (minus tail) cm. per gm. per rat.	0.032	0.029	0.036
Tail length cm. per gm. per rat.	0.029	0.027	0.033
Pituitary % body weight	0.003	0.0029	0.0032
Adrenal % body weight	0.0041	0.0040	0.0042
Kidney % body weight	0.49	0.51	0.53
Gastrocnemius % body weight	0.241	0.221	0.251
G. I. tract and contents of body weight	7.8	8.25	8.56
Thyroid and Tracheal ring % body weight	0.017	0.019	0.020
Heart, Lungs and Thymus % body weight	1.325	1.275	1.435
Spleen % body weight	0.165	0.173	0.178
Liver % body weight	3.62	3.51	3.78

TABLE 2. Summary of autopsy weights and measurements.

CONCLUSIONS

Reserpine and the total extract of Rauwolfia do not cause significant increase in weight in rats when given in daily oral doses of 100 $\mu\text{g./kg.}$ and 300 $\mu\text{g./kg.}$ body weight respectively. Both decrease the voluntary food and water intake in rats in the above doses. Reserpine causes significant inhibition of water excretion whereas with total extract of Rauwolfia the inhibition appears to be slight. Reserpine is shown to cause more positive nitrogen balance than the control and it is not possible to reconcile this finding with the fact that it did not cause a significant increase in weight. Nor is any explanation forthcoming for the smaller nitrogen balance among animals treated with total Rauwolfia extract than the controls. The weights of the various organs in the treated groups are also less than the untreated group (Table 2.) though there is no significant difference in the body weights of rats in the three groups. This may be explained on the basis of water retention in extracellular tissues in the treated groups.

The cause for weight gain in human beings treated on Rauwolfia preparations, remains obscure.

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