Sales of dietary supplements have skyrocketed over the past few years. Despite widespread interest in and use of these products, information about the safety and efficacy of dietary supplements in humans is generally sparse compared with the information available about prescription drugs. Herbalists and laypersons have used herbs for centuries, but most nonherbal dietary supplements came into vogue only within the past few decades, further limiting the information available about these products. The companion volume, Toxicology and Clinical Pharmacology of Herbal Products addressed herbal dietary supplements, whereas Dietary Supplements: Toxicology and Clinical Pharmacology focuses on nonherbal dietary supplements. Supplements were chosen for inclusion based on their popularity, toxicity, and the quantity and quality of information available. Some supplements described here are no longer available as dietary supplements (e.g., gamma-hydroxybutyric acid and related substances, L-tryptophan), but are available through various channels, either legal or illegal. Others are advertised as dietary supplements, although the Food and Drug Administration does not view them as such (e.g., hydrazine sulfate).

The aim of this book is to present, in both comprehensive and summary formats, objective information on nonherbal dietary supplements from the most reliable sources, with an emphasis on information not readily available elsewhere (i.e., detailed descriptions of case reports of adverse effects, pharmacokinetics, and chemical and biofluid analysis). It is not designed to be a prescriber’s handbook; the intended audience is both forensic and health care professionals, particularly researchers and clinicians interested in more detailed information than is available in most “herbal” or “natural product” references.

Although information about dietary supplements is widely available on the Internet, it is usually provided by product distributors and is designed to sell products rather than provide objective information about product efficacy and toxicity. Even reviews of dietary supplements in journals, newsletters, books, and electronic databases can be biased or incorrect. In compiling information to be included in Dietary Supplements: Toxicology and Clinical Pharmacology, emphasis was placed on original studies published in reputable, peer-reviewed journals. Older studies as well as more current literature were utilized for completeness. Where appropriate, information was obtained from meta-analyses, systematic reviews, or other high-quality reviews such as those written by recognized experts. Case reports of adverse effects and interactions, although anecdotal
in nature, were used to identify and describe uncommon, but potentially serious, adverse events that may not have been noted in controlled studies because of small sample size or short duration. The detail in which studies in this section is described is a function of the popularity of the supplement, the extent to which study results conflict with each other and with advertised efficacy claims, the attention recent supplement studies have received in both lay and medical news, and other factors described in the text.

This volume begins with an updated discussion of the legal aspects of dietary supplements. Each of the following supplement monographs includes a review of the product’s history, current promoted uses, sources and chemical composition, and descriptions of available products, which are kept general owing to the myriad of ever-changing products on the market. Product quality is also discussed in this section. For those supplements that are endogenous to humans, the physiologic role is then described. The pharmacologic effects of the products, divided into in vitro/animal data and clinical studies, are reviewed. The in vitro/animal data included were chosen to provide an explanation for the product’s clinical effects in humans and to show the rationale for clinical studies. It should be noted that because of the nature of dietary supplement claims (see Part I, Legal/Regulatory Aspects), some promoted product uses might not have been studied in humans; conversely, known pharmacologic and therapeutic effects might not be promoted commercially. As a result, in most chapters there is a mismatch between the information in the Current Promoted Uses and Clinical Studies sections.

The Pharmacokinetics section covers absorption, tissue distribution, elimination, and body fluid concentrations. Such pharmacokinetic information is not usually included in other sources and may be useful in forensic investigations, or in the clinical setting when the product is used in patients with renal or hepatic insufficiency. A section on Adverse Effects and Toxicity follows, which includes detailed information on case reports of adverse reactions to the supplement. The Interactions section discusses interactions between the supplement and drugs or foods, as well as the effects of drugs on endogenous levels of the supplement if it is an endogenous compound. The Reproduction section is generally limited, owing to lack of information. Methods of Chemical and Biofluid Analysis are included for forensic professionals and for those investigating the product in clinical studies. Each monograph ends with a discussion of Regulatory Status of the product. The amount of information included in each of these sections varies according to availability.

At the end of each monograph is a summary presenting key information in bulleted form. A table at the end of the book summarizes supplement toxicities and adverse effects, drug interactions, and use in special populations (e.g., pregnancy and lactation, renal and hepatic impairment). The source of this information (animal data, in vitro effects, clinical trials, case reports, and theoretical concerns) are given. This section is intended for quick reference, and readers should refer to the chapter for more detailed discussion.

Adverse reactions to dietary supplements appear to be uncommon compared with those attributed to prescription drugs. This may be a function of health care and forensic professionals’ unfamiliarity with a product’s pharmacology and toxicology or assumption that a product is “natural” and therefore safe. Thus, an adverse reaction may go
unrecognized or be attributed to a prescription medication. It is hoped that the information in *Dietary Supplements: Toxicology and Clinical Pharmacology* will be used to solve clinical or forensic problems involving dietary supplements, to promote dialog between health care professionals and patients, and to stimulate intellectual curiosity about these products, fostering further research on their therapeutic and adverse effects.

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