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DIEFFENBACHIA: USES, ABUSES AND TOXIC CONSTITUENTS: A REVIEW

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Summary

Dieffenbachia may well be the most toxic genus in the Araceae. Calcium oxalate crystals, a protein and a nitrogen-free compound have been implicated in the toxicity, but the available evidence is unclear. The plants have also been used as food, medicine, stimulants, and to inflict punishment.

Introduction

Dieffenbachia is a very popular ornamental plant which belongs to the Araceae. One member of the genus, *D. seguine*, was cultivated in England before 1759 (Barnes and Fox, 1955). At present the variegated *D. picta* and its numerous cultivars are most popular. The total number of *Dieffenbachia* plants in American homes is estimated to be in the millions.

The plants can be 60 cm to 3 m tall, and have large spotted and/or variegated (white, yellow, green) leaves that may be 30 - 45 cm long and 15 - 20 cm wide. They grow well indoors and in some areas outdoors. Unfortunately, however, *Dieffenbachia* may well be the most toxic genus in the Araceae, a family known for its poisonous plants (Fochtman *et al.*, 1969; Pamel, 1911). As a result many children (Morton, 1957, 1971), adults (O'Leary and Hyattsville, 1964), and pets are poisoned by *Dieffenbachia* every year (Table 1). Ingestion of even a small portion of stem causes a burning sensation as well as severe irritation of the mouth, throat and vocal cords (Pohl, 1955). In severe cases the swelling of tongue and mouth can cause choking (Hardin and Arena, 1974) and death (Marderosian, 1966). When stems are bitten the resulting stomatitis may be severe enough to bring about aphonia and render victims speechless for several days (Arnold, 1978; Everist, 1967; Mitchell and Roor, 1979; Ricciuti, 1978; West, 1957). In other cases speech can become unintelligible (Lampe and Fagerström, 1968). These symptoms have led to the common name of dumb cane (Sloane, 1707): "If one Cut this cane with a Knife, and put the tip of the Tongue to it, it makes a very painful Sensation, and occasions such a very great irritation on the

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TABLE 1

Poisoning by *Dieffenbachia* (compiled from Food and Drug Administration 1976, 1977, 1980)

Year	Number of persons poisoned by		% of total poisoned by	
	Dieffenbachia[a]	All plants[a]	*Dieffenbachia*[a]	All plants
1977				
Under 5 years of age[a]	689	6226		11.06
1976				
Under 5 years of age[b]	376		44.92	
Over 5 years of age[c]	51		6.09	
Age unknown	58		6.93	
Total	485	837		57.94
1975				
Under 5 years of age[b]	312		4.5	
Over 5 years of age[c]	80		11.5	
Age unknown	3		0.4	
Total	420			

[a]Reporting periods, tabulations, and plants listed may vary. Therefore reports may not be equivalent.
[b]1 - 4.
[c]5 - 76.

salivary Ducts, that they presently swell, so that the person cannot speak, and do nothing for some time but void Spittle in a great degree, or Salivate, which in some time goes off, in this doing in a greater degree, what *European Arum* does in a lesser, and from this its quality, and being jointed this *Arum* is called Dumb-Cane". Other common names are no less sinister: Comida de Culebra (Costa Rica), Hoja de Puerco (Honduras), Giftiger Aron (Germany), and the English Poisonous Arum (Barnes and Fox, 1955).

Even in non-fatal cases, severe corrosive burns occur in the mouth, larynx, esophagus, and stomach. These may be complicated by respiratory failure, bradycardia, muscle twitching, cramps, vomiting, diarrhea, and hypertension (Drach and Maloney, 1963). Death following *Dieffenbachia* poisoning is a very real possibility (Morton, 1971) and on occasion victims can be saved only through the insertion of tubes into the trachea.

Nursery-garden workers who cut *Dieffenbachia* stems into sections for propagation may suffer from inflammation of parts which come in contact with the plant or its juice (Morton, 1971). When *Dieffenbachia* sap enters the eye it causes immediate intense pain, watering and blepharospasms. After about one hour the eyelids become "grossly swollen" (Lim, 1977). Eyes cannot be opened due to gross and diffused oedema. The conjunctiva may become injected and chemosed (Lim, 1977). In one case a large abrasion involving more than half the cornea surface was observed (Lim, 1977). Pupil size was normal and reacted "briskly" to direct light, but visual acuity was reduced to 6/24 (a considerable reduction).

Altogether it seems wise to heed the advice that "Strangers must be warned of these Canes, they looking like those of Sugar". (Sloane, 1707).

Uses

The toxic and irritant qualities of *Dieffenbachia* have been known and utilized for years. In the upper Amazon, Indians combined *D. seguine* with curare to make arrow poisons (Remington and Wood, 1918). Inhabitants of Caribbean Islands chewed *D. seguine* to bring about male sterility that lasts 24 - 48 hours (Barnes and Fox, 1955; Walter and Khanna, 1972). Fresh juice of this species, when administered to male rats, renders them sterile for 40 - 90 days, whereas in females the sterility lasts 30 - 50 days (Madaus and Koch, 1941; Walter and Khanna, 1972).

On a more positive note, preparations containing *Dieffenbachia* were used to treat gout, dropsy, sexual impotence, and frigidity (Fochtman *et al.*, 1969). "Pieces of [its] Stalk [were] cut, and put into Baths and Fomentations for Hydropick Legs and are thought very effectual" (Sloane, 1707). In addition, *D. seguine* was used to open obstructions and against inflammations. Sliced root was employed against gout (Barnes and Fox, 1955).

According to one report (Sloane, 1707) "The Root is of more force than the Fruit or Leaves; besides, the first qualities, being of very small parts, and opening Obstructions, Fomentations are made of them against Inflamations and Obstructions of Hypochindres and Reins; and the Oil is good against those Evils, and supplies that of Capers, and *Lilies.* The Roots sliced and boiled in Wine, made into Baths, and used to the Feet, it is of great use against old and late Gouts" (Sloane, 1707). And, despite the toxicity "it is eat by *Indians* for want of better Meat" (Sloane, 1707).

One idea advanced regarding the possible use of *Dieffenbachia* is that if the discharge brought about by its juice "...hath the same Quality as that occasioned by Mercury, and if the narcotic Quality could be corrected, it might, perhaps, be of great use in Physic..." (Hughes, 1750). Nothing seems to have come of this suggestion, but a Physician who accompanied the Duke of Albemarle, formerly Jamaica, says that the juice of Dumb-Cane, mixed with a certain portion of fresh fat, is the sovereign remedy in dropsies, externally used, by rubbing the part affected with this ointment (Hughes, 1750).

Industrial uses of *Dieffenbachia* include the granulation of sugar (Barnes and Fox, 1955).

Abuses

In Germany during World War II, it was "...discovered that the juice of... *Caladium seguinum* [*Dieffenbachia seguine*], swallowed or injected, produces... after a certain time, particularly in male animals, but also in females, a lasting sterility" (International Military Tribunal, Nuernberg, 1946). Actual "Sterilization experiments... to ascertain the efficacy of a drug known as *Caladium seguinum* (Schweigrohr) [*D. seguine*] were suggested to Himmler by... Pokorny in 1941... who reported that Dr. Madaus [Madaus and Koch, 1941] had found... that *Caladium seguinum* produced sterility in animals... As a result of Pokorny's suggestion experiments were conducted upon concentration camp prisoners... [and] all efforts were made to cultivate the plant in large quantities" (Trials of War Criminals, 1949a). However, there were questions whether plants cultivated in Europe would produce "... the same effective substances in sufficient quantities..." (Trials of War Criminals, 1949b). Himmler himself was interested in the possibility of using *Dieffenbachia* and suggested that Dr. Madaus should be offered "...possibilities of doing research in cooperation with the Reich Physician SS, on criminals..." (Trials of War Criminals, 1949b). As it turned out the experiments were carried out on concentration camp inmates. Fortunately the "...experiments... reached a dead end because the *Caladium seguinum* [*Dieffenbachia seguine*] grows only in North (*sic*) America and during the war could not be imported in adequate quantities. Dr. Koch's attempts to grow this plant from seed... have been successful... but the process is very slow and the yield is not sufficient..." (Trials of War Criminals, 1949b). And, as with so much of Nazi Concentration Camp science, the work seems to have been bad. According to testimony at the war trials "...the findings of Madaus and Koch... are certainly valid, but they do not prove anything with regard to... *Caladium seguinum* [*Dieffenbachia seguine*]; they are rather... part of the general poisonous effect..."

No less cruel and equally reprehensible was the use of *Dieffenbachia* to punish Jamaican slaves; their mouths were rubbed with cut stalks (Fochtman *et al.*, 1969). In an ironic twist, a criminal rubbed *Dieffenbachia* in the mouth of a witness who could not testify as a result, and this led to acquittal for the accused (Barnes and Fox, 1955).

Toxic constituents

The toxic effects of *Dieffenbachia* have long been attributed to the presence of calcium oxalate crystals (Dore, 1964; Pohl, 1955), perhaps because they are so common and numerous (Hilgers, 1867 - 1868). In other words, this explanation appears to have been intuitive and not based on experimental evidence. More careful investigations suggested that calcium oxalate is probably not the major reason for the toxicity and pointed to a "proteinaceous" agent (Pohl, 1964). Subsequent investigations have implicated the calcium oxalate crystals (perhaps merely as piercing agents), a proteolytic enzyme (named dumbcain), a cyanogenic glycoside, a substance which causes contraction of smooth muscles (Fochtman *et al.*, 1969; Ladeira *et al.*, 1975; Walter, 1967; for reviews, see: Arnold, 1978; Brodersen *et al.*, 1979; Everist, 1962; Mitchell and Roor, 1979; Ricciuti, 1978; Tamplon, 1977), asparagine (Arena, 1974), and protoaenomoine which causes swelling of the pharynx and larynx (Morton, 1971). However, the exact cause for *Dieffenbachia* toxicity remains unknown and even pharmacological studies (Kubala and Anton, 1977) have not provided clarification.

Calcium oxalate

Raphides (two types) and raphide idioblasts have been reported in *Dieffenbachia maculata* cv Rudolph Roehrs (Sakai and Nagao, 1980). Large raphides, 120 μm in width with wide grooves, were observed in spindle-shaped, obtuse-end idioblasts (165 μm long by 40 μm in diameter). Smaller raphides, 25 μm by 0.4 μm, with grooves and barbs were noted in idioblast cells which resemble those on the adjacent parenchyma (Sakai and Nagao, 1980). The crystals resemble those in taro (*Colocasia esculenta*), *Alocasia*, and *Xanthosoma* (Black, 1918; Sakai and Hanson, 1974; Sakai *et al.*, 1972, Sunell and Healey, 1979). When fresh tissue is sectioned the needles are extruded in rapid succession in a manner which could be similar to what may happen during a bite (Dore, 1964). The lance-like structure of the raphides suggests that they may (1) facilitate entrance of the irritant, and (2) prevent surrounding tissue from sealing the cut (Sakai and Nagao, 1980).

Despite the absence of direct evidence (Sakai and Nagao, 1980), calcium oxalate crystals have been implicated in the toxicity of *Dieffenbachia* (Drach and Maloney, 1963), possibly because of similar suggestions for taro (Arnold, 1944; Black, 1918) and one theory is that the raphides activate kinin-liberating mechanisms (Walter and Khanna, 1972). However, subsequent work suggests that the raphides are not the cause of the toxicity or at least are not the primary reason for it (Pohl, 1964) as is the case in taro and *Xanthosoma* (Moy *et al.*, 1979; Osisiogu *et al.*, 1974). Another argument against the theory that the calcium oxalate raphides are the cause of poisoning is their presence in other plants, some of which cause no irritation even on being eaten raw (Asenjo *et al.*, 1944; Horner and Franceschi, 1978; Horner *et al.*, 1978). Still, protein-free (and therefore presumably nontoxic) extracts of *Dieffenbachia* do exhibit"... only the mechanical effects due to the crystals..." in test animals (Occhioni and Rizzini, 1958; Rizzini and Occhioni, 1957).

Of particular importance for horticulturists are reports that some cultivars are less toxic than others (Barnes and Fox, 1955; Mitchell and Roor, 1979), and that significant differences in calcium oxalate content were noted among seedlings of a *D. picta* cv Exotica hybrid (Zettler and Rhodes, 1975). The range among the seedlings was from 31.6 to 66.0 mg calcium oxalate per g dry weight whereas the parent plant contained 55.2 mg/g. Marked visual phenotypic differences were also noted among the progeny but a relationship between foliar variegation and oxalate levels was not evident. These findings are a clear indication that it would be possible to select (by tissue culture and from seedling populations) clones of *Dieffenbachia* which have a low calcium oxalate (and raphide) content and are both attractive and horticulturally acceptable. To the extent that calcium oxalate raphides are part of the toxicity mechanism, such clones can also be expected to be less (or non-) harmful to children, adults and pets.

Protein

A proteolytic enzyme called "dumbcain" (Walter, 1967; Walter and Khanna, 1972) has been isolated from *Dieffenbachia.* This enzyme was assumed "...to explain most of the poisonous properties attributed..." to those plants (Walter and Khanna, 1972). Proteins were also isolated by other workers who have shown that trypsin digestion reduces or eliminates the toxic effects of *Dieffenbachia* extracts (Brodersen *et al.*, 1979; Fochtman *et al.*, 1969; Pohl, 1964; Occhioni and Rizzini, 1958; Rizzini and Occhioni, 1957). On the other hand, analyses of the active fraction of stem juice has shown that it contains no nitrogen, and incubation with trypsin or chymotrypsin did not hinder the usual effects (Ladeira *et al.*, 1975; Pohl, 1955). Thus the role of protein and/or proteinaceous substance(s) in *Dieffenbachia* toxicity is not clear and remains subject to speculation.

Histamine

Release of histamine has been implied (Pohl, 1955) or implicated in *Dieffenbachia* toxicity (Fochtman *et al.*, 1969; Occhioni and Rizzini, 1958; Rizzini and Occhioni, 1957). However, other workers (Ladeira *et al.*, 1975) have suggested that the active principle is not similar to histamine.

Kininin

Release of kinins as a result of injury by oxalate crystals or protease activity has been suggested for *Dieffenbachia* on the basis of work with venoms and other plants (Walter and Khanna, 1972).

Other compounds

In taro (*Colocasia esculenta*) at least part of the acridity has been attributed to an ethanol- and boiling-water-labile factor (Moy *et al.*, 1979). It is possible, therefore, that similar factor(s) may be present in *Dieffenbachia.* Sapotoxins which have been detected in both taro (Barosah, 1944) and *Xanthosoma atrovirens* (Clark and Waters, 1934) are probably also present in *D. picta* and *D. seguine* (Barnes, 1953).

Unidentified glycosides have also been implicated in *Dieffenbachia* toxicity (Drach and Maloney, 1963). One possibility is a cyanogenic glycoside which yields HCN on hydrolysis (Walter, 1967). Other possibilities are compounds related to a glucoside of 3,4-dihydrobenzaldehyde, the irritating substance in *Pinella ternata*, Araceae (Suzuki, 1969), or 3,4-diglycosilicbenzaldehyde, an irritant in taro, *Colocasia esculenta* var. *antiquorum*, Araceae (Suzuki *et al.*, 1975).

Speculation

Three facts stand out in the available information about *Dieffenbachia* toxicity. First, calcium oxalate raphides do not play a major role in the toxic effects of *Dieffenbachia.* In some taro (*Colocasia esculenta*, Araceae) cultivars, there is even an inverse relation between toxicity and calcium oxalate content (L. A. Sunell, University of California, Irvine, personal communication). If crystal-induced lacerations were required for entry by the toxic principle, toxicity would decrease with a drop in raphide and/or druse content. Second, only the precipitate of the stem juice obtained following "...centrifugation at 3 °C at 10 000 rpm for 1 h..." contained the toxic principle which had no nitrogen in its molecule and apparently no protein (Ladeira *et al.*, 1975). Third, treatments with proteolytic enzymes do not always eliminate toxicity. A speculation consistent with these facts and a theory regarding the acridity of taro (J. C. Caygill, Tropical Products Institute, London, personal communication) is that raphides pierce the tissues and facilitate the entry of at least an enzyme and a substrate and possibly also mucilages. The latter may provide a matrix in which the enzymes change the substrate rendering it toxic. Consequently, it is possible that if *Dieffenbachia* extracts are subjected to proteolysis or protein inactivation before the substrate has been modified by the enzyme, toxicity may be reduced or lost. On the other hand, if proteolysis or inactivation are delayed, toxicity would be retained. These speculations could explain the apparently contradictory reports in the literature.

Assuming that this speculation is correct and even if the toxic principle(s) in *Dieffenbachia* remain(s) unidentified, it would be possible to select cultivars which are free of toxicity or relatively harmless. If the toxic action requires the participation of more than a single agent, selection of plants which lack or are deficient in one of the components would result in non-toxic cultivars. Earlier work with *Dieffenbachia* (Poole *et al.*, 1976; Zettler and Rhodes, 1975), taro (Strauss *et al.*, 1980), and *Caladium* (Kamemoto and Sheffer, 1978) has demonstrated that variability does exist in previously neglected (from the selection and breeding standpoint) genera and can be obtained easily. Methods for the induction of flowering (Alamu and McDavid, 1978), tissue culture (Arditti and Strauss, 1979), and seed germination (Jackson *et al.*, 1977; Strauss *et al.*, 1979) are available and could be applied to *Dieffenbachia* for the purpose of producing non-toxic or low-toxicity cultivars.

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