Second Edition

Pharma-Ecology

The Occurrence and Fate of Pharmaceuticals and Personal Care Products in the Environment

Patrick K. Jjemba

WILEY

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Preface

Pharma-ecology aims at studying and minimizing the impact of pharmaceutical and personal care products (PPCPs) on the environment. Personal care products broadly include a number of compounds used in our daily lives ranging from soaps, detergents, perfumes, aftershaves, cleaning agents, disinfectants, sprays, deodorants, and similar products. PPCPs are designed to target our individual ailments, a usage that may inadvertently disregard their effects on the ecosystem. Initial interest in these compounds on nontarget organisms in the environment was expressed in 1965 by E. Stumm-Zollinger and G.M. Fair. However, their concerns about PPCPs went unnoticed until a review by M.I. Richardson and J.M. Bowron was published two decades later. Since then, an exponential number of studies reported the presence of these compounds in the environment, with most reports focusing on the presence of these compounds in various matrices. The first edition published 10 years ago brought some understanding, minimizing the impact of PPCPs on the environment. This edition has incorporated recent advances in this area since the first edition was published. The occurrence and fate of these compounds in the environment is dynamically changing, and the impact of these compounds is undergoing a lot of scrutiny. The second edition updates the readership about this important subject and pursues the continued need to bridge the gap between medicine/public health and environmental science. Each chapter is introduced with key learning objective and ends with a set of review (often) open-ended questions. The latter engages readers about the presented information in each chapter. Both of these additions will be very beneficial for individuals interested in a deeper understanding of pharma-ecology and research opportunities. Those aspirations are helped by an extensive set of key references provided in each chapter.

Chapter 1 introduces the intertwined relationship between our health and the ecosystem. From a historical perspective, it draws interesting parallels between extensive use of agrochemicals (i.e. pesticides, herbicides, fungicides, and fertilizers) under the Green Revolution and increased dependency on PPCPs in relation to environmental degradation. It highlights important

differences in PPCP usage between countries and regions. **Chapter 2** delves into a detailed analysis of the most highly prescribed pharmaceuticals notably antihypertensive, sedatives, and analgesics that have consistently contributed more than 50% of all prescriptions in the United States and other developed countries. **Chapter 3** focuses on the use of antimicrobial agents. Current usage varies between countries indicating differences in patient expectations, attitudes, marketing, and physician practices. Antimicrobial modes of action are examined, and elements of antibiotic resistance presented. **Chapter 4** details the usage of other pharmaceuticals that are individually rarely prescribed but equally important in public health. Their modes of action, bioavailability, and implications for the environment are discussed. **Chapter 5** is devoted to personal care products including fragrances and musks, detergents, and disinfectants. The occurrence and detection of PPCPs in the environment is explored in **Chapter 6**. This chapter is not intended to be a catalog of detection methods and related instrumentation as analytical methods tend to be compound specific. Rather, it summarizes the most important methods such as GC-MS and LC-MS to help the reader understand the advantages and disadvantages of each method, highlighting the general challenges of detecting these chemicals. Related to these analytical methods and challenges, readers are also guided on how to distinguish high quality data from less rigorous monitoring information. **Chapter 7** introduces the principles of pharmacology notably pharmacokinetics and pharmacodynamics designed for deciphering interactions between drugs and living systems and applies them to analyzing the fate of PPCPs in the environment. Ecotoxicity of PPCPs on simple and more complex nontarget organisms using advanced risk assessment approaches is explored in **Chapter 8**. **Chapter 9** focuses on technologies for removing or reducing the impact of PPCPs in the environment. There is a growing interest in this subject in emerging economies including Brazil, South Africa, China, and India as well as well-established European economies in developing regulatory guidelines. The last chapter presents ideas about designing a regulatory framework for limiting emission of PPCPs in the environment, building a more consistent cradle-to-grave approach that appeals to multiple disciplines and stakeholders.

PPCPs are an important and indeed indispensable part of our individual well-being. To that effect, medical professionals are trained to primarily minimize or eliminate our pain and suffering from disease. The book attempts to bridge some of the gaps facilitated by our individualized usage of PPCPs and potential ecotoxicological implications. It is intended for students and scholars in toxicology, ecology, microbiology (mostly environmental), chemistry (including medical chemists), agriculture, and healthcare delivery (i.e. public health, nursing, pharmacy, veterinarians, and physicians) as well as policy makers. Environmentally conscious members of the general public will also find some parts of the book informative. Considering the range of these

seemingly fragmented disciplines, individual readers may be dissatisfied with the level of coverage of one aspect or another, particularly aspects that directly relate to their respective discipline. However, it is my sincere hope that such dissatisfaction can be used to inform stakeholders in other fields, a trend that will truly serve the purpose of advancing this subject.

This edition came to fruition with a lot of patience and technical editorial support for Jonathan Rose, Aruna Pragasam, and Grace Paulin (Wiley Publishing). Dr. Emmanuel F. Ashong, MD graciously provided valuable suggestions about clinical usage of pharmaceuticals and related endpoints. I acknowledge the support and encouragement from my wife, Enid, daughter, Patricia, and sons, Daniel and Eric while writing this book. It is dedicated to my parents Daniel (deceased) and Racheal Kayondo as well as my uncle Bethel Mulondo (deceased) for their love and sacrifices to ensure that we get a decent education.

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1

Usage of Pharmaceutical and Personal Care Products

LEARNING OBJECTIVES

1) Intertwine between human health and the ecosystem based on historical perspectives of environmental degradation.
2) Potential consequences of our increased dependency on extensive PPCP use vis-à-vis lessons from agrochemical (i.e. pesticides, herbicides, fungicides, and fertilizers) usage.
3) PPCP classification for environmental studies.
4) Historical pharmaceutical consumption trends in the United States and other developed countries highlighting global differences.

The human impulse for a cure runs quite deeply, and our first instinct whenever we feel sick or are inclined to sickness is to medicate. As the baby boomers age, so is their increased demand for state-of-the-art medical care. The pharma–patient transaction has transformed itself from the previous practice of selling pharmaceutical products to selling a lifestyle. Amiss from that transformation, however, is the need to appreciate the intertwined relationship between the health of ecological systems and the ecology of health. Both of these concepts collectively refer to the health of humans as determined, at least in part, by the condition of their ecological surroundings. These considerations have led to the emergence of what is referred to as ecosystem health, a science aimed at integrating our desire to assess and monitor ecosystems and health-related problems in a more holistic fashion, environmental degradation, and ecology (Rapport et al. 2001; Jjemba and Robertson 2005). Ecology is the study of the distribution, activities, and interactions of organisms with their habitat. Thus, ecosystem health necessitates the identification and characterization of natural and anthropogenic sources of environmental contaminants that can compromise our health, a need to predict their movement and persistence both in time and space, and determining how pathogens (typically the target of pharmaceuticals) and nontarget organism respond to the presence of such compounds. To

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that effect, pharmaceutical and personal care products (PPCPs) are increasingly being recognized as emerging contaminants in the environment.

Pharmaceutical or pharmaceutical substance in this context refers to the actual active pharmaceutical ingredients. PPCPs are a diverse group of chemicals that include prescription and nonprescription medications, veterinary drugs, nutritional supplements, and diagnostic agents as well as a variety of consumer products such as fragrances, sunscreens, and cosmetics. To that effect, PPCPs are referred to by several other names such as compounds of emerging concern (CECs) or trace organic compounds (TrOC). This book is intended to examine the usage of these chemicals, occurrence in the environment, and ecotoxicity and highlight efforts to minimize their presence (and introduction in the environment) as well as remove them from various matrices in the environment.

Dr. David Kessler, a former US FDA chief, once indicated at a direct-to-consumer (DTC) national conference that the more the pharmaceutical industry wears the public health hat, the more drugs it will ultimately sell. The pharmaceutical industry has traditionally included medical chemists, pharmacists, physicians, nurses, marketing experts, and other public health professionals. Microbiologists and other biologists have had a limited role of examining physiological processes as they relate to disorders, pathogens, and pathogen control, particularly through the use of antibiotics. However, it has traditionally excluded other disciplines such as engineers and ecologists. Over time, the per capita consumption of pharmaceutical compounds and the range of choices have steadily increased. This is especially true in developed countries as more natural and synthetic compounds are discovered. For example, total drug sales in Canada doubled from $6.6 billion in 1996 to $13.8 billion in 2004 (Campbell 2007). Similarly, consumption in the United States steadily grew over time, with over half the population using a prescription drug in a 30-day timeframe. In fact, approximately 20% of the population took three or more prescriptions, and 10% used five or more prescriptions in a 30-day timeframe (Figure 1.1). Separate statistics from the United States also showed increased usage of prescription pharmaceuticals with age (Figure 1.2).

The increase in pharmaceutical use also coincided with the detection of these compounds in the environment. First brought to the attention of the scientific community by the work of Richardson and Bowron (1985), focus on the fate of these compounds did not really catch on until the late 1990s when Halling-Sørensen et al. (1998) and Jørgensen and Halling-Sørensen (2000) published extensive reviews about the issue of drugs in the environment. The consumption of pharmaceutical products is mostly driven through advertising with more and more individuals becoming aware of conditions that were once less noticeable as significant or even of concern. Such consumption is typically not accompanied by basic fundamental questions about:

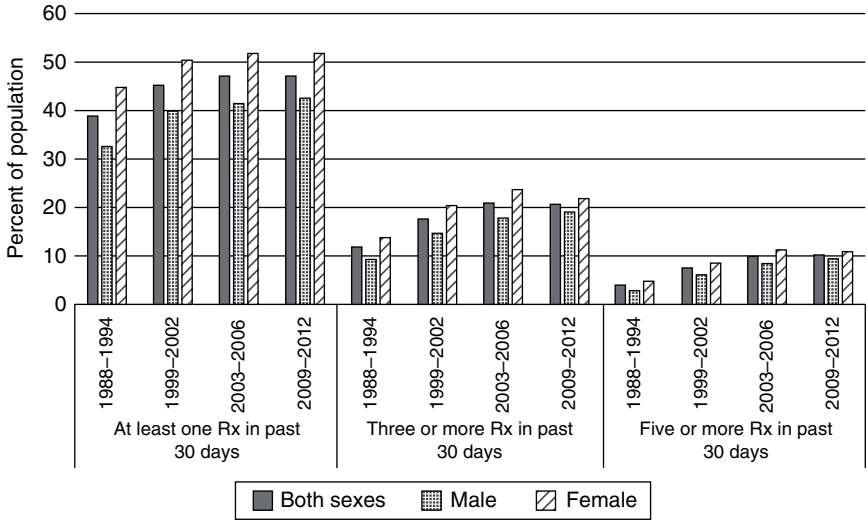

Figure 1.1 Prescription drug use in past 30 days in the United States (1988–2012). *Source:* Data from cdc.gov/nchs/hus/contents2015.htm#080 (accessed 20 March 2016).

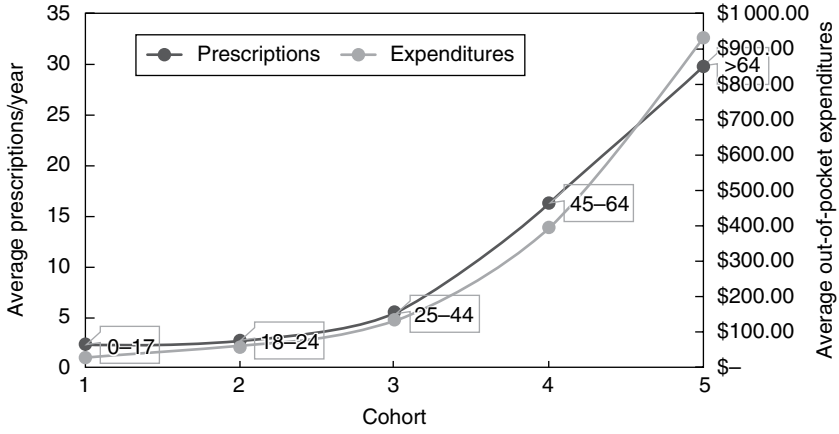

Figure 1.2 Prescription and out-of-pocket expenditure in the United States by cohort. Cohorts 1, 2, 3, 4, and 5 belonged to age groups 0–17, 18–24, 25–44, 45–64, and over 64, respectively. *Source:* Data from Kallaos et al. (2007).

1) How a particular drug is able to achieve what it does to make one feel relieved (i.e. mode of action).
2) How much of the active ingredient that is consumed is actually used to make one feel better or even get cured.
3) If not all of the drug is used by our ailing bodies, what happens to the excess.

A similar complacence prevailed during the early days of the Green Revolution when unlimited quantities of agrochemicals (i.e. pesticides, herbicides, fungicides, and fertilizers) were applied, generating tremendous increases in plant yield. Although those yield increases mitigated world hunger, it ultimately became clear that their continued use without proper precautions could be detrimental to the ecosystem and to our well-being. Those realizations were prompted by celebrated publications such as Rachel Carson's (1962) *Silent Spring*. It is important to realize that PPCPs are not very different from agrochemicals and, in a number of instances, they are actually used in equal (or even higher) quantities than agrochemicals (Hirsch et al. 1999). However, while there are some similarities between PPCPs and other organic pollutants, there are also some dramatic differences. For one, PPCPs tend to be more polar and, in most instances, have acidic or basic functional groups. This attribute poses challenges when it comes to efforts to completely remove PPCPs from the environment once they are introduced and also contributes to the difficulties we face in trying to detect their presence in the environment. Besides being biologically active, PPCPs also have other unique attributes as they:

1) Are typically composed of large chemically complex molecular structures.
2) Have parent neutral compounds that are associated with salts to form polymorphic solid states.
3) Generally have multiple ionizable sites that are spread throughout the molecule.

These attributes enable them to serve their therapeutic purposes but are also important in their fate and impact on the environment as parent, metabolites, or glucuronide moieties. Thus, the lessons learned from other organic pollutants cannot be transplanted wholesale to address issues of PPCPs in the environment.

PPCPs are characterized or classified based on chemical structure, their effects (i.e. mode of action), or their use (i.e. therapeutic purpose). That stated, however, it is important to note that even within those classifications, PPCPs are quite diverse and therefore not expected to have a homogeneous set of characteristics once they get into the environment. This is in contrast to other conventional pollutants such as polyaromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), dioxins, BTEX (i.e. benzene, toluene, ethylbenzene, and xylene), herbicides, and pesticides that are, within each group (or class), not very variable even with a variation in the number of carbons or type of substitutions at a position within the molecular structure. This diversity in PPCPs is very apparent even in classes of compounds that target the same organ and/or are for the same therapeutic use. They are deliberately designed to be biologically very active, which plainly means they have exceptional ability to affect biochemical and physiological functions of biological systems.

However, by the same token, this ability can also divergently affect ecosystems. All of these observations lead us into ecological issues and the need to develop a clear understanding of how various organisms in the environment interact with PPCPs.

The properties of the molecule are important determinants of its biological activity. Thus, specific mode of action that is widely researched during drug development may provide relevant information about likely effects on nontarget organisms in the environment. The primary focus of medical science is, first and foremost, to concentrate on relieving pain and suffering. However, some of the practices currently in place to achieve this noble cause seem to set up a chain reaction that relieves pain to an individual but exposes the ecosystem to even more aggressive or subtle maladies even across generations (i.e. multi-generational exposure). Although not a new concept, making the leap from an individual patient to an ecosystem may seem mind-boggling for a medical practitioner trained to address the issues of individuals as they file through the clinic. However, it is important to remember that a group of individuals (e.g. using a particular antibiotic) of the same species comprise a population. Beyond that, a group of populations in the same locale may be genetically related (e.g. humans and other primates) or unrelated (livestock and earthworms; fish and algae) but can perform a similar function. Populations assemble into a community exploiting the same resources, usually competing for those resources. In that sense, members of a community exert a similar set of functions ultimately comprising a self-sustaining but complex ecosystem. From this brief individual–population–community–ecosystem outlay, it is apparent that linking our understanding of community, culture, and health with ecology requires us to build bridges across disciplines, disciplines that are still mostly quite fragmented and driven by specialization. Building such bridges will enable members of the respective disciplines to appreciate the complexity of issues pertaining to the presence and fate of PPCPs in the environment and to start seriously elucidating whether PPCPs are detrimental in those settings. Considering how important PPCPs are to our well-being, we would collectively need to devise ways of how to deal with such detriments as an informed society. This book attempts to put those issues in the limelight to expand the already increasing interest in this complex subject.

The use of pharmaceuticals has also become an integral part of livestock production. In industrialized countries, livestock, similar to other sectors of agribusiness, involves the maintenance of large flocks or herds in very close quarters, otherwise referred to as confined animal feeding operations (CAFOs) (Figure 1.3). Within the United States, CAFOs are defined as having ≥1000 animal units (US EPA 2000). The country has more than 6600 CAFO units. Such confined conditions can be a prime avenue for the rapid spread of diseases. To minimize disease spread in CAFOs, animal husbandry experts have relied on an increased use of pharmaceuticals to maintain viable livestock.

Figure 1.3 Examples of confined animal feeding operations (CAFOs). Such operations typically rely on subtherapeutic doses of antibiotics and other forms of pharmaceutical compounds to ensure healthy and fast-growing herds or flocks.

Thus, it is a common practice to regularly administer a range of pharmaceuticals including antibiotics, antiacids, anesthetics, antihelminthics, anti-inflammatory steroids, antiparasitic compounds, emetics, estrous synchronizers, growth promoters, sedatives, tranquilizers, insecticides (against ticks and flies), and nutritional supplements to the livestock. Most commonly used in livestock management are antibiotics for specific therapeutic and subtherapeutic reasons (Table 1.1). A number of these products may be administered to the herd or flock for relatively long durations, whereas some are used occasionally. Currently, data about the quantities of antibiotics used in livestock production in various countries are not systematically collected in a standardized fashion. Thus, Jensen (2001) estimated 150 000 kg of antibiotics was used in Denmark in 1997, of which more than 100 000 kg was primarily used as growth promoters. The Animal Health Institute estimated 9.3 million kilograms of antibiotics was used in the United States, of which only 1.3 million kilograms was for nontherapeutic purposes (AHI 2002). More recently, Hollis and Ahmed (2013) reported 13.5 million kilograms of antibiotics used in the US livestock compared with 3.75 million kilograms for human consumption. About 70% of US livestock use is for nontherapeutic purposes (UCS 2001).

Table 1.1 Pharmaceutical and growth promoters routinely used in the livestock industry.

Livestock	Product	Purpose
Poultry	Coccidiostats such as monensin, lasalocids, salinomycin, and narasin	Antiprotozoals and antibiotics to guard against coccidiosis. These ionophores are also used in cattle and swine as growth promoters. They generally have a different mode of action compared with other antibiotics
	Arsenical, e.g. roxarsone and arsanilic acid	Improve growth performance and bird pigmentation
	Antibiotics such as tylosin, bacitracin, and virginiamycin	Control bacterial infection and improve feed consumption, leading to large/heavier birds
Swine	Antibiotics such as apramycin, tylosin, bacitracin, carbadox, olaquindox, tiamulin, and avoparcin	Control enteritis, dysentery, and colibacillosis. Also generally improves growth possibly due to better feed consumption. Avoparcin has also been used in cattle and poultry, but it has been banned in the EU and Australia
Cattle	Hormones such as estradiol, testosterone, and progesterone. Active ingredients include zeranol, melengestrol acetate, and trenbolone acetate	Used in the beef industry to increase the rate of weight gain and feed use efficiency. Some of these are applied in the feedstuff, as suppositories or as implantable pellets (subcutaneously)
	Hormones such as bovine somatotrophin (BST)	Improve milk production in dairy
	Long-term antibiotics such as tylosin	Control liver abscesses
	Short-term antibiotics such as tetracycline, sulfamethazine, and oxytetracycline	Used periodically to control/prevent bacterial infections
	Antihelminthics such as ivermectins and fenbendazole	To control parasites
	Lactams such as amoxicillin, cyclosporine, erythromycin, novobiocin, penicillin, etc.	Treatment of mastitis, a major infection that can cripple the dairy industry
	Nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, meloxicam (Metacam), ketoprofen, etc.	A variety of veterinary ailments such as pain including the pain exerted by mastitis. Also used in other domestic animals including pigs and dogs
Aquaculture	Antibiotics such as sulfadimethoxine, ormethoprim, and oxytetracycline	Applied to the water or as part of the feedstuff for fish, shrimp, and shellfish. Some are applied by injecting individual animals
	Tricaine methanesulfonate	Used in fish as a chorionic gonadotropin to enhance spawning. Applied intramuscularly, i.e. as an injectable
Apiary (beekeeping)	Oxytetracycline (Terramycin), tylosin, and lincomycin	Used to control foulbrood larva disease caused by *Paenibacillus larvae* in honey bees

Reports indicate that tylosin, tetracycline, and bacitracin are three of the most used antibiotics in livestock production within the United States (Sarmah et al. 2006). The macrolide tylosin is a broad-spectrum antibiotic with excellent antibacterial activity against most Gram-positive (including *Mycobacterium* sp.) and some Gram-negative bacteria, vibrios, coccidian, and spirochete. *In vitro*, it acts by inhibiting the synthesis of proteins as it binds on the ribosomes (McGuire et al. 1961; Weisblum 1995). It consists of mainly tylosin A, which comprises approximately 80–90% together with three other constituents, i.e. tylosin B (desmycosin), tylosin C (microcin), and tylosin D (relomycin), on a 16-membered lactone ring attached to an amino sugar (mycaminose) and two neutral sugars called mycarose and mycinose (McGuire et al. 1961). It is very stable at neutral pH but becomes very unstable under acidic or alkaline conditions. This attribute may have very significant effects on its stability in the environment. It targets the 50S ribosomal subunit, inhibiting the transcription and eventually leading to death of the cell (Retsema and Fu 2001). More than 634 million poultry were exposed to macrolides such as tylosin and tilmicosin in the United States annually (Hurd et al. 2004).

Sulfonamides are widely used in human and livestock against Gram-positive and some Gram-negative pathogens. In livestock, they are in some instances used at prophylactic levels to prevent disease outbreaks. In fact, sulfonamides are some of the most widely used antibiotics in the livestock industry. Their attributes and mode of action will be more extensively discussed in Chapter 3. They are excreted as parent compound or acetic acid conjugates, which eventually revert to the parent compound. Bacitracin is a polypeptide antibiotic that is commonly added to livestock (i.e. chicken, turkey, cattle, swine) feedstock. It is very soluble in water and has a high molecular weight. Similarly, the β-lactam moenomycin A is also widely used as a growth promoter in livestock feed.

In general, these drugs are administered to the livestock through water and foodstuff although some may be injected, applied in dips, or used during spraying events. They are administered to individual animals or to the entire herd. In the United States, some of the antibiotics are approved for use in livestock for the treatment and prevention of diseases, whereas others are approved for use as growth promoters. For example, virginiamycin was approved for use in cattle, turkeys, swine, and chickens primarily as a growth promoter and prevention or control of diseases. It was licensed for use in the US livestock industry in 1975. The wide use of this specific compound has raised concern in some circles as it is very similar to other streptogramins such as Synercid (see Chapter 3), which are dependable antibiotics used against enterococcal infections (Werner et al. 1998; Claycamp and Hooberman 2004). Such transfer of resistance is possible as animal-derived-resistant enterococci may colonize humans directly when humans interact with animals (e.g. farm workers), consume tainted animal products, or consume other farm produce that have had

contact with animal products such as improperly treated animal manure (Landers et al. 2012). Enterococci are otherwise part of the normal human enteric microflora, although they occur in low abundance (i.e. <1% of the enteric bacterial population). They are also widely distributed in other animals and a common contaminant on mishandled foods. They are an important causative agent of nosocomial infections (Murray 1997; Witte 2001).

The exact mechanisms of how pharmaceuticals, especially antibiotics, exert growth promotion attributes in livestock are not clearly known, but it is suspected that the antibiotics control minor infections that do not make the animals sick, ultimately increasing feed utilization (Ferber 2003). In practice, most of the antibiotics are used for both therapeutic and subtherapeutic (i.e. growth promotion) purposes although the latter use may be more predominant (Jin 1997; Mitema et al. 2001). In the European Union, the nontherapeutic use of most antibiotics for agriculture was banned, with the exception of avilamycin, monensin, flavophospholipol, and salinomycin (Kümmerer 2004). These four were spared from the ban because they were deemed significantly different from compounds used in human health.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have also been used in livestock, particularly in Southern Asia (Oaks et al. 2004; Cuthbert et al. 2006; Swan et al. 2006). Whether for livestock or human needs, the usage of pharmaceutical compounds in most developing countries is even harder to track precisely as some pharmaceuticals typically available through prescription only (e.g. most antibiotics) can be easily obtained over the counter without a prescription in developing countries (WHO 2001).

Some antibiotics are also used in horticulture to control contamination of micropropagation, in plant tissue culture, and in controlling bacterial diseases of fruit trees (Levy 1992; Falkiner 1998; Hollis and Ahmed 2013). Commonly used in horticulture are cephalosporins, neomycin, novobiocin, polymyxin, and sulfaguanidine. More than 20 tons of streptomycin and tetracycline are used by the horticulture industry in the United States per annum. Substantial amounts of antibiotics are also used in aquaculture. They are either directly added to the water (therapy) or as part of the feed, resulting in high concentrations in the water and adjoining sediments. An examination of the levels of use of various PPCPs for various purposes is outlined below.

1.1 Pharmaceutical Consumption Trends

Accurate statistics about the production and consumption of the individual pharmaceutical compounds are not readily available because of privacy and industry competition issues. However, some crude estimates can be based on the number of prescriptions. For example, in the United States, which uses more than half of the world's medications, the most dispensed 200 drugs

registered 2.13, 2.82, and 2.32 billion prescriptions in 2003, 2004, and 2005, respectively. Based on those statistics, antihypertensive and cardiovascular drugs were the most prescribed, contributing 26–27% of the prescriptions for the top 200 most prescribed drugs (Figure 1.4). Sedatives, hypnotics, and antipsychotic drugs ranked second (19–23% of the top 200 most prescribed drugs), followed by analgesics and anti-inflammatory agents (14–15%) and antimicrobial agents (10–11%). As a parallel comparison, antihypertensive and cardiovascular drugs as well as antipsychotic drugs were the three most frequently purchased drugs in Canada in 2004, collectively accounting for 54% of the expenditure on prescription medicine in the country (Morgan et al. 2005). In subsequent monitoring, antihypertensives, antidepressants, and cholesterol-lowering drug topped the prescription volumes; accounting for 32.7% of the total prescriptions in 2012 (Morgan et al. 2013). In the United States, 110–140 million (i.e. 5–6% of the top 200 prescriptions) gastrointestinal medication prescriptions were dispensed between 2003 and 2005. Through that same duration, 2.5–4.3% of the prescriptions were medications used mostly for respiratory infections (2.5–3.6%), oral contraceptive and reproductive therapy (2.5–4.3%), thyroid hormones (2.9–3.5%), diuretics and electrolytes (3.9–4.1%), or antidiabetics (3.3–4.2%) (Figure 1.4).

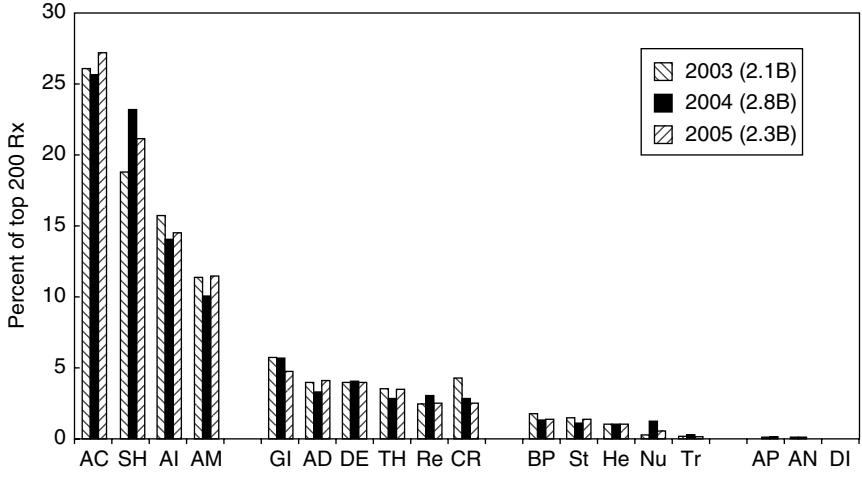

Figure 1.4 The percentage of drugs prescribed in the United States for 2003–2005 as a fraction of the top 200 most prescribed drugs. Note that the total of the top 200 most prescribed were 2.1, 2.8, and 2.3 billion for 2003, 2004, and 2005, respectively. AC, antihypertensive/cardiovascular medication; SH, sedatives/antipsychotics; AI, analgesics/anti-inflammatory; AM, antimicrobial; GI, gastrointestinal; AD, antidiabetic; DE, diuretics/electrolytes; TH, thyroid drugs; Re, respiratory; CR, contraceptives/reproductive therapy; BP, biophosphonates and other anti-bone loss; St, steroids; He, hematology; Nu, nutritional; Tr, triptan; AP, antineoplastics; AN, anesthetics; and DI, dopaminergics and immunomodulators.

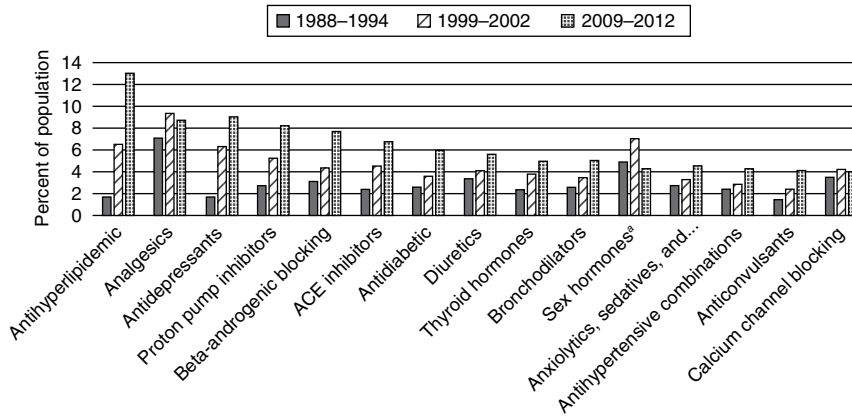

Figure 1.5 Selected prescription drug classes used in past 30 days in the United States (1988–2012). *a*Percent provided by CDC for sex hormones was only for females. Since they are approximately half of the population, it was halved and expressed on per total population basis. Source: Data from cdc.gov/nchs/hus/contents2015.htm#080 (accessed 20 March 2016).

Other key prescriptions belonged to biophosphonates and anti-bone loss (1–1.4%), steroids (1–1.5%), hematology (1%), and nutritional (0.2–1.2%) categories. Antineoplastics, dopaminergics and immunomodulators, anesthetics, and triptans were least prescribed among the leading 200 prescriptions during those three years. For various reasons, recent consumption data since 2005 have become harder to compile, but the CDC recently summarized prescription of selected pharmaceuticals in the United States between 1988 and 2012 (Figure 1.5).

Significantly missing from the CDC compilation are antibiotics and other less frequently prescribed but important pharmaceuticals such as biophosphonates, triptans, anesthetics, immunomodulators, and nutritional and hematology drugs. For convenience, the trends compiled from 2003 to 2005 (Figure 1.4) have been used to categorize pharmaceuticals in highly prescribed (Chapter 2), antimicrobial (Chapter 3), and other pharmaceutical groups (Chapter 4) as a basis for examining their usage and cursory examination of their modes of action. To complete the picture, Chapter 5 is devoted to personal care products of environmental concern.

Study Questions

1 List known common drivers of the increased use of PPCPs in developed countries.

2 Can you elaborate how individual use of PPCPs can have ecosystem ramifications?

3 What are some of the common pharmaceutical used in agriculture and livestock management and for what reason?

4 In the absence of hard sales numbers, what alternative methods can be used to estimate pharmaceutical consumption?

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