Comparative Plasma Levels of Mephenesin and its Carbamic Acid Ester. (22894)

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Mephenesin carbamate induces, in laboratory animals, profound skeletal muscle relaxation of considerably longer duration than that of its parent compound, mephenesin. Studies in the dog have indicated that mephenesin is oxidized to mephenesic acid or conjugated with glucuronic acid prior to urinary excretion. The fact that mephenesin carbamate is not oxidized to mephenesic acid in the dog may account for the relatively higher and more persistent plasma levels (with consequent prolonged pharmacologic activity) seen after its administration (1). The present study compares, in man, the plasma levels of mephenesin with those of its carbamic acid ester following oral administration at equal dosage of the respective drugs.

Methods. Control blood samples were obtained from 4 healthy male subjects, who then received single doses of 3 g of either mephenesin or its carbamic acid ester, orally with water. Citrated blood samples were obtained from each subject at ½, 1, 2 and 4 hours after administration of the drugs. The blood samples were spun down and plasma levels of the drugs were determined using a modification of the chromotropic acid method of Titus (2). One week later, in a cross-over experiment, the entire procedure was repeated, each subject receiving the alternate drug.

Results. Mephenesin initially attained higher plasma levels than did the carbamic acid ester. Its superiority persisted for only about 15 minutes. As shown in Fig. I, mephenesin carbamate was slower to reach its peak plasma level of approximately 13 μg per ml of plasma, but at 2 hours after administration of the drugs, mephenesin carbamate plasma levels exceeded those of mephenesin by 10 μg per ml, on the average. Four hours after administration of the drug, mephenesin was no longer detectable in the plasma, whereas after the same time interval, the average plasma concentration of mephenesin carbamate was 7 μg per ml. No free mephenesin was detected in the plasma of those subjects receiving mephenesin carbamate.

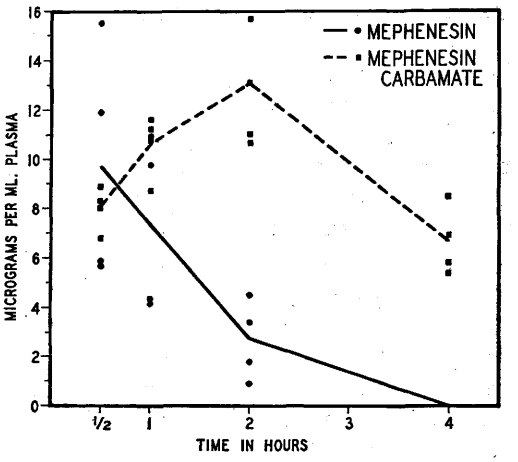

FIG. 1. Plasma levels of mephenesin and its carbamic acid ester during a 4-hr interval.

Summary. Mephenesin and its carbamic acid ester were orally administered to 4 normal males, the plasma levels of the respective drugs were determined at various intervals in each subject for 4 hours following administration of the drugs. Significantly higher and more persistent plasma levels were attained by mephenesin carbamate, as compared to those of mephenesin. No free mephenesin was found in the plasma of those subjects receiving mephenesin carbamate.

1. Dresel, P. E., and Slater, I. H., PROC. SOC. EXP. BIOL. AND MED., 1952, v79, 286.

2. Titus, E., Ulick, S., and Richardson, A. P., *J. Pharm. and Exp. Therap.*, 1948, v93, 129.

Received October 26, 1956. P.S.E.B.M., 1957, v94.