

oxide, which have a like effect on protoplasm, are isosteres. That this is true is shown in Table 1.

It is thus obvious that in their isosteric properties as in their anesthetic or pathological effects on certain lowly organisms, carbon dioxide and nitrous oxide are nearly identical.

TABLE 1  
THE ISOSTERIC PROPERTIES OF CARBON DIOXIDE AND  
NITROUS OXIDE\*

	CO <sub>2</sub>	N <sub>2</sub> O
Number of exterior electrons	22	22
Molecular weight	44	44.02
Viscosity, at 20°C and 1 atm	148 × 10 <sup>-6</sup>	148 × 10 <sup>-6</sup>
Critical pressure (atm)	77	75
Critical temperature	31.9°	35.4°
Heat conductivity, at 100°C	0.0506	0.0506
Density of liquid, at -20°C	1.031	0.996
Density of liquid, at 10°C	0.858	0.856
Refractive index of liquid, D line, 16°C	1.190	1.193
Dielectric constant of liquid, at 0°C	1.582	1.598
Magnetic susceptibility of gas, at 16°C and 40 atm	0.12 × 10 <sup>-6</sup>	0.12 × 10 <sup>-6</sup>
Solubility in H <sub>2</sub> O, at 0°C	1.780	1.305
Solubility in alcohol, at 15°C	3.13	3.25

\* Certain discrepancies appear to exist between the values in the foregoing table (in part from Langmuir, 3) and other recent work. Where the values given by authors differ, the agreement between the two gases CO<sub>2</sub> and N<sub>2</sub>O is, nevertheless, surprisingly close. Thus, the dielectric constants in Lange's *Handbook of physics and chemistry* (5th ed.) are 1.000985 for CO<sub>2</sub> and 1.00116 for N<sub>2</sub>O, at 0°C and 1 atm. As temperatures and pressures are not always stated, I have kept strictly to the Langmuir values, except for several additions.

Nitrogen and carbon monoxide have no effect on slime mold protoplasm (except for a brief initial injury due to shock, which is not uncommon in treating protoplasm with reagents). These two gases, both the biologically inert nitrogen and the usually active carbon monoxide, have closely similar isosteric qualities. Carbon monoxide poisoning in mammals is due to combination of the gas with hemoglobin. This is a different matter than the effect of the gas on protoplasm which lacks most mammalian characteristics.

That certain properties of protoplasm, not only purely physical qualities such as viscosity and elasticity but complex chemical ones such as respiration, are similar in primitive forms of protoplasm and in higher forms of life, including man, is indicated by the following experiment: A 3- to 5-day chick heart reacts to carbon dioxide in a manner identical to the protoplasm of a slime mold. The chick embryo contains blood not yet distributed in an organized system extending throughout the tissue; yet, though blood is present, the embryo, unlike the adult chick as a whole, reacts as does a primitive form of living matter (5).

The correlation between pathogenicity and isosterism may ultimately prove to hold for only a few isolated

cases. Gases and other reagents may be found which are not isosteres but to which protoplasm shows similar reaction. However, such a correlation will not have been proved false until two isosteres are found which have wholly different effects on living matter.

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## Control of Hemorrhagic Syndrome and Reduction in X-Irradiation Mortality With a Flavanone<sup>1</sup>

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A hemorrhagic diathesis is now believed to be characteristic of the mammal exposed to the ionization of single-dose radiation and, to a lesser degree, to repeated radiation. Following sub- or midlethal doses of total body radiation this bleeding is uncontrollable and is a primary factor in mortality. The disturbance is one of generalized bloody extravasation with oozing into practically every organ and tissue. In the dog, exitus is usually preceded by profound intrapulmonary and/or intraintestinal hemorrhage.

A direct influence of ionizing radiation on vascular integrity has not been proved. Earlier studies have implicated thrombocytopenia as a causal factor in the hemorrhagic picture (5).

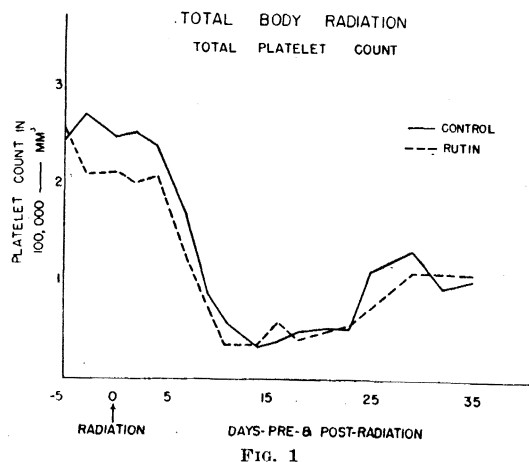
Recent investigations indicate the presence of an increased quantity of heparin or heparin-like material in the blood of dogs following acute whole-body exposure to ionizing radiations. In these animals certain anti-heparin substances, such as toluidine blue and protamine, restored prolonged *in vitro* and *in vivo* coagulation time to normal (2). This technique served to halt the hemorrhagic tendency, although all treated dogs succumbed about 22 days after being exposed to 450 r, while control untreated dogs usually died after 11 days (1).

As the result of studies in this laboratory it was felt that control of vascular integrity might be of benefit to the organism in which hypocoagulability exists. In this condition, prevention of vascular damage might reduce the hemorrhagic extravasation. It would appear that the function of critical organs already suffering from some degree of direct destruction by ionizing irradiation is further impaired by the bloody ooze of capillary destruction. By maintaining the vascular structure, an in-

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creased opportunity for eventual restoration of organ function should be afforded.

Cognizant of the import of the nonspecific toxicity of massive doses of irradiation and of uncombated infection as causal influences in irradiation mortality, both of which are also under study here, an examination of some



protective and regulatory factors in maintaining the vascular integrity has been undertaken. The recent availability of the flavanol glycoside, rutin,<sup>2</sup> with which clinical instances of increased capillary fragility were controlled (3, 4), prompted its trial. In this preliminary report a summary of some of the data obtained with its use is presented. Details will be given in subsequent reports.

Fifty normal adult dogs similar in size were selected and divided into a control group of 25 dogs and a treated group of 25 dogs. The latter received 50 mg of the glycoside 3 times a day orally, commencing one week prior to irradiation and continuing throughout the course of the test. Except for the administration of rutin, the two groups of dogs were treated identically.

A standard single dose of total-body X-irradiation of 350 r<sup>3</sup> (approximately the middlethal dose) was delivered to each dog used in these tests. Following the irradiation, 16 of the 25 (64%) untreated dogs succumbed in 13-30 days after X-irradiation, whereas only 3 of 25 (10%) rutin-treated dogs died 16, 28, and 31 days post-radiation.

Widespread premortem ecchymoses and intrapulmonary and intrainstestinal hemorrhages were seen in all 16 untreated dogs which succumbed. Three of the surviving dogs of this group manifested subcutaneous ecchymoses and intestinal hemorrhages. Although characteristic widespread hemorrhage was seen in 2 of the 3 rutin-treated dogs which failed to survive, the 22 remaining

<sup>2</sup> A crystalline glycoside of quercetin. Furnished by the Eastern Regional Research Laboratory, Philadelphia, through the courtesy of J. F. Couch, and also by the Abbott Laboratories, North Chicago, Illinois.

<sup>3</sup> Radiation was administered from a Picker Industrial X-ray machine of 250 KVP, 15 ma, 37" t.s.d., and 14.22 mm parabolic aluminum and 0.53 copper filters with a half-value layer for copper of 2.15 mm.

exposed dogs were relatively free from petechiae and ecchymoses during the postradiation period of 40-60 days and at autopsy.

Studies of the peripheral blood of the two groups of dogs showed little or no difference in the postradiation depression of the hematological elements, especially the thrombocytes and leucocytes in the treated and control dogs. Illustrating this similarity, Fig. 1 shows the means of the platelets of the two groups of animals.

In the group given the glycoside several dogs were observed to develop a severe thrombocytopenia and leucopenia which persisted for 10-14 days. Recovery eventually ensued. In distinct contrast, recovery in untreated dogs with persistent severe depression of blood elements has rarely been observed in this laboratory.

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## A Rapid Chemical Test for Some Plant Virus Diseases<sup>1</sup>

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In a search for possible chemical reactions that might be of aid in the diagnosis of virus diseases of fruit trees, it was found that an alkaline extract of certain virus-infected peach or sweet cherry leaves produced, under certain conditions, a brilliant red coloration. A procedure was developed whereby the reaction could be used as a quantitative measure for some plant virus diseases. Although several thousand tests have been made during the past few months, this report can be of only a preliminary nature pending a more exhaustive study. Nevertheless, it seems desirable to report the procedure at this time because of its potential usefulness.

Thus far most of the studies have been confined to virus diseases of cherry and peach trees, and the discussion that follows is based on work with these plants. Leaf tissue was used as the source for all analytical material. An ordinary paper punch, with a diameter of approximately 6 mm, was used to obtain disks of leaf tissue as samples of standard size. For routine work, only one disk was taken from each leaf, midway between the base and tip and midway between the midrib and margin of the leaf.

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