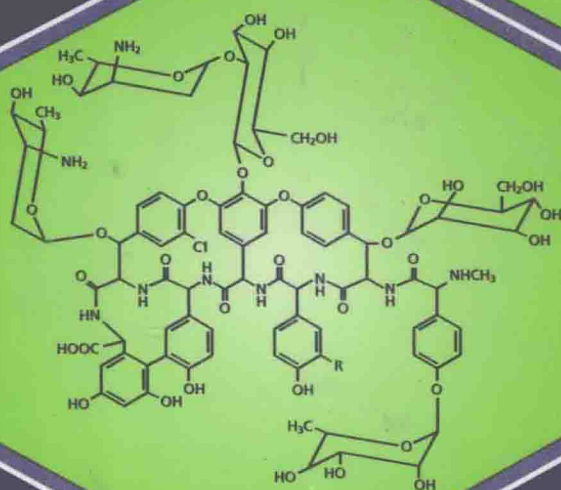


DRUG RESIDUES IN FOODS

*Pharmacology,
Food Safety, and
Analysis*



Nikolaos A. Botsoglou
Dimitrios J. Fletouris

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Σχίσσας την φροντίδα λεπτήν
κατά μικρόν περκρρόνει τα πράγματα,
ορθώς διαίρων καὶ σκοπών.
Κάν απορής τι των νοημάτων,
αφείξ ἀπελθε, καὶ κατὰ την γνώμην πάλιν,
κίνησον αὐθις αὐτό καὶ ζυγώθρισον.

ΑΡΙΣΤΟΦΑΝΗΣ, Νεφέλαι

*Divide your thoughts to small places
and search the things around you one by one,
by dividing in the right way and examining them.
And if you reach a point and you stumble in one of your thoughts,
leave it and go elsewhere, and then back to the same bring your mind,
and re-evaluate it.*

Aristophanes, Nephelae

Preface

As protein needs for the growing world population expand, maximization of animal productivity has become a matter of major concern. Through improved technology, new animal hybrids are being developed, highly productive strains of livestock are being bred, and imported breeds are being introduced into new localities with the sole intention of increasing productivity and quality of animal products. Modern farming systems involving intensive rearing of animals in restricted areas are being optimized so that adequate supplies of food of animal origin for the increasing world population can be produced at reasonable prices.

The rearing conditions of a large number of animals in close confinement and the high stocking densities in intensive aquaculture could hardly be more favorable for the frequent incidence and rapid spread of diseases. Many practices in modern animal husbandry, such as livestock marketing, movement of very young animals, and certain forms of intensification, can further act as trigger factors for the initiation and development of clinical diseases. This has led to an increasing use of a great variety of drugs for therapeutic, preventive, or growth in promoting applications in animal and fish farming.

Drugs, however valuable for increasing food animal productivity they may be, present a concern for public health, considering the potential presence of their residues in the edible products of treated animals. Extra-label or illegal use of sometimes dangerous drugs in food animals are examples of applications that may cause a real health hazard.

Surveillance of animal-derived food for drug residues through toxicological and analytical investigations has stimulated public awareness during the last two decades, and in turn has forced all partners in the food chain and health authorities

to apply control techniques in the various steps of production on the farm and in the slaughterhouse, in food-processing factories, and at sale points.

Currently, extensive research is carried out for an increasingly stringent and better defined interdisciplinary control. Regulatory authorities around the world demand progressively more information, not only on new drugs but also on older and established compounds where re-registration may be required to ensure that up-to-date standards of safety, quality, and efficacy are attained. New analytical methods are being developed for screening, quantification, and confirmation of residues in food as, in parallel with human medicine, innovative drugs are being introduced into animal farming, whereas the detection requirements for the parent drugs and/or their metabolites are frequently changed downward.

The relevant scientific information grows daily. With so extensive a literature, valuable pieces of information on the issue of drug residues in foods are scattered widely throughout the world. This book tries to bring together such information into one compact volume so as to give all the necessary knowledge to anyone who is involved in food production and the control of food safety.

Data are summarized in tables throughout the volume in the same way. An abundance of such material, along with figures and examples, makes this publication a solid reference book. Particular food safety issues—such as the fate of residues during food cooking—that, although important, are rarely considered in literature, are included also in this book. Apart from these unique features, this book seeks to discuss analytical problems in current methodology, giving special emphasis to the more promising screening and confirmatory procedures for routine monitoring of drug residues in foods. Preference is given to recently developed automated multiresidue methods, and attempts are made, where feasible, to provide ideas for better approaches to existing analytical methodology.

The book contains 30 chapters covering topics related to drug residues in foods. It is divided into three parts. The first part, consisting of nine chapters, deals with the drugs potentially used in food-producing animals. Chapter 1 discusses drug usage, and Chapter 2 provides some important pharmacokinetic considerations on the fate of drugs in terrestrial and aquatic species. The next six chapters are dedicated to the most significant groups and sub-groups of drugs potentially used in food-producing animals. All the necessary information on the chemical structures of the parent drugs and their metabolites, dosages and routes of drug administration in the targeted species, and absorption, distribution, biotransformation, and excretion data are fully detailed for a rather high number of individual members within each sub-group. Special emphasis is given to the residue depletion profile of the potentially used drugs and their metabolites in all edible animal products. Chapter 9 discusses benefits versus risks of drug usage in food-producing animals, providing answers to frequently asked questions such as how to address the development of antimicrobial resistance.

The second part deals with the significance and control of drug residues in foods. Chapter 10 discusses the toxicological, pharmacological, technological, and other risks associated with the drug residues present in the edible animal products. Chapters 11 to 13, the reader can find information on the regulatory outlines all over the world, make an approach to the global harmonization issue of the regulatory requirements, and get an idea on the incidence of violative residues in the United States, Canada, Europe, and other countries. Factors of management and/or biological origin involved in food contamination are discussed in Chapter 14. Chapter 15 summarizes the cost of residues in the livestock industry, whereas Chapter 16 deals with the residue avoidance management. Chapter 17 reviews on the stability of residues during food storage, cooking, and processing. Consumer perception and concerns are discussed in Chapter 18.

Starting with a description of the analytical challenge in Chapter 19, the third part, which is devoted to analytical attitudes, proceeds with a detailed description in Chapter 20 of modern sample preparation procedures including solid-phase extraction, matrix solid-phase dispersion, use of restricted-access media, supercritical fluid extraction, and immunoaffinity cleanup. Flexible derivatization techniques including fluorescence, ultraviolet-visible, enzymatic, and photochemical derivatization procedures are presented in Chapter 21.

The next two chapters are dedicated to separation and detection techniques. Principles of liquid chromatography, gas chromatography, thin-layer chromatography, supercritical fluid chromatography, and capillary electrophoresis are reviewed in Chapter 22. Properties of microbiological, immunochemical, and all known physicochemical detection systems are discussed in Chapter 23. Modern confirmation techniques based on coupling chromatographic methods with diode array, mass spectrometric, and infrared spectroscopic detectors are surveyed in Chapter 24, while method validation parameters are examined in Chapter 25. Chapter 26 deals with major quality criteria for selecting an analytical method, interpretation of the analytical results, and strategies for monitoring the food supply for drug residues.

Chapters 27, 28, and 29 of Part III give an overview of all microbiological, immunochemical, and physicochemical methods presently available in the field of drug residue analysis. In addition, the relative advantages and disadvantages of the different methods are assessed. Particular emphasis is given to the most promising methods in terms of simplicity, rapidity, reliability, and applicability, and their analytical features are fully detailed. In the final chapter, future trends in the analysis of drug residues in foods are summarized.

The book is indented neither as a pharmacology text nor as a residues analysis text; tries to bridge that gap. Because so much specialist knowledge is now available, the real challenge is to try to encapsulate this, creating a stimulus and direction for greater in-depth study. Our objective is that the content of this book will serve as an invaluable tool to those with a professional interest in

food safety such as food scientists and technologists, toxicologists, veterinarians, clinicians, food and analytical chemists, biologists and biochemists in state service, private laboratories, academic service, industry, and the regulatory sphere. This book is also intended for use as a primary textbook by those who wish to learn about the feed–animal–food chain contamination as part of their formal education, such as undergraduate, graduate, and postgraduate students. It will also be useful to scientists whose training is not primarily in analytical work but who are faced with the difficult task of analyzing food for drug residues.

We are indebted to all of our colleagues for their assistance with this work. Special appreciation is due to the efficient library service at Aristotle University of Thessaloniki. Finally, a word of thanks to our families for their understanding and constant encouragement to proceed in the face of a large task.

Nikolaos A. Botsoglou
Dimitrios J. Fletuvris

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