FROG MELANOPHORE DISPERSING ACTION OF MEPROBAMATE

Martha Ann Robinson and George T. Scott

Department of Zoology
Oberlin College, Oberlin, Ohio

Received December 23, 1959

Investigation of a possible antagonism between adrenalin and meprobamate* (1) (Equinil, Miltown) revealed a marked effect of the ataraxic on melanophore expansion in frogs. The action of meprobamate was found to be mediated by the activity of the pituitary gland.

The frog Rana pipiens normally assumes a darker color on a dark background and tends to blanch on a light background. This adjustment is brought about by the degree of melanophore pigment dispersal which is under the control of the intermediate lobe of the pituitary (2). Secretion of the hormone intermedin causes dispersal of melanophore pigment (3). In fact the degree of pigment dispersion is a good index of the internal secretion of intermedin (4).

Twenty-four frogs were placed on a light background under fluorescent illumination so as to bring about maximum pigment concentration (punctate stage) in the melanophores. The frogs weighing 20-30 grams were then injected intra-peritoneally with 1.0 ml. of 0.3% meprobamate (100-150 mg/kg. body weight). Microscopic observation was made on melanophores in the web of

*Meprobamate was obtained through the courtesy of Wyeth Laboratories, Philadelphia, Pa.

the foot. After 1 hour the melanophore pigment began to become dispersed and after 3 hours had reached the state of maximum dispersal (reticulate stage). This effect prevails for approximately 24 hours after which the melanophores return to the concentrated state characteristic of an animal on a light background. After approximately 2 hours a general reduction in muscle tonus was observed and the dilator pupillae muscles of the eyes were noticeably relaxed. At the end of a 25 hour period normal muscle tonus was reestablished. In no case did the tranquilizer prove fatal.

In order to determine whether the pituitary gland was involved in the action of meprobamate in the induction of melanophore pigment dispersal, one dozen frogs were hypophysectomized under ether anesthesia. Blanching of the animals began within one-half hour and continued 4 to 5 hours when the permanent maximum concentration (punctate stage) was reached. After a recovery period of 12 to 24 hours meprobamate was injected in the dosage indicated above. The drug in the absence of the pituitary gland was absolutely refractory.

Meprobamate likewise was refractory on the isolated frog-skin test or when placed in Ringer perfusate.

Frogs with pigment dispersed due to meprobamate were observed to undergo concentration within 10 minutes when given 0.1 ml. of 1:1000 adrenalin. The influence of adrenalin persisted approximately 10 hours after which the cells usually returned to the dispersed state characteristic of meprobamate.

The conclusion is drawn from these experiments and others not reported here that meprobamate causes the release of intermedin from the pituitary gland. The drug could be acting directly on the gland or on brain centers with influences

transmitted to the hypophysis by way of the infundibulum.

Further work is in progress involving other ataraxics and other animals and will be ready for publication in the summer of 1960.

References

1. F. M. Berger, Inter. Rec. of Med. and Gen. Prac. Clinics, 169: No. 4, 184 (1956).
2. L. T. Hogben and F. R. Winton, Proc. Roy. Soc. B: 93, 318 (1922).
3. L. T. Hogben, The Pigmentary Effector System. Oliver and Boyd, London (1924).
4. L. T. Hogben and F. R. Winton, Proc. Roy. Soc. B: 95, 15 (1923).