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THE PHARMACOLOGY OF GALINSOGA.*[1]

A SERIES OF MICRO-RESPIROMETER STUDIES.

BY MARTIN A. YAVORSKY WITH EDWARD C. REIF.[2]

Preliminary experiments on the pharmacology of Galinsoga (1) indicate the presence of a principle or principles in the plant, which cause a drop in the blood pressure of the dog when certain preparations are injected intravenously

The chemistry of the plant has been studied by Dr. Karl Muller (2). No reference, however, has been made to the presence of a potent or active constituent.

The purpose of this paper is to describe certain experiments that were conducted to increase our knowledge of the pharmacology of Galinsoga and to add more information concerning the oxygen consumption by tissues, especially the influence upon the same by plant drugs.

It is a well-known fact that tissues removed from the body of a recently killed animal will, if suspended in a suitable medium, utilize oxygen for an indefinite period. Oxidations in animal tissues can be studied by means of a microrespirometer, various types of which are described by Warburg and his collaborators (3).

Extensive studies on the influence of certain compounds on the oxygen consumption of many tissues have been made by Voegtlin, Rosenthal and Johnson (4), (5).

The action of Vitamin C on the oxidations of tissue *in vitro* has been reported by Harrison (6).

Oxygen consumption by the tissues used in this series of experiments was

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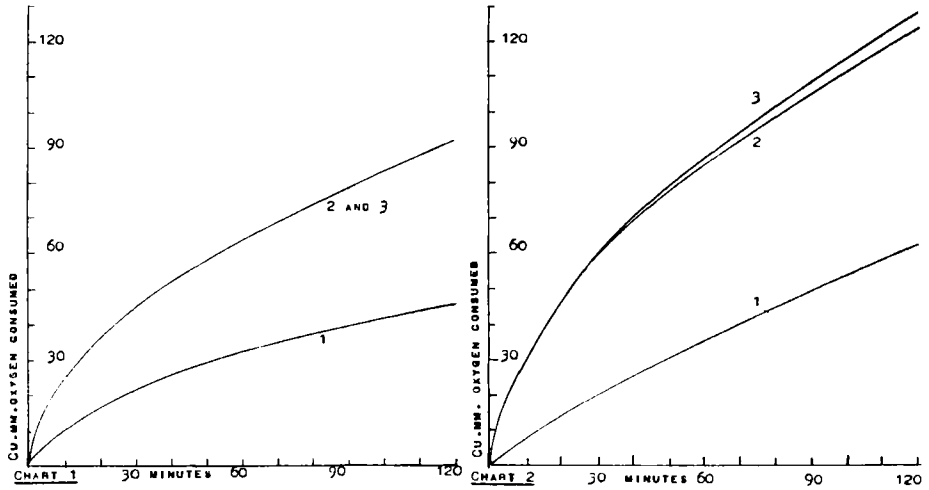
measured in the Warburg vessels with the Haldane Barcroft manometers, using the technique described by Warburg (3).

The heart tissue of the healthy guinea pig was selected for the studies on Galinsoga. The tissue was finely minced according to the method used by Voegtlin and collaborators (4). This fresh tissue was used in 100-mg. quantities, accurately weighed and immediately transferred to the respirometer trough. All results are reported on a basis of 100 mg. of fresh tissue. Air was the source of oxygen and the carbon dioxide was absorbed by a solution of sodium hydroxide contained in a separate compartment in the respirometer trough. With few exceptions the experiments were run for a period of two (2) hours.



Experiment No. 1.—Object: To determine the influence of a 1% Infusion of Galinsoga.

1.—100 mg. of heart tissue in Locke's Solution. 2 and 3.—100 mg. of heart tissue in 1% Infusion of Galinsoga.

Results: The effect of the Infusion of Galinsoga on the same heart tissue is clearly shown. The increase in oxygen consumption caused by similar quantities of the same infusion was 95.5%.

Experiment No. 2.—Object: To determine if a stronger infusion would cause a relatively greater increase in oxygen consumption.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 2% Infusion of Galinsoga. 3.—100 mg. of heart tissue in 2% Infusion of Galinsoga.

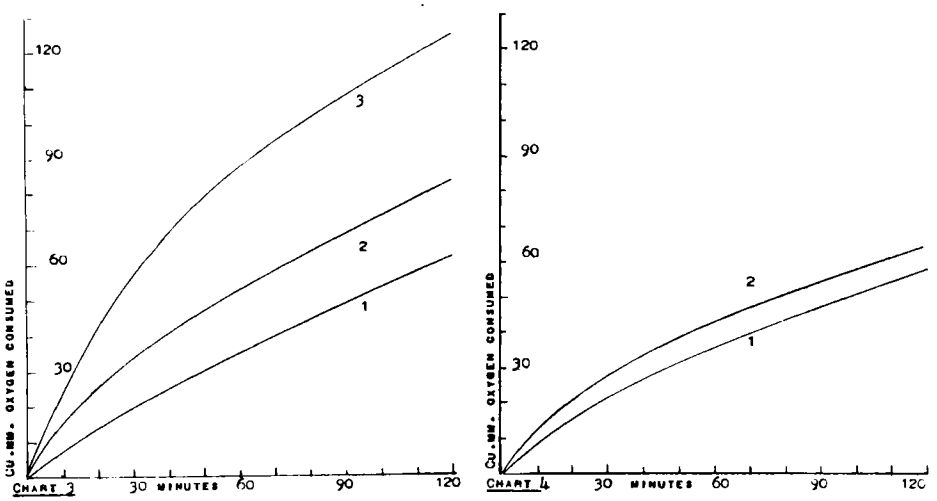
Results: This infusion caused an increase of 106.5 to 108% in the oxygen consumption. It appears as though the double strength infusion contains little more of the active constituents than the 1% infusion.

The material used consisted of the dried leaves, stems not over three (3) mm. in diameter and flowers of *Galinsoga parviflora*. Infusions were made of this material according to the general method by adding boiling water to the material and allowing to stand for one (1) hour before filtering. These infusions were made using 1 and 2 Gm. of the drug for 100 cc. of the finished product, respectively. After filtration these preparations were buffered with the salts used in the preparation of Locke's Solution and in the same concentrations, dextrose being omitted. In all experiments where an infusion was used, 3 cc. was the quantity added to the respirometer trough.

It must be understood that, while in each series of experiments heart tissue from different animals was used and the influence of Galinsoga varied somewhat with the heart tissue, the final figures are comparative in as much as a control tissue is run with each experiment.

CONCLUSIONS.

1. An increase in oxygen consumption by heart tissue is caused by 1% and 2% Infusion of Galinsoga.



Experiment No. 3.– Object: To determine if aging of the infusion would cause a change in the activity of the preparation.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 2% Infusion of Galinsoga 8 days old. 3.—100 mg. of heart tissue in 2% Infusion of Galinsoga freshly prepared.

Results: The infusion 24 hours old caused an increase in oxygen consumption amounting to 108.3%.

The infusion eight (8) days old increased the oxygen consumption to the extent of only 34.1%, showing a considerable loss on aging.

Experiment No. 4.—Object: To determine if the infusion made by extraction with cold water was as active as the one prepared with boiling water.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 1% infusion made by the cold process.

Results: Indicate the possibility that the principle is only slightly soluble in cold water. The infusion was prepared by macerating 1 Gm. of the material in cold water for twelve hours; filtered and buffered with Locke's Solution in the usual manner.

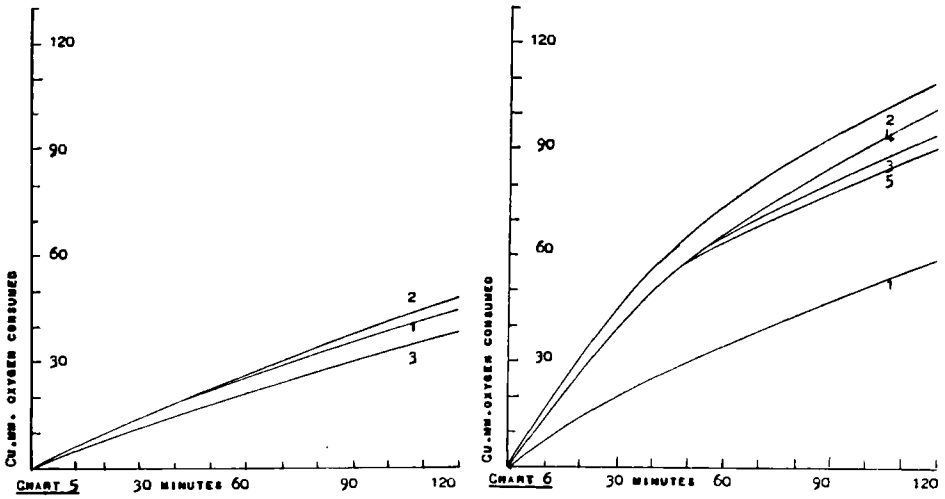
2. Increase in oxygen consumption is not proportional to the concentration of the infusions used.

3. The principle or principles responsible for stimulation are apparently destroyed as the infusion undergoes aging.

4. The principle or principles are apparently not extracted with cold water.

5. Inulin, levulose and dextrose show little influence on oxygen consumption.

6. Saponin causes a slight inhibition.

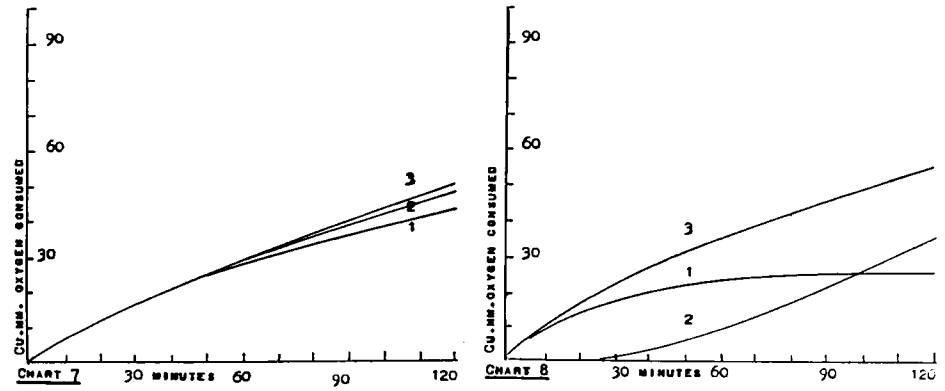


Experiments Nos. 5 and 6.—Object: To determine if the identity of the potent constituent could be determined by the study of certain principles often found in plants. The substances selected for this study were Inulin and Saponin. As indicated by the charts they were studied separately and added to an Infusion of Galinsoga.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in Locke's Solution containing 0.2% Inulin. 3.—100 mg. of heart tissue in Locke's Solution containing 0.2% Saponin. (Chart 5.)

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 1% Infusion of Galinsoga. 3.—100 mg. of heart tissue in 1% Infusion of Galinsoga plus 0.2% Saponin. 4.—100 mg. of heart tissue in 1% Infusion of Galinsoga plus 0.5% Inulin. 5.—100 mg. of heart tissue in 1% Infusion of Galinsoga plus 0.2% Saponin. (Chart 6.)

Results: Note—The infusion used in these experiments was 24 hours old, kept cool. As shown by Charts 5 and 6 Saponin causes a slight inhibition in oxygen consumption which is also evident when it is added to the Infusion of Galinsoga.



Experiment No. 7.—Object: To determine the influence of Levulose and Dextrose.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 0.2% Levulose added to Locke's Solution. 3.—100 mg. of heart tissue in Locke's Solution containing 0.2% Dextrose.

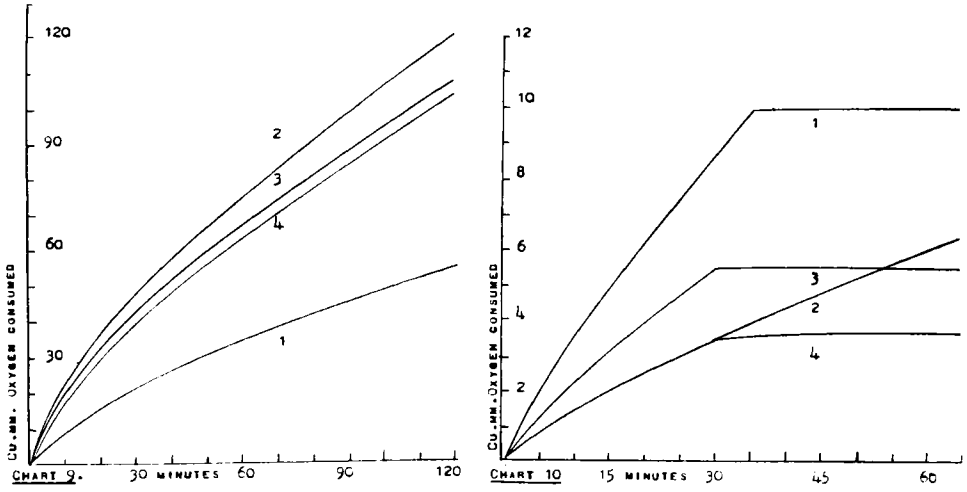
Result: Levulose and Dextrose show little effect on the oxygen consumption of heart tissue.

Experiment No. 8.—Object: To determine the activity of a crystalline mass obtained during the method commonly used for the isolation of a glucoside. A strong infusion was pre-

pared; treated with Litharge; filtered; Hydrogen Sulphide was passed through the filtrate; filtered; concentrated on a water-bath; product was a sticky brown mass containing crystals. 100 mg. of the heart tissue was suspended in Locke's Solution containing 100 mg. of this crystalline mass. A control was run to determine the uptake of Oxygen by 100 mg of the same material. A heart tissue control in Locke's Solution was also run.

Results: 1.—Oxygen uptake by 100 mg. of the mass of crystals. 2.—100 mg. of heart tissue in Locke's Solution containing 100 mg. of the crystalline mass. 3.—100 mg. of heart tissue in Locke's Solution.

Curve 2 shows an inhibition ot oxygen consumption when the crystals are added to the Locke's Solution in which is suspended the heart tissue.



Experiment No. 9.—Object: To study the influence of an Infusion of Digitalis on the oxygen consumption of heart tissue and to compare the activity of the same with the activity of an Infusion of Galinsoga.

1.—100 mg. of heart tissue in Locke's Solution. 2.—100 mg. of heart tissue in 1% Infusion of Galinsoga. 3.—100 mg. of heart tissue in 1% Infusion of Digitalis. 4.—100 mg. of heart tissue in 1% Infusion of Digitalis.

Results: Curves 3 and 4 indicate the action of Infusion of Digitalis in the quantities and concentration used is uniform and that Infusion of Digitalis increases the oxygen consumption of heart tissue. Infusion of Digitalis in the quantities used caused an increase of 76.3 and 83%, respectively. Infusion of Galinsoga in the same concentration caused an increase of 105% in oxygen consumption.

Experiment No. 10.—Object: To determine the oxygen uptake by 1 and 2% Infusions of Galinsoga. No tissues were used in this experiment.

1.—1% Infusion of Galinsoga. 2.—Same. 3.—2% Infusion of Galinsoga. 4.—Same.

Results.—While the infusion in the quantities used in these experiments show little in the way of oxygen uptake: blank should always be run and proper corrections made.

7. Infusion of Digitalis apparently contains a principle which causes an increase in oxygen consumption.

8. This series of experiments suggest the possibility that studies of the influence of drugs on the oxidative processes in animal tissues to be measured by the use of a micro-respirometer might be the basis of the following investigations.

(*a*) The potency of principles in plant and animal drugs.

(*b*) The activity of the various fractions that occur during the investigative stages of drug extraction.

(*c*) The activity of various cardiac drugs on cardiac muscle and other tissues.

(*d*) The development of a method of biological assay for the standardization of the cardiac group of drugs.

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PHYTOCHEMICAL NOTES.*[1]

No. 112. PRELIMINARY CHEMICAL EXAMINATION OF CORYDALIS AUREA.

BY HAROLD EPPSON.

Thirty-five kilograms of air-dried herb collected in full bloom near Laramie, Wyoming, at an altitude of about 7400 ft. were percolated with alcohol in a Lloyd extractor, yielding 8920 Gm. of extractive, calculated on a moisture-free basis.

The alcoholic extract was extracted with petroleum ether, yielding an oily extract that weighed 1382 Gm. This was saponified with alcoholic KOH in the usual manner.

Isolation of Dimyristylcarbinol.—The saponified petroleum-ether extract was heated to remove the alcohol. Upon cooling a solid, waxy, yellow-red material formed on the surface. Additional similar material was obtained from the ether extract of the saponified fat. After repeated recrystallization from alcohol and methyl alcohol a light cream-colored material was obtained which melted at 81–82°. The acetylated product, after two recrystallizations from alcohol, melted at 44–45°. Elementary analyses yielded the following results:

	I.	II.	Computed for $C_{29}H_{58}O_2$.
C	79.4%	79.5%	79.3%
H	13.3%	13.4%	13.3%

Upon saponification the acetate yielded as saponification values, 124, 119 and 120, respectively. The regenerated alcohol, after recrystallization from both methyl and ethyl alcohol, melted at 81–82°. Elementary analyses yielded the following results:

	I.	II.	Computed for $C_{27}H_{56}O$.
C	81.6%	81.8%	81.7%
H	14.2%	14.2%	14.2%

* Scientific Section, A. PH. A., Madison meeting, 1933.

[1] From the laboratory of Edward Kremers.