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Leptazol and Diuresis.*

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Not uncommonly drugs have been introduced into medical practice for one purpose and subsequently found to be much more useful in other fields of therapy. This statement applies to the drug now known as Nikethamide in N.N.R. and the B.P., a drug which was originally marketed some 20 years ago under the name of Coramine and which, as the name implies, was at that time considered as a drug useful in the therapy of certain forms of cardiac disease. Nikethamide is now known to have little direct action upon the heart and blood vessels but in 1940 it was found in this laboratory that the drug is markedly diuretic if given in sufficiently large doses.[1] About the same time that Nikethamide was introduced. Leptazol, B.P.,[2] or Metrazol, N.N.R., was synthesized and marketed under the name of Cardiazol as a cardiac stimulant. Since leptazol is now known to have little direct action upon the heart and blood vessels,[3] it was decided to find out if it too might have diuretic properties.

Leptazol was injected subcutaneously into 6 groups, each of 21 healthy, adult albino rats averaging between 250 and 300 g body weight in doses of 0, 1, 5, 10, 25, and 50 mg per kilo body weight respectively. A dose of 100 mg per kilo body weight was found to be lethal to a majority of rats and was discarded early in the investigation. Up to the time of the experiment, the animals had had Purina Fox Chow Checkers and water *ad libitum*. They were then weighed, given the appropriate dose of leptazol or isotonic saline in a volume of 1 cc of isotonic saline per kilo body weight and placed in large funnels suitable for the collection of urine. At hourly intervals after injection, the animals were reweighed and the volume of urine noted.

Over the 6 hours during which the readings were taken, the average rate of urine formation was 34.4 cc per kilo per 24 hours and the rate of output was at no time affected by the injection of the several doses of leptazol, the output in the control group receiving injections of saline only being at the rate of 36.8 cc per kilo per 24 hours. These results were in marked contrast to those obtained with nikethamide in which the rate of urine formation was augmented to as much as 10 to 20 times the normal or control rate, as previously reported.[1]

Leptazol did increase the loss in total body weight. Most of this effect occurred during the first hour after injection of the drug and if the increased loss is expressed as a percent of the loss in total body weight of the controls given isotonic saline only, then it was calculated that for the 1 mg dose the increased loss averaged 7%, for the 5 mg dose 57%, for the 10 mg dose 100%, for the 25 mg dose 157%, and for the 50 mg dose 129%. By the end of 6 hours after injection, the cumulative loss of total body weight in the controls was similar to that in the rats receiving leptazol with the exception of the 25 and 50 mg doses of leptazol and rats receiving these large doses of leptazol still had a cumulative loss in total body weight which averaged 39% over that in the controls.

Conclusion. It was not possible to demonstrate that leptazol had a diuretic action in albino rats when given in doses up to the lethal dose.

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1 Boyd, E. M., and Forde, J. D., *J. Pharm. and Exp. Therap.*, 1940, **70**, 279.

2 *Third Addendum to the British Pharmacopoeia*, 1932, Constable and Co., London, 1941.

3 Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics*, Macmillan, New York, 1941.