lower the concentration of creatine in the myocardium. This is surprising and may be due to the variable carbohydrate intake, a point which is being examined. The addition of glycine or dl-alanine to the diet definitely raised the amount of creatine in the heart muscle, d-glutamic acid was not so effective. The relative effects of the various amino acids, particularly over short periods of time in the same manner as used by Beard and Barnes[1] for skeletal muscle, should be determined.

8177 C

Sodium Propyl-methyl-carbinyl Allyl Barbiturate, a Short Acting Hypnotic.

EDWARD E. SWANSON. (Introduced by K. K. Chen.)

From the Lilly Research Laboratories, Indianapolis.

Fitch, Waters, and Tatum[1] in their extensive work on barbituric acid hypnotics emphasized the importance of employing short acting members for surgical procedures. Among the different derivatives synthesized by Shonle and his associates,[2, 3, 4] the sodium salt of propyl-methyl-carbinyl allyl barbituric acid appears to have the desirable promptness and brevity of action. The same compound has been prepared by Tabern and Volwiler.[5]

By following Eddy's scheme of recording results,[6] it was found that in rats by intraperitoneal injection the minimal anesthetic dose (M.A.D.) was 40 mg. and the minimal lethal dose (M.L.D.) 110 mg., per kg. Twenty mg. per kg. by the same route of administration were sufficient to induce sleep. These animals, 220 in number, weighed on the average 94 gm. In dogs by intravenous injection of a 5% solution at the rate of 1 cc. per minute, the M.A.D. was ascertained to be 25 mg. and the M.L.D. 50 mg., per kg. By mouth in the same species of animal the M.A.D. was determined to be 35 mg. and the M.L.D. 90 mg., per kg. A total of 83 dogs were used.

---

1 Fitch, R. H., Waters, R. M., and Tatum, A. L., *Am. J. Surg.*, 1930, **9**, 110.

2 Shonle, H. A., Keltch, A. K., and Swanson, E. E., *J. Am. Chem. Soc.*, 1930, **52**, 2440.

3 Shonle, H. A., and Kleiderer, E. C., *J. Am. Chem. Soc.*, 1934, **56**, 2489.

4 Shonle, H. A., *J. Am. Chem. Soc.*, 1934, **56**, 2490.

5 Tabern, D. L., and Volwiler, E. H., *J. Am. Chem. Soc.*, 1934, **56**, 1139.

6 Eddy, N. B., *J. Pharm. and Exp. Therap.*, 1928, **33**, 43.

TABLE I.
Comparison of Sodium Propyl-methyl-carbinyl Allyl Barbiturate, Pentobarbital Sodium, and Sodium Amytal in Dogs.

Drug	Dogs used	M.A.D. by vein: Amt. required mg. per kg.	M.A.D. by vein: Duration of anesthesia min.	M.A.D. by vein: Time necessary for complete recovery hr.	M.A.D. by vein: Time necessary for complete recovery min.	M.A.D. by mouth: Amt. required mg. per kg.	M.A.D. by mouth: Appearance of ataxia after injection min.	M.A.D. by mouth: Duration of anesthesia min.	M.A.D. by mouth: Time necessary for complete recovery hr.	M.A.D. by mouth: Time necessary for complete recovery min.
Sodium Propyl-methyl-carbinyl Allyl Barbiturate	5	25	70	7	50	35	4	75	12	10
			70	7	20		4	140	12	45
			50	7	10		3	160	12	43
			80	7	35		3	120	12	10
			50	7			5	140	12	15
Aver.			64	7	23			127	12	24
Pentobarbital Sodium	6	25	35	9		40	5	140	17	
			30	8	30		5	110	18	
			65	8	30		8	135	15	
			45	7	30		5	145	12	30
			35	8	30		5	130	13	30
			45	9			8	60	14	
Aver.			42	8	30			120	15	
Sodium Amytal	6	45	65	16		70	8	135	22	
			65	15	30		8	150	22	
			50	14			10	180	22	
			55	16	30		8	150	24	
			65	16			8	175	24	
			60	14			10	105	20	
Aver.			60	15	20			149	22	20

A comparison of the onset and duration of action of sodium propyl-methyl-carbinyl allyl barbiturate in dogs with those of sodium amytal and pentobarbital sodium is shown in Table I. It will be noted that when given by mouth the appearance of ataxia occurred slightly sooner with the new barbituric acid derivative. Its duration of anesthesia was, on the average, longer than that with pentobarbital sodium and comparable to that with sodium amytal. However, the time for complete recovery after the administration of sodium propyl-methyl-carbinyl allyl barbiturate was approximately half that with sodium amytal, and slightly shorter than that with pentobarbital sodium.

Similar to sodium amytal and pentobarbital sodium, the new compound by intravenous injection proved to protect rabbits from 4 but not 5 M.L.D.'s of strychnine or cocaine—34 animals being employed for this purpose. Its preanesthetic value in rats was found to be 25% of the M.L.D. according to the method of Barlow and his coworkers.[7] In this case, the drug was given subcutaneously, and the subcutaneous M.L.D was determined to be 140 mg. per kg. In 5 dogs which were repeatedly injected by vein with anesthetic doses, every other day for 8 days, there was no loss of hypnotic and anesthetic effect. Furthermore, it required no more than the M.L.D. (50 mg. per kg.) to kill the same animals. Obviously, no tolerance was developed by repeated administration. The new hypnotic when injected intravenously in anesthetic doses did not appear to be excreted in the urine. Like all other members of the same group, sodium propyl-methyl-carbinyl allyl barbiturate causes lowering of blood pressure and depression of respiration, especially if given rapidly by vein. The body temperature may also fall slightly. No inhibition of the vagus in dogs was observed when anesthetic doses were employed. In this respect, sodium propyl-methyl-carbinyl allyl barbiturate is different from sodium amytal but similar to pentobarbital sodium.

Clinical investigations have been carried out by Doctors G. F. Kempf and L. G. Zerfas, and separate reports will be made by them elsewhere. In general, their results bear out the essential points enumerated above, particularly with reference to the promptness and brevity of action.

[7] Stormont, M. F., Lampe, I., and Barlow, O. W., *J. Pharm. and Exp. Therap.*, 1930, **39**, 165.