157. *The Action of Japan Camphor upon the Heart.*

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Clinical experiences show that Japan camphor dissolved in oil, when injected subcutaneously, produces usually a marked beneficial effect on the circulation in cases of cardiac weakness. This effect is due partly to vaso-constriction by stimulation of the medulla oblongata, as demonstrated in animal experiments (Wiedemann,¹⁾ Alexander-Lewin²⁾ and others), and probably also to the improved heart beats; but as to how the heart is affected by Japan camphor little has hitherto been known definitely, in spite of numerous experiments with mammalian and amphibian hearts (Heubner,³⁾ Baum,⁴⁾ Alexander-Lewin,²⁾ Seligmann,⁵⁾ Joachimoglu,⁶⁾ Fröhlich, Pick,⁷⁾ Nakazawa⁸⁾ and others).

In our experiments, therefore, to elucidate the mode of action of Japan camphor upon the heart, the difference between the effects of the drug administered by various methods were minutely studied and the following results were obtained.

Subcutaneous Injection of Camphor into Rabbits.

First the effects produced by the subcutaneous injection of 0.5 c.c. of a 10 per cent solution of Japan Camphor in oil upon the circulation of urethanized rabbits with exposed heart were observed. It was only after a while that the heart beat began to augment, gradually increasing in its amplitude with the lapse of time, without showing any perceptible change in the general blood pressure.

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- 1) Wiedemann, Arch. f. exp. Path. u. Pharm., **6** (1876), 216.
 - 2) Alexander-Lewin, Arch. f. exp. Path. u. Pharm., **27** (1890), 226
 - 3) Heubner, Arch. f. Heilk., **9** (1870).
 - 4) Baum, Zbl. f. d. med. Wiss., **8** (1870).
 - 5) Seligmann, Arch. f. exp. Path. u. Pharm., **52** (1905), 333.
 - 6) Joachimoglu, Arch. f. exp. Path. u. Pharm., **80** (1917), 259.
 - 7) Fröhlich, u. Pick, Arch. f. exp. Path. u. Pharm., **84** (1918), 250
 - 8) Nakazawa, Tohoku Journ. of exp. Med., **4** (1923), 373.

Intravenous Injection of Camphor into Rabbits.

Moreover, even when Japan camphor, dissolved in glyceric- or glycol-ether, was intravenously injected in small doses (0.2 c.c. of 10 % solution), the augmentation of the heart-beat began only some minutes later and not directly after the injection, just as in the case of the subcutaneous injection, though with larger doses (0.5 c.c. or more) the force of contraction of the heart was depressed directly after the injection. These facts indicate that the stimulant effect of Japan camphor on the heart is characterised by a prolonged latent period which is not found in its depressant effect upon the heart.

Application of Camphor to Isolated Frogs' Hearts.

a) Experiments with excised hearts prepared after Straub's method. Further, in the experiments with isolated hearts prepared and nourished after Straub's method, when Japan camphor was added in a concentration as low as 1 in 5000 to Ringer's solution used as an artificial blood, though directly after the introduction of the drug the heart-beat often became weaker for a moment, after 15–20 minutes, it became stronger than normal and the heart continued to beat very strongly, with a slight diminution of the frequency, as reported already by Joachimoglu.¹⁾ In fact, when this solution containing camphor which had been in contact with the heart for about 15–20 minutes, was applied to another isolated frog's heart, its beat was sometimes augmented directly after the administration. On the contrary, Japan camphor in higher concentrations was constantly observed to cause only depressant effect upon isolated hearts directly after the administration.

b) Perfusion of isolated frogs' hearts. When the isolated frog's heart was perfused through the vena cava from a Mariotte bottle with Ringer's solution containing camphor in various low concentrations as 1 in 10,000–20,000, no stimulant effect developed in any of these concentrations, depressant effect constantly being manifest, unlike in the experiments with the isolated frog's heart prepared after Straub's method. The results of these experiments with isolated frogs' hearts show clearly that camphor does not stimulate the heart at any concentration, unless the drug remains in contact with the tissues for a while.

1) Joachimoglu, Arch. f. exp. Path. u. Pharm., **80** (1917), 259.

Action of Campherol upon the Heart.

Furthermore, campherol, isolated after Schmiedeberg's method¹⁾ from its glycuronic acid combinations in the urine excreted from a dog poisoned by Japan camphor, appeared to increase the force of heart-beat immediately after the intravenous injection into the rabbit, unlike in the case of Japan camphor; and when campherol was injected intravenously into the frog with exposed heart, the amplitude of heart-beats distinctly increased directly after the injection.

These facts suggest that Japan camphor itself does not produce any direct stimulant action upon the heart, though it depresses the heart; and that some of its intermediate products in the body does appear to stimulate the organ.

1) Schmiedeberg u. Hans Meyer, Zeitschr. f. physiol. Chemie, **3** (1879), 422.