

Preface

I realize that this book will create a great deal of controversy. It has never been easy to challenge the consensus because the System - of any kind, in any context - will try to preserve the *status quo*, by all means possible. Having spent 37 years in the field of organic, organometallic, computational, and medicinal chemistry, and having published 77 papers, including 7 reviews and book chapters on different aspects of radical chemistry, I feel obliged to share my knowledge, analyses, and conclusions. Hopefully, this account will raise the level of awareness among the general public and initiate the discussion that, in turn, may entail major cultural changes, as well as a revision of the consumer basket. The beneficiaries will be all of us - ourselves, our children, our beloved ones, the society, as a whole - who will live a healthier, and longer, life. I would like the food consumption to be not a routine procedure for gaining nutrients that the body needs, but a science-based process with complete predictability of its overall impact and fate of every food component entering the human body.

This book can be read on two different levels. First, it may be read by ordinary people with a limited, if any, scientific background. Throughout, the book has been written with this audience in mind. At times, the science presented might seem overwhelming: busy schemes with multiple structures, electrons

movements, charges, and intimidating chemical names. I hope that you won't be easily discouraged. Even if the chemical content of a given chapter is hard to understand, the scientific evidence presented, the citations from original documents, conclusions drawn, and recommendations made can be easily comprehended. Some chapters, such as 5 - 8, 12, and 13, are very light in chemistry and can be easily understood by a layperson. One of the important features of this book is that it does not have a textbook structure when the chapters, in order to be understood, need to be read in the sequence given. In fact, you can start the journey from any chapter, based on your interests, tastes, and preferences.

The second group of readers will be represented by professionals from the food industry, academia, and government agencies, as well as consumer protection and advocacy groups. I do not expect everybody in the scientific community to agree with the content and ideas put forth in this book. But I do hope that the information and knowledge presented will become a wake-up call for the general public, regulatory agencies, legislators, business leaders, and scientists coming to the realization that the current state of affairs is not satisfactory, to say the least, and it needs to be fixed - urgently.

The book comprises thirteen chapters. Chapter 1 is a general introduction to the chemistry and biology of antioxidants used in the food industry. Chapter 2 presents the enzymes located in the alimentary canal and explains, step by step,

what kind of chemical transformations are possible when organic compounds enter the human body. Chapter 3 introduces the concept of an “antioxidant,” provides an explanation why phenol is a problematic compound, and how the antioxidants work to preserve the body systems from oxygen-centered radicals. Chapter 4 introduces a “hazardous drug” oxymoron, along with an ongoing saga on Bisphenol A. Chapter 5 is critical for the overall understanding since it explains why the word “natural” is not synonymous with “safe” and “benign.” Chapter 6 compiles the known procedures for evaluating antioxidants and comments on their validity and transferability. Chapter 7 might be quite shocking for an unsuspecting reader, providing examples of much touted antioxidants that happened to also be carcinogens! Chapter 8 is critical from a conceptual standpoint: mistakes are continuously made, and people get hurt even when there is enough scientific evidence that could be used in order to adequately protect the general public. Chapter 9 is a cross-section of the consumer basket discussing items of immediate relevance to our everyday life. I sense that some conclusions made will be quite disappointing to heavy coffee, tea, and wine drinkers, but, in the long run, everybody will benefit from an acquired knowledge and modified habits. Chapter 10 deals with perils of cosmetics by using, as representative samples, some selected products, such as hair color and sunscreen lotion. Chapter 11 introduces another problematic compound, benzene, along with more complex, and more dangerous, aromatic structures called *Polynuclear Aromatic Hydrocarbons (PAH)*. Chapter 12 sets forth a conceptually new theory according to which food products should be totally free

of phenolic and benzenoid compounds. Lastly, Chapter 13 concludes with comments of a general nature to further underscore an inadequacy of the current state of affairs and the urgency of the changes proposed.

I hope this book is widely read. If we are to avoid the blunders of the past, then we need to change the direction and start benefiting from the knowledge base created by the scientists. We did not have this chance a decade ago. Now is the right time.

Chapter 5

The Concept of “Naturalness”: Is “Natural” Synonymous with “Good” and “Harmless”?

One of the major misconceptions the public has, and continuously suffers from, is the concept of “naturalness.” Being “natural” is often perceived as being healthy and good for the human body. In public consciousness, the term “natural” is nearly synonymous with being beneficial for health. In public debates, when people run out of arguments, they tend to say, “It is natural!” as the end point of a discussion, as the strongest argument in dispute, and as the last proof given in rebuttal. Let us carefully consider “naturalness” to better understand why, in fact, we should be concerned about current perceptions and attitudes.

The term “natural” means that the compound in question was isolated from its natural source. It can be of plant, animal, or mineral origin. Over the decades, the public was fed stories that *synthetic compounds* are evil and foreign to the

human body. And because of their very nature, they are not compatible with a natural subject, the human body.

Now let us look at the origin of, say, plant-derived compounds. Evolution has placed them in roots, stems, and leaves of plants for various reasons. They can play an important role in the chemical communication between plants and animals, or they can be the constituent parts of the defense mechanisms evolved over the centuries. They can also be intermediate compounds in the complex biosynthetic pathways, or metabolites of the plant enzymatic system. There are literally *hundreds of compounds isolated from plants that cannot be found in the human body. So, these natural compounds are as foreign to the human body as any other organic compound synthesized in the laboratory.* The mere fact that the structure is present in the plant, a natural subject, does not automatically make it benign to any other natural subject, such as the human body. And the public should not let their guard down as soon as they hear the words “plant” or “natural.”

The “natural” hype is created by the media, unscrupulous scientists, and manufacturers who have tremendously benefited from selling plant- and animal-derived products, such as food or herbal supplements. In 1996, total sales of such products amounted to \$12.2 billion, while in 2006, it reached a whopping \$22.3 billion! To convince the potential buyer that their advertisements are valid, companies often include references to ancient medical books. It is true that some

sources, such as Chinese and Indian folk volumes contain prescriptions describing how to treat wounds and how to cure diseases. How valid are these claims and to what extent should we trust them? Ancient folk, hundreds and thousands of years ago, in any part of the globe, did not have very many tools in their possession. There was no science, no understanding of biochemical processes on a molecular level, no theory of atom structure, no theory of chemical bonding, and no methods for structural elucidation. The list can go on and on. All major scientific theories, laws, and methods were discovered much later, in the 19th and, mostly, 20th centuries. At the time, what people had available to them were just natural materials, i.e., plants, animals, and minerals. Understandably, by seeing that their compatriots were dying from diseases and wounds, they tried to apply extracts of natural origin in order to help the human race survive. The outcome of those early experiments on humans is documented in various folk medical books.

Now I would like you to decide how valid those claims can probably be. How were the results of the treatments judged? By what scientific criteria? What was the qualification of people, as medical professionals and scientists, feeding this information to the writers of those “medical” books? Were there any toxicological studies carried out to fully evaluate an interaction of the natural extract with body systems? Was any follow-up research carried out to find out what happened to those patients years later? Maybe the wound healed, but the person died in six months from a cancer-like disease. Were the studies randomized? Were the data

statistically valid? Were any epidemiological studies carried out? The answers to all these questions are NO! And for an obvious reason: because the whole scientific disciplines were not even in existence at the time and people were just doing their best to save their loved ones. Should we follow their footsteps today, in the 21st century?

To further emphasize that “natural” is not synonymous with “good” and “benign,” let us consider compounds which are natural, but are known to be toxic to humans. For example, the venom secreted by snakes, spiders, and bees. Evolution has placed these complex organic, organometallic, and inorganic mixtures into the bodies of these creatures for good reasons; for example, to protect themselves, to decapacitate the prey, or to feed their offspring. Today, the structures of many venom components have been established by using a totality of modern instrumentation available to scientists. It has even become an emerging interdisciplinary field - at the interface of organic, medicinal, analytical, and computational chemistries - directed at drug development. Or, consider the toxins isolated from marine organisms. Many of them have highly sophisticated chemical structures, but the power of modern chemistry has allowed not only to establish the structures of the natural molecules, but also to synthesize them in the organic laboratory. Venoms and toxins are just two examples among many. They are “natural,” but why don’t we see any advertisements, on TV or in print, suggesting that we all take a drop, or two, of snake venom before going to bed? The answer is: “Because it kills too fast.”

Then where is the logic? When it is natural and it kills too fast, we do not advertise it. But, when it is natural and it does not kill fast, then we worship its “naturalness” and try to sell it for a profit. If we are so much misled, and disoriented, that the word “natural” has become synonymous with “credible,” then why don’t we ask the public to go around and eat grass and leaves in the city streets and parks? Maybe it is just too early. Maybe a bit later, down the road, when the public will become completely brainwashed and ready for the next “discovery,” then it will be the next big thing to watch on TV. Of course, there will be supporting references to some ancient books that would have originated from Third World countries, sometimes unrecognizable by the general public. Paradoxically, it “works” well in a country with a highly advanced scientific culture, federal institutions, technological infrastructure, and an educated populace!

The credibility of natural compounds, as inherently harmless, is further damaged by the fact that they are heavily represented in the list of human carcinogens prepared by the authoritative International Agency for Research on Cancer (IARC).¹ According to the current selection system, the carcinogens are carefully evaluated based on human and animal data, mechanistic and other relevant information, and are grouped into several major categories: Groups 1, 2A, 2B. Summarized below are the group numbers, their IARC definitions, and the names of natural compounds.

IARC Group 1. *Carcinogenic to humans.*

Asbestos (magnesium silicate; *Chrysotile*, a fibrous variety);
Beryllium (chemical element) and beryllium compounds;
Cadmium (chemical element) and beryllium compounds;
Estrogens, steroidal (female hormones);
Nickel (chemical element) compounds;
Silica (quartz or cristobalite);
Solar radiation;
Aflatoxins (isolated from marine organisms);
Areca nut (fruit of a palm tree *Areca catechu*);
Betel quid (with/without tobacco);
Herbal remedies containing plant species of the genus *Aristolochia*;
Shale oil (a crude dark oil obtained from shale by heating);
Salted fish (Chinese-style);
Wood dust.

IARC Group 2A. *Probably carcinogenic to humans.*

Androgens (male hormones);
Adriamycin (from *Streptomyces peucetius*);
Aristolochic acids;
Lead (chemical element) compounds;
Creosotes (wood distillate).

IARC Group 2B. Possibly carcinogenic to humans.

Caffeic acid (from coffee seeds);

Cycasin (from *Cycas revoluta*);

Daunomycin (from *Streptomyces peucetius*);

Fumonisin B1 (from *Fusarium moniliforme*);

Lead (chemical element);

Mitomycin C (from *Streptomyces caespitosus*);

Monocrotaline (natural alkaloid);

Ochratoxin A (from *Aspergillus ochraceus*);

Safrole (from essential oils, such as *sassafras*);

Sterigmatocystin (from mold *Aspergillus versicolor*; *A. nidulans*).

The current format does not allow for a detailed analysis of each and every compound, or groups of compounds, present. But the sheer volume of this purely representative list indicates that the natural compounds are abundantly present in all three categories (IARC: Groups 1, 2A 2B), ranging from household names, such as asbestos, lead, coffee, and estrogen, to more exotic *afatoxins*, *safrole*, and *sterigmatocystin*. The message for the unsuspecting public is that *natural compounds of very different origins can be carcinogenic*. Among them are minerals (*asbestos*, *silica*), plants (palm tree, herbs), molds (*Sterigmatocystin*), essential oils (*Safrole*), bacteria (*Mitomycin C*), rocks (shale oil), and chemical elements (Be, Cd, Ni, Pb).

Natural compounds are widely present in the list of chemicals compiled by the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (EPA).² The measure was first enacted as a ballot initiative in November 1986, and later on, it became universally known as the “Safe Drinking Water and Toxic Enforcement Act of 1986,” or just Proposition 65.² It requires the Governor of California to publish, at least annually, a list of chemicals known to the State to cause cancer or reproductive toxicity.

While many compounds are duplicates of those present in the IARC list, the representative data from California’s OEHHA list are shown below in a different format. First, there is no grouping according to the *level of proven carcinogenicity*, as that in the IARC list (*Carcinogenic to humans; Probably, and Possibly carcinogenic to humans*).¹ Second, the date when a given natural compound was first introduced is reported, providing us with a better feel as to how long a given compound is known, to the State and to the scientific community, to be really “bad.”

OEHHA list: Compounds derived from plants.

- (1) Aflatoxins (date listed: January 1, 1988);
- (2) Areca nut (date listed: February 3, 2006);
- (3) Herbal remedies (*Aristolochia*) (date listed: July 9, 2004);

- (4) Betel quid with tobacco (date listed: January 1, 1990);
- (5) Betel quid without tobacco (date listed: February 3, 2006);
- (6) Mitomycin C (*Streptomyces caespitosus*) (date listed: April 1, 1988).

OEHHA list: Compounds derived from wood and natural minerals.

- (7) Carbon black (coal mines) (date listed: February 21, 2003);
- (8) Coke oven emissions (coal distillate) (date listed: February 27, 1987);
- (9) Creosotes (wood distillate) (date listed: October 1, 1988);
- (10) Shale oils (date listed: April 1, 1990);
- (11) Asbestos (magnesium silicate; *Chrysotile*) (date listed: February 27, 1987);
- (12) Silica, crystalline (date listed: October 1, 1988).

OEHHA list: Compounds isolated from humans.

- (13) 17 β -Estradiol (female hormone) (date listed: January 1, 1988);
- (14) Estrone (female hormone) (date listed: January 1, 1988);
- (15) Testosterone (male hormone) (date listed: April 1, 1988);
- (16) Progesterone (natural hormone) (date listed: January 1, 1988).

OEHHA list: Chemical elements.

- (17) Lead and lead salts (date listed: 1987-1992);
- (18) Nickel and nickel compounds (date listed: 1987-2004);
- (19) Arsenic and arsenic compounds (date listed: 1987, 1997).

OEHHA list: Beverages.

(20) Caffeic acid (from coffee seeds) (date listed: October 1, 1994).

There are already wake-up calls for the general public. Following years of uncontrollable use of herbal supplements, finally, in 2004, the U.S. Food and Drug Administration (FDA) stepped in and banned *ephedra*, a Chinese weight-loss herb linked to a number of deaths. In 2002, the FDA released a warning about potential liver damage from the *kava root*, one of the most popular herbal supplements sold in the country. But this is just a tip of the iceberg! People who are on “legitimate” medication do not often realize that there is a compatibility issue between a prescribed medication and tens, or even hundreds, of organic compounds present in the herbal supplement. *Drug compatibility* is a factor carefully, and professionally, studied by physicians and pharmacists before any drug is released into the market, and also in post-market tests. Unfortunately, some people, while buying a prescribed medicine do not even disclose the nature of the supplements taken by them, either occasionally or on a regular basis. And this can be the reason for allergies, severe complications, drug inefficiency, or even a patient’s death.

The take-home lessons from this chapter are the following. First, the word “natural” is not a synonym for “safe.” The consumption of chemical compounds synthesized, over the centuries, in Mother Nature’s laboratory can be as

detrimental as exposure to any other “synthetic” compound. Second, please EDUCATE yourself, and QUESTION each and every advertisement on natural products that you see on TV, or find in your mailbox.

The chemistry of natural products is a very important part of organic chemistry, and it has been around for many decades. I am fully supportive of this research, but only when the research is conducted by qualified professionals on the highest level possible, and the results are not overinterpreted, or misrepresented. There is a cultural gap between the academic and corporate worlds. In academia, the scientists consider it their civic duty to use their professional knowledge, expertise, and every resource at their disposal, to inform, educate, and protect the general public. In contrast, the corporate world, by its very definition, has different values, objectives, and frame of references.

Bibliography

- [1] <http://www.iarc.fr/>.
- [2] <http://www.oehha.org/prop65/>.