Coffee is one of the most beloved beverages in the world, making it the second most globally traded commodity (just behind crude oil). The conventional notion that drinking coffee might be detrimental to human health derives from studies carried out in the 1950s and 1960s. This research failed to account for cigarette smoking which, as was discovered later, confounded and masked coffee’s benefits. Since then, and especially since the new millennium, research evidence for coffee’s health benefits has mounted significantly. More and more large and long-term studies have demonstrated that coffee offers protection against type 2 diabetes, assorted cancers, and neurodegenerative diseases including Parkinson’s and Alzheimer’s diseases.

Coffee: Emerging Health Effects and Disease Prevention is the first book to present a contemporary and comprehensive summary of the newly-understood bioactive effects of the many compounds in coffee. The breadth and depth of coverage is extensive and balanced, focusing on the following topics: coffee constituents and their bioavailability; pro- and antioxidant properties; the health benefits and disease prevention effects of coffee; and potential negative health impacts. Multiple chapters describe coffee’s positive impacts on health and various diseases, including type 2 diabetes, neurodegenerative diseases, cancer and cardiovascular and liver diseases. Coffee’s positive effects on mood, suicide rate and cognitive performance are addressed, as are the negative health impacts of coffee on pregnancy, insulin sensitivity, dehydration, gastric irritation, anxiety, and withdrawal syndrome issues.

Written by many of the top researchers in the world, this volume is a must-have reference for food professionals in academia, industry, and governmental & regulatory agencies whose work involves coffee.

The Editor
Dr Yi-Fang Chu was Head of the Global Coffee Wellness Research Group at Kraft Foods Global Inc., Glensview, Illinois, USA. He is currently with PepsiCo Global Nutrition, Barrington, Illinois.

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Coffee
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Coffee is a drink of acuity, of precision, of intellect. To truly understand this drink, one has to go back in time. Coffee was discovered in Ethiopia and brought to the Arab region in the sixteenth century. At that time in history, the Arab civilization was carrying the world forward. For example, they invented zero, which gave to the world elegant solutions to mathematical problems. It is no surprise that the region became fascinated with coffee, a drink that stimulated its penchant for precision and intellect.

Coffee was brought to Western Europe in the seventeenth century. At that time, most of Europe was often mildly drunk. Why? Because if you lived in London or Paris, you could not drink water from various sources without worries about water-borne diseases. Instead of a coffee break at 10 o’clock in the morning, people would have a “beer break.” Paintings and literature from that era depict people’s amusingly besotted behaviors throughout the whole day. Coffee drinking slowly replaced this practice. As the industrial revolution started to take shape in that region, workers simply could not afford to be drunk while operating heavy industrial machines. Coffee was the perfect solution to help fuel the revolution. Work and coffee grew inseparable in the modern age. Perhaps coffee makes the age possible at all. Now as we have moved into the twenty-first century, coffee is the world’s most popular drink after water. It is a daily comfort to millions and a necessity to many more.

In consumers’ minds, coffee is also often considered a guilty pleasure. At the turn of the twenty-first century, scientific tools started to become powerful enough to enable the discovery of what was previously deemed undiscoverable. Surprisingly, consumption of this indulgent drink began to show links to positive health impacts. As scientists continue to dig deeper, reports of good news about coffee constantly outweigh negative or neutral findings. In this book, we summarize the evolving state of the science related to coffee’s health implications.

This book is divided into three main parts: (i) background and chemistry in Chapters 1–3, (ii) potential benefits in Chapters 4–13, and (iii) potential concerns in Chapters 14–18. We aim to be fair, objective, and evidence based. We are blessed with terrific contributions from a diverse group of experts from 12 different coffee-loving countries. Our ultimate goal is to refresh dialogue and intellectual debate about coffee’s impacts on health, hopefully leading to better understanding collectively. On a personal level, we hope that this book can provide some useful information and eventually make you look at your daily cup just a bit differently. Who knows? Maybe, there really is more to coffee than just the ability to keep us awake!

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<tr>
<td>3-APA</td>
<td>3-Amino-propionamide</td>
</tr>
<tr>
<td>3MS</td>
<td>Modified Mini-Mental State Examination</td>
</tr>
<tr>
<td>ABCA1</td>
<td>ATP-binding cassette transporter A1</td>
</tr>
<tr>
<td>ACh</td>
<td>Acetylcholine</td>
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<tr>
<td>AChE</td>
<td>Acetylcholinesterase</td>
</tr>
<tr>
<td>AD</td>
<td>Alzheimer’s disease</td>
</tr>
<tr>
<td>AFB1</td>
<td>Aflatoxin B1</td>
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<tr>
<td>ALT</td>
<td>Alanine aminotransferase</td>
</tr>
<tr>
<td>APOE</td>
<td>Apolipoprotein E</td>
</tr>
<tr>
<td>APP</td>
<td>Amyloid precursor protein</td>
</tr>
<tr>
<td>ARCADE</td>
<td>Alcohol-Related Cancers and Genetic Susceptibility in Europe</td>
</tr>
<tr>
<td>ARE</td>
<td>Antioxidant response element</td>
</tr>
<tr>
<td>AST</td>
<td>Aspartate aminotransferase</td>
</tr>
<tr>
<td>AUB</td>
<td>Area under baseline</td>
</tr>
<tr>
<td>BACE</td>
<td>β-Amyloid precursor cleaving enzyme</td>
</tr>
<tr>
<td>BDA</td>
<td>Butene-1,4-dial</td>
</tr>
<tr>
<td>BMDL</td>
<td>Benchmark dose lower confidence limit</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CA</td>
<td>Caffeic acid</td>
</tr>
<tr>
<td>CAIDE Study</td>
<td>Cardiovascular Risk Factors, Aging and Dementia Study</td>
</tr>
<tr>
<td>CAMP</td>
<td>Cyclic adenosine monophosphate</td>
</tr>
<tr>
<td>CASI</td>
<td>Cognitive Abilities Screening Instrument</td>
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<tr>
<td>CCl4</td>
<td>Carbon tetrachloride</td>
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<td>CCR</td>
<td>Cytochrome-c-reductase</td>
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<td>CEN</td>
<td>European Committee for Standardization</td>
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<td>CGA</td>
<td>Chlorogenic acid</td>
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<td>CHD</td>
<td>Coronary heart disease</td>
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<td>ChEI</td>
<td>Cholinesterase inhibitor</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
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<tr>
<td>CIAA</td>
<td>Confederation of the European Food and Drink Industry</td>
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<tr>
<td>Cmax</td>
<td>Peak plasma concentration</td>
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<tr>
<td>COMT</td>
<td>Catechol-O-methyltransferase</td>
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<td>CPT</td>
<td>Cyclopentyltheophylline</td>
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<td>CQA</td>
<td>Caffeoylquinic acid</td>
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<tr>
<td>CQLAL</td>
<td>Caffeoylquinic acid lactone</td>
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<td>CREB</td>
<td>cAMP response element-binding protein</td>
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<tr>
<td>CRP</td>
<td>C-reactive protein</td>
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<tr>
<td>CTGF</td>
<td>Connective tissue growth factor</td>
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<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>--------------</td>
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<tr>
<td>CVS</td>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>diCQA</td>
<td>Dicaffeoylquinic acid</td>
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<tr>
<td>DIFEQ</td>
<td>Derivative 3,4-diferuloyl-1,5-quinolactone</td>
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<tr>
<td>Disorders and Stroke</td>
<td>Alzheimer’s Disease and Related Disorders Association</td>
</tr>
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<td>DPCPX</td>
<td>Dipropylxanthine</td>
</tr>
<tr>
<td>DRI</td>
<td>Dietary reference intake</td>
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<tr>
<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
</tr>
<tr>
<td>ECM</td>
<td>Extracellular matrix</td>
</tr>
<tr>
<td>EFSA</td>
<td>European Food Safety Authority</td>
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<tr>
<td>EGFR</td>
<td>Epithelial growth factor receptor</td>
</tr>
<tr>
<td>ERK</td>
<td>Extracellular signal-regulated protein kinase</td>
</tr>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>FBOs</td>
<td>Food business operators</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FDE</td>
<td>FoodDrinkEurope</td>
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<tr>
<td>FQA</td>
<td>Feruloylquinic acid</td>
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<tr>
<td>FINE Study</td>
<td>Finland, Italy and The Netherlands Elderly Study</td>
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<tr>
<td>GABA</td>
<td>( \gamma )-Aminobutyric acid</td>
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<tr>
<td>GC-MS</td>
<td>Gas chromatography-mass spectrometry</td>
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<tr>
<td>GDNF</td>
<td>Glial-derived neurotrophic factors</td>
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<tr>
<td>GERD</td>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td>GFP</td>
<td>Green fluorescent protein</td>
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<tr>
<td>GGT</td>
<td>( \gamma )-Glutamyl transferase</td>
</tr>
<tr>
<td>GIP</td>
<td>Insulin-like polypeptide</td>
</tr>
<tr>
<td>GLP-1</td>
<td>Glucagon-like peptide 1</td>
</tr>
<tr>
<td>GPD</td>
<td>Gastric potential difference</td>
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<td>GST</td>
<td>Glutathione-S-transferase</td>
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<tr>
<td>HCC</td>
<td>Hepatocellular carcinoma</td>
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<tr>
<td>HDLs</td>
<td>High-density lipoproteins</td>
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<tr>
<td>HPA</td>
<td>Hypothalamic–pituitary–adrenal</td>
</tr>
<tr>
<td>HPLC-MSn</td>
<td>High-performance liquid chromatography mass spectrometry ion scan</td>
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<tr>
<td>HR</td>
<td>Hazard ratio</td>
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<tr>
<td>HRT</td>
<td>Hormone replacement therapy</td>
</tr>
<tr>
<td>hsCRP</td>
<td>High-sensitivity C-reactive protein</td>
</tr>
<tr>
<td>HSCs</td>
<td>Hepatic stellate cells</td>
</tr>
<tr>
<td>HT</td>
<td>Hydroxytryptophan</td>
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<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>IC50</td>
<td>Half-maximal inhibitory concentration</td>
</tr>
<tr>
<td>IDC</td>
<td>Instant decaffeinated coffee</td>
</tr>
<tr>
<td>IL</td>
<td>Interleukin</td>
</tr>
<tr>
<td>INF-( \gamma )</td>
<td>Interferon-( \gamma )</td>
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<td>IR</td>
<td>Irritation index</td>
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<tr>
<td>IRMM</td>
<td>Institute for Reference Materials and Measurements</td>
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<td>IVGTT</td>
<td>Intravenous glucose tolerance test</td>
</tr>
<tr>
<td>JECFA</td>
<td>Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives</td>
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List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>JNK</td>
<td>c-Jun N-terminal kinase</td>
</tr>
<tr>
<td>LC-MS/MS</td>
<td>Liquid chromatography tandem mass spectrometry</td>
</tr>
<tr>
<td>LDL</td>
<td>Low-density lipoprotein</td>
</tr>
<tr>
<td>LES</td>
<td>Lower esophageal sphincter</td>
</tr>
<tr>
<td>LMP</td>
<td>Last menstrual period</td>
</tr>
<tr>
<td>LXRα</td>
<td>Liver X receptor-α</td>
</tr>
<tr>
<td>MAO</td>
<td>Human monoamine oxidase</td>
</tr>
<tr>
<td>MAPK</td>
<td>Mitogen-activated protein kinase</td>
</tr>
<tr>
<td>MAPT</td>
<td>Microtubule-associated protein tau</td>
</tr>
<tr>
<td>MMSE</td>
<td>Mini-Mental State Examination</td>
</tr>
<tr>
<td>MOE</td>
<td>Margin of exposure</td>
</tr>
<tr>
<td>MOS</td>
<td>Mannooligosaccharides</td>
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<tr>
<td>MPTP</td>
<td>1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MWM</td>
<td>Morris water maze</td>
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<tr>
<td>NF-kB</td>
<td>Nuclear factor-κB</td>
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<tr>
<td>NINCDS-ADRDA</td>
<td>National Institute of Neurological and Communicative Disorders and Stroke</td>
</tr>
<tr>
<td>NMDAR</td>
<td>N-Methyl-d-aspartate receptor</td>
</tr>
<tr>
<td>NMP</td>
<td>N-Methylpyridinium</td>
</tr>
<tr>
<td>NOAEL</td>
<td>No observed adverse effect level</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>NTP</td>
<td>National Toxicology Program</td>
</tr>
<tr>
<td>NVP</td>
<td>Nausea and vomiting in pregnancy</td>
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<tr>
<td>OGTT</td>
<td>Oral glucose tolerance test</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>ORAC</td>
<td>Oxygen radical absorbance capacity</td>
</tr>
<tr>
<td>OTA</td>
<td>Ochratoxin A</td>
</tr>
<tr>
<td>PAH</td>
<td>Polycyclic aromatic hydrocarbon</td>
</tr>
<tr>
<td>PD</td>
<td>Parkinson’s disease</td>
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<tr>
<td>PGA</td>
<td>Pyroglutamate</td>
</tr>
<tr>
<td>PKA</td>
<td>Protein kinase A</td>
</tr>
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<td>PS</td>
<td>Presenilin</td>
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<td>RAWM</td>
<td>Radial-arm water maze</td>
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<tr>
<td>RCT</td>
<td>Reverse cholesterol transport</td>
</tr>
<tr>
<td>ROS</td>
<td>Reactive oxygen species</td>
</tr>
<tr>
<td>RR</td>
<td>Relative risk</td>
</tr>
<tr>
<td>RR</td>
<td>Risk ratio</td>
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<td>SCAA</td>
<td>Specialty Coffee Association of America</td>
</tr>
<tr>
<td>SD</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>SR-BI</td>
<td>Scavenger receptor class B type I</td>
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<tr>
<td>TGF</td>
<td>Transforming growth factor</td>
</tr>
<tr>
<td>TICS</td>
<td>Telephone Interview for Cognitive Status</td>
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<td>Tmax</td>
<td>Time reached for peak plasma concentration</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Tumor necrosis factor alpha</td>
</tr>
<tr>
<td>TRAP</td>
<td>Total radical-trapping antioxidant parameters</td>
</tr>
<tr>
<td>VLDL</td>
<td>Very low-density lipoprotein</td>
</tr>
<tr>
<td>WCRF</td>
<td>World Cancer Research Fund</td>
</tr>
</tbody>
</table>
Acknowledgement

As a student of science, I am deeply honored to serve as Editor for this book. I am also profoundly grateful to the many authors who carved out time from their busy schedules to contribute.

This book would not have been possible without the enthusiasm and support of Richard Black, Chief Nutrition Officer at Kraft Foods. Richard demonstrates how effective a leader can be by believing in his troops, which in turn brings out the best in people. I also want to thank Barbara Lyle for taking a chance on me when I was a new PhD graduate.

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1 Introduction
Thomas Hatzold

1.1 Coffee—a Popular Beverage

Billions of cups of coffee are enjoyed every year by consumers around the world. Coffee consumption is common among both younger and older adults, and at all times of the day: early morning upon waking, for breakfast, after a meal, and even in the evening. It is taken at home, at work, and in cafés, bars, and restaurants. The preparation methods range from café ristretto, a special type of espresso containing little water, to large cups of “regular” coffee. It is taken as black coffee or with addition of other food ingredients such as sugar or other sweeteners, milk or nondairy creamer, and in the form of special preparations such as cappuccinos, lattes, or flavored coffees.

Coffee is consumed for its unique aromatic taste and stimulating effects. The pleasant taste originates from the roasting process, where the bitter tasting and the characteristic volatile aroma components are formed [1]. More than 1000 different aroma compounds have been identified in coffee, making it a complex and diverse beverage. Moreover, the effects of coffee can be either stimulating or relaxing, depending on the situation one finds oneself in and how one feels [2].

Consumers may take coffee for emotional reasons because they enjoy it; it may help them relax or improve their mood. Other reasons for drinking coffee may be more rational; it may help one to wake up, be stimulated, have improved concentration, or avoid falling asleep when wakefulness is desired. Coffee is also used for social reasons, which is evident from the 400-year history of coffee houses, where people meet while enjoying their coffee.

Coffee is one of the most popular drinks in Western countries. In many countries, most adults consume this beverage. In the United States, for example, only 22% of adults never drink coffee [3].

1.2 Coffee from a Nutritional Perspective

Coffee is a unique drink and could be regarded as a healthy beverage choice. If taken as black coffee, it is virtually free of saturated fatty acids, sodium, and sugar. Further, it contains an insignificant amount of energy: 2 kcal/178-g serving [4]. However, many consumers add sugar, milk, or cream to their coffee. The amount of calories provided daily by sweetened
coffee has been calculated as 130 kcal/day (consumers of this beverage only), which is less than half of the estimated 321 kcal/day obtained from all sweetened beverages (including sodas/colas), based on intake data from the United States [5]. Consumers who want to control their calorie intake or consumption of nonessential nutrients such as sugar or saturated fat may choose to add noncaloric sweeteners and low-fat milk to their beverage.

Certain so-called gourmet coffee beverages should be consumed in moderation. These include cappuccino and lattes that contain ingredients such as cream, full-fat milk, and sugar. These beverages can contain up to 240-kcal/237-mL serving [6], but beverages with significantly lower energy levels are also available. An intake study of college women indicated that gourmet coffee drinkers consumed an additional 206 kcal/day and 32 g sugar/day compared with nonconsumers [7].

Roast coffee produced by traditional roasting processes can be regarded as a natural food or food ingredient. It is a single ingredient product without additives and thus fulfills the criteria for the term “natural” that was established by the UK government, for example [8]. In certain roast coffee products, the only other substances used are packaging gases such as carbon dioxide, an inert gas that preserves the flavor. In other roast coffee products, other technologies such as vacuum packaging may be used for this purpose.

1.3 POTENTIAL BENEFICIAL EFFECTS OF COFFEE

The health aspects of coffee drinking have been subject to many controversial debates. This history is nicely summarized in Ian Bersten’s book Coffee, Sex & Health, a history of anti-coffee crusaders and sexual hysteria [9]. As the author points out:

... even though coffee, tea and cocoa all contain caffeine, seemingly the root cause of many problems to do with health, coffee seemed to be the only one of the three that had a health image problem.

Even today, a substantial number of articles about coffee are negative. In the United Kingdom, for example, 51% of media publications on coffee, caffeine, and health are negative, 22% are neutral, and 27% positive [10].

Only recently have scientists begun to document the potential health benefits of coffee drinking, whereas research data on the acute/short-term stimulating properties of coffee due to caffeine are well known. Caffeine is naturally found in about 60 different plants including tea leaves, cocoa beans, guaraná, and kola nut. It is also added to many soft drinks including energy drinks and to medicinal products such as analgesics and cough syrups [11,12].

Acute caffeine effects on the central nervous system have been reviewed extensively [13–15]. Although these effects are not the focus of this book, they are briefly summarized here.

At common consumption levels, the most important acute effect of caffeine and its predominant metabolites (paraxanthine and theophylline) is the blockade of adenosine A₁ and A₂A receptors. This leads to activation of a variety of neurotransmitter systems and finally to the well-known effects on improved arousal, vigilance, and attention. There is evidence that caffeine has the potential to improve cognitive functions that are timed such as reaction time, decision-making, or cancellation tasks. Its influence on mood depends on the amount of caffeine consumed, individual differences, and arousal states. In real-life simulations, caffeine appears to improve performance of artificial tasks and simulations of driving and industrial work.