5865

Effect of Ultraviolet Rays on Pharmacological Potency of Digitalis.

DAVID I. MACHT.

From the Pharmacological Research Laboratory, Hynson, Westcott & Dunning, Inc., Baltimore, Maryland.

Digitalis varies markedly in its pharmacological activity, even the alcoholic extracts deteriorating often within a comparatively short time. In view of the extreme differences of opinion held by pharmacologists and pharmacists in regard to the effect of ultraviolet rays on digitalis, the present investigation was undertaken. A standard tincture was kept in the ice-chest in the dark. Samples of this were irradiated with an Alpine Sun lamp, and with a water-cooled Kromayer lamp with and without various filters, and the pharmacological activity of the tinctures after assay was determined by 4 different methods: (1) the official one-hour frog method,[1] (2) the cat method of Hatcher and Brodie,[2] (3) the phytopharmacological method of Macht and Krantz,[3] and (4) the goldfish method of Pittenger and Vanderkleed.[4] The great majority of animal experiments were performed on cats because, in the author's experience, that is the most reliable method for assaying digitalis. About 100 cat experiments were performed in connection with the present investigation. Each sample or fraction of digitalis tincture was tested on at least 3 cats and in cases where the readings obtained showed a wide divergence, as many as 8 cats were sometimes used to obtain the average minimal lethal dose. The phytopharmacological method was found to be particularly adapted to comparative study of various samples of digitalis simultaneously and under identical conditions of light, temperature, barometric pressure, etc. At least one hundred sets of such experiments were performed and each control, as well as each sample of digitalis tincture, was tested on 8 or 10 healthy seedlings of *Lupinus albus*. The frog and goldfish methods were used only to corroborate the results obtained by the cat and phytopharmacological experiments. Each sample was tested on at least 10 goldfish and 12 frogs.

It was found that irradiation with ultraviolet rays of tinctures

[1] United States Pharmacopoeia. Tenth Revision (Tincture Digitalis, Assay), 1926.

[2] Hatcher and Brodie, *Am. J. Pharmacy*, 1910, **82**, 360.

[3] Macht and Krantz, *J. Pharm. and Exp. Therap.*, 1927, **31**, 11.

[4] Pittenger and Vanderkleed, *J. Am. Phar. Assn.*, 1925, **24**, 427.

exposed to the mercury vapor lamp in the quartz tubes produced deterioration of the tincture within ten minutes. Prolonging the irradiation produced greater deterioration up to a certain point, usually up to one and a half hours of exposure. After this point has been reached further irradiation for a limited period of time produces photochemical changes resulting in a greater toxicity or "potency" of the drug as tested by the methods mentioned above. Still further irradiation, for a period longer than two and a half hours, produces a second and more marked deterioration of the tincture. By the use of various filters it has been found that the longer ultraviolet rays produce little or no change in the tincture while the shorter rays produce even more rapidly the sequence of events noted above. This is particularly true when a gas filter, consisting of a mixture of chlorine and bromine and transmitting waves of 2400 to 2800$\mu\mu$, was used in conjunction with a Kromayer lamp. Specimens of digitalis tincture irradiated through such a filter first show a deterioration in potency but after exposure for over an hour the tincture begins to get more toxic or "potent". It is evident that exposure to ultraviolet rays produces progressive photochemical changes. There is also a possibility that several chemical reactions may be taking place simultaneously, these being produced by rays of different wave length. This is to be determined by study of individual rays with a monochromator.

The effects produced by x-rays and radium were also studied by the author, and it was found that exposure to both x-rays and radium emanations, as well as radium itself, produced marked deterioration of the tincture, as shown by the weaker action of digitalis on animal preparations. The phytopharmacological properties of such a tincture, however, are quite different from those of another exposed to ordinary ultraviolet rays. X-rays and radium render the digitalis tincture very much more toxic for plant tissues, while exposure to the ultraviolet rays of a mercury lamp makes it weaker for the same kind of plants.