BASHAR SAAD
OMAR SAID

GRECO-ARAB AND ISLAMIC HERBAL MEDICINE

Traditional System, Ethics, Safety, Efficacy, and Regulatory Issues




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By

Bashar Saad, PhD
Professor of Cell Biology and Immunology, Arab American University, Jenin, Palestine, and Qasemi Research Center, Al-Qasemi Academic College, Israel

Omar Said, PhD
Pharmacologist, Senior researcher of Arab Herbal Medicine, Antaki Center for Herbal Medicine Ltd, Kufur Kanna and the Galilee Society R&D Center, Israel

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FOREWORD

There was a huge enlightenment in the Arab world at a time when Europe was in the grip of the Dark Ages, stifled by Church authority. A major part of this explosion of intellectual freedom was the creation of an entirely new coherent medical system, based on the medicine of the Greeks, the Egyptians, and even of India, that developed into a rational, experimental, and thorough corpus with its theories and treatment protocols, pharmacies, hospitals, libraries, and thousands of new medicines and combinations used for the first time along with differential diagnosis. It became a foundation stone of modern medicine and also of herbal medicine in the West. And it still exists. Arabic medicine today stands alongside Ayurvedic and Chinese medicine as one of the great traditional medical systems of the world and is popularly used in all Muslim countries from Pakistan to Morocco. However, it is relatively unknown and unappreciated as a system in its own right, and today, at a time when natural medicine is a primary source of new therapies and remedies, there is still a great deal to be learnt from it.

This book sets out to reveal the potential of Arabic medicine and especially medicinal plants as a living and vital medical resource today. In this it is quite unique, especially because of its coverage of research on the herbs, and much of it was carried out in the authors' own labs. As far as I am aware, no other professional-level book covers the pharmacology and science of so many important herbs that are widely used in Arabic countries but are still relatively unknown in the West. Take, for example, *Nigella* (black seed). It is a central herb in Arabic medicine used as a powerful anti-inflammatory and antiseptic. The authors have researched this herb and there are also hundreds of papers, including clinical studies, published on it in the world scientific literature, yet the herb is still unknown and unused in the West except as a spice. This book might well raise its profile worldwide. There has been an assumption in the past that all the herbs of Arabic medicine are already known and used in modern professional herbalism and the health industry. This is not so [1], and this book can be very helpful in introducing a host of novel plants, together with research on them.

Professor Bashar Saad and Dr. Omar Said have written what may well become a classic text on Arabic medicine, not only because of its pharmacological and scientific material, but also because of its interdisciplinary nature. It is a fascinating exploration of the richness of the past knowledge, combined with ethnopharmacology of Arabic medicine today, safety and pharmacology of Arabic medicinal plants, botany, clinical aspects, Arabic medical principles, and so on. The authors are uniquely qualified to write this book, because they themselves embody the interdisciplinary wisdom

needed for it. Indeed, they would stand alongside some of the greats of ancient Arabic medicine, who transcended boundaries of subject and discipline. Many times I have walked with the authors over the Galilee hills and listened as they picked out a small hidden herb, identified it, described its Latin, Arabic, English, Hebrew, and ancient names, described its uses and the debates surrounding it in the ancient literature, told me what is in it chemically, described how it performs in the lab and how it should be formulated into a finished remedy, and told stories of, for example, of how the Bedouin of the Negev desert or the Druze of Syria might use it today. The authors are accomplished scientists in the fields of pharmacology, cell biology, and immunology and bring this unique and original aspect of modern science to the herbal wisdom. Besides, the authors are involved in the Galilee Society's botanical garden of medicinal plants, the largest garden devoted to medicinal plants in the Middle East. Thousands of children go there every year and are taught about the traditional medicine of the region. And it should also be mentioned that working and researching on traditional Arabic medicine in Israel and Palestine, regions of conflict, has not been easy.

Today, it is acknowledged that much of modern drug discovery depends on natural product concepts. The first steps are usually the work by ethnopharmacologists in the field and pharmacologists in the lab. This book breaks new ground in opening up a forgotten resource for both drug discovery and new natural product medicines.

STEPHEN FULDER

REFERENCE

1. Fulder SJ,Said O.Steps towards revival of Graeco-Arabic medicine in the Middle East: a new project. *HerbalGram* 2009;83:36–45.

PREFACE

At the beginning of the twenty-first century and despite the great progress in modern medicine, traditional Arab–Islamic medicine continues to be practiced within the Mediterranean as well as most Arab and Islamic countries. A very important factor that has enhanced the present popularity and widespread use of Arab herbal-based medicines is the belief that they are prepared according to the principles of Greco-Arab and Islamic medicine, which was developed during the Golden Age of Arab–Islamic civilization. This civilization spanned from the seventh to the fifteenth century and extended from Spain to Central Asia and India. It became a wellspring of brilliant medical developments and innovations, as well as of great achievements in astronomy, mathematics, chemistry, philosophy, and arts. Arab and Muslim scientists significantly contributed to the development of modern Western medicine, accomplishing far more than mere translation. A closer look at their activity during the medieval period shows that they translated classical medical texts not only from Greece, but also from Persia, India, and China. From this, Arab and Muslim scientists were able to synthesize and develop a rich and universal medical system based on scientific methods and experimentation. The works of Arab and Muslim scholars gained widespread use and were used in European medical schools. For instance, the Arab and Muslim physicians Al Tabbari, Rhazes, Al-Zahrawi (Albucasis), Al-Biruni, Avicenna, Ibn al-Haitham, Ibn al Nafees, Ibn Khaldun, and Ibn Zuhr (Avenzoar) are regarded as among the great medical authorities of the ancient world and the medieval world, physicians whose textbooks were used in European universities up to the sixteenth century. They were among the first to make accurate diagnoses of plague, diphtheria, diabetes, gout, cancer, leprosy, rabies, and epilepsy. Avicenna's and Rhazes's works on infectious diseases led to the introduction of quarantine as a means of limiting the spread of these diseases. Arab physicians laid down the principles of clinical investigation and drug trials, as well as animal tests. They mastered operations for hernia and cataracts, filled teeth with gold leaf, and prescribed spectacles for defective eyesight. The physicians and scientists of the Islamic Golden Age, who were of diverse religious and ethnic backgrounds, passed on rules of health, diet, and hygiene that are still largely valid.

The high degree of development achieved in Greco-Arab and Islamic medicine is observable in a statement of Avicenna (980–1037), who defined medicine in his *Canon of Medicine* as "the science from which we learn the states of the human body with respect to what is healthy and what is not; in order to preserve good health when it exists and restore it when it is lacking." He further stated that "we have to understand

that the best and most effective remedy for the treatment of patients should be through the improvement of the power of the human body in order to increase its immune system, which is based on the beauty of the surroundings and letting him listen to the best music and allowing his best friends to be with him." Another statement concerning therapeutic methods was made by Rhazes (846–930): "if the physician is able to treat with foodstuffs, not medication, then he has succeeded. If, however, he must use medications, then it should be simple remedies and not compound ones." Arab–Islamic medicine influenced Western medical circles to such an extent that it was included in the curriculum of European medical schools for many centuries. It became a foundation stone of modern medicine and also of herbal medicine in the West. And it still exists. Arab-Islamic medicine today stands as one of the great traditional medical systems of the world and is popularly used in all Arab and Islamic countries from Pakistan to Morocco.

The Eastern region of the Mediterranean is covered with at least 3600 plant species of which 700–800 are noted in medieval medical books for their use as medicinal herbs. Recent ethnopharmacological studies have demonstrated that more than 450 medicinal plants have continued to be employed in the treatment and prevention of human diseases within the Mediterranean as well as most Islamic countries. Some of these plant species have been investigated and their bioactive ingredients extracted to treat various human diseases.

This book is the first academic book in the field of Arab herbal medicine that explores and introduces aspects of Arab herbal medicine using original ethnopharmacological surveys conducted by our group in the Mediterranean area. This book includes 19 chapters, embracing particularly historical aspects and present uses of traditional Arab–Islamic herbal medicine. Chapters 1–5 focus on historical background, medical innovations introduced by Arab physicians, common roots of Arab medicine and Western medicine, and methodology of drug discovery and therapy in Arabic and Islamic medicine. Chapters 6–10 present a comprehensive review of the methodology of drug discovery, method of therapy, and commonly used herbal medicines in the Arab–Islamic world and their tremendous potential in modern drug discovery. Chapters 11–14 combine overviews of state-of-the-art *in vitro* and *in vivo* techniques, as well as clinical trials of traditional herbal medicine. Chapters 15 and 16 cover medical ethics in Arabic and Islamic medicine, uses of medicinal plants, and methods of extracting their active ingredients. Chapter 17 examines the use of food therapy in Arab–Islamic medicine. Chapters 18 and 19 focus on demographic and regulatory issues, as well as on drug development from herbal sources.

For convenience, all dates given in book are those of the Christian calendar, unless otherwise specified. The designation AD is used only when there is a need to distinguish a date from an earlier BC date. General references to a century rather than to a specific year refer to centuries of the Christian era.

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CHAPTER 1

An Overview of Greco-Arab and Islamic Herbal Medicine

1.1 INTRODUCTION

Natural products, such as plant, fungal, and bee products, as well as minerals, shells, and certain animal products, represent the oldest form of medical treatment. Currently, many of the commonly used drugs are of herbal origin and about 25% of the prescription drugs contain at least one herbal-derived active ingredient or synthetic compound, which mimics a plant-derived compound. There are over 80,000 plants that have medicinal uses throughout the world and usually a specific part of the plant is used for medical preparations such as tablets, infusions, extracts, tinctures, ointments, or creams. The pharmacological action of these medicines is often described in very general terms, such as carminative (an agent that prevents formation of gas in the gastrointestinal tract or facilitates the expulsion of said gas), laxative (an agent that induces bowel movements or loosens the stools), demulcent (an agent that forms a soothing film over a mucous membrane, relieving minor pain and inflammation of the membrane), antitussive (cough suppressants), or antiseptic (antimicrobial substances that are applied to living tissue/skin to reduce the possibility of infection). Unlike synthetic drugs, which usually consist of a single and often synthetic chemical, herbal-based medicines contain multiple constituents.

In the history of science, Arabic medicine, Islamic medicine, Arab–Islamic medicine, Greco-Arab medicine, or Greco-Arab and Islamic medicine are terms that refer to medicine developed during the Golden Age of Arab–Islamic civilization (seventh to fifteenth century), which extended from Spain to Central Asia and India (Figure 1.1). This civilization became the center of brilliant medical developments and innovations, as well as great achievements in astronomy, mathematics, chemistry, philosophy, and artistic culture. Arab and Muslim scholars translated and integrated scientific knowledge of other civilizations into their own. As will be seen in the following chapters, however, Arab–Islamic medicine was not simply a continuation of Greek ideas but a venue for innovation and change. These included the discovery of

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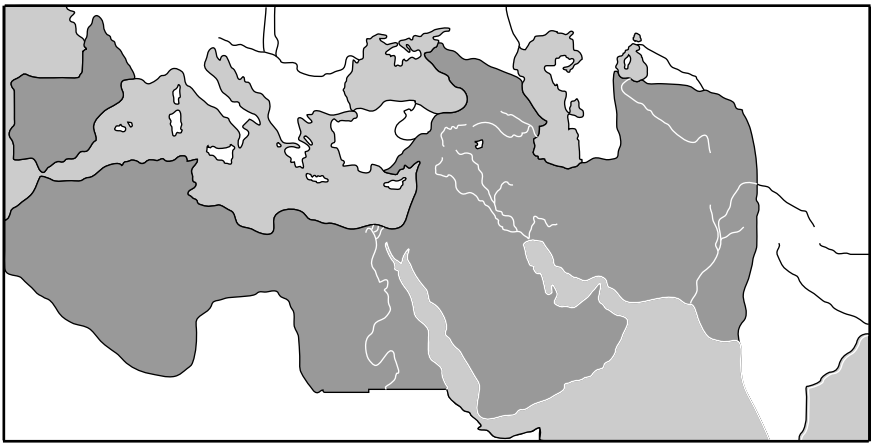

FIGURE 1.1 The medieval Arab–Islamic Empire at its largest extension.

the immune system, the introduction of microbiological science, and the separation of pharmacological science from medicine. Medicine in general is considered to be one of the most illustrious and best known achievements of Arab–Islamic civilization, which influenced Western medical circles to such an extent that it was included in the curriculum of medical schools up to sixteenth century.

Despite great progress in allopathic medicine, Arab–Islamic medicine has continued to be practiced within the Mediterranean as well as most Arab and Islamic countries (Table 10.2), where cultural beliefs and religion often lead to self-care or home remedies in rural areas and consultation with traditional healers. In addition, Arab–Islamic therapies are most often utilized by people who have faith in spiritual healers and herbalists. These people are the first to be consulted for problems such as infertility, impotence, diabetes, obesity, epilepsy, psychosomatic troubles, and many other diseases (see Chapter 10). The popularity of herbal preparations based on Greco-Arab and Islamic medicines has increased worldwide in the past four decades, probably because of the sustainability of this medicine over the years. Other factors include the notion that herbal-based drugs are safe (see Chapter 13), that they are relatively inexpensive, the restricted access to physicians imposed by managed care, and the adverse effects of synthetic drugs.

Chapter 10 provides an overview of Greco-Arab and Islamic medicine practiced in countries other than those in the Middle East, such as Iran, India, Turkey, Maghreb region, and Pakistan [1–10]. India is the only country where Greco-Arab medicine has an official status. It was introduced by Arabs and soon took firm roots in the subcontinent. Greco-Arab and Islamic medicine as practiced in Muslim communities of the Indo-Pakistan subcontinent is known as Unani-Tibb. "Tibb" is an Arabic word meaning "medicine," while "Unani" is thought to be derived from "Ionan" (meaning Greek), acknowledging the influence of early Greek medicine on Greco-Arab and Islamic medicine. A Unani physician is known as a *hakim*. However, the Unani

medicine currently practiced in the Indo-Pakistan subcontinent is vastly different from its Greco-Arab roots. It benefited from the native medical system or folk medicine in practice at the time in various parts of central and southern Asia, mainly Ayurvedic medicine and Chinese medicine.

Herbal medicines are classified in many European countries as drugs; in the United States, they are sold as dietary supplements. Unfortunately, in the Arab–Islamic world as well as in China and India, they are mostly sold over the counter without regulation. As discussed in Chapter 11, safety assessment of herbal products has often been neglected since prolonged and apparently safe use is usually considered as evident. Nevertheless, evidence of the toxicity of such products has accumulated. This is not surprising, since herbal products are complex mixtures of secondary metabolites, many of which are potentially toxic (e.g., hepatotoxic and nephrotoxic). Therefore, the widespread use and popularity of herbal-based medicines raises concerns and fears over the professionalism of practitioners and safety, quality, and efficacy of these products. In regard to safety, biomedical journals have reported serious side effects, particularly hepatotoxicity. These matters are covered extensively in Chapters 11 and 12.

The popularity of natural product-based therapies is rapidly increasing and global sales of herbal products top $100 billion a year. In 2008, $4.8 billion were spent in the United States and a large center of complementary and alternative medicine has been established recently at the NIH (National Institute of Health). And more recently, the NIH has sponsored large clinical trials of botanicals such as St. John's Wort and Ginkgo.

In the course of the following chapters, we intend to reveal the complexities, encourage comparisons, and offer answers to questions such as the following: How did Arab–Islamic medicine reach such high levels of knowledge and practice? How did Arab–Islamic scholars lay the foundations of modern Western medicine and pharmacology? How did Arab and Muslim physicians discover and successfully treat diseases? How did Arab and Muslim scholars lay the foundation for clinical trials and animal testing? And finally we give an overview of currently used medicinal plants in the Arab world and their efficacy and safety. This book is organized around 19 major topics, reflected by the titles of these chapters: (1) An overview of Greco-Arab and Islamic herbal medicine, (2) History of Greco-Arab and Islamic medicine, (3) Herbal medicine, (4) The Arab–Islamic roots of Western medicine, (5) Contributions of Arab and Islamic scholars to modern pharmacology, (6) Natural drugs in Greco-Arab and Islamic medicine, (7) Method of therapy in Greco-Arab and Islamic medicine, (8) Commonly used herbal medicines in the Mediterranean, (9) The current state of knowledge of Arab herbal medicine, (10) Greco-Arab and Islamic medicine practiced outside the Middle East, (11) Biosafety of herbal medicine, (12) Arab medicinal plants: from traditional uses to scientific knowledge, (13) Modern *in vitro* test systems, (14) Modern *in vivo* evaluations and clinical trials, (15) Medical ethics in Arab and Islamic medicine, (16) Medicinal herbs and extracting their active ingredients, (17) Food therapy, (18) Drug development from herbal sources, and (19) Herbal remedies: use and demographic and regulatory issues. In this introductory chapter, we will give a brief overview of the main topics of this book.

1.2 THE GOLDEN AGE OF ARAB–ISLAMIC CIVILIZATION

The development of Arab–Islamic civilization started in the Arabian Peninsula, the homeland of the Arabs. The Peninsula is predominantly deserted and the tribes who inhabited this area were nomadic, that is, they traveled from one grazing land to another. The great unifying power of these nomadic Arabs was clearly the Prophet Mohammad (peace be upon him) (570–632) from the Quraysh tribe that ruled Mecca. Though Mecca was a prosperous caravan city, it was still tied to traditional social customs and was governed by the tribal societies of the desert. Each tribe worshipped its own gods in the form of objects from nature but all Arabs worshipped one object in common, the *Kaaba*, a large black stone at Mecca, which made Mecca significant as a place of worship and pilgrimage. The Prophet was able to unite the nomadic tribes and to create a strong nation, able to defeat the two powerful empires at that time, the Persian and Byzantine Empires.

The Byzantines and Persians were the first to feel the power of unified Arabs. At Yarmuk in 636, the Arabs defeated the Byzantine army (Table 1.1). Syria fell in 640. A decade later, the Arabs had conquered the entire Persian Empire. Egypt, the Maghreb (North Africa), and Spain were all conquered and under Arab rule by the 720s. Arab expansion in Europe ended after the loss of the Battle of Tours in 732. The Arabs not only conquered new lands, but also became scientific innovators through originality and productivity. They preserved the cultures and knowledge of the conquered lands, tolerated religious minorities within land they had conquered, and were careful to protect the purity of their religion, language, and law from any foreign influence.

The first problem after the death of the Prophet was who should be caliph, the spiritual and secular successor to the Prophet (PBUH). The first four caliphs were elected by a tribal council of elders and are referred to as the Orthodox Caliphs, ruling from 632 to 661. However, as the empire grew, this form of government became increasingly inadequate. In addition, tribal and clan rivalries continued. Finally, the Umayyad clan took over and established the Umayyad Dynasty (661–750). From now on, the dynastic principle of one family choosing the caliph would dominate. From the start, the Umayyads saw that they must adapt Byzantine and Persian techniques for ruling their empire. Therefore, they instituted some major changes. They moved the capital from Medina in Saudi Arabia to a much more central location, Damascus in Syria, created the first Muslim coinage, and also adapted and further developed Byzantine and Persian bureaucratic methods as well as postal communication and transmission of news. In 750, a revolt led by Abbas, a governor of Persia, overthrew the Umayyads and established the Abbasid Dynasty (750–1258). The victorious Abbasids moved their capital to Baghdad to signify a break with the Umayyads. However, the reconstituted Umayyads set up a rival Arab state and put their capital at Cordoba. Even as the Abbasids, in particular the Caliphs Harun al-Rashid (ruled from 786 to 809) and Al-Mamun (ruled from 813 to 833) and their heirs, turned Baghdad into the smartest, most creative, and most modern city of the world, the Umayyads led by Abd Al Rahman I and his heirs set out to do the same thing in Cordoba, Grenada, and the other Andalusian cities.

TABLE 1.1 Timeline of Arab Islamic Civilization

Year	Historical Event
570	The Prophet Mohammad is born in Mecca
622	The Prophet and followers emigrate to Medina. The first year of Islamic calendar
632	Death of the Prophet
632	Muslim armies consolidate their power over Arabia
634–644	Muslim forces advance through the Persian and Byzantine empires
636	Battle of Yarmuk. Byzantine emperor Heraclius is defeated by Muslim army in Syria
642	Arabs conquer Byzantine Egypt and expand into North Africa
656	Mohammad's son-in-law, Ali, succeeds to the leadership of Islam
661–750	**Umayyads rule in Damascus**
711	Tariq with a mixed force of Arabs and Berbers invades Spain
712	Muslims advance into Sind (modern-day Pakistan) and Central Asia
725	Muslims occupy Nimes in France
750–945	**Abbasids rule in Baghdad**
756–929	**Umayyad emirs rule in Spain**
762	Al-Mansur founds Baghdad
786	Haroun al-Rashid becomes caliph in Baghdad
792	The first papermaking factory in the Muslim Empire is built in Baghdad
813–823	Al-Mamun reigns in Baghdad. He founds the House of Wisdom
823	Beginning of Muslim conquest of Sicily
909–1171	**Fatimids expand in North Africa**
929–1031	**Umayyad caliphate reigns in Spain**
969	Fatimid conquer Egypt and transfer their capital to Cairo in 973
976	Al-Azhar university is founded in Cairo
1058	Seljuks take Baghdad
1090	Cordoba is sacked by Almoravids
1096	First Crusade. Christians rule in Jerusalem in 1099
1145–1232	Almohads rule in Spain
1171	Saladin overthrows the Fatimids in Egypt
1171–1250	Ayyubid Dynasty rules in Egypt and Syria
1187	Saladin returns Jerusalem to Arab–Islamic rule
1206–1406	**Mongol Empire**
1492	Christian Reconquest of Spain
1453–1922	**Ottoman Empire**
1494–1566	Suleiman I guides the Ottoman Empire to its fullest extent, ranging from Morocco to the Caspian Sea and the Persian Gulf and into Europe through the Balkans to Hungary
1922	End of the Ottoman Empire

All dates given in the table are those of the Christian calendar. Bold entries denote dynastic rule.

Under the Abbasid Caliphs, Islamic civilization entered a Golden Age. And while in Europe, learning seemed to be at its lowest point, the Arabs created a highly sophisticated civilization. The period from the seventh to roughly the end of the fifteenth century is known as the Golden Age of Arab–Islamic civilization. During this period, the vigorous desert tribesman from Arabia assimilated and interpreted the Byzantine, Persian, and Indian cultural traditions into their own. Perhaps the most important catalyst was Islam itself that encouraged study, thinking, and discussion, as well as a scientific understanding of the world. Historians of Arab science point to various statements in the Qur'an and in the body of other statements attributed to the Prophet (PBUH): "Even if you must go to China, seek knowledge." or "Acquire knowledge, because he who acquires it in the way of the Lord performs an act of piety; who speaks of it, praises the Lord; who seeks it, adores God." Another recognized trigger for the rise of Arab intellect was the acknowledged intellectual traditions of the older societies that fell under Arab and Muslim influence. Places such as Alexandria, Damascus, Tunis, Spain, the Byzantine lands, Persia, and India had been urban and intellectual centers for many centuries when the Arab armies arrived. So people who had long been trained in the ways of research, study, debate, and invention were eager to continue their work within the Arab context. Thanks to Arab and Muslim scholars, ancient Greek knowledge, acquired from their contact with Byzantine scholars, was kept alive and was eventually transferred to the West in the twelfth century and after. But not only did Arab and Muslim scholars preserve the heritage of Greek science and philosophy, they added to it by writing commentaries and glossaries, thus adding to what eventually became the Western intellectual tradition.

The Arab–Islamic Empire covered a period of roughly nine centuries, from the middle of the seventh to the end of the fifteenth century, when the Arab–Islamic world was divided into three independent empires, the Ottoman Empire in Turkey, the Safavid Empire in Persia, and the Mughal Empire in the Indo-Pakistan subcontinent. In the eighteenth and nineteenth centuries, Islamic regions fell under the sway of European imperial powers. Following World War I, the remnants of the Ottoman Empire became European protectorates [1–18].

1.3 THE DEVELOPMENT OF ARAB MEDICAL SCIENCES

The health care practices of the medieval Arab–Islamic community over a large area and nine centuries were not uniform. The everyday practices and the public health of the Arab–Islamic world were affected by many factors: fasting laws and dietary regulations during the holy month of Ramadan, hygiene and burying the dead by Muslims as well as by non-Muslims, the climatic conditions of the vast area, the living conditions of nomadic, rural, and urban communities, the amount of travel undertaken for commerce, or for pilgrimage, the maintenance of a slave class and slave trade, the injuries and diseases attendant upon army camps and battles, and the incidence of plague and endemic diseases [4–6].

As mentioned above, the Abbasids moved the Islamic capital to Baghdad by the tenth century. The city became the center of scientific knowledge and research activity

and emerged as the capital of the scientific and cultural world. In addition to Baghdad, Seville, Toledo, Granada, and other cities established themselves as centers for medical sciences, which were strongly supported and promoted by Abbasid Caliphs. The eagerness of the Arabs for learning resulted in the translation of substantial amounts of Greek, Persian, and Indian medical texts into Arabic. In parallel, Arabs established and promoted their own medical sciences in theories and practices that became highly influential in Western science and teaching. During the Arab–Islamic Golden Age, collaborative works of physicians and scientists from different nations and ethnic groups raised the dignity and caliber of the medical profession. Disease was seen by Arab and Muslim physicians as a problem that can be challenged. The Prophet (PBUH) was credited with many statements on health care problems and their treatments. For instance, "The one who sent down the disease sent down the remedy." and "For every disease, God has given a cure." He was also credited with articulating several specific medical treatments, including the use of honey, olive oil, figs, and cupping. But most importantly, whereas other societies usually feared the sick and afflicted, at best isolating them and at worst leaving them somewhere to die, the Prophet had a very compassionate and forgiving view of the sick.

As a result, health care services rose in esteem from that of a menial calling to the rank of a learned profession, which became known as Greco-Arab and Islamic medicine. This medicine had advanced from ephemeral talisman and theology to real hospital wards, mandatory examination for doctors, and the use of technical terminology. Baghdad and Cairo had hospitals that were open to both male and female patients, staffed by attendants of both sexes. These hospitals contained libraries, pharmacies, intern systems, externs, and nurses. There were mobile clinics to reach the disabled, the disadvantaged, and those in distant areas, regulations were imposed by the health authorities to maintain quality control on drugs, medical ethics was introduced, and pharmacy became separated from medicine and a licensed profession.

Baghdad and Cordoba became the main centers for Arab development of herbal medicines. Al-Zahrawi (Albucasis, tenth century) of Cordoba wrote *The Book of Simples*, an important source for European herbal medicine. The Andalusian botanist Abu al-Abbas al-Nabati introduced the use of experimental scientific methods in the thirteenth century. He also introduced empirical techniques in the testing, description, and identification of numerous *materia medica*. Al-Nabati separated unverified reports from those supported by actual tests and observations. This allowed the study of *materia medica* to evolve into the science of pharmacy. Later on, Ibn al-Baitar, who lived in Damascus, published *The Book on Drinks and Foods*, a collection of different drinks and foods. It is considered as one of the most prestigious books in the medieval pharmacopeia in which the drugs are classified in alphabetical order. Other pharmacopoeia books include that written by Abu-Rayhan Biruni in the eleventh century and Ibn Zuhr (Avenzoar) in the twelfth century. Daoud al-Antaki used different herbs for treating patients and published a book on medicinal herbs summarizing the knowledge of his predecessors. Al-Antaki in the sixteenth century described in his book 57 plants that were used as a source for simple drugs, or frequently as one ingredient in complex herbal-based preparations. He

described the plant and the way it was used by physicians. For instance, birthwort, carob, castor oil plant, common fennel, common myrtle, Persian cyclamen, saffron, serapias, sycamore fig, and Syrian bryony. Furthermore, Al-Antaki mentioned foreign plants that were brought to the area for their medicinal properties, such as cornelian cherry, purging croton, and gardenia. He also described pharmacological uses of typical agricultural crops, such as caraway, carrot, wild coriander, pear, quince, sugar cane, and walnut. The traditional and medicinal uses of many of these plants are described in Chapters 3, 8, and 17.

The development of medicine and pharmacy in the Arab–Islamic world laid the foundations for the development of modern Western medicine and pharmacy. Arabs contributed many insights of their own to the development of medicine while acknowledging the knowledge they received from other civilizations. It is important to mention that they translated classical medical texts not only from Greek, but also from Persian, Indian, and Chinese sources. This synthesis resulted in a richer and universal medical system, based on scientific rules and experimentation. Al Tabbari (838–870), Al-Razi (Rhazes, 864–930), Al-Zahrawi (Albucasis, 936–1013), Al-Biruni (973–1050), Ibn Sina (Avicenna, 980–1037), Ibn al-Haitham (960–1040), Ibn al-Nafis (1213–1288), Ibn Khaldun (1332–1395) (Figure 1.2), Ibn al-Baitar (1197–1248), and Ibn Zuhr (Avenzoar, 1091–1161) are regarded as among the great medical authorities of the medieval world and as physicians whose textbooks were used in European universities up to the sixteenth century. They made accurate diagnoses of plague, diphtheria, diabetes, gout, cancer, leprosy, rabies, and epilepsy. Avicenna's and Rhazes's works on infectious diseases led to the introduction of quarantine as a means of limiting the spread of these diseases. Other physicians laid down the principles of clinical investigation, drug trials, and animal tests, and uncovered the secret of sight. They mastered operations for hernia and cataract, filled teeth with gold leaf, and prescribed spectacles for defective eyesight. And they passed on rules of health, diet, and hygiene that are still largely valid today. Physicians of different languages and religions cooperated in building a medical organization whose outlines are still visible in current medical practices. While, as mentioned above, medieval Arab–Islamic medicine laid the foundation of modern medicine, some of the currently practiced therapies may seem irrelevant to the modern world. These include magical procedures and folkloric practices of local tradition.

The development and the recognition of the independent, academically oriented status of pharmacy as a profession charged with the preparation of safe and effective drugs started in Baghdad during Al-Mamun's caliphate (813–833). The main objectives of pharmacists were directed not only toward the translations and interpretations of accumulated data on natural product-based drugs, but increasingly toward the search for the potential of natural products as sources for new drugs, and they even started to elucidate physicochemical properties of these products. Drugs were classified according to their effects on the human body, for example, diuretics (promote urination and thus expel toxins), expectorants (remove mucous accumulation), topical antiseptic cleansers, stimulants (prescribed to increase blood flow and raise energy level), tonics (general strength building and disease prevention), analgesics and anesthetics, digestive aids, and oral health agents. Pharmacists, or

FIGURE 1.2 Ibn Khaldun (1332–1406). The fame of Ibn Khaldun in modern scholarship is due to his writing of the Muqaddimah, or "Introduction." In the Muqaddimah, he laid the foundations of a new science, "Ilm al-Umran," or the science of human social organization.

saydalaneh in Arabic, managed to introduce a large number of new drugs to clinical use, including senna, camphor, sandalwood, musk, myrrh, cassia, tamarind, nutmeg, cloves, aconite, ambergris, and mercury. They also developed syrups, juleps, and pleasant solvents such as rose water and orange blossom water as means of administering drugs. The first pharmacy shop was apparently in Baghdad, founded in 762, and medicines were manufactured and distributed commercially, and then dispensed by physicians and pharmacists in a variety of forms: ointments, pills, elixirs, confections, tinctures, suppositories, and inhalants. *Saydalaneh* were required to pass examinations and be licensed and were then monitored by the state [1–18].

As discussed in detail in Chapter 16, the selection of potential natural products as sources for new drugs was based on traditional knowledge developed in the

pre-Islamic era based on a long history of trial and error, and then by theoretical and practical knowledge introduced by Islam. These include natural products mentioned in the Holy Quran or in the *Hadith* of the Prophet (PBUH), notably honey, milk, dates, black seeds, olive leaf, and olive oil. In addition, theoretical and practical knowledge developed in other medical systems, which became available to Arab–Islamic scholars after the translation of foreign scripts, played a central role in developing new medicines. The works of Galen, Hippocrates, and the Indian physicians Sushruta and Charaka were translated into Arabic. Arab–Muslim physicians developed hundreds of new natural product-based remedies. They were not guided by a long history of trial and error, but mainly by scientific methods, which led to the development of evidence-based medication. Avicenna discussed in his book, on simple drugs (*materia medica*), the nature and quality of drugs (see Chapter 7), and the way that compounding them influences their effectiveness. He stated "You can tell the potency of drugs in two ways, by analogy and by experiment. We say experimenting leads to knowledge of the potency of a medicine with certainty after taking into consideration certain conditions."

Arab–Islamic medicine considers all components of existence with equal importance, from breath and body to the soul and matter; both spiritual and physical health are treated equally. Hence, the body should be treated as a whole and not just as a series of organs and tissues. Physicians noted that there are individual differences in the severity of disease symptoms, and in the individual ability to cope with disease and healing. Hippocrates thus laid the foundations of the modern theory that thoughts, ideas, and feelings, which he proposed to originate in the brain, can influence health and the process of disease. Rhazes supported this concept by his recommendation: "The physician, even though he has his doubts, must always make the patient believe that he will recover, for state of the body is linked to the state of the mind." Later on, Avicenna who defined medicine as "the science from which we learn the states of the human body with respect to what is healthy and what is not; in order to preserve good health when it exists and restore it when it is lacking" supported the views of Rhazes. He stated that "We have to understand that the best and most effective remedy for the treatment of patients should be through the improvement of the power of the human body in order to increase its immune system, which is based on the beauty of the surroundings and letting him listen to the best music and allowing his best friends to be with him."

It is now clear that the mind and the body interact, influence, and regulate each other. The perception of stress can lead to production of "stress hormones" as well as mediators of the immune system, for example, cytokines and free radicals. Stress hormones act in a feedback pathway to regulate their own production and the production of certain immune products. These immune products act on the brain to modify behavior and the ability to perceive and to respond to stressful challenges by inducing lethargy, fever, and nausea.

Based on the recommendations of Rhazes and Avicenna, patients were treated through a scheme starting with physiotherapy and diet, and if this failed, drugs were used. Rhazes's treatment scheme started with diet therapy; he noted that "if the physician is able to treat with foodstuffs, not medication, then he has succeeded. If,

however, he must use medications, then it should be simple remedies and not compound ones." Drugs were divided into two groups, simple and compound drugs. Physicians were aware of the interaction between drugs; thus, they used simple drugs first. If these failed, compound drugs consisting of two or more compounds were used. If these conservative measures failed, surgery was undertaken.

The Greek and Roman humor theory of the human body or humoralism had a great influence on the development of the Greco-Arab medical system. Hippocrates was the first who applied this idea to medicine and it became strongly accepted in the medical canon through the influence of Galen. The humoral theory was adopted and further developed by Arab–Muslim physicians and it became the most commonly held view of the human body among European physicians until the advent of modern medical research in the nineteenth century [1–8]. Chapter 7 provides an overview of method of therapy used in Greco-Arab and Islamic medicine.

1.4 COMMONLY USED HERBAL MEDICINES AND DIETS IN THE ARAB AND ISLAMIC WORLD

Medicinal plants and their products have been used traditionally across the world for the prevention and treatment of almost all known types of diseases. Clinical and basic scientific research confirmed the efficacy and action mechanism of several plants for treating several ailments, including liver disease, diabetes, skin diseases, and hypertension. As a result, about 25% of the currently prescribed drugs are of herbal origin. For instance, milk thistle (*Silybum marianum*) has been shown to have clinical applications in the treatment of liver diseases, including toxic hepatitis, fatty liver, cirrhosis, ischemic injury, radiation toxicity, and viral hepatitis, via its antioxidative, antilipid peroxidative, antifibrotic, and anti-inflammatory properties. Furthermore, milk thistle has shown immunomodulating and liver regenerating effects. Another example is *Nigella sativa* (black seed). The seeds of this plant are known to have many medicinal properties and are widely used in Greco-Arab and Islamic medicine. Therapeutic potential and toxicological properties of the seeds have been extensively studied. A Medline search using "*Nigella sativa*" or "black seed" reveals more than 700 citations, including antioxidant, anti-inflammatory, antimicrobial, hypotensive, antinociceptive, choleretic, uricosuric, antidiabetic, antihistaminic, immunomodulatory, anticancer, and antifertility effects.

Chapter 8 provides an overview of traditional uses, safety, and efficacy of commonly used medicinal plants in the Eastern region of the Mediterranean (Lebanon, Jordan, Israel and Palestine) where more than 3600 plant species are found and about 450–550 plants are noted for their medicinal uses. Plant parts used included leaves, flowers, stems, roots, seeds, and berries [3, 4, 10, 19–21].

Food plays an important role in Arab–Islamic medicine in maintaining a healthy body, soul, and spirit. Muslims are commanded to follow a set of dietary laws outlined in the Holy Quran where almost everything is permitted, except what God specifically prohibited. Later on, when the Islamic empire covered all of Arabia, half of Byzantine Asia, all of Persia, Egypt, the Maghreb (North Africa), and Spain, Arabs and Muslims

became exposed to foreign and multinational culinary heritages. Furthermore, great developments in scientific fields, the establishment of "modern" hospitals, and growing socioeconomic conditions of Islamic empire increased the awareness of the relationship between food and health. During this period, a type of Islamic food therapy developed that was a blend of Quranic teaching and Greek medicine.

As discussed in depth later in Chapter 17, the foods favored by the Prophet were dates, honey, olive oil, and black seeds. Concerning olive oil, he said "Eat olive oil and massage it over your bodies since it is a holy tree." Black seeds were regarded as a medicine that cures and prevents all types of diseases. The Prophet once stated, "The black seed can heal every disease, except death." Dates are mentioned in 20 places in the Quran. The Prophet is reported to have said: "if anyone of you is fasting, let him break his fast with dates. In case he does not have them, then with water. Verily water is a purifier."

1.5 SAFETY AND EFFICACY OF HERBAL MEDICINES

The widespread use and popularity have also brought concerns and fears over quality, efficacy, and safety of the "natural" products available on the market as well as the professionalism of practitioners. It is well known that adulteration, inappropriate formulation, or lack of understanding of plant and drug interactions can lead to adverse reactions that are life threatening or lethal to patients. Safety assessment of herbal-based preparations has often been neglected since traditional and prolonged use is usually considered evidence of its safety. Another important factor is the belief that these medicines are prepared according to the principles of the Greco-Arab tradition that forms the basis for the current conventional product. However, a history of traditional usage is not always a reliable guarantee of safety since it is difficult for traditional practitioners to detect or monitor delayed effects (e.g., mutagenicity), rare adverse effects, and adverse effects arising from long-term use. Most reports concerning toxic effects of herbal medicines are associated with hepatotoxicity although reports of kidney, nervous system, blood, cardiovascular, dermatologic effects, mutagenicity, and carcinogenicity have also been published in the biomedical literature. Chapter 11 gives a systematic safety review of herbal medicine and the contribution of Arab scholars to toxicology. Standards for safety, quality control, use of modern cell biology and biochemistry, and *in vitro* as well as *in vivo* techniques for the evaluation of medicinal plants are also discussed [11, 19–21].

There is little doubt that the use of the concept of Greco-Arab and Islamic herbal therapy has shown remarkable success in healing acute as well as chronic diseases. As mentioned above, Arab and Muslim physicians were the first to use scientific methods in the field of medicine and pharmacy, including the introduction of quantification, animal testing, and clinical trials. Hospitals in the Arab–Islamic world featured the first drug tests, drug purity regulations, and competency tests for physicians. In his *Comprehensive Book of Medicine*, Rhazes documented clinical cases of his own experience and provided very useful recordings of various diseases. He also introduced urinalysis and stool tests. Avicenna (980–1037) introduced experimental

medicine and systematic experimentation and quantification in physiology. He discovered the contagious nature of diseases and described many medical treatments, including clinical trials, risk factor analysis, and the idea of a syndrome in the diagnosis of specific diseases. His book, *The Canon of Medicine*, was the first book dealing with evidence-based medicine, randomized controlled trials, and efficacy tests. Concerning the medical documentation, the first documented description of a peer-reviewed publication process was written by Ishaq bin Ali al-Rahwi (854–931). In his work, *The Ethics of the Physician*, he stated that a physician must always make duplicate notes of a patient's condition. When the patient was cured or had died, the notes of the physician were examined by a local medical council of other physicians, who would review the practicing physician's notes to decide whether the treatment had met the required standards of medical care. Chapter 12 discusses the status of Greco-Arab and Islamic herbal medicine, including the efficacy and safety of specific medicinal preparations, prepared according to scientific and traditional knowledge of Greco-Arab and Islamic medicine.

1.6 MODERN *IN VITRO* AND *IN VIVO* TEST SYSTEMS

Under international regulations, animal tests play a crucial role in developing new knowledge that provides the basis for a new drug development. The appropriate use of animals in biomedical research and safety testing is an indispensable part of the process for acquiring the knowledge necessary to control or treat disease and injury. Regulatory bodies worldwide require preclinical efficacy and safety data for new drugs based on animal tests before human clinical trials can be conducted. Animal studies are mandatory in order to reduce the risks for people and allow the safe creation of new therapies. Drug development is a time-consuming, costly, and complicated research process. Thousands of chemical compounds must be synthesized or purified (in the case of natural products) and tested in order to find a desirable therapeutic result. The Food and Drug Administration in the United States (FDA) estimates that it takes approximately 8.5 years to study and test a new drug before it can be approved for the general public. This estimate includes preclinical *in vitro* studies and animal testing, as well as clinical trials using human subjects. The appropriate and responsible use of animals is a mandatory part of biomedical research and pharmaceutical product safety testing. They significantly reduce the probability of side effects occurring during testing in humans. Around 70% of serious adverse effects that occur in humans are identified at the animal testing stage. In addition, animal tests enable researchers to determine which experimental compounds in advanced development are unsuitable for use in humans either because the risk of potential toxicity is too great or because they do not have the desired pharmacokinetic profile. Therefore, animal testing is extremely beneficial in minimizing the risks to humans in clinical trials. Chapter 14 provides an overview of *in vivo* test methods used for both toxicity and efficacy studies.

Culturing cells is the most widely used *in vitro* method in pharmacology, toxicology, and biomedical research. In general, *in vitro* test systems represent the

first phase of the evaluation procedure. *In vitro* cell culture methods have the advantage of relatively well-controlled variables and are generally accepted as a very effective method for safety testing. Advantages of these systems over classical methods, such as long-term studies on experimental animals, include relatively well-controlled variables, decreased costs, a reduced time to completion, and reduced number of animals necessary to complete the study. Although some advanced *in vitro* systems are available that allow prediction of the local effects of test pharmaceuticals, even the most sophisticated *in vitro* test cannot yet be used to measure systemic effects, for example, blood pressure or fever.

Given the well-known problem of using two-dimensional cell culture pharmaceutical test systems, more realistic three-dimensional tissue constructs are required in order to create more *in vivo*-like cell culture conditions, where cells and tissues do not exist in isolation but communicate with and are interdependent on neighboring tissue. The breakthrough might be to develop human three-dimensional *in vitro* test systems and tissue equivalents that could serve as *in vitro* model systems during the initial stages of drug discovery. Chapter 13 provides an overview of *in vitro* test methods used for both preclinical toxicity and efficacy tests.

1.7 DRUG DEVELOPMENT FROM HERBAL SOURCES AND REGULATORY ISSUES

Herbal-based drug discovery research is a multidisciplinary approach combining ethnopharmacology and traditional knowledge on the one hand and botanical, phytochemical, biological, toxicological, pharmacological, and molecular techniques on the other hand. As mentioned above, about 25% of the currently used prescription drugs contain at least one herbal-derived active ingredient and several herbal-based drugs either have recently been introduced to the market or are currently involved in late-phase clinical trials. Although herbal-derived compounds continue to provide an important source of new drug leads, numerous challenges are encountered including the procurement of plant materials, for example, the selection and implementation of appropriate high-throughput screening bioassays and the scale-up of active compounds.

It is generally believed that the standardization and regulation of plant materials is not required when used by the rural communities for their primary health care. Nevertheless, regardless of whether the medicinal plant is to be used by local communities or by industry, a systematic approach is required for a traditionally used plant, as is done in modern medicine. It is necessary to standardize all stages of herbal-based drug discovery: from cultivation, ethnopharmacology, utilization, isolation, and identification of active constituents to efficacy evaluation, pharmacology, safety, formulation, and clinical evaluation.

In general, many herbs are effective when consumed as whole or as extracts. Current trends, however, are directed toward the use of purified herbal-derived agents that can serve not only as new drugs themselves but also as drug leads suitable for optimization by medicinal and synthetic chemists. Even when new chemical

structures are not found during drug discovery from medicinal plants, known compounds with new biological activity can provide important drug leads. In this respect, the sequencing of the human genome paves the ways for identification of thousands of new pathologically active molecules. With the help of modern *in vitro* and *in vivo* screening assays directed toward these targets, known herbal-derived compounds may show promising and possibly selective activity. Several known herbal-derived compounds have already been shown to act on newly validated molecular targets (e.g., indirubin selectively blocks cyclin-dependent kinases). Other herbal-derived compounds have also been shown to act on novel molecular targets, thus reviving interest in members of these frequently isolated plant compound classes. In Chapter 19, we concentrate on important aspects of the herbal-based drug discovery: from collection of plant material to efficacy and safety evaluation through preclinical studies and phytochemical standardization.

REFERENCES

1. Esposito JL. *The Oxford History of Islam*. Oxford University Press, 2000.
2. Hitti PK. *History of the Arab*. St. Martin's Press, 1970.
3. Saad B, Azaizeh H, Said O. *Arab botanical medicines*. In: Watson RR, Preedy VR (Eds.), *The Encyclopedia of Botanicals in Clinical Practice*. CABI Publishing, 2008.
4. Saad B, Azaizeh H, Said O. Tradition and perspectives of Arab herbal medicine: a review. *eCAM* 2005;2:475–479.
5. Pormann PE, Savage-Smith E. *Medieval Islamic Medicine*. Edinburgh University Press, 2007.
6. Morgan MH. *Lost History: the Enduring Legacy of Muslim Scientists, Thinkers, and Artists*. National Geographic Society, 2007.
7. Bilal A, Jamal A. Unani system of medicine. *Pharmacogn. Rev.* 2007;1(2):210–214.
8. Hajar Al Bin Ali HA. History of medicine. *Heart Views* December 2001–February 2002; 2(4).
9. Deuraseh N. Health and medicine in the Islamic tradition based on the book of medicine (*Kitab al-Tibb*) of Sahih Al-Bukhari. *JISHIM* 2006;5:2–14.
10. Said O, Zaid H, Saad B. Greco-Arab and Islamic herbal medicine and cancer treatment/ prevention. In: Watson RR, Preedy VR (Eds.), *Bioactive Foods and Extracts: Cancer Treatment and Prevention*, Taylor & Francis Group, 2009.
11. Saad B, Azaizeh H, Abu Hijleh G, Said O. Safety of traditional Arab herbal medicine. *eCAM* 2006;3:433–439.
12. Ibn Sena(Avicenna). *Al Qanun Fi al Teb.* Book 6. Dar Alfiker, Bairut, Lebanon, 1994, pp 77–78 (in Arabic).
13. al-Antaki D. *Tadhkirat Uli l-al-Bab wa l-Jami li-L-'Ajab al-'Ujab.* Cairo, 1935 (in Arabic).
14. Ibn Albitar. *Aljamea Limufradat Aladwiya Walaghdiya*. Dar Bulaaq, Cairo, 1974 (manuscript from twelfth century).
15. Souayah N, Greenstein JI. Insights into neurologic localization by Rhazes, a medieval Islamic physician. *Neurology* 2005;65:125–128.

16. Ar-Razi. *Kitab al-Hawi Fi Al-Tibb li-Muhammad Ibn Zakariyya ar Ra-Razi*, Vol. 1Al-Osmanya, Hyderabad, 1956.
17. Ar-Razi.In: Al-Bakry Al-Siddiky H (Ed.), *Al-Mansuri Fi Al-Tibb (The Book of Medicine for Mansur)* Institute of Arab Manuscripts, Arab League Educational Cultural and Scientific Organization, Kuwait, 1987(in Arabic).
18. Abun-Nasr J. *A History of the Maghrib in the Islamic Period*. Cambridge University Press, 1987.
19. Pak E, Esrason KT, Wu VH. Hepatotoxicity of herbal remedies: an emerging dilemma. *Prog. Transplant*. 2004;14:91–96.
20. Fugh-Berman A. Herb–drug interactions. *Lancet* 2000;355:134–138.
21. Rousseaux CG, Schachter H. Regulatory issues concerning the safety, efficacy and quality of herbal remedies. *Birth Defects Res*. 2003;68:505–510.