

SECOND EDITION

Toxic Plants of North America



George E. Burrows & Ronald J. Tyrl

 WILEY-BLACKWELL

TOXIC PLANTS OF NORTH AMERICA

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Second Edition

GEORGE E. BURROWS
AND RONALD J. TYRL

 **WILEY-BLACKWELL**

A John Wiley & Sons, Inc., Publication

This edition first published 2013 © 2013 by John Wiley & Sons, Inc.
First edition published 2001 © Iowa State University Press

Wiley-Blackwell is an imprint of John Wiley & Sons, formed by the merger of Wiley's global Scientific, Technical and Medical business with Blackwell Publishing.

Editorial offices: 2121 State Avenue, Ames, Iowa 50014-8300, USA
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
9600 Garsington Road, Oxford, OX4 2DQ, UK

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Library of Congress Cataloging-in-Publication Data

Burrows, George E. (George Edward), 1935–
Toxic plants of North America / George E. Burrows, Ronald J. Tyrl. – 2nd ed.
p. cm.
Includes bibliographical references and index.
ISBN 978-0-8138-2034-7 (hardback : alk. paper) 1. Poisonous plants–North America. I. Tyrl, Ronald J. II. Title.
QK100.N6B87 2013
581.6'59097–dc23

2012015386

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Set in 9.5/12 pt Sabon by Toppan Best-set Premedia Limited

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Contents

1	Introduction	3	46	Liliaceae	751
2	Adoxaceae	11	47	Linaceae	808
3	Agavaceae	15	48	Malvaceae	812
4	Aloaceae	24	49	Meliaceae	825
5	Amaranthaceae	28	50	Nitrariaceae	830
6	Anacardiaceae	35	51	Oleaceae	836
7	Annonaceae	50	52	Oxalidaceae	840
8	Apiaceae	53	53	Papaveraceae	844
9	Apocynaceae	81	54	Phyllanthaceae	860
10	Aquifoliaceae	127	55	Phytolaccaceae	864
11	Araceae	131	56	Pinaceae	870
12	Araliaceae	145	57	Plantaginaceae	878
13	Asteraceae	150	58	Poaceae	888
14	Berberidaceae	257	59	Polygonaceae	998
15	Boraginaceae	266	60	Primulaceae	1010
16	Brassicaceae	282	61	Pteridaceae	1017
17	Calycanthaceae	308	62	Ranunculaceae	1022
18	Campanulaceae	311	63	Rhamnaceae	1055
19	Cannabaceae	315	64	Rosaceae	1064
20	Caprifoliaceae	319	65	Rubiaceae	1095
21	Caryophyllaceae	323	66	Rutaceae	1100
22	Celastraceae	333	67	Sapindaceae	1110
23	Chenopodiaceae	338	68	Scrophulariaceae	1125
24	Convolvulaceae	365	69	Solanaceae	1130
25	Coriariaceae	376	70	Taxaceae	1177
26	Crassulaceae	380	71	Thymelaeaceae	1186
27	Cucurbitaceae	387	72	Urticaceae	1192
28	Cupressaceae	395	73	Verbenaceae	1198
29	Cycadaceae	402	74	Viscaceae	1209
30	Dennstaedtiaceae	410	75	Zamiaceae	1215
31	Ebenaceae	423	76	Zygophyllaceae	1221
32	Equisetaceae	430	77	Families with Species of Questionable Toxicity or Significance	1234
33	Ericaceae	434	78	Identification of Toxic Plants	1280
34	Euphorbiaceae	450			
35	Fabaceae	491			
36	Fagaceae	675			
37	Fumariaceae	690			
38	Gelsemiaceae	700			
39	Ginkgoaceae	705			
40	Hypericaceae	710			
41	Iridaceae	717			
42	Juglandaceae	722			
43	Juncaginaceae	727			
44	Lamiaceae	731			
45	Lauraceae	743			
				Appendix A. Plant Taxa Listed by Their Principal Adverse Effects and Main Organs Affected	1285
				Appendix B. Plants of Concern for Dogs, Cats, and Other Pets	1288
				Glossary	1289
				Index	1308

TOXIC PLANTS OF NORTH AMERICA

SECOND EDITION

Chapter One

Introduction

We humans have an intimate relationship with the plants that surround us. We take them for granted as we use them for food, clothes, and shelter. We use them medicinally; indeed, more than one-third of our modern pharmacopoeia has its origins in plant products. We please our senses, decorate our living spaces, and express our feelings for one another with them. Plants are an essential part of many of our religious and social rites. Paradoxically, some of the plants we prize for these varied uses may also pose a threat to us or to our domesticated animals. Toxic plants are very much a part of our environment. Until their effects, ranging from mild irritation or discomfort to rapid death, become apparent, they are often ignored or simply overlooked. Because of their ubiquity, there is a need for a comprehensive treatment of toxic plants likely to be encountered in North America, north of the Tropic of Cancer, growing wild or cultivated. The first edition of this book was written in response to that need.

OBJECTIVE AND SCOPE OF THE FIRST EDITION

The objective of this undertaking was to write a comprehensive treatment of toxic plants that brought together the currently available information on (1) their morphology and distribution, (2) the disease problem or problems associated with them, (3) their toxicants and mechanisms of action, (4) the clinical signs and pathologic changes associated with their toxicity, and (5) the principal aspects of treatment. The perspective of the first edition was primarily veterinary science.

Compilation of the information presented in the first edition began in the 1980s as a series of articles for the *Oklahoma Veterinarian* and an agricultural extension publication, *Poisonous Plants of Oklahoma and the Southern Plains*. Well received, these publications dealt primarily with native plants and their toxicity for livestock. Initially, the present book was anticipated to do the same for the

United States. Gradually, however, its scope and depth of coverage evolved—larger area, more plant families, and greater detail than first envisioned. These changes came about in part because of the increasing popularity of ornamental plants for both house and garden. There has been a corresponding increase in awareness of toxicity problems associated with some of them.

OBJECTIVE AND SCOPE OF THE SECOND EDITION

In the 11 years since publication of the first edition, a wealth of toxicologic information has been compiled—unknown toxicants identified, mechanisms of intoxication elucidated, and additional reports of problems published. In addition, there has been a corresponding increase in taxonomic knowledge with significant changes in the classification of plant families and genera and associated changes in nomenclature. Because of this almost exponential increase in our knowledge of toxic plants, work on a second edition was initiated in 2009.

In addition to compiling and presenting the literature of the last decade, we have also slightly altered the perspective of this edition. We have included information about four additional aspects of plant toxicology; they are summarized in the following subsections.

Intoxications in Humans—The first edition focused primarily on veterinary science because of our professional backgrounds and the need for such a book in the discipline. In this second edition we have attempted to place increased emphasis on human intoxications because the information acquired about both humans and other animals is often interrelated and supportive. For the most part, plant intoxications in humans, while not uncommon, do not pose the lethal risk (with the exception of *Datura* and *Cicuta*) seen with livestock and other animals, but they nevertheless may be numerous and sometimes serious as revealed in annual

reports from Poison Control Centers (Litovitz et al. 2001; Bronstein et al. 2007). It may be expected that in most instances similar disease problems will occur in both humans and animals with a few exceptions.

For some taxa, we have included information about problems associated with herbal products as examples of their intoxication potential but a comprehensive discussion of adverse reactions to these products is beyond the scope of this book. In addition we have included some information about potential bioterrorism threats because of the serious problem presented by the extreme toxicity of some plants such as those possessing type 2 ribosome-inactivating proteins—most notably *Ricinus communis* and species of *Adenia* (Pelosi et al. 2005; Stirpe and Battelli 2006; Monti et al. 2007; Stirpe et al. 2007; Ng et al. 2010). Considerable information on the mechanisms of intoxication is emerging because of the interest in effects of plant toxicants as models for various human disease problems such as Huntington's disease, ALS, Alzheimer's disease, and Parkinson's disease (Tukov et al. 2004; Bradley and Nash 2009; Cox 2009; Pablo et al. 2009; Tunes et al. 2010).

Treatments for humans are given in very general terms because physicians and medical institutions may have different treatment protocols. General references for specific procedures include Greene and coworkers (2008) and Lee (2008) for gastrointestinal decontamination and use of ipecac, and Froberg and coworkers (2007) for plant poisonings specifically in humans.

Intoxications in Wildlife and Captive Animals—In this edition, a special effort has also been made to document the effects of poisonous plants on wildlife, both free roaming and captive. References for specific information about particular genera and species are included throughout the book. General references to be consulted include Fowler (1981, 1999) and Van Saun (2006).

The reader should keep in mind that in general most wild herbivores respond similarly to plant toxicants as do our domesticated animals, with a few exceptions such as those compounds produced by *Quercus* (oak), *Centaurea* (star thistle), *Acroptilon* (knapweed), and *Pinus* (pine). Some plants are invariably toxic to most wild animal species, for example, cardiotoxic and cyanogenic plants as well as species of *Lantana* (lantana) and *Nicotiana* (tobacco) (Basson 1987). Other plants, however, may affect wild animal species quite differently as illustrated by responses to tannins, especially those produced by species of *Quercus* (the oaks).

With respect to toxic plants, species of wildlife are not necessarily immune to their effects, but avoid problems associated with their toxic secondary compounds by ignoring some plants, eating only small

amounts, and/or exhibiting natural gastrointestinal/hepatic degradation/detoxication of these noxious compounds (Fowler 1981; Laycock 1978). Unfortunately, captive or domesticated wild species may have access to toxic plants with which they have not coevolved or which they have not encountered previously. In some instances, boredom of captive animals may lead to ingestion of toxic plants in their enclosures. Such problems have been reported in a variety of herbivores ranging from elephants to tortoises.

There are also other reasons for ingestion of toxic plants by wild animal species, including poorly nourished, hungry animals which may be nonselective in their eating habits or to seasonal variations in palatability or acceptability of otherwise noxious plants in their environment. Thus management plays a vital role in animal intoxications (Pfister et al. 2002). Additional reviews regarding the role of secondary plant compounds on nutritional toxicology of birds and herbivores are available (Cipollini and Levey 1997; Dearing et al. 2005; Torregrossa and Dearing 2009).

Role of Plant Secondary Compounds in Plant Intoxications—An additional problem given increased attention in this second edition is the role of secondary plant compounds as toxicants in honey and or their affect on bees. A number of general reviews on these subjects are available: Patwardhan and White (1973), White (1981), Detzel and Wink (1993), Faliu (1994), Adler (2000), and Kempf and coworkers (2010). Some attention has been given to the problem of milk and meat tainting but without exhaustive discussion. Reviews are available but this is a subject not given great coverage with respect to noxious noncultivated plant species (Richter 1964; Armitt 1968a,b). Methyl sulfide is clearly a factor in tainting and probably many plants that have sulfur-containing constituents are likely culprits (Patton et al. 1956; Gordon and Morgan 1972).

Role of Fungal Endophytes in Plant Intoxications—Great interest is now directed toward the role of fungal infections of plants as contributors to the synthesis of toxicants in host plants. The fungi involved in these infections may be endophytes or epiphytes. In some instances the toxins may be produced exclusively by the fungus, whereas in others the toxicants may be produced by both the plant and the fungus (Wink 2008). Examples of these situations are the presence of an endophytic fungus in *Hypericum perforatum*, which produces hypericin similar to the host plant, and an endophyte in *Podophyllum peltatum*, which produces podophyllotoxin again similar to the host plant. In contrast, an endophytic strain of the

fungus *Fusarium oxysporum* also produces podophylotoxin but in *Juniperus recurva*, a totally unrelated species (Eyberger et al. 2006; Kour et al. 2008; Kusari et al. 2008).

Because these fungi, especially the endophytes, are in many instances clearly beneficial to the host plant, there is good reason to expect that more of these symbiotic relationships will be identified in the future (Rodriguez et al. 2009; Rudgers et al. 2009). Likewise, there are probably many fungi–plant–toxicant relationships yet to be demonstrated. Although at present most involve the Poaceae (grasses), other plant families are increasingly being associated with toxin-producing fungi. In some instances, these endophytes are exploited to promote grass protection and production and as potential sources of beneficial natural products (Easton 2007; Kuldau and Bacon 2008; Belesky and Bacon 2009; Aly et al. 2010). Numerous endophytes have been isolated from some plant species, for example, 183 different fungi from *Catharanthus roseus* in India (Kharwar et al. 2008). For additional discussion of this relationship see the treatment in Poaceae (Chapter 58).

COMPILATION OF INFORMATION

The information presented in this treatise on toxic plants is based upon reports extracted from the toxicological, veterinary, human, agronomy, chemical, biochemical, and physiological literature and from our personal observations. References are numerous. In the past, descriptions of intoxication problems were sometimes poorly documented, and a large amount of unsubstantiated anecdotal information was incorporated in earlier publications in such a form that it eventually became accepted as fact. Experimental studies have since confirmed or rejected much of this information. An effort has been made to document each point selectively to avoid being excessive, but it is anticipated that the incorporation of many references provides starting points for readers to delve more deeply into any topic.

The information presented is intended to be of interest to veterinarians, agricultural extension agents, horticulturists, animal scientists, botanists, personnel at poison control centers, physicians, pharmacists, agronomists, range scientists, toxicologists, wildlife biologists, ecologists, farmers, ranchers, students, and the general public. The book may be used as a textbook for graduate-level courses or as a general reference. The incorporation of tables associating the clinical signs and pathology of intoxications with specific plant genera and species permits its use in applied situations.

As always with a book such as this one, the caveat that it is not complete must be stated. As investigations of plants progress, there will be the discovery of new toxic

species and the reassessment of the intoxication problems caused by known ones.

ORGANIZATION AND FORMAT

In this edition, the plant family continues to serve as the organizational unit for the toxicological data compiled. Each chapter is devoted to the toxic taxa of one family. To facilitate access and review, the information is organized into seven sections: “Taxonomy and Morphology,” “Distribution and Habitat,” “Disease Problems,” “Disease Genesis,” “Clinical Signs,” “Pathology,” and “Treatment.” Embedded in these sections are boxes with salient points of information, photographs, line drawings, distribution maps, and illustrations of chemical structures and toxicologic pathways.

With respect to the taxonomy of the toxic plants being described in this work, concepts of families, genera, and species are based on current classifications. When significant changes in classification and/or nomenclature have occurred, older names are given as synonyms in parentheses below the currently accepted names. Readers, especially those who used the first edition, may discover that “new” scientific names are used for several familiar species, genera, and families in this edition. The majority of these changes reflect the accumulation of additional taxonomic data by taxonomists and thus revised interpretations of character importance and phylogenetic relationships. In some instances, these name changes are mandated by the *International Code of Botanical Nomenclature* (McNeill et al. 2006), and a few changes were made to make the names in this book consistent with those appearing in the *Flora of North America North of Mexico* (Flora of North America Editorial Committee 1993+) and the PLANTS Database (USDA, NRCS 2012). These two works are becoming the standard references for taxonomy and nomenclature in North America. Abbreviated explanations of the reasons for these changes are presented in the “Taxonomy and Morphology” sections.

The common names cited are those based on our experience and their citation in floristic works and standardized lists such as the PLANTS Database and the Weed Science Society of America’s (2010) *Composite List of Weeds*. Author citations (name or abbreviation of name of person or persons who published the taxon’s name) are taken from Brummitt and Powell’s (1992) *Authors of Plant Names*.

The descriptions given for each family describe the range of morphological variation for only its North American species. When a range of values is given for the numbers of genera and species in a family, differences in opinion among taxonomists are indicated. Unless otherwise attributed, information about the taxonomy and

biology of each family was compiled primarily from Cronquist (1981), Kubitzki (1990+), Flora of North America Editorial Committee (1993+), Heywood and coworkers (2007), Mabberley (2008), Judd and coworkers (2008), and Bremer and coworkers (2009).

To avoid repetition and conserve space, morphological features of the genus that are the same as those given for the family are generally not repeated; rather, those features that are characteristic of or unique to the taxon are used. If a genus is monotypic or represented in North America by a single species, its morphological description is based on the species' appearance. The morphological descriptions of the genera and species are composites of those appearing in state and regional floras encompassing the distributional ranges of the taxa. Principal sources are listed in the references.

Should exact identification of a plant suspected to be toxic be needed, it is anticipated that the reader will use floras specific for his or her locale to determine or confirm identification. Perhaps, as some taxonomists predict, plant identification may become almost as simple as reading a universal barcode in the grocery store as technology evolves and we make progress in determining DNA sequences in plants (Bruni et al. 2010).

Line drawings, distribution maps, and chemical structures are based in part upon those appearing in the references cited below. Original line drawings are primarily the work of Bellamy Parks Jansen and Sheryl Holesko. Other drawings were obtained from the government publications listed in the references and were prepared by Regina Hughes and numerous other artists. Drawings have also been used with permission from *Flora of Missouri*, by J.A. Steyermark (1975). The maps and chemical structures are composites of the information available in both the references cited and the general literature.

In addition to the 76 chapters presenting the toxicologic problems associated with each plant family, a chapter is included describing 44 families with species of questionable toxicity or significance, a glossary, diagnostic synopses of the most important families, tables cross-referencing disease syndromes and clinical signs, and a comprehensive index.

HISTORICAL PERSPECTIVE

We would be remiss in this endeavor if we did not recognize those who have gone before us and whose work has served as a foundation for this book. There are many individuals who should be recognized, and it is with some trepidation that we list them, because many who will not be included have also made substantial contributions to our understanding of toxic plants. Certainly L.H. Pammel and J.M. Kingsbury have been instrumental in providing a foundation and model upon which to write a book on

toxic plants. Their efforts contributed greatly to our understanding of the effects of plants on livestock. Their work is especially significant because of the meager information they had in many instances upon which to base their conclusions about toxicity. Also of great importance were the efforts of early investigators and observers such as V.K. Chesnut and C.D. Marsh. The remarkable, astute observations of Marsh continue to be the basis for our understanding of the effects of many toxic plants as will be illustrated by the number of literature citations to his work throughout this book.

When reviewing those who have had great impact on our present state of knowledge of plant-caused problems, we cannot fail to recognize the personnel of the U.S. Department of Agriculture's Agricultural Research Service (USDA, ARS) Poisonous Plants Research Laboratory at Logan, Utah. These ARS scientists, both past and present, have had an immense impact on our understanding and ability to deal with the ever-present problems of plant intoxications in livestock. Many individuals have been involved in the lab's work, and the references throughout the book attest to their extensive efforts. With the passage of time, we are becoming increasingly indebted to workers in Australia, Brazil, India, South Africa, and other countries for their vital contributions to our understanding of the effects of toxic plants.

We are also indebted to the many personnel at state experiment stations who have contributed to the body of knowledge on the toxicity of plants, especially those in the western states. Worthy of particular note is the exceptional work conducted in Texas. Names that appear repeatedly in the toxicological literature and our references include I.B. Boughton, W.T. Hardy, and F.P. Mathews. Dr. Mathews was instrumental in opening the Locoweed Research Laboratory in Alpine, Texas, in 1930 and was responsible for many years for investigating the plant-related livestock problems in West Texas and surrounding areas.

DEDICATION

Following in the footsteps of Dr. Mathews was Dr. James W. Dollahite, a young veterinarian from west central Texas and an individual who had a profound influence on the discipline of toxicology. His life and contributions were eloquently summarized by E.M. Bailey (1998) and are excerpted here with permission. Born in 1911, Dr. Dollahite was raised near Johnson City, Texas. He received his DVM. in 1933 from the Agricultural and Mechanical College of Texas. He worked for the U.S. government and practiced until World War II, when he served as an army veterinarian, later retiring as a lieutenant colonel in the Air Force Reserve. Following the war, he went back into veterinary practice in Marfa, Texas, but developed an

interest in toxicology. Dr. Dollahite combined his practice and a part-time position with the Texas Agricultural Experiment Station in Alpine to further his interests in plant toxicology. He also worked for a time at the USDA research facility in Beltsville, Maryland. In 1956 he started a full-time experiment station position and was responsible for moving the Alpine Research Station, begun by Dr. Mathews, to Marfa, where it became the Marfa Toxic Plant Research Station. During this time he drove many miles over West Texas and southern New Mexico, investigating toxic plant problems and conducting his toxic plant research. He closed the Marfa station in 1958 and moved his research endeavors to College Station, where he was a member of the veterinary research section of the College of Veterinary Medicine. Because there was no formal toxicology program at the time, he received his MS in veterinary physiology in 1961. He became an associate professor of pathology in 1964 and a professor in 1965. In 1968 he transferred to the Department of Veterinary Physiology and Pharmacology, where he was instrumental in establishing a doctoral program in toxicology in 1969.

Dr. Dollahite was a charter and founding diplomate of the American Board of Veterinary Toxicology (1966–1967). He continued his research until his retirement from Texas A&M in 1975. He continued to work on toxic plants at the USDA, ARS Veterinary Toxicology and Entomology Research Laboratory until his full retirement in 1980. He died in 1984.

Dr. Dollahite played a very important role in the development of veterinary toxicology in Texas, especially toxic plant research, and in the development of veterinary toxicology as a specialty within the American Veterinary Medical Association. However, these facts, dates, and accomplishments are but one aspect of the real man. One of us (GEB) had the opportunity to spend a week in 1979 traveling with him in a review of the toxic plants of Texas. It was this time that provided a glimpse of the person of whom others had long been aware. The respect paid to him by those with whom he had been associated in the field was impressive. He was truly a remarkable individual, not only for his powers of observation of clinical signs in diseased animals and contributions to our knowledge of toxic plants but also for his personal attributes. The legacy of his life was much more than professional success. He was an exemplary individual in many ways. We are sure that he would like to be remembered as a man of great faith in God, who made every effort to deal with others with respect, kindness, and gentleness. He had great integrity and was a gentleman in every sense of the word. He is truly a worthy role model.

It is with this in mind that we dedicate this book to Dr. J.W. Dollahite.

ACKNOWLEDGMENTS

The writing of both editions of this book have been conducted as traditional academic endeavors, that is, reviews of the literature and an attempt to synthesize in a readable fashion the wealth of information accumulated. Initially the effort involved just the two of us, but as the writing of each edition progressed, more and more individuals volunteered encouragement, support, time, and expertise. It is therefore necessary and certainly most appropriate to recognize formally their contributions at this point.

Thanks are expressed to Gayman Helman for critically reviewing all aspects of each chapter in the first edition and making valued suggestions as to what additional information might be included, especially as pertains to the pathologic descriptions. Special thanks to Drs. Zane Davis, Ben Green, James Pfister, and Kevin Welch of the Poisonous Plant Research Laboratory (USDA, ARS) at Logan, Utah for constructive comments on portions of chapters in their specific areas of interest in this second edition.

To our wives, Connie Burrows and Lynda Tyrl, special thanks are given. Their tireless assistance with the odious and tedious editorial tasks, especially in the later stages of writing of the first edition, was invaluable. Their words of encouragement represented vital contributions. Their patience and understanding during the writing of this second edition is especially appreciated.

Likewise, completion of work on the first edition was facilitated by the technical assistance of Sheryl Holesko and Paula Shryock, staff members of the Department of Anatomy, Pathology, and Pharmacology and the Department of Botany at Oklahoma State University. Thanks to each are extended.

Completion of both editions could not have been accomplished without the support provided by the science and loan librarians in the Edmon Low Library of Oklahoma State University. We gratefully acknowledge the efforts of Vicki Phillips, Jimmy Johnson, Helen Clements, Steve Locy, Kevin Drees, Kiem Ta, Lynne Simpson, Heather Moberly, Suzanne Reinman, and John Phillips who helped us locate the many obscure or ambiguous technical papers or decipher the ambiguous literature citations.

Special thanks are due the individuals and organizations, in particular the Smithsonian Institution, Oklahoma State University, the Oregon State University Jed Colquhoun Photo Collection, the Samuel Roberts Noble Foundation, and the Texas AgriLife Extension Service, who kindly granted us permission to use their striking photographs; their names appear below their photos. Photos not attributed are our own. We definitely must acknowledge the many publications of the various agencies of the United States Department of Agriculture that

were the source of the many line drawings that appear throughout the book.

The financial assistance provided by the College of Veterinary Medicine via its long-term support of George E. Burrows's research on toxic plants is gratefully acknowledged. Long-term access to the library and herbarium collection at the Royal Botanic Gardens, Kew, UK for Ronald J. Tyrl is also treasured.

Finally, the individuals responsible for the transition of our manuscripts to the two editions of this book certainly must be recognized. With respect to the first edition, our profound thanks to Gretchen Van Houten and Judi Brown of Iowa State University Press for their patience and ability to understand our vision of the book's final form. A special thanks to Rosemary Wetherold, our editor, whose careful work ensured accuracy, consistency, and clarity throughout the book. We also gratefully acknowledge the efforts of Nanette Cardon, our indexer, who organized in a most logical fashion the plethora of names and terms that appear in this book. A final thanks to Fred Thompson, our production editor, whose editorial and organizational skills facilitated the entire production process.

Completion of this second edition was facilitated by the staff at Wiley-Blackwell and Toppan Best-Set Premedia Ltd. Our thanks to our editorial program coordinator Susan Engelken for her words of understanding and encouragement during the last stages of our writing and compiling illustrations; to our production editor Erin Magnani for translating our vision of the appearance of this second edition into reality; to project manager Stephanie Sakson for her assistance in the production phase; and to our commissioning editor Erica Judisch who thoughtfully considered our requests for deviations from the traditional Wiley-Blackwell style. Special thanks is due to our copy editor Maria Teresa M. Salazar who so carefully reviewed our manuscript and corrected our many inconsistencies, mistakes, and ambiguities.

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Chapter Two

Adoxaceae E.Mey.

Elderberry or Moschatel Family *Sambucus*

Widespread in temperate regions of the northern hemisphere, the Adoxaceae, commonly known as the elderberry or moschatel family, comprises 4 or 5 genera and 225–245 species, of which 3 genera and approximately 29 species are present in North America (Judd et al. 2008; Mabberley 2008; USDA, NRCS 2012). The two largest genera *Viburnum* (about 220 species) and *Sambucus* (about 20 species) were originally classified in the Caprifoliaceae. Morphological and molecular phylogenetic studies, however, indicated a closer phylogenetic relationship to the genera of the Adoxaceae, thus their repositioning (Donoghue et al. 1992; Eriksson and Donoghue 1997; Bremer et al. 2009). It must be noted that the USDA PLANTS database (USDA, NRCS 2012) does not yet reflect this change in classification, however the forthcoming volume 18 of the *Flora of North America* will. Intoxication problems have been associated only with *Sambucus*.

erect herbs, shrubs, small trees; stems ill scented when bruised; leaves simple or pinnately compound; cymes; flowers 5-merous; ovaries inferior; fruits berry-like drupes with 1 or 3–5 stones.

Plants small trees or shrubs or perennial herbs. **Leaves** simple or 1-pinnately compound; opposite; venation pinnate; margins entire or serrate; stipules present or absent. **Inflorescences** cymes; terminal. **Flowers** perfect; perianths in 2-series. **Sepals** 5; fused; reduced. **Corollas** radially symmetrical; typically rotate. **Petals** 5; fused. **Stamens** 5; epipetalous. **Pistils** 1; compound, carpels 3–5; stigmas 1–3, capitate; styles absent or short; ovaries wholly or partially inferior. **Fruits** drupes or berry-like drupes with 1 or 3–5 stones.

SAMBUCUS L.

Taxonomy and Morphology—Comprising 20–25 species, *Sambucus*, commonly known as elderberry or elder, is a cosmopolitan genus (Huxley and Griffiths 1992; Judd et al. 2008). Species are sources of wine and jelly, several are cultivated ornamentals, and the wood of some is used to make musical instruments. Native Americans and settlers used the plants medicinally for a variety of ailments. In North America, 5 native and introduced species are present (USDA, NRCS 2012):

<i>S. ebulus</i> L.	dwarf elderberry
<i>S. nigra</i> L.	common elderberry, black elder
(= <i>S. caerulea</i> Raf.)	European elderberry, bourtree
(= <i>S. canadensis</i> L.)	American elder, sweet elder
(= <i>S. mexicana</i> C.Presl ex DC.)	Mexican elder, tapiro, blueberry elder
(= <i>S. neomexicana</i> Woot.)	
<i>S. racemosa</i> L.	red elderberry, European red elder, stinking elderberry
(= <i>S. callicarpa</i> Greene)	
(= <i>S. microbotrys</i> Rydb.)	
(= <i>S. melanocarpa</i> [A.Gray] McMinn)	
(= <i>S. pubens</i> Michx.)	

Although long recognized as distinct species, the American taxa *S. canadensis* and *S. caerulea* are now classified as subspecies of the European *S. nigra* (Bolli 1994; USDA, NRCS 2012). Bolli treats *S. mexicana* as a synonym of *S. nigra* subsp. *canadensis*. Early toxicologic reports used *S. canadensis*.

Because the morphological features of *Sambucus* are essentially the same as those of the family, they are not repeated here. The genus is distinguished from *Adoxa* and *Viburnum* by differences in habit, leaf dissection, and fruit features (Figures 2.1 and 2.2).



Figure 2.1. Line drawing of *Sambucus nigra* subsp. *canadensis*. Illustration by Bellamy Parks Jansen, courtesy of Oklahoma State University.



Figure 2.2. Photo of *Sambucus nigra* subsp. *canadensis*.

moist soils; cultivated ornamentals

Distribution and Habitat—*Sambucus nigra* subsp. *canadensis* is the elderberry commonly encountered in moist sites of fields, borrow ditches, and woods of eastern North America. Populations of subsp. *canadensis* formerly called *S. Mexicana* occur in montane regions of Mexico and south into Central America (Bolli 1994). Subspecies *caerulea* is found in valleys and on slopes in the open woodlands of western North America from British Columbia to Durango, Mexico (Bolli 1994). Ornamental introductions from Europe, *S. nigra* and *S. ebulus*, occasionally escape from cultivation (Figures 2.3–2.5).

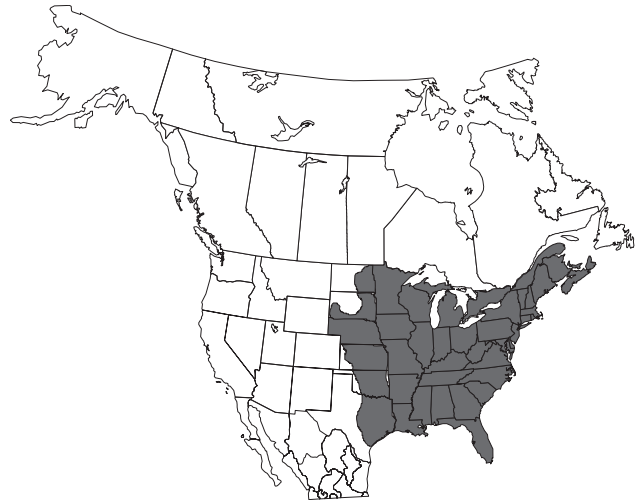


Figure 2.3. Distribution of *Sambucus nigra* subsp. *canadensis*.

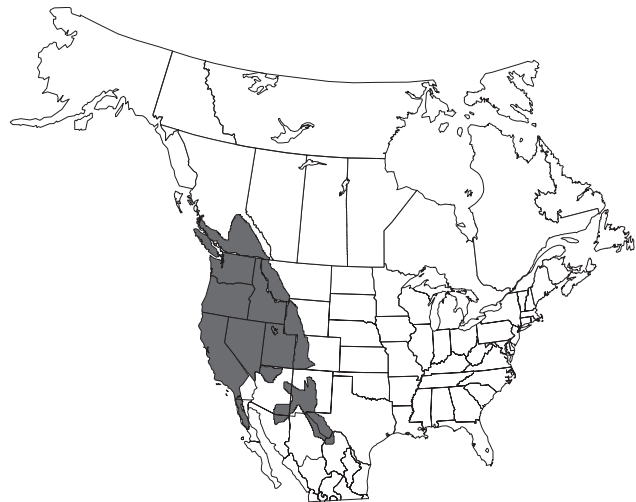


Figure 2.4. Distribution of *Sambucus nigra* subsp. *caerulea*.

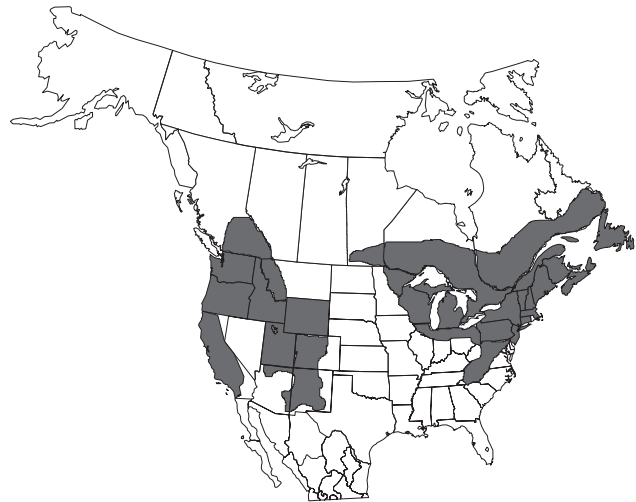


Figure 2.5. Distribution of *Sambucus racemosa*.

low risk of digestive disturbance, all plant parts; low risk of abrupt neurologic cyanide effects

Disease Problems—Species of *Sambucus* are used for food and medicines. The edible drupes are used to make pies, wine, and jelly, and the numerous medicinal uses of the genus have caused some individuals to consider it a complete pharmacy in itself (Millspaugh 1974). The leaf buds were considered to be potent cathartics and the sap a laxative.

Despite its widespread use and therapeutic reputation, the genus causes problems. Tinctures made from the leaves and flowers have caused diuresis and circulatory problems, terminating in exhaustion and profuse sweating (Millspaugh 1974). An Asian species has been shown to be highly lethal in mice, 20% in feed causing 80% mortality and 10% in feed causing 10% mortality (HongLi et al. 2004). However, repeated i.p. administration of methanol extracts of *S. ebulus* to rats were lethal only at exceptionally high dosage and generally caused only anorexia and lethargy (Ebrahimzadeh et al. 2007). In another case, European plants of *S. nigra* were identified as a cause of sudden death in two Jardine's parrots on the basis of finding the leaves in the stomachs and crops (Griess et al. 1998).

Although it is clear that species of *Sambucus* contain bioactive constituents, they are uncommon causes of disease. Ingestion of the roots and/or stems has been associated with digestive tract problems (Cooper and Johnson 1984). The roots and stems produce purgative effects, and the drupes, when eaten raw, may produce similar results, including nausea and vomiting (Pammel 1911). In a case in the 1800s, a boy in Scotland developed severe vomiting and bloody diarrhea after eating leaves of *Sambucus*. A second child exhibited mild neurologic signs after eating the flowers (Pammel 1911). In another episode, 11 of 25 people who drank elderberry juice made 2 days previously developed nausea and vomiting (Kunitz et al. 1984). Other signs seen in some individuals included abdominal pain, weakness, dizziness, and numbness. One individual became stuporous and required hospitalization. The severity of signs was directly correlated with the amount of juice consumed. Cyanide was not detected in the blood of those affected.

In some circumstances the leaves of *Sambucus* are cyanogenic, and the stems have been associated with accumulation of nitrate, but these conditions have not been demonstrated to pose a substantial risk to livestock.

irritant terpenoids present; cyanogenic glucosides present but low risk

Disease Genesis—The toxicants responsible for the digestive tract problems have not been identified, although triterpenoids, such as oleanolic acid, are present in the leaves of *S. nigra* and *S. nigra* subsp. *canadensis* (reported as *S. canadensis*; Inoue and Sato 1975). The stones/seeds contain a heat-labile resinous substance (Frohn and Pfander 1984). Lectins or hemagglutinins are present in both the bark and fruit of *S. nigra* (Kaku et al. 1990; Mach et al. 1991). Any of these types of toxicants could be responsible for irritation of the digestive tract.

Species of *Sambucus* have traditionally been thought to be toxic because of the presence of cyanogenic glucosides in the foliage and fruit. *Sambucus nigra* contains several phenylalanine-derived glucosides, including holocalin, prunasin, sambunigrin, and zierin (Jensen and Nielsen 1973; Seigler 1977). Presumably other species contain a similar array of these compounds. The risk of intoxication, however, is quite low but cannot be entirely ignored. In this respect, there are occasional reports of cyanide intoxication in cattle confirmed by serum and plant HCN analysis (Meiser 2001). For the most part, the propensity to produce adverse effects of any type is lost when the berries are cooked or fermented to make jellies or wine (Pogorzelski 1982; Cooper and Johnson 1984). The digestive tract problems are not consistent with cyanide intoxication (Figures 2.6 and 2.7).

Of unknown significance are the presence of type 2 ribosomal-inhibiting proteins (RIPs) of no apparent toxicity potential. These are 2-chain RIPs similar to those of *Ricinus* referred to as nigrins and ebulin (Girbes et al. 2003). In contrast to those of ricin, these RIPs have single amino acid substitutions at the high affinity sugar-binding sites of the facilitator B chain.

humans: rarely: abrupt onset: vomiting, colic, profuse salivation, diarrhea

livestock: rarely: abrupt onset: weakness, apprehension, ataxia, labored respiration, collapse, seizures

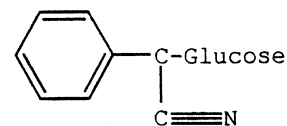


Figure 2.6. Chemical structure of prunasin.

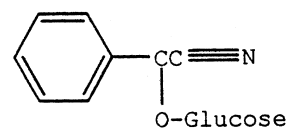


Figure 2.7. Chemical structure of sambunigrin.

Clinical Signs—In cases involving irritation of the digestive tract, there is abrupt onset of vomiting, colic, excess salivation, and diarrhea. These problems may be accompanied by increased heart and respiratory rates, tremors, and paralysis.

When cyanide intoxication occurs in livestock, the clinical signs typically appear soon after consumption of plant material and include weakness, apprehension, ataxia, labored respiration, collapse, and tetanic seizures. A more detailed discussion of the signs and diagnosis is presented in the treatment of the Rosaceae (see Chapter 64).

no lesions; activated charcoal; sodium thiosulfate

Pathology and Treatment—There are few if any distinctive pathologic changes. A few scattered, small hemorrhages on the heart and visceral surfaces may be present. Prevention of toxicant absorption via activated charcoal and relief of any persistent vomiting are important considerations in treatment. For cyanogenesis, the standard, well-established response employing sodium thiosulfate with or without sodium nitrite is appropriate. A complete discussion of this approach is presented in the treatment of the Rosaceae (see Chapter 64).

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Chapter Three

Agavaceae Endl.

Agave Family

Agave

Nolina

Comprising 17 or 18 genera and approximately 550 species native to warm, mostly arid regions of both the Old World and the New World, the Agavaceae is commonly known as the century plant or sisal family (Verhoek and Hess 2002). The first common name reflects the monocarpic habit of some of the species of *Agave*. Because of the harsh growing conditions occupied by most species, plants grow vegetatively for many years or even decades. They are acaulescent, with a rosette of fleshy, firm leaves that may become quite massive. When flowering does occur, a flowering stem bearing a massive terminal inflorescence is quickly produced. The plant subsequently dies as the seeds mature. The second common name, *sisal*, reflects the family's economic importance. Strong, durable fibers for cordage and matting are extracted from the leaves of a number of species. Species of both *Agave* and *Yucca* are frequently used in landscaping, especially in xeric sites.

Taxonomists differ in their opinions as to the circumscription of the family and even whether it should be recognized as a distinct taxon. Verhoek (1998) and Seberg (2007a) narrowed its circumscription to encompass only 8 or 9 genera and about 300 species. Originally described by Endlicher in 1841, Cronquist (1981) submerged it in the Liliaceae, Bogler and Simpson (1996) in the Amaryllidaceae, and Bremer and coworkers (2009) in the Asparagaceae. However, phylogenetic analyses of morphological, cytological, and molecular characters support the family's recognition as distinct (Bogler and Simpson 1995, 1996; Bogler et al. 2005). We therefore employ in this treatise the Verhoek and Hess (2002) treatment of the Agavaceae in the *Flora of North America*.

subshrubs or herbs; leaves simple and typically long

Plants subshrubs or herbs; perennials; from caudices or crowns; evergreen; caulescent or acaulescent; succulent or not succulent; bearing perfect flowers or polygamodioecious. **Leaves** simple; alternate; basal or cauline and crowded; sessile; spreading or reflexed; fibrous or fleshy; blades linear or lanceolate or oblong; venation parallel; apices acute, often spine tipped; margins entire or serrate; stipules absent. **Inflorescences** spikes or racemes or panicles; bracts absent or present. **Flowers** perfect or imperfect, similar; perianths in 1-series or 2-series; radially or slightly bilaterally symmetrical; campanulate or tubular or funnel-form. **Perianth Parts** 6; all alike; petaloid; in 1 or 2 whorls; free or fused; greenish white to white to cream or yellow to orange. **Stamens** 6. **Pistils** 1; compound, carpels 3; stigmas 3; styles 1 or 0; ovaries superior or inferior; locules 3 or appearing to be 6; placentation axile. **Fruits** capsules or berries. **Seeds** numerous or 3; flattened or globose.

Yucca used as emergency stock feed; saponins in the leaves and seeds

Because they are found mainly in dry desert-type ranges, members of the Agavaceae are well recognized for their value as emergency stock feeds (Wootton 1918; Forsling 1919). Especially valued are species of *Yucca*, commonly known as Spanish bayonet or soapweed. Members of the genus *Yucca* are also known as sources of steroidal saponins, which are composed of two groups, varying mainly in the glycosidic ether linkages. The spirostanols (monodesmosidic) have spirostan aglycones with mainly C-3-linked sugars, whereas the furostanols (mono-, di-, or tridesmosidic) are typically 26-C aglycones with glycosidic linkages at C-3 and C-26 and are composed of 2–5 or even up to 11 sugars (Hostettmann and Marston 1995). Although saponins are generally considered to be irritants of the digestive tract, the use of these forages for feed is not accompanied by noteworthy digestive disturbances (Wootton 1918; Forsling 1919). Even when chopped and fed to cattle at up to 9 kg/day, *Yucca*

produced only mild diarrhea. Bloat was a more serious problem. Best results were obtained when cottonseed meal was given in addition to the chopped *Yucca*. *Nolina* and *Agave lecheguilla* were not as useful for feed.

AGAVE L.

Taxonomy and Morphology—Comprising some 200 species, *Agave*, commonly known as agave or maguey, is the largest genus of its family and certainly the most important (Reveal and Hodgson 2002). Its name comes from the Greek *agavos*, meaning “admirable,” and presumably refers to the showy appearance of the plants in flower (Huxley and Griffiths 1992). In addition to being a source of fiber, *Agave* is the source of popular Mexican beverages and food (Gentry 1982). The sap, consumed fresh, is known as aguamiel; fermented, it is the source of pulque, and of mescal or tequila when distilled. Archaeological evidence indicates that species of the genus have been used for food for at least 9000 years. Humans consumed, both raw and boiled, the soft, starchy, white meristems of the short stems; the white bases of the leaves; the immature flowering shoots; and the flowers of some species. In the 1960s, thousands of tons of leaves were fed to herds of dairy cattle in northeastern Mexico; and in Baja, California, panicles of flowers were cut and fed to range cattle (Gentry 1982). Various species of the genus are also grown as ornamentals, especially for architectural effect, and are now propagated worldwide. In North America, some 30 species are present. Only 1 is of toxicologic importance:

A. lecheguilla Torr.

lechuguilla

succulent perennial herb; basal rosette of long and spiny leaves; flowers yellow, borne on elongated stalk

Plants succulent herbs; perennials; from small, suckering, few-leaved rosettes, 30–50 cm in diameter and 40–60 cm high. **Leaves** 30–50 cm long; ascending to erect; light green to yellow green; stiff; blades linear lanceolate; adaxial surfaces concave; abaxial surfaces convex; apices spine tipped; margins easily separated from blade when dry, coarsely serrate, teeth retrorse. **Inflorescences** spikes or racemes or rarely panicles; flowers borne in 2s or 3s; peduncles 2.5–3.5 m long; bracts present. **Flowers** perfect; funnellform. **Perianth Parts** yellow or tinged with red or purple; linear; ascending. **Stamens** clasped by perianth parts after anthesis. **Pistils** 1; ovaries inferior, fusiform. **Capsules** oblong to pyriform; short beaked. **Seeds** flattened; black (Figures 3.1 and 3.2).

deserts; open sites; rocky soils



Figure 3.1. Line illustration of *A. lecheguilla*.



Figure 3.2. Photo of *Agave lecheguilla*.

Distribution and Habitat—All species of *Agave* are native to the Americas and generally occupy open, arid sites and a variety of soil types. One of the most abundant species in terms of numbers of rosettes, *A. lecheguilla*, also has one of the most extensive ranges (Gentry 1982). A common component of different desert communities, it is found in rocky sites, especially limestone, often as the dominant plant. Where locally abundant, it may provide a captivating sight of desert beauty when numerous plants are in bloom (Figure 3.3).



Figure 3.3. Distribution of *Agave lecheguilla*.

mainly sheep and goats; abrupt onset; liver disease with photosensitization after eating leaves for several weeks

Disease Problems—The spines on the leaf margins and the tips appear so menacing that it is difficult to comprehend that *A. lecheguilla* is eaten. As is so often the case in arid environments, problems due to ingestion usually occur in late winter or spring when there is little other forage available. Affecting primarily sheep and goats, the disease, known as lecheguilla fever, goat fever, or swell-head, is a type of hepatogenous photosensitization with jaundice (Schmidt and Jungherr 1930; Jungherr 1931). Cattle are affected much less commonly. In years when the plant is browsed extensively, morbidity rates may be as high as 30% in sheep and goats. Interestingly, during the same winter–spring period, mule deer may subsist extensively on lecheguilla without apparent ill effects (Brownlee 1981).

The toxic potential of other species of *Agave* is essentially unknown; they may be mechanically injurious and/or contain irritants causing a purpuric dermatitis (Ricks et al. 1999). In Mexico, the young, tender flowering stems or quoties of *A. americana* are cooked. They become sweet and juicy and are eaten like stalks of sugar cane. If the fibrous pulp is not spit out, phytobezoars rarely may form in the stomach and require surgical removal (Villarreal et al. 1985).

saponins, crystalloid cholangiohepatopathy, calcium salts of a saponin

Disease Genesis—Early studies indicated the presence of two toxicants: a photodynamic agent and a hepatotoxic saponin (Mathews 1937, 1938b). It is now clear that saponins such as smilagenin are also capable of causing hepatogenous photosensitization (Kellerman et al. 1991) (Figure 3.4).

The destructive effects of the toxins appear to affect the liver in a manner that renders it incapable of eliminating a photodynamic agent, presumably phyloerythrin. Whether an additional photodynamic factor is present is not resolved, but it is probably of only academic interest, because the action of smilagenin can account for all the observed disease effects (Figure 3.5).

Similar-appearing bile duct crystal structures and the accompanying lesions are now recognized to be present in hepatogenous photosensitization caused by taxa from other families such as *Panicum* (see Chapter 58) and *Tribulus* (see Chapter 76). Interestingly, although these are diverse genera, they share a potential to cause disease through saponins (Kellerman et al. 1991). For *A. lecheguilla*, not only is smilagenin considered the cause, but

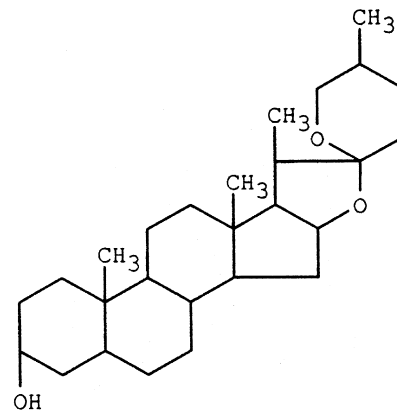


Figure 3.4. Chemical structure of smilagenin.

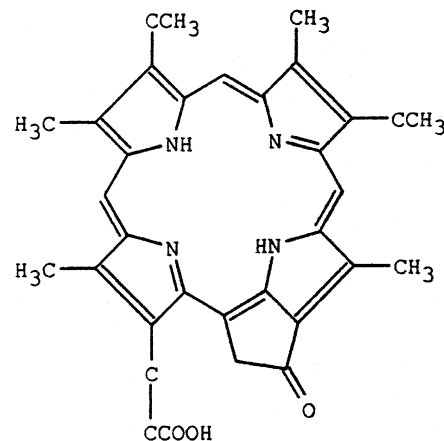


Figure 3.5. Chemical structure of phyloerythrin.

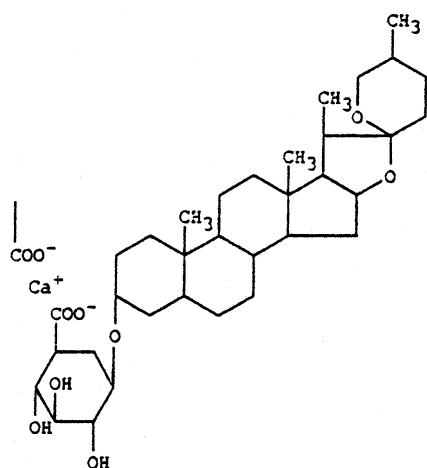


Figure 3.6. Chemical structure of the Ca^{2+} salt of epismilagenin β -D-glucuronide.

the biliary crystals are also now known to be calcium salts of a sapogenin, probably smilagenin rather than cholesterol (Camp et al. 1988) (Figure 3.6).

In addition, smilagenin has been shown to have abortifacient potential when given intravenously (Dollahite et al. 1962). Saponins are much like cardenolides: they are composed of a steroid sapogenin nucleus (the genin or aglycone) and one or more sugars attached at C-3 (Shoppee 1964). Thus smilagenin may be found with several different combinations of sugars to give various saponins. Lechuguilla leaves have about 1% (up to 2%) sapogenin, almost exclusively smilagenin (Wall et al. 1962). The concentrations are similar in dead leaves, but up to 2-fold higher in the plant's center, generally known as the heart or cajolla, which is selectively eaten by deer and livestock. The fruits and seeds contain lesser amounts of other sapogenins. Concentrations are quite consistent from site to site but may vary slightly during the year (highest in September and October) (Wall et al. 1962). Smilagenin is also found in *A. vilmoriniana* of Mexico, the consequences of which are not known (Wall et al. 1954). *Agave sisalana* contains high concentrations of the sapogenins, hecogenin, and tigogenin (Teixeira et al. 1989). Limited feeding studies on sisal residues following extraction revealed few indications of any toxicity potential, although the toxicants may have been leached out (Figueiredo 1975). Species of *Yucca* also contain similar concentrations of sapogenins but mainly sarsasapogenin rather than smilagenin (Wall et al. 1954). *Agave americana* is reported to accumulate unique 6-sided calcium oxalate raphides (Wattendorff 1976; Kellerman et al. 1988).

It should be pointed out that as with other disease problems involving the liver, animals need not be eating agave plants at the time of appearance of clinical signs. If

hepatic changes are severe, regeneration and recovery may require an extended period. During this time, animals otherwise appearing normal will be susceptible to stresses that may precipitate the onset of signs of intoxication (Burrows and Stair 1990).

mucoid discharge from eyes and nose; swelling of head and ears; edema of face, lips, jaw; pruritis; weakness; emaciation

elevation of serum bilirubin, hepatic enzymes

Clinical Signs—After feeding upon *A. lecheguilla* for several weeks or more, the animal may be listless and not inclined to keep up with the flock. A stringy, thick mucoid discharge may hang from the eyes and nose. Close examination will reveal icterus of the sclera and visible mucous membranes. In some cases the head and ears will be swollen, and when the head is handled, edema of the face, lips, and underside of the jaw may be readily detected. The edema may cause the animal to rub and scratch its head for several days. These are manifestations of photosensitivity and will likely be accompanied by purplish discoloration of the coronary bands. There will be progressive debilitation, weakness, and emaciation, and the urine may be a clear dark yellow or brown. Death may occur several days to a week or more after onset of signs. Cattle exhibit more diffuse skin changes. Clinicopathologic changes during the course of the disease include marked elevation of serum bilirubin and hepatic enzymes.

gross pathology: thickened skin, head, especially ears; crusty, ulcerative areas

Pathology—In instances where photosensitization occurs, the most obvious changes will be in the skin of the head. There may be marked thickening of the skin and ears, with a gelatinous appearance extending into the deeper corium. Sloughing of patches, cracking, and even sloughing of an ear are features occasionally observed. Crusty and ulcerative or proliferative areas may be present, especially around the lips, eyes, and nose. The kidneys may be swollen and greenish black, with numerous gray foci. Typically the liver is brownish yellow.

microscopic: liver moderate necrosis, bile duct clefts or crystals; renal tubules dilated, with flattened epithelium

Microscopically, edema of the skin will be accompanied by necrosis and a polymorphonuclear infiltrate in the deeper corium. The renal tubules will be distended with albumin and casts of pigment and cellular debris. Individual epithelial cells may show fatty degeneration and necrosis, with some tubules dilated and lined by a flattened epithelium. In the liver, fatty change, zonal necrosis, and bile pigment in macrophages are readily apparent, but the most distinctive lesions are the crystals or clefts in bile ducts. They may be surrounded by a brownish amorphous material filling the ducts or granuloma formation with necrosis of the biliary epithelium. Crystals may also be present in bile canaliculi and Kupffer cells. Originally the birefringent, acicular crystals were thought to be cholesterol, which they closely resemble (Mathews 1937, 1938a,b). They are now known to be calcium salts of a sapogenin. The crystals are best retained when acetone is substituted for alcohol to dehydrate tissues during processing for microscopic examination.

supportive care, provide shade

Treatment—Recovery from the disease is based upon general supportive care to allow the animal to regain adequate liver and kidney function. The animal may be protected from sunlight, but this is not generally necessary for survival. A discussion of the use of zinc salts for prevention of intoxication is presented in the following treatment of *Nolina*.

NOLINA MICHX.

Taxonomy and Morphology—Native to the southwestern United States and Mexico, *Nolina* comprises approximately 30 species and is closely related to *Dasyli- rion* (Hess 2002). The genus has also been positioned in the Nolinaceae by Bogler (1998) and Seberg (2007b); in the Ruscaceae by Judd (2003); and in the Asparagaceae by Bremer and coworkers (2009). Although molecular phylogenetic studies do suggest the separation of *Nolina* from *Agave* and *Yucca* (Duvall et al. 1993), we here continue to follow Hess's (2002) positioning in the Agavaceae, until generic and familial relationships are fully resolved. *Nolina* honors P.C. Nolin, an eighteenth-century French agriculturalist. Of the 14 species in North America, 3 are of toxicologic concern:

<i>N. bigelovii</i> (Torr.) S.Watson	Bigelow's beargrass
<i>N. microcarpa</i> S.Watson	sacahuista, small-seed nolina
<i>N. texana</i> S.Watson (= <i>N. affinis</i> Trel.)	sacahuista, bunchgrass

subshrubs or herbs; forming tussocks; leaves simple, long, narrow

Plants subshrubs or herbs; from large, woody, subterranean, or aerial caudices; tussock appearing. **Stems** present or absent. **Leaves** simple; alternate; numerous; basally clustered; sessile; spreading or arching; thick or thin; fibrous or fleshy; blades narrowly linear; apices often spine tipped; margins entire or serrate; stipules absent. **Inflorescences** panicles; pedicels jointed; bracts present. **Flowers** small; numerous; perfect or imperfect, similar; campanulate or funnelform. **Perianth Parts** 6; free; white. **Stamens** 6. **Pistils** 1; ovaries inferior. **Capsules** ovoid; 3-lobed or 3-winged. **Seeds** 1–3; globose; grayish white or brown to blackish (Figures 3.7 and 3.8).

deserts; open sites

Distribution and Habitat—All species of *Nolina* are native to the southwestern United States and the Sonoran and Chihuahuan deserts of northern Mexico. They occupy a variety of soil types and habitats. Some species may be used occasionally as ornamentals in the southern states (Figures 3.9–3.11).

sheep and goats eating flower buds, open flowers, and ripe fruits for several weeks; abrupt onset; liver disease with photosensitization,

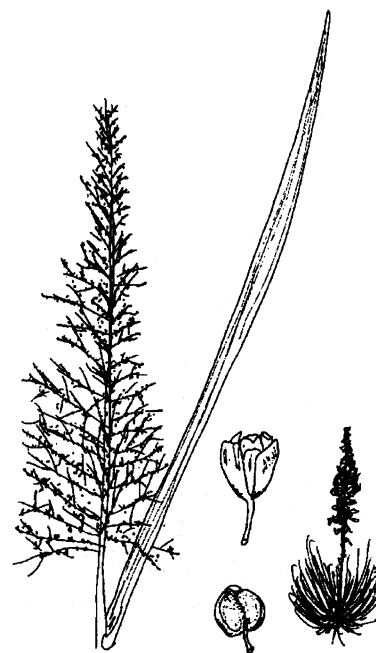


Figure 3.7. Line drawing of *Nolina bigelovii*.



Figure 3.8. Photo of a single plant of *Nolina bigelovii*. Courtesy of Stan Shebs.



Figure 3.9. Distribution of *Nolina bigelovii*.

Disease Problems—Although animals are seldom in situations where they are forced to eat *Nolina* species, these plants are considered useful forage in some parts of their ranges (Mathews 1940). The value of *Nolina* as forage is probably reflected in its crude protein concentrations: 19% in the buds but only 5–6% in the leaves (Huston et al. 1981). Only the flower buds, open flowers, and ripe fruit present a significant hazard of the occurrence of photosensitization similar to that from *Agave lecheguilla*.

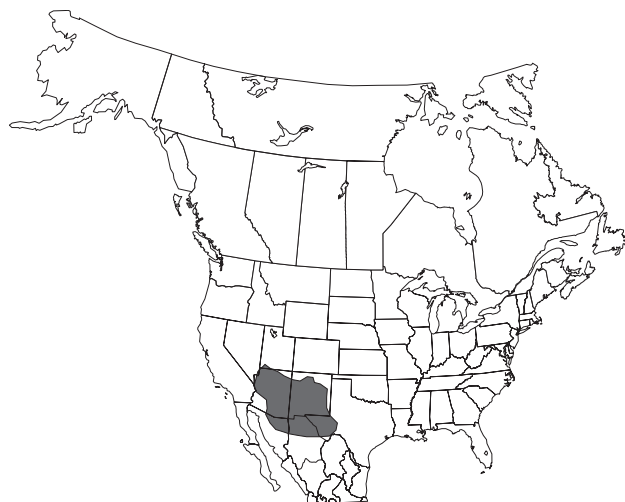


Figure 3.10. Distribution of *Nolina microcarpa*.



Figure 3.11. Distribution of *Nolina texana*.

This apparent localization of toxicant in *Nolina* minimizes problems, because large numbers of flowers are not produced each year, but rather only every 5 or 6 years, depending on the species (Mathews 1940). In years when flowers are not so abundant, plants may indeed be useful as forage. However, when flowers are profuse, *Nolina* lives up to its reputation as the most common cause of photosensitization in New Mexico (Hershey 1945). Sheep and goats relish the buds and flowers but disdain the leaves. In contrast, cattle eat the leaves in the winter but seldom consume the toxic buds and flowers. Thus, sheep and goats are at considerable risk, whereas cattle are typically seldom affected (Mathews 1940; Hershey 1945; Norris and Valentine 1954). In some localities the leaves are harvested for making brooms and the trimmings are fed to cattle (Nabhan and Burns 1985). When the outer

leaves are removed, they are replaced with succulent new growth, which is readily grazed by cattle.

crystalloid cholangiohepatopathy; sapogenins suspected but not confirmed as cause of disease

Disease Genesis—The toxicant in *Nolina* is unknown, but the similarities in effects produced to those caused by other photosensitizing plants favor sapogenins. *Nolina* and several other genera cause a hepatotoxicity characterized by the presence of crystalloid material in the bile ducts. It now appears that most of these other genera contain toxic sapogenins (Kellerman et al. 1991). Thus, it is likely that similar toxins account for the effects produced by *Nolina*. Early studies failed to show sapogenins in the genus, but only leaves and whole plants were evaluated (Wall et al. 1954). Because it is the buds and flowers that are toxic, the negative results of the leaf analyses may have been misleading. An additional observation of interest is that the toxicant seems to be somewhat volatile, given that oven-dried plant material, originally used in toxicity experiments, was reported to be considerably less toxic after storage for 2 years (Samford et al. 1991). Whatever the identity of the toxin, it appears to affect the liver in a manner that renders it incapable of eliminating a photodynamic agent, presumably phylloerythrin. Photosensitization is reported to be worse when animals eat *Nolina* in pastures of green grass rather than in hay (Mathews 1940). At present it seems reasonable to consider *Nolina* intoxication from eating buds and flowers as hepatogenous photosensitization. A more detailed discussion of photosensitization is given in the treatment of Poaceae, in Chapter 58. As little as 0.5% body weight (b.w.) of dry *N. microcarpa* can cause serious disease (Rankins et al. 1989). *Nolina texana* is similarly toxic but may require a slightly higher dosage, in excess of 1% of b.w. (Mathews 1940). Although we know little of the toxicity potential of the many other species in this genus, it seems prudent to regard them with suspicion.

In contrast to the liver derangement produced by ingestion of the buds and flowers, a wasting disease developed in rats and partridges that were fed seeds (Rankins et al. 1986; Smith et al. 1992). This may be indicative of a different toxin in the seeds or a difference in absorption and site of action of the toxin.

head swollen; edema of ears, lips, and face; pruritis; icterus; dark brown urine

Clinical Signs—The disease appears sporadically in sheep and goats that have been eating *Nolina* for a week or more. Initially their appetite is much reduced, and then in another day or two the animals become depressed and reluctant to move about. Pruritis, with rubbing of the head and ears, may be noted for several days, and the urine may be dark yellowish brown. Upon close inspection, there is very obvious icterus; the sclera and mucous membranes are intensely yellow. The ruminal contents become quite dry because of dehydration, and there is a marked increase in fluid passage through the digestive tract (Rankins et al. 1989). By this time the head is quite swollen and the ears, lips, and face reddened and edematous—hence the name *bighead*.

Most of the time, the animals stand in any shade available. Debilitation is progressive, with a copious sticky discharge from the eyes and nose and with death following in 1–2 weeks (Mathews 1940). The swelling and sloughing of the skin may be severe enough that the ears may be lost, even in animals that eventually recover (Hershey 1945). In some instances, animals referred to as “fevered” may become ill and die without signs of photosensitization. It is of interest to note that *Nolina* given to rats readily produced severe illness and death, but there was no evidence of liver involvement. The disease appeared to be of a metabolic wasting type without elevation of serum hepatic enzymes, for example, GGT and AST, and was readily reversible by eliminating *Nolina* from the feed (Rankins et al. 1986). This implies considerable variation among species in the signs of intoxication.

elevation of serum bilirubin and hepatic enzymes

Clinicopathologic changes during the course of the disease include elevation of serum calcium, decrease of potassium and phosphorus, and marked elevation of bilirubin and serum hepatic enzymes. Alkaline phosphatase is elevated during the early phases (Rankins et al. 1988).

gross pathology, edema, skin of head

Pathology—The gross lesions, which are essentially the same as those produced by *A. lecheguilla*, are limited to the skin of the head and to the liver and kidney. The skin of the head may be thickened with a gelatinous, subcutaneous edema and areas of shallow ulceration. The kidneys may be swollen and dark greenish brown to black, whereas the liver will be a light yellowish brown, perhaps with a greenish sheen.

microscopic, liver, moderate necrosis with bile duct clefts or crystals

Microscopically, there will be distortion of the hepatic cords and fatty degeneration of centrilobular cells. The characteristic lesions are thickened bile ducts filled with debris and crystalloid material or with clefts apparently left from previous crystals (Mathews 1940). The last change seems typical for several of the hepatogenous photosensitizing plant genera.

supportive care, provide shade; possible preventive effects of zinc, mixed grazing with sheep and cattle

Treatment—The most obvious approach to alleviating distress of the disease is to remove the animals from sunlight. However, even where this is possible, it does little for the underlying and much more serious problem of liver disease. Typically, the case fatality rate is high, especially if browsing of *Nolina* continues after signs of disease are manifested. Good nursing care to allow the liver to recover, often difficult to do under range conditions, is the primary approach.

A more specific approach is suggested by observations of the beneficial effects of zinc in preventing facial eczema due to the fungus *Pithomyces chartarum* (Smith and Towers 1985). Because facial eczema is somewhat similar to *Nolina* intoxication, the preventives might be expected to be interchangeable. The value of zinc oxide for therapeutic use after disease onset is questionable, but when given intraruminally at a daily dose of 30 mg/kg b.w., it seems to provide some benefit (Rankins et al. 1988, 1993). Additional studies are needed to clearly delineate treatment conditions and the response. However, zinc supplementation appears to be of promise, at least as a preventive if not as a therapeutic. If it is used, care must be taken to avoid toxic amounts; 1 part zinc oxide to 3 or more parts water (w/v) to provide 20–30 mg/kg b.w. daily by oral drench is protective against facial eczema (Smith and Towers 1985). It may be given less often, provided the dose is increased proportionately. The foregoing recommendations are for zinc oxide; zinc sulfate is more toxic. In addition to drenching, zinc may also be effective when given in the drinking water or by spraying it on the pasture. It must be emphasized that zinc is not a proven treatment for *Nolina* intoxication at present.

Grazing systems employing a mixture of cattle, sheep, and goats together is an effective means of reducing disease losses, especially when combined with a pasture ration program (Merrill and Schuster 1978).

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