(*b*) Pregnant rats, intraperitoneal, 0.67 mg./Kg./hr.

(*c*) Male rats, intraperitoneal, 1.85 mg./Kg./hr.

(*d*) Male rabbits, repeated intravenous injection, 0.183 mg./Kg./hr.

(*e*) Male rabbits, intravenous infusion, 0.562 mg./Kg./hr.

(*f*) Male monkey, subcutaneous, 0.127 mg./Kg./hr.

(*g*) Male guinea pigs, intraperitoneal, found unsatisfactory for the methods used.

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A Study of a Strychnos Species*†

By F. V. Lofgren‡ and Dale L. Kinsley§

The genus *Strychnos* occupies a rather unique position in the vegetable kingdom because its various species exhibit widely varying physiological actions. While some of the species thus far examined from a chemical and physiological standpoint are exceedingly poisonous, others are entirely harmless, and in numerous cases highly prized as foods. The poisonous action is due mainly to the alkaloids strychnine and brucine. These alkaloids have been found to exist in all the different parts of some species. In other species, however, only certain parts are poisonous, thus indicating that the alkaloids may be localized.

In 1928 a quarantined plant of the species *Strychnos spinosa* was received from the U. S. Bureau of Plant Industry to be planted in the botanical garden at the University of Florida. The growth of this plant was not successful although it was able to exist. Upon inquiry at the Sub-Tropical Experiment Station at Homestead, Florida, it was learned that this species was thriving and producing fruits. Interest was aroused as to the alkaloidal content and toxicity.

After making a careful review of the literature it was found that the only investigations of this species had been on the fruits and even then conflicting results were reported concerning the toxicity and the presence of alkaloids. Also, through the years, the true identity of this plant had become confused.

This investigation was undertaken in the light of these reports to attempt to clear up these contradictions and uncertainties and

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to investigate the entire plant pharmacognostically.

HISTORY

Flacourt (1), in 1661, is the first to give an account of this plant which he called *Caniram vontac*. He states that the plant is also known as *Cydonium bengalense*. This according to an illustration of Plukenett (2) is not *Strychnos spinosa*.

Plukenett (2), in 1670, before the adoption of the binomial system of nomenclature, gives the name *Cucurbitifera arbor spinosa, fructu male aurei facie, aromatica*.

In 1791, Lamarck (3) gave this plant its present name of *Strychnos spinosa*. He calls this species synonymous with Flacourt's *Caniram vontac* and Plukenett's *Cucurbitifera arbor spinosa*. Poiret (1), in 1804, gave a complete description of this plant and called it *Vomique epineuse*. In 1842, Harvey (4) gave it the name *Brehmia spinosa*.

SCIENTIFIC NAMES AND SYNONYMS

The plant has several scientific names. As mentioned, *Strychnos spinosa* and *Brehmia spinosa* are said to be identical. "Index kewensis" (5) gives *Strychnos spinosa*, *Strychnos vuntac* and *Strychnos madagascariensis* as synonymous. The latter is misleading because Poiret (1) describes a strychnos species growing in Madagascar and calls it *Strychnos madagascariensis*. Yet, according to Poiret's description, it is characteristically different from *Strychnos spinosa*. Other names reported are *Vulgairment abre a Savonette* (1), *Strychnos ramis spinosa* (3) and *Vontaca Flacourt* (6).

Synonyms commonly ascribed to *Strychnos spinosa* are Kafir orange and Natal orange. Others are Vuntac (7), Calabash (8), Litonga seed (9), spiny spinosa (10), Vouavountaka (11) and Voavotaka (12). Native African synonyms are Klapper, Zulu um Hlala and Tonga Usuala (13).

REPORTED TOXICITY

The consensus is that the pulp of the fruit is edible, being described by most investigators as delicious. The seeds, on the other hand, have produced several contradictions as to their toxicity, three workers (14, 15, 16) stating that they are toxic and six investigators (5, 8, 17, 18, 19, 20) saying that they are nonpoisonous. Gilg (21) and Tunmann and Rosenthaler (22) seem to correlate these two views as to toxic effects when they state that the fruits are sometimes poisonous, sometimes nonpoisonous. Interesting is Small's (15) statement in which he says, "The seeds of the Kafir orange are so poisonous that great care must be exercised in eating the pulp in which the seeds are imbedded, in order to eliminate all seeds," in contrast to Flükiger's (7) statement, "they are nontoxic—in fact harmless."

The references which give their views negatively all agree that the seeds contain no alkaloids, while those investigators giving positive conclusions do not state definitely the causative substance giving such action. Perhaps the reasons for these two views may be answered by Gilg (21) when he infers that the toxicity is due to a bitter principle and not to an alkaloid.

Another possible answer to these contradictory opinions is the doubt which exists as to the real identity of the species. Those persons who have examined the fruits obtained their specimens from Africa. Gilg raises this doubt when he writes that "...the true *Strychnos spinosa* is indigenous only to Madagascar and that the species of the African mainland which we have designated up to now by that name belongs to a different very well defined characterized species."

There has been no experimental work on the toxicity of the leaves, stems and shell of the fruit (pericarp) reported in the literature.

EXPERIMENTAL

Fruits, stems and leaves of *Strychnos spinosa* were obtained from the Agricultural Experiment Station, Department of Agriculture, University of Florida, Homestead, Florida. A small quantity of fruit was also obtained from De Soto City (Highlands County), Florida. Two shipments of fruit were received from Homestead, one containing immature fruits, the other ripe fruits.

The stems received were divided between the last year's growth which was green in color, and the older stems, which had a whitish gray color.

Preparation of Material.—The seeds were removed from the pulp of the fruit and dried in an oven at a temperature of 37° C., as were the shells of the fruit, leaves and stems.

The hardness of the dried seeds caused extreme difficulty in getting a representative powdered sample. The ground samples that were obtained were the result of numerous grindings and regrindings with power and hand mills.

TABLE I.—RESULTS OF THE DETERMINATION OF ALKALOIDS IN *Strychnos spinosa*

	Method		
Part Used	U. S. P.	Stas–Otto	Continuous Extraction
Seeds of mature fruits	Negative	Negative	Negative
Seeds of immature fruits	Negative	Negative	Negative
Shells (pericarp)	Negative	Negative	Negative
Leaves	Negative	Negative	Negative
Stems (old)	Negative	Negative	Negative
Stems (new)	Negative	Negative	Negative

Examination for Presence of Alkaloids.—Three methods for extracting alkaloids were used, *i. e.*, (*a*) the U. S. P. method for nux vomica, using chloroform and ether as the extractive, (*b*) the Stas–Otto method and (*c*) a continuous extraction (Soxhlet) using alcohol acidulated with tartaric acid. Table I gives the results of the examinations for the presence of alkaloids.

Toxicological Studies.—Mice were put on a diet of the ground seeds. Some were given the unextracted seeds and some were given the marc of extracted seeds. No deaths occured in six days.

In order to assure that a sufficient dose was taken at one time and to determine if other parts of the plant were toxic, capsules were made up of the powdered material of the different parts of the plant. These capsules were then administered to guinea pigs. One-gram doses were given. After four hours the guinea pigs had shown no ill effects or any noticeable change.

An extract was made of the powdered seeds. This extract was concentrated so that 1 Gm. of the dried extract was equal to 10 Gm. of the powdered seeds. One-gram doses of the extract were administered to guinea pigs. No ill effects or change in reaction was observed.

Taxonomic Study.—In order to be sure that our present species growing in southern Florida was the true *Strychnos spinosa*, it was thought that a taxonomic comparison should be made between our sample and the descriptions given by earlier botanists.

Specimens were obtained from Homestead, Florida, and sent to the Division of Plant Exploration and Introduction, Division of Plant Industry, U. S. Department of Agriculture, Washington, D. C., to be examined. They replied that they could not give a critical determination of the plant because there is not a good collection of herbarium specimens of African plants in this country, and that their determination had to be based on literature. They also replied that the specimen sent did not compare with the original *Strychnos spinosa* specimen which was introduced in 1903 (14) and that there probably had been a transposition of labels somewhere through the ensuing years, or that this specimen was from another introduction. However, after studying the specimen, they could see no reason which would lead them to doubt that the plant was the true *Strychnos spinosa*.

The material sent to Washington has been preserved and placed in the Herbarium of the U. S. National Arboretum (Sheet No. 74,479). This will give a means for any future worker to check the identity of the material discussed in this paper and thus precludes the risk of this work becoming valueless if the identification is found to be incorrect.

Histology.—The histology of the plant parts, including cross sections of the seed, shell, leaf and stem, was studied for the purpose of identification. Also the diagnostic elements in the powdered material of each of these plant parts were observed and described. The results of these studies are embodied in a thesis which is on record in the library of the University of Florida.

CONCLUSIONS

From the qualitative chemical examinations for the presence of alkaloids in *Strychnos spinosa* growing in Florida, it has been found that alkaloids are absent in the seeds, shell, stems and leaves. It is possible that an examination of the roots of this species might reveal the presence of alkaloids, although it is highly improbable. It must be remembered also that this plant is a native of Madagascar and tropical Africa and that a change in environmental conditions might not be conducive to the formation of alkaloids in the plant, which have been reported by some authors.

Toxicological examination of the seeds, shell of the fruit, stems (old and new) and leaves on guinea pigs and mice has shown *Strychnos spinosa* to be nontoxic.

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Method of Evaluating Relative Efficacy of Disguising Agents for Distasteful Drugs*

By W. Arthur Purdum†

During the long era of medical ignorance and superstition, it was common belief that medicines should be repulsive in taste or malodorous in order to drive the "evil humours" from the body. The public of today, as a whole, is not so ignorant of medical matters as were its ancestors even as little as a century ago. This has been brought about to a large extent by health education in the public schools, news accounts of the latest discoveries in pharmaceutical chemistry and pharmacodynamics, feature articles by physicians and men in allied professions appearing in newspapers and magazines, and by public lectures and radio addresses. The combined effect has been to make the public conscious of the fact that a dose of medicine need not be bitter, acrid, or nauseating, in order to be efficacious. Consequently, the physician who can prescribe effective therapeutic agents in palatable forms is more certain of success than one who has no regard for palatability. Disagreeable tasting substances are not relished by persons in good health and surely they should not be inflicted on ailing persons (for whom nausea and vomiting are not uncommon), if it is possible to avoid them.

Medicines which are administered in solid form present no serious problem with respect to taste. Provided they are not too bulky, they may easily be given in the form of cachets, capsules, coated pills or coated tablets, in which the taste of the medicament is entirely concealed. On the other hand, infants and most small children, as well as some adults, are unable to swallow such forms of medication, particularly cachets and large capsules. When such is the case, a liquid preparation must be given. Moreover, drugs in the liquid state are more quickly absorbed and thereby exhibit their therapeutic effects more promptly than solid forms of medication. Furthermore, there are a great number of drugs which are more conveniently dispensed in the liquid state. Many of these liquids are quite distasteful, solutions of iodides and bromides being notable examples.

This study was undertaken in an effort to devise a method for appraising the value of pharmaceutical vehicles as disguising agents for distasteful drugs and then to use the method for evaluating some of the more common vehicles as agents to disguise certain unsavory medicaments. A search of available literature revealed that very little has been done in this direction. Many vehicles have been recommended for distasteful drugs, but in the majority of cases there has been no obvious scientific basis for these recommendations.

Since the prime purpose of a vehicle is to lessen or completely overcome the disagreeableness of the medicament, it is rational to assume that the threshold of taste of the medicament varies directly with the disguising power of the vehicle employed,

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