SCIENTIFIC SECTION

BIOASSAYS OF RODENTICIDES.*

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The deviations of chemical assay of a product are generally smaller than the deviations of physiological assay. For this reason chemical assays have been developed for many drugs and chemicals, with the tacit assumption that the results of chemical assay indicate the physiological activity. However, some information has been published suggesting that this assumption is not always true (1).

The chemical assay of opium for the morphine content has been studied by many chemists throughout the world and has been the subject of several international conferences. Bioassays have shown that various lots of opium, each containing 10% of morphine, vary in their physiological activity because of the antagonistic and/or potentiative action of the other alkaloids of opium. The determination of the strychnine content of nux vomica preparations is not an indication of physiological potency because of the potentiating action of brucine which is also present. Similarly the determination of quinine may not be a true expression of the clinical value of cinchona bark, because of the effect of the remaining alkaloids.

Chemical assays of chemicals have been believed to be true indexes of physiological activity. Careful investigations have shown that this is an unwarranted assumption. Chemical assays of epinephrine may be misleading since the *lævo* form is very much more active than is the *dextro*. Similar deviations in the activity of optically active products have been encountered. The presence of apparently small traces of impurities which do not affect the chemical assay, may often produce marked discrepancies in physiological action. The chemical assay of sodium chloride, for example, is no indication of its suitability for use in the preparation of perfusion solutions. The chemical assay of arsenious oxide is no indication of its toxicity because the size of particles has a very marked effect upon rate of solution and therefore upon pharmacological and physiological properties (2).

During the course of fifteen years intensive pharmacological, chemical and toxicological studies upon strychnine alkaloid and salts, as related to their use in the control of rodents and predatory animals by this Bureau during the last half century, occasional variations in field results have been very forcibly brought to our attention. In the early days we were inclined to attribute very great deviations to the general variability of the animal population upon which control measures were being exercised. A number of studies have been undertaken with a view to reducing these animal variations by proper attention to varied factors such as diet, time and method of administration. However, these studies finally lead us to the

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belief that there must be variations in the clinical effectiveness of "C.P." strychnine products. Definite chemical standards were developed for purity, size of particle, specific rotation and melting points, with the hope that conformity to such standards would reduce the observable fluctuations in results when these products were used as rodenticides. Unfortunately field as well as laboratory tests have shown that a series of samples of "C.P. Strychnine," which conform *in every particular* to the chemical requirements, exhibit marked variations in physiological activity (Table I). Results of chemical and pharmacological study will be presented in detail in a separate communication.

TABLE I.—CHEMICAL AND BIO-ASSAY OF STRYCHNINE ALKALOIDS.

Manufacturer.	Sample Number.	Alkaloidal Content, %.	$LD_{100\%}$ Rats, Mg./Kg
A	1	99.31	Over 25.0
	2	...	" 25.0
	3	...	20.0
	4	...	20.0
	5	...	17.5
	6	...	17.5
	7	...	15.0
	8	...	15.0
	9	99.70	12.5
	10	...	Below 10.0
B	1	98.86	7.5
	2	98.91	7.5
C	1	...	20.0
	2	98.68	15.0
	3	...	12.5
	4	...	7.5
	5	...	7.5
	6	...	7.5
D	1	...	20.0
	2	98.28	15.0
	3	99.30	15.0
	4	...	15.0
	5	...	12.5
	6	...	10.0
E	1	...	12.5
	2	...	10.0
	3	98.60	7.5
Range:	.	98.28–99.70	7.5—over 25

A number of red squill preparations, in powder or liquid form, have been offered for sale for the control of rats and mice. Some of these powders are made by oven drying, others by sun drying the red squill bulbs (3). Unsatisfactory results obtained in a few rat control campaigns undertaken on a large scale led to the biological assay of squill preparations upon rats. Deviations of one thousand per cent in toxicity have been found. A bioassay has been developed and specifications drawn to prevent repetition of these failures.

The presence of small quantities of free sulphuric acid in a few lots of commercial thallium sulphate caused very poor acceptance by various rodents with very poor field results. After these findings were confirmed on laboratory animals studies were made which led to development of methods of correcting this. A bio-

assay of the commercial material would have shown this poor acceptance and permitted correction before undertaking an intensive and expensive field trial.

Limited experience with zinc phosphide has shown that material of the same chemical purity obtained from two different manufacturers varied greatly in palatability on laboratory as well as field-scale tests. The chemical assays did not reveal any cause for this variation.

In preliminary laboratory scale studies with other rodenticides, similar discrepancies in palatability and toxicity have been observed upon products which are of apparently identical chemical purity.

CONCLUSION.

Bioassays of rodenticides are necessary, since chemical assays often fail to indicate their physiological activities.

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THE TOXICITY OF PROPYLENE GLYCOL.*

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In recent years propylene glycol has assumed a position of somewhat increasing pharmaceutical interest as a vehicle and solvent. Seidenfeld and Hanzlik (1) have reported extensive toxicity studies in which propylene glycol is compared with glycerol and ethylene glycol. Hunt (2) has discussed the use of ethylene and propylene glycols as medicinal solvents and has shown that systemically propylene glycol is much less toxic than ethylene glycol.

We have compared the acute toxicities of propylene glycol and glycerol in rats by intramuscular, subcutaneous and intravenous injection and have obtained results which show satisfactory agreement with those obtained by Seidenfeld and Hanzlik (1). In addition, the acute and chronic toxicities of propylene glycol administered orally in rabbits have been studied.

The propylene glycol used in these studies is the Alpha Propylene Glycol (1, 2 Propane Diol).

Acute Toxicity.—Propylene glycol was injected in undiluted form intramuscularly and subcutaneously in rats. Parallel groups of rats were similarly injected with undiluted glycerol. With the large doses administered to establish the minimum fatal dose, all of the rats showed profound depression, analgesia and coma. With sub-lethal doses, the toxic symptoms persisted for a longer time in the glycerol-injected animals than in those injected with propylene glycol. In the larger doses, glycerol produced greater local tissue damage than was observed with propylene glycol in corresponding percentages of the M. L. D. The results of these experiments given in Table I show that propylene glycol is much less

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