TOXIC PLANTS

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Preface

The dependency of the human race on plants as renewable sources of many foodstuffs, drugs, textiles, fuel, and building materials is generally acknowledged. However, the harmful effects produced by certain plant constituents, which result in an increasing incidence of poisoning cases in the United States each year, are not so widely appreciated. This book is not intended to be a comprehensive treatise on all substances from plants that are lethal or otherwise injurious to humans or livestock. Instead, owing to tremendous recent advances in the understanding of the chemical nature of their toxic principles, it reviews selected toxic plants which have been hitherto inadequately documented in previous texts.

The eight chapters of this book were originally presented as a symposium at the 18th Annual Meeting of the Society for Economic Botany, held at Coral Gables, Florida, in 1977. All the contributors are active researchers in the subject areas they describe, and several of the chapters have been updated since the symposium. Four main aspects of the study of toxic plants are discussed in the book. These are the problems affecting the generation of accurate scientific and clinical data on poisonous plants, recent studies on some plants with lethal and severe toxic effects, an objective review of harmful domestic plants, and accounts of dermatitis-producing plants which cause humans a great deal of suffering.

It is hoped that the book will be of interest to both the specialist and nonspecialist reader. It should be of use to agronomists, botanists, chemists, horticulturalists, pharmacognosists, and health professionals, including physicians, pharmacists, and veterinarians, as well as the staffs of poison control centers. Equally, enthusiasts in gardening, floriculture, and those with a concern for threats to human health in the environment should find this book informative.

In the first paper, John M. Kingsbury, a widely acknowledged writer on North American poisonous plants, provides a stimulating and provocative look at the uneven quality of the sources of information in this area. He also probes the possible consequences of increased legislation on the sale of domestic ornamental plants.

George Hatfield discusses poisonous mushrooms in the first of three papers on drastic poisons from plants. He reviews some recent advances on the structure, toxicity, mechanism of action, and methods of treatment of mushroom toxins. Richard F. Keeler provides an overview of the economic consequences when livestock accidentally graze on forage containing poisonous plants. He cites examples of toxins occurring in plants of the lily and nightshade families, including those which produce deformities in livestock offspring. Since extracts of tobacco leaves and blighted potato seedlings have shown teratogenic effects in laboratory animals, they are possible human health hazards.

Certain seed proteins are the most toxic plant constituents known. For example, the rosary pea is a colorful tropical seed used to make commercially available necklaces in the United States; it contains abrin, a protein similar to cholera, tetanus, and diphtheria bacterial toxins. Alexander McPherson describes methods to isolate and characterize complex proteinaceous substances from pokeweed and other plants.

Ara Der Marderosian and Frank Roia Jr. have attempted to eliminate some of the misapprehensions concerning the safety of household plants in a chapter which combines their laboratory screening results with an extensive literature review. An important section of their chapter is a discussion of clinical practices used in the management of poisoning cases involving plants.

The final three papers focus on plants which are toxic externally to humans. A. Douglas Kinghorn discusses the irritant compounds to the eyes and skin found in the spurge family, which occur in species found in the home, garden, and commerce. Some of these are particularly significant because they have been shown to promote skin cancer in mice. Harold Baer has been involved in the most extensive study to date on plants such as poison ivy and poison oak, which cause much human suffering in the United States. He reviews the chemical nature of the active principles and immunological studies done on them, including those with human volunteers. Neil Towers describes agents from the composite family that generate allergic contact dermatitis. One plant in this family, *Parthenium hysterophorus*, is curious in that it has caused severe dermatitis in India, though not in other countries where it grows.

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The authors of each chapter are to be thanked for the time and effort they have spent in preparing manuscripts. Special thanks are also due to Dr. Julia Morton, the local organizer of the meeting, for providing cordial Floridian hospitality, and to my colleagues at the Department of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Drs. Norman Farnsworth, Harry Fong, and Edward Mika, for their interest and helpful suggestions throughout all stages of this project.

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Contents

1 The Problem of Poisonous Plants

John M. Kingsbury

The major human problems associated with poisonous plants derive from the basic problem of a confused, seriously inadequate, and often misunderstood body of literature on the subject.

Plants produce and present toxicity in a multitude of complex ways (Kingsbury 1964; Clarke and Clark 1967; Lampe and Fagerström 1968; Morton 1971; Hardin and Arena 1974). Although vertebrates have evolved an array of mechanical and biochemical defenses against these toxins, few systems of the vertebrate body are immune to damage by some toxic compound from some plant source (Kingsbury 1975). Toxicity, by and large, involves an interrelationship among dose, absorption, detoxification, and excretion. At present, the "layman" might believe that toxicity involves the plant alone.

The word *problem* is anthropocentric, implying a human point of view. From that vantage point the problem of poisonous plants is not their direct toxicity to man alone but also the inconvenience and economic loss associated with the poisoning of domestic animals and the cost of preventing or reducing such happenings. Quality and accessibility of information is central to effective management of all these problems. This chapter examines five specific topics related to such information.

Plants with Known Toxic Constituents Are Not Always Poisonous

Primary compounds can be defined as those required for a plant's basic metabolism. Secondary compounds, loosely, are all others. In the past twenty years, knowledge of the identity, complexity, and quantity of secondary compounds in plants has increased geometrically. Patterns are beginning to emerge from the masses of data that phytochemists have produced. One of these relates to toxicity.

In living organisms probably no metabolic cycle is entirely complete or completely balanced. Secondary compounds perhaps first appeared in evolution as end products in incomplete cycles. Many of these compounds would be toxic to the organisms producing them if allowed to accumulate or become concentrated in living tissues. When plants made the landward migration hundreds of millions of years ago, they lost the ability to dissipate water soluble and lipid soluble wastes directly into the ambient environment. Land plants evolved self-protective ways of handling potentially toxic secondary compounds by removing them physically into metabolically inactive locations (e.g., bark) or by converting them into nontoxic compounds via specific chemical reactions. At the same time, plants found that secondary compounds gave them an opportunity for effective defense against attack by herbivorous insects. Coevolution of complex patterns of insect attack and plant defense involving secondary compounds leads to the conclusion that, whatever the reason for their initial appearance on the evolutionary scene, toxic secondary compounds are now fundamental to the success of plants in defending themselves, and that their defense by this means is mainly against the pervasive pressures of herbivorous insects. That many of these secondary compounds are also toxic to herbivorous vertebrates seems almost accidental as far as the selective value to plants is concerned (Kingsbury, 1978).

J. A. Duke (personal communication) has recently summarized a vast amount of information about plants and toxic secondary compounds in two tables. The first lists chemicals known to occur in plants that are also given in the 1975 *Registry of Toxic Effects of Chemical Substances*. Duke's second table lists the plants containing these compounds. These lists name about 750 toxic compounds in more than 1,000 species of plants.

One might infer from these lists that all the plants named are potentially toxic. In order for a plant to be functionally poisonous, however, it must not only contain a toxic secondary compound but also possess effective means of presenting that compound to an animal in sufficient concentration, and the secondary compound must be capable of overcoming whatever physiological or biochemical defenses the animal may possess against it. Thus, the presence of a known poisonous principle, even in toxicologically significant amounts, in a plant does not automatically mean that either man or a given species of animal will ever be effectively poisoned by that plant. Plants should not be listed as poisonous unless they have been reported to have poisoned a person or animal, or can reasonably be shown to satisfy the other requirements just discussed.

The Uneven Quality of Existing Information

In this context reliable information about actual poisonings becomes especially important. We look to the scientific literature for accurately defined cases of poisoning or, better yet, experimental confirmation of poisonings. The quality of the scientific literature as a whole comes immediately into question. It is spotty. Some sources are modern and the work excellent. Others are ancient, and that fact is often obscured by the tendency of authors to retain what appears to be useful information even when they are not immediately able to identify its origin. For example, the source of information about the toxicity of *Daphne mezereum* as it appears in a contemporary compendium of poisonous plants can be traced back (Kingsbury, 1961), reference by reference, to experiments with dogs conducted by M. J. B. Orfila before 1800. Even though his work was experimental (not always the case in those days), Orfila added little to the literature that had not already been set forth by Dioscorides nearly two millennia earlier. This is not an isolated example. A significant amount of information in contemporary compendia is derived innocently from ancient sources or observations. Persons using such compendia have an obligation to recognize and evaluate for themselves the quality of the individual pieces of information collected therein.

Access to Information Requires Preliminary Accurate Identification

An important contemporary source of information about plant poisoning in man is in the records of poison control centers as collected and analyzed by the National Clearinghouse for Poison Control Centers. Also, these inform us about the use of information by those dealing with human ingestion of toxins. Since the advent of the "childproof" safety cap on bottles of prescribed medicines and the consequent rapid decline in the incidence of poisoning by aspirin, poisonous plants have moved into first place as a reported category in the annual Clearinghouse reports (HEW 1976).

Since toxic plants do not bear labels, ingestion of plants represents a serious problem for poison control centers. Access to whatever scientific information may exist about a given plant, then, must first involve accurate determination of the botanical identity of the ingested material by someone at the poison control center. Rarely do such personnel have the necessary technical background to accomplish this. Reliance on a common name reported by a parent when a child has ingested a plant (the usual case) can result in treatment errors. A survey of plant ingestions reported by poison control centers brings this and collateral problems into sharp relief (Kingsbury 1969). Without an accurate plant name, access to the literature is defeated before it has begun, and tallies of ingestions by poison control centers are no better than the identifications that accompany them.

Physicians react to inadequate information by playing it safe. Few ingestions of plants result in hospitalizations, and fewer yet in mortalities. Yet many result needlessly in induced vomition, gastric lavage, a sense of frustration on the part of the physician, and a state of panic on the part of the parent. Much of this national agony could be prevented if the information base were reliable and capable of being accurately employed by personnel at poison control centers and by pediatricians in private practice.

Should Poisonous Ornamental Plants Bear Labels?

Reliable access to existing information could be obtained if plants bore accurate labels like cans of drain cleaners. Federal agencies have recently pursued that objective. They propose that the most dangerous plants in interstate commerce be labeled as hazardous. Plant nurserymen and commercial horticultural associations have resisted vigorously. While the federal agencies believe that some plants are fundamentally dangerous, horticulturalists argue that they are not dangerous as people use them. Both sides turn to a patently imperfect scientific literature to defend their positions. Neither side gives attention to the current overreaction of poison control centers. The resolution of this adversary position will come eventually, no doubt, from the courts.

Whatever the resolution, it is impossible to restrict or even to label effectively all species of plants containing potentially troublesome levels of toxic secondary compounds. As pointed out earlier, such a list might include over 1,000 species right now, with more added frequently. However, many food plants contain toxic secondary compounds that for one reason or another do not actually cause trouble in normal human ingestions. A line will have to be drawn somewhere.

It can be argued that labeling potentially dangerous plants takes American humanity farther down the road toward dependence on government for protection from cradle to grave. The greater such dependence, the more dangerous the omissions. Common sense and individual intelligent appraisal tend to fall by the wayside. Is furthering this trend wise in relation to such a pervasive element of the human environment as plants? A single, simple rule could obviate the necessity for warning labels on plant materials, a rule such as "Don't eat anything not commonly recognized as wholesome." Those who would experiment with wild plants as food should accept the burden of identifying materials accurately and learning whether they might be poisonous or not before they use them, or else accepting the consequences. Society at large should not be penalized for the stupidity of a very few.

If governmental agencies require labeling of some very dangerous ornamental plants (which may be a good idea as an educational aid), how are they to approach the problem of the other occasionally dangerous plants that are not labeled? In labeling some, does not the government lead the public to assume that the absence of such a label implies that the plant is never dangerous to the public under any circumstances? In any event, given the present state of information, determining which of our plants are truly the most dangerous is an exercise in uncertainty.

The Difficulty of Improving the Present Body of Information

Toxicity is rarely an all-or-none phenomenon. Species of plants vary in their content of toxic compounds owing to unpredictable extrinsic and genetic factors (Kingsbury 1960). Vertebrate species and individual animals vary in susceptibility. To describe adequately the toxicity of a given species of plant to man and the larger vertebrates is thus difficult without experiments involving a variety of plant materials fed to many individuals. Larger domestic vertebrates are expensive, and the facilities needed to experiment humanely and productively with such animals are neither easily nor cheaply obtained. Whereas the toxicity of insecticides and food additives can be explored with thousands of laboratory animals, establishing the LD_{50} of "nightshade" to "cattle" is a practical impossibility. Furthermore, to describe the functional toxicity of a particular plant adequately requires the professional capacities of a range of specialists, from botanists to pathologists or animal husbandmen to clinical toxicologists. Institutions at which appropriate teams of investigators can be brought together and provided with the necessary facilities are few. Thus, the experimental generation of useful new information about poisonous plants as they relate to man and his domestic vertebrates is an unusually difficult practical problem.

REFERENCES

Clarke, E. G. C. and M. L. Clark. 1967. *Garner's Veterinary Toxicology*, 3d ed. Baltimore: Williams and Wilkins.

Hardin, J. W., and J. M. Arena. 1974. *Human Poisoning from Cultivated Plants*, 2d ed. Durham, N.C.: Duke University Press.

HEW. 1976. "Tabulations of 1974 Case Reports." In *National Clearinghouse for Poison Control Centers Bulletin*. Bethesda, Md.: U.S. Department of Health, Education and Welfare.

Kingsbury, J. M. 1960. "Poisonous Plants of Particular Interest to Animal Nutritionists." *Proc. Cornell Univ. Nutr. Conf. Feed Manuf.* 1960:14–23.

—— 1961. "Knowledge of Poisonous Plants in the United States—Brief History and Conclusions." *Econ. Bot.* 15:119–30.

—— 1964. *Poisonous Plants of the United States and Canada*. Englewood Cliffs, N.J.: Prentice-Hall.

—— 1969. "Phytotoxicology. I. Major Problems Associated with Poisonous Plants." *Clin. Pharmacol. Ther.* 10:163–69.

—— 1975. "Phytotoxicology." In L. J. Casarett and J. Doull, eds., *Toxicology: The Basic Science of Poisons*, pp. 591–603. New York: Macmillan.

—— 1978. "Ecology of Poisoning." In R. F. Keeler, K. R. Van Kampen, and L. F. James, eds., *Effects of Poisonous Plants on Livestock*. New York: Academic Press.

Lampe, K. F. and R. Fagerström. 1968. *Plant Toxicity and Dermatitis*. Baltimore: Williams and Watkins.

Morton, J. F. 1971. *Plants Poisonous to People in Florida and Other Warm Areas*. Miami: Hurricane House.

2 Toxic Mushrooms

George M. Hatfield

No other group of plants has a more infamous reputation for being toxic than the mushrooms, which are fleshy, spore-bearing structures of certain ascomycetes and basidiomycetes. Some mushrooms, such as those containing the deadly amatoxins, certainly deserve this reputation, but the vast majority of the several thousand species of fungi in this group have not been reported to be toxic. Of course, not all species have been tested for toxicity in laboratory animals or through human ingestion. But from the data available only about 100 species are known to produce toxic effects when ingested, and of these fewer than 10 can rightfully be considered deadly.

Although no complete data are available regarding the occurrence of mushroom intoxication in the United States, the incidence does appear to be rather low. For 1975 the National Clearinghouse for Poison Control Centers reported over 170,000 poisoning cases due to all causes (Food and Drug Administration 1977). These cases were reported to the Clearinghouse by participating poison control centers and do not represent the total number occurring in the United States, since many poisonings are treated by private physicians and by hospitals not associated with a poison control center. Of the total, only 1,508 (0.9 percent) were due to mushroom ingestion. Only 128 cases developed symptoms, and of these, 71 required hospitalization. No deaths were reported for 1975, but on the average two or three fatal intoxications are reported each year in the United States (Buck 1964; Benedict 1972). Over 70 percent of the cases reported to the Center for 1975 were in children under the age of 5. The accidental ingestion of mushrooms by this age group tends to inflate the statistics, since most of these cases do not actually represent intoxications. Only 4 of the 1095 cases for the under-5 age group required hospitalization.

In the United States some of the most reliable statistics dealing with mushroom poisoning are for Colorado, where the Rocky Mountain Poison Center has acted as a clearinghouse for nearly all poisonings in that state.

Colorado has averaged about 20 cases per year, of which approximately one-third required hospitalization (Mitchel 1976). The incidence of mushroom poisoning can be expected to increase in the future, since the collection of wild mushrooms for food is becoming increasingly popular.

Until recently, one of the most widely used methods of categorizing toxic mushrooms was that utilized by Tyler (1963) in his comprehensive review of the subject in 1963. All poisonous species were grouped into four pharmacologic categories: protoplasmic poisons, neurotoxins, gastrointestinal irritants, and those producing disulfiram-like effects. Since Tyler's review, tremendous progress has been made toward establishing the chemical nature of the constituents of mushrooms that are responsible for their toxic effects, and a chemical classification is now possible, as shown in table 2.1. The

Table 2.1 Constituents of Toxic Mushrooms

Toxic Constituent	Mushroom
Amatoxins	*Amanita*, *Galerina*, *Conocybe*, and *Lepiota* species
Ibotenic acid, muscimol	*Amanita muscaria*, *A. pantherina*, and *A. cothurnata*
Psilocybin, psilocin	*Psilocybe*, *Panaeolus*, *Conocybe*, and *Gymnopilus* species
Muscarine	*Inocybe*, *Clitocybe*, and *Amanita* species
Coprine	*Coprinus atramentarius*
Gyromitrin	*Gyromitra esculenta*
Unknown	*Chlorophyllum*, *Cortinarius*, *Entoloma*, *Hypholoma*, and *Tricholoma* species

toxic components of a few species remain unidentified; they make up the last group in the table. With the exception of the *Cortinarius* species and *Hypholoma fasciculare* (Huds. ex Fr.) Kummer, the mushrooms listed in this group produce primarily gastrointestinal effects such as nausea, vomiting, and/or diarrhea. Little or nothing is known about the nature of the toxic constituents of these mushrooms, primarily because no suitable animal model exists to study this type of toxicity. Reviews by Tyler (1963) and Benedict (1972) can be consulted for information regarding the effects of these mushrooms.

Table 2.1 serves as an outline of the review to follow. Only species for which the active constituent(s) has been identified will be covered. Fortunately, this includes the majority of the mushrooms that have been reported to cause human intoxications. The review covers information available up to September 1977.