

MYCOTOXIC FUNGI, MYCOTOXINS, MYCOTOXICOSES

An Encyclopedic Handbook

Volume I

**Mycotoxic Fungi
and Chemistry of Mycotoxins**

edited by

Thomas D. Wyllie

Lawrence G. Morehouse

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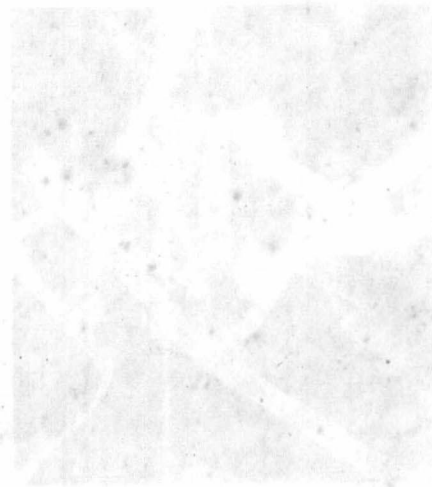
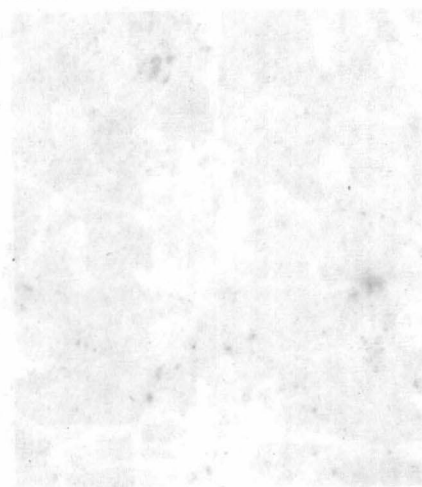
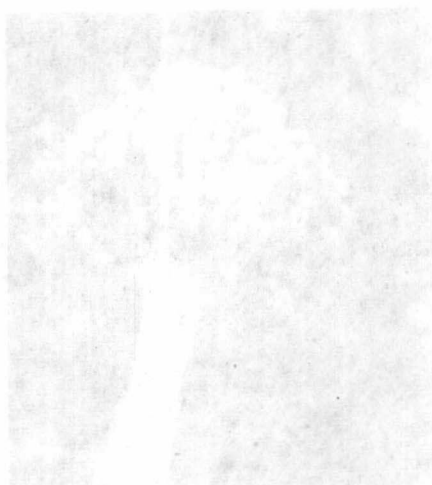
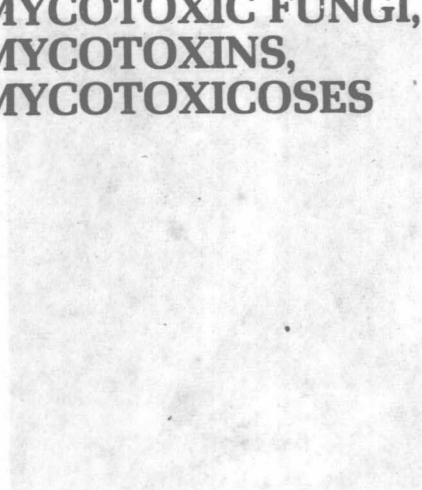
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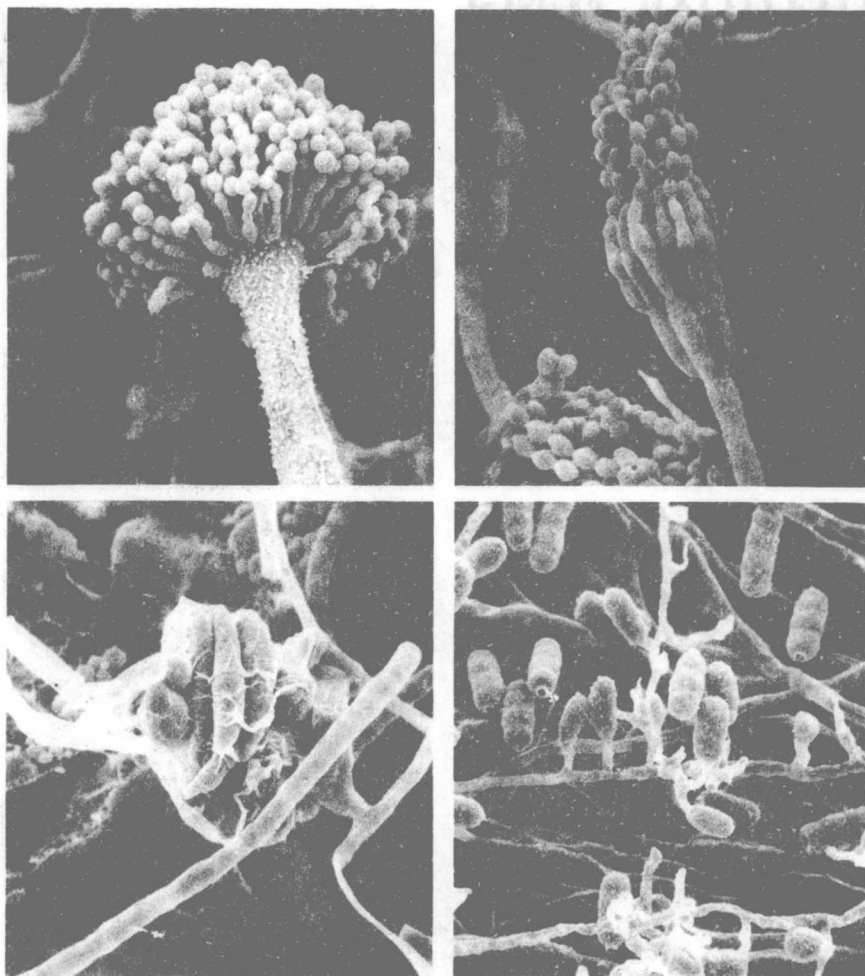
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MYCOTOXIC FUNGI, MYCOTOXINS, MYCOTOXICOSES



1. The mycotoxins are secondary metabolites of certain fungi which are capable of producing them. They are usually produced in the form of spores or hyphae. The mycotoxins are usually produced in the form of spores or hyphae. The mycotoxins are usually produced in the form of spores or hyphae.



Scanning electron micrographs of four important mycotoxigenic fungi. From upper left clockwise: *Aspergillus flavus*, conidial head, 1050X; *Penicillium islandicum*, conidial head, 1400X; *Pithomyces chartarum*, conidiospores, 700X; *Fusarium tricinctum*, young macroconidia, 1750X. Photomicrographs courtesy of Dr. M. F. Brown, Department of Plant Pathology, University of Missouri-Columbia.

FOREWORD

Mycotoxic fungi and their resulting threat to food and feedstuffs worldwide continue to have an extensive impact on the welfare of human and animal populations. Since early times these fungi have made their mark, but only lately have we been able to appreciate the extent of their impact. As recently as 1960, a major and widespread mycotoxicosis was initially thought to be a strange, new "X disease," probably of viral origin. The discovery of the role of peanuts in an aflatoxicosis was the leading factor contributing to increased interest and concern in the United States and, indeed, worldwide. In the ensuing 17 years there has been a more organized effort devoted to understanding and, hopefully, controlling the problem created by these fungi.

The range of food and feedstuffs potentially affected by mycotoxic fungi and the numbers of microbial species has been extensively increased in recent years. Although the epidemic occurrences seem to have lessened, the endemic and more subtle effects, no less destructive, appear to be increasing. In part this results from an awareness brought about by new knowledge and the ability to document cause and effect relationships.

A wealth of knowledge about mycotoxic fungi, their toxins, and the resulting toxicoses has been documented in scientific literature throughout the world. This encyclopedic handbook brings this large volume of knowledge together through the collective efforts of experts analyzing the documentation in every facet of the field. From the isolation, culture, and identification of suspect or known mycotoxic fungi, to the chemistry of toxins and toxicoses, the subjects are synthesized and set forth for the reader in an orderly, accessible manner. The organization

and indexing are designed to make these three volumes readily usable as standard, working references. Their comprehensiveness and international scope of subject coverage makes them an invaluable reference for students, scientists, physicians, veterinarians, animal health specialists, public health and regulatory personnel, and many others involved with the planning, production, and use of food and feed-stuffs.

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PREFACE

This three-volume Encyclopedic Handbook of mycotoxic fungi, mycotoxins, and mycotoxicoses assembles information on the fungi, their toxic metabolites, and the diseases associated with them. Well-documented mycotoxicoses are discussed, and comment is made on less well-known disease syndromes suspected to have a mycotoxic origin. There are 11 countries represented by 46 contributing authors. This affirms the international scope and nature of the mycotoxin problem, and emphasizes the importance of specific disease syndromes in certain locales, while suggesting that mycotoxic fungi known to cause disease in one country may be present in another with only negligible impact on animals and man. From such information, we infer that the factors responsible for the production and consumption of toxic compounds probably are controllable through a shift in agricultural procedures or food processing, marketing, shipping, and storage practices. These approaches are well-documented and generally recognized as effective ways to eliminate mycotoxin problems. Less often considered is the contribution to control of the problem by changing current production methods.

This Handbook has been designed to afford an effective introduction to, and review of, the complex field of mycotoxicology. We were especially concerned that the research scientist, practicing veterinarian, and physician as well as individuals responsible for the production and safeguarding of our food supply be able to locate readily pertinent information about the subject. The book is therefore organized into sections on mycotoxic fungi, specific toxins, affected animal species, and is extensively cross-referenced.

The Handbook collates information pertaining to the identification and manipula-

tion of mycotoxic fungi, chemistry of toxic compounds, and their physical and chemical properties. Methods of their extraction, isolation, and identification are defined. Metabolism of the toxins and their effect on man, domestic and laboratory animals, poultry, aquatic species, and plants is described. In addition, gross and cellular pathology, as well as possible control or treatment of the diseases they cause, are discussed in detail.

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INTRODUCTION

An association of toxic substances with plants and plant products used for human or animal consumption has been made since biblical times, with ergotism representing one of the first suspected effects of such compounds. In modern times discussions of mold-produced poisons appeared in 1924 concerning Aspergillus toxicity in cattle; in 1931 on stachybotryotoxicosis in horses; in 1936 on Fusarium toxicity and digestive disturbances in swine; in 1940 on moldy corn poisoning in horses; in 1943-44 on alimentary toxic aleukia caused by the consumption of Fusarium contaminated cereals in the U.S.S.R. In 1954, production of clinical and pathologic symptoms of "X disease" in cattle associated with toxic Aspergillus spp. was reported, and in the mid and late 1950s there were reports of disease of cattle and swine caused by feeding moldy corn. Since 1960, when "Turkey X disease" was reported, incriminating aflatoxin in its etiology, numerous studies have been conducted on the nature of the "aflatoxin family" of compounds and the various clinical problems encountered as a result of their consumption. The impact of the discovery of "aflatoxicosis" as a distinct disease syndrome, and the subsequent implication of aflatoxins as potential carcinogens in the human food chain, was felt on an international scale. It rapidly became a matter of great concern to scientists and others interested in the production, manufacturing, and handling of food and feed products, and to livestock and poultry producers. It is considered a potentially major threat to public health. Although research with aflatoxin has received major emphasis and this effort continues, attention has now also turned to other mycotoxins concerning their cause and effect relationship with known disease syndromes or their possible implication in a number of idiopathic diseases. Hence,

the concern for "aflatoxin" and "aflatoxicoses" has become a broader one for "mycotoxins" and "mycotoxicoses."

A wide variety of fungi and fungal metabolites have come under scrutiny. Findings of recent years have far-reaching implications that include not only the quality of food of both plant and animal origin, but also the availability of "clean products." Aspects of this subject were discussed in the recent symposium on mycotoxins during the 1975 Annual Meeting of the American Society for Microbiology and are published in Microbiology - 1975 (edited by David Schlessinger). The influence of "naturally occurring" mycotoxin residues has had a major impact on food industries of the world and is reflected in the controlled movement of some food and feed foodstuffs across international borders. The ultimate concern is that some of the mycotoxins are carcinogenic, and thus human health may be directly threatened. Although emerging and underdeveloped nations of the world may be more concerned with the simple availability of food of any quality, in the United States the concern for a loss of quality in the food supply is reflected in the food additives amendment of the Federal Food, Drug, and Cosmetic Act, Chapter IV, section 402 (a)1. Further deliberations of the zero tolerance policies on possible carcinogens in the food chain likely will depend, at least in the United States, on the sophistication of analytic methods of detection balanced against the wisdom of our scientists and lawmakers to determine reasonable legal limits for mycotoxins in foodstuffs and feedstuffs. Other concerns include the influence of mycotoxins on recreation and conservation interests as some of these substances involve fish and wildlife. Little information is available concerning the potentiation of mycotoxins by other mycotoxins, antibiotics, pesticides, and other environmental pollutants.

It was apparent to us that despite the many scientific reports, monographs, symposia, and textbooks on various aspects of mycotoxins and mycotoxicoses, a need existed to bring together in a single work, current information on a wide range of toxic fungal metabolites, the fungi that produce them, and the resultant diseases they cause. Therefore, our major objective was to organize the Handbook for maximum ease of cross-referencing between the parts devoted to mycology, chemistry of toxins, and the disease syndromes elicited by them. Each contributor was given license to explore a subject as he willed and in his own method of expression, and to assume responsibility for reviewing and citing pertinent literature in his area of expertise. Thus, the uniformity of format would be attained but individual expression by authors would remain. Furthermore, the objective of a complete reference work as well as a practical bench-level guide could be achieved.

ORGANIZATION OF THE HANDBOOK

The Handbook is divided into three volumes:

- Volume 1 Mycotoxic Fungi and Chemistry of Mycotoxins
- Volume 2 Mycotoxicoses of Domestic and Laboratory Animals,
 Poultry, and Aquatic Invertebrates and Vertebrates
- Volume 3 Mycotoxicoses of Man and Plants: Mycotoxin Control
 and Regulatory Practices

(see Contents of this volume and Contents Of Other Volumes for further details).

The Handbook is composed of six parts and supporting subsections that provide ancillary information on concepts and information of a more generalized nature. The first is concerned with mycology. It is designed to acquaint the uninitiated with the characteristics of the mycotoxic fungi. It permits one to determine whether an isolate obtained from suspect feed or foodstuffs could be a mycotoxic form.

Part 1 begins with a comprehensive key to the genera of fungi that have been reported as producers of mycotoxins regardless of their significance in the causation of disorders of animals or man. Therefore, several genera are included that are not widely recognized as "mycotoxic" fungi. The genera covered are illustrated for ease of identification. Subsequent subsections deal with keys to the species of the major "mycotoxic" genera. In general, the authors have made statements about the types of substrate and environmental conditions that favor growth of an organism, production of its characteristic toxins, and the animals affected by them.

Taxonomic treatment of any group of fungi rarely is accepted universally. Usually, the controversies surrounding a particular group are not overly severe. Treatment of the genus Fusarium, however, is another matter. Several attempts have been made to classify the fusaria over the years. Some treatments are cumbersome and difficult to use; other are usable, but oversimplified in the view of many experts. In fact, no single taxonomic treatment is universally accepted today, and we suspect that there will be additional attempts to classify this group of fungi in the future. The treatment used in this Handbook is an attempt to select a middle-of-the-road approach to the fusaria. The treatment is more detailed than the Snyder and Hansen classification which is generally accepted by the plant pathology community. However, in the view of the author of this section, the Snyder and Hansen classification was based primarily on the plant pathogenic properties of the fusaria and not on their mycotoxigenic properties, and therefore we

considered it to be inappropriate for the Handbook. The present treatment allows for a multidisciplined recognition of the fusaria to species as they appear in the international literature, while at the same time allowing those preferring a more simplified taxonomy to utilize the key. All synonymies between the various classifications are included in the detailed description of the species to facilitate recognition by the researcher regardless of taxonomic preference.

With respect to the treatment of the major mycotoxic genera, each genus is keyed to species but no attempt is made to include all species in a given genus. Only those recognized, reported, or suspected of being mycotoxigenic are included.

Part 2 is concerned with the chemistry of mycotoxins. It is designed as both a bench-level guide and as a reference source. Our intention was to assemble specific information on the physical and chemical properties of the toxins, methods of extraction, isolation, purification, and identification and to give full treatment to the biochemistry and physiologic effects of each toxin. Entrance to more in-depth consideration of a topic is provided by very detailed referencing on each subject covered. All references are fully titled for the benefit of the reader in evaluating the pertinence of each individual reference to his interest. This section is organized by toxin, and aside from the chemical information presented, information concerning the fungi involved and the animal species affected is given. The section is fully cross-referenced into Part 1 (Mycology of Mycotoxic Fungi) and Part 3 (Mycotoxicoses) for rapid access to supporting information in those fields.

Part 3 is concerned with the mycotoxicoses. It was specifically designed to offer information about mycotoxicoses to the research scientist, practicing veterinarian and physician, and individuals interested in livestock, poultry, and aquatic animal production. The section is organized by animal species. Part 3, Section 1 presents an overview of diagnostic procedures for mycotoxicoses in animals, followed by Sections 2 through 6 on mycotoxicoses of cattle, sheep, horses, swine, and poultry, respectively. Hence individuals who specialize in given categories of animal species, either in production, disease therapy, or in specific research areas may gain a rapid overview as well as an in-depth insight into the mycotoxicoses that have been reported in that particular species. This section is also cross-referenced to the causal fungi and specific toxins involved.

The subject matter covered by animal species includes information on the path-

ology, clinical symptomatology, occurrence, and potentiating factors and control or treatment for each disease. The study of mycotoxicoses is an emerging science, and there is obviously far more known about some than others. However, in this Handbook we speak to the reported mycotoxicoses and indicate the extent of the knowledge at this time. Some redundancy was unavoidable, but where it occurs, it has been permitted with the intent of allowing each section to stand independently without referring the reader to a wider spectrum of disease or species of animal than necessary.

Part 3, Section 7 represents the major coverage on laboratory animals, although the Handbook contains other discussions by some authors who have specific experience with certain mycotoxins on individual laboratory animal species. The contribution in Section 8 covers the range of available knowledge on mycotoxicoses in the aquatic species, including both vertebrates and invertebrates. It also is organized on a specific species basis with each toxin covered.

Part 3, Sections 9 through 13 deal with mycotoxicoses of man and specific conditions in man known or suspected of being associated with the consumption of mycotoxins. The section is not organized strictly on a "system basis." However, reference is made to the central nervous and digestive systems, i. e., aflatoxicosis and alimentary toxic aleukia; skin, i. e., toxic verrucarins and roridins, sporidesmin, ergotism, stachybotryotoxicosis; cardiovascular system, i. e., cardiac beriberi, and general effects of mycotoxins on vascular permeability; hemic and lymphatic system, i. e., bone marrow depressant effects; urinary system, i. e., possible role of ochratoxins in nephropathies of man. Section 12 speaks to the role of mycotoxins in human pulmonary disease. An introduction to the overall section on human mycotoxicoses covers the dietary and epidemiologic considerations of the mycotoxic problem in humans.

We believe that the diseases described and referenced in the Handbook represent a comprehensive treatment of mycotoxic fungi and mycotoxicoses. We realize that a broader range of idiopathic disease syndromes may be ascribed to the mycotoxins in the future as our knowledge of the fungi, the toxins, and the diseases increase. It is also emphasized that the intent in this work was to deal with the effect of a single mycotoxin on a single species. However, a variety of fungi, producing a variety of compounds, acting in concert, may be involved in the diseases

described herein. Inferences to this effect are made in various chapters of the Handbook where it seemed appropriate. It is further realized that enhancement of mycotoxicoses by other disease organisms, or vice versa, may occur, and evidence of this is beginning to appear in the literature. Studies suggest that some agents may predispose organisms to general debilitating effects and increase susceptibility or sensitivity to disease incited by bacteria, viruses, or toxins.

Part 4 is concerned with the effects of the mycotoxins on higher plants, bacteria, and algae, thus completing the review of the effects of mycotoxins on animal and plant life.

Part 5 is concerned with control procedures for mycotoxic fungi. The growth of these fungi both in the field and in storage is discussed. The manner in which fungal growth and subsequent toxin production can be restricted or inhibited is outlined. Facts related to the utilization or salvage of the product are given. The section briefly summarizes the general concepts alluded to by many of the authors during their discussion of various specific fungi, substrates, and uses, regarding methodology related to their manipulation.

Part 6, the concluding chapter of the Handbook, is devoted to regulatory aspects of the mycotoxin problem in the United States. Mycotoxins currently controlled by law are discussed as well as some indication of where regulation of mycotoxins in food and feedstuffs may be headed in the future.

In summary, we trust that this format has provided an access to the field of mycotoxins for mycologists, plant pathologists, biologists, food scientists, chemists and biochemists, toxicologists, veterinarians, physicians, and others interested in livestock and poultry production and aquatic species. Individuals in various scientific disciplines can refer immediately to their area of interest for information and for rapid guidance to other areas of concern. Supporting sections include procedures for diagnosing a mycotoxicosis, the current concepts of proper storage facilities, of contamination of raw food and feedstuffs by mycotoxins, control and marketing implications, and current legal and FDA regulations concerning mycotoxins in their food supply.

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