SCIENCE OF SPICES & CULINARY HERBS
LATEST LABORATORY, PRE-CLINICAL, AND CLINICAL STUDIES

Editors:
Atta-ur-Rahman
M. Iqbal Choudhary
Sammer Yousuf

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(Volume 6)

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CONTENTS

PREFACE

Spices and culinary herbs have been among the richest sources of medicines, fragrances, and recreational substances since antiquity. The modern concept of "food and medicine homology" is largely based on the use of spices as food and medicine. We have recently coined the term "phytodietoceuticals" for all those plant parts that are not only rich in nutrition but also prevent and treat diseases. Extensive research studies on spices and culinary herbs have proven their utility as anti-oxidants and anti-infectious, anti-inflammatory and neuroprotective agents. Volume 6 of the *e*book series titled "*Science of Spices & Culinary Herbs"* is an excellent compilation of ethnobotanical, phytochemical, pharmacological and clinical work being conducted on the most commonly consumed spices and herbs globally. The book series is an attempt to demystify the existing information about these fascinating natural products by presenting comprehensive reviews of scientific studies and their results. This makes *e*book series a must to have in general libraries, pharmaceutical R&D institutions, and nature-based healthcare facilities.

The review by Ceyda Sibel Kilic provides an excellent account of the ethnomedicinal uses and phytochemistry, as well as pharmacological, dietary, and cosmetic applications of aniseed or anise (*Pimpinella anisum* L.). *Sinapis alba* L., commonly called white or yellow mustard, is the focus of the article contributed by Hattab *et al.* The authors have explained the taxonomy, phytochemical methods, essential oil extraction, and chemical and biological properties of aniseeds. Maithanil *et al.* updated the literature review on world-famous herb cinnamon bark powder (*Cinnamomum verum* J. Presl), covering recent work on tremendous health benefits and mechanisms of action, largely due to the presence of its main constituent, cinnamaldehyde. Recent studies on the globally famous spice tamarind (*Tamarindus indica* L.) were reviewed by Ahmad *et al*. The authors have explained the phytochemicals of the pulp of tamarind and their pharmacological and clinical properties. Curcumin, a key constituent of *Curcuma longa*, has been the subject of extensive research in recent years due to its numerous medicinal properties. Badavath *et al.* reviewed the work conducted on the synthetic analogs of curcumin for improved anticancer and anti-oxidant properties. *Glycyrrhiza glabra* L. is the source of licorice derived from its dried roots and rhizomes and used as a natural sweetener. Aksoyalp *et al.* commented on the novel aspect of licorice pharmacology. They reviewed recent studies on the interplay between the use of licorice constituents and human gut microbiota and resulting therapeutic effects on neurodegenerative diseases.

We gratefully acknowledge the scholarly contributions of all authors and the production team of Bentham Science Publishers for a job very well done. Among them, Mrs. Fariya Zulfiqar (Manager Publications) and Mr. Mahmood Alam (Editorial Director) of Bentham Science Publishers deserve special recognition. We sincerely hope that the contributions of the authors and the production team will help readers better understand and appreciate the therapeutic effects and disease-preventive potential of colorful, tasty, and aromatic spices and herbs.

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CHAPTER 1

Pimpinella anisum L. (Anise, Aniseed)

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Abstract: *Pimpinella anisum* L. is an aromatic species of the Apiaceae (Parsley) family, commonly known as anise or aniseed. Fruits of the plant, which are also known as seeds, have widespread usage throughout the world for culinary and medicinal purposes, in cosmetics industry, and also is used in the flavoring of some alcoholic beverages, candies *etc*. Usage of the plant for medicinal purposes dates back to ancient Egypt and the plant is currently being used mainly for its digestive properties and hormonal activities such as increasing milk production in breast feeding mothers. The plant is sometimes confused with star anise, another species called *Illicium verum* Hook. f. from Schisandraceae family due to the fact that they both have *trans*-anethole within the composition of their volatile oils, though anise is an annual herbaceous plant and star anise is an evergreen tree. In this chapter composition, traditional usages, biological activities and some issues related to the utilization of this world-renowned plant are focused on.

Keywords: *Pimpinella anisum*, anise, aniseed, Apiaceae, Parsley family, volatile oil, anethole.

INTRODUCTION

Pimpinella anisum L. is an annual plant of the Apiaceae family, formerly known as Umbelliferae. The plant is known to be cultivated since ancient Egypt (for at least ~4000 years) for its beneficial usages. While texts of ancient Egyptians stated the usage of the plant for digestive problems, as diuretic and against toothache, Greeks and Romans also mentioned the cultivation and uses of the plant for different purposes; furthermore, it has been used in China as a traditional remedy since the 5th century [1, 2]. It is reported to be used in embalming of Scythian kings [3]. The plant is reported to be used in Serbia during medieval times as carminative, digestive, against splenomegaly, stomachache, female genitalia disorders, bruising, to increase spermatogenesis, lactation [4]. The plant

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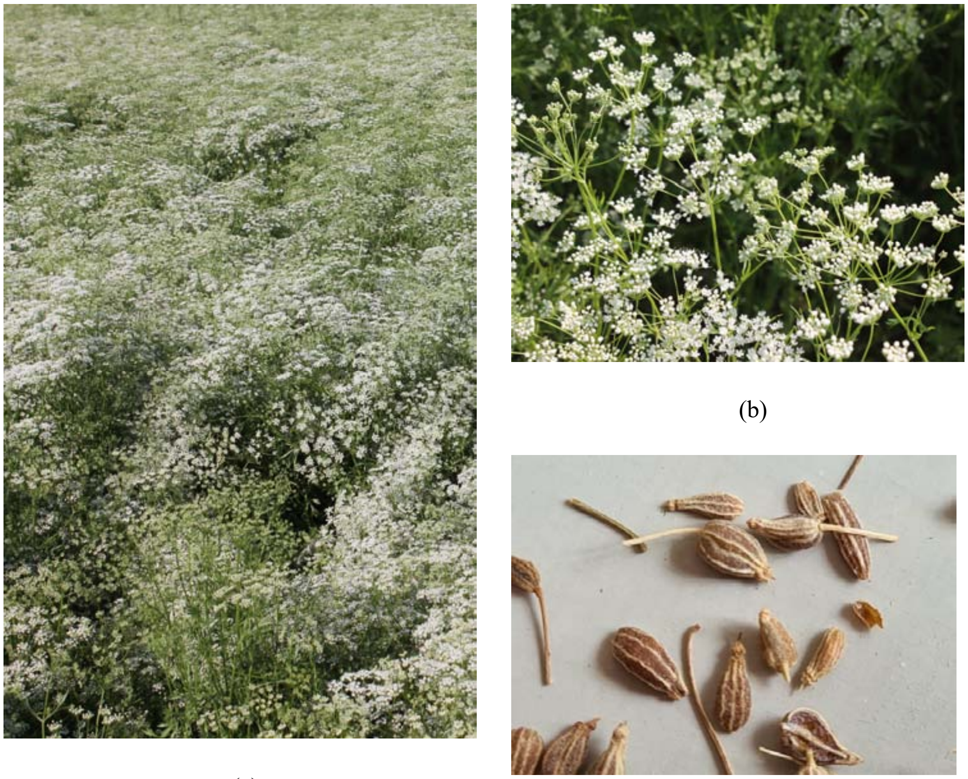
Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

is still being used traditionally in many countries as an anticonvulsant and for the treatment of gastrointestinal, inflammatory, dermatological diseases, against nightmares, melancholy, seizures, epilepsy [5 - 7]. Not only the seeds, but volatile oil of the fruits/seeds are also being used for their medicinal activities [8].

In addition to the plant's utilization for medicinal and culinary purposes, volatile oil obtained from the seeds is used in the cosmetic industry in the making of toothpastes, lotions, soaps, skin care products; used in the production of different alcoholic beverages in different countries (e.g. rakı in Türkiye, ouzo in Greece, Anisette or Pastis in France, anesone in Spain, Sambuca in Italy and arak mainly in Armenia and Syria) [1, 9]. A Cuban refreshment called Pru was also prepared with the species once, however basic Pru recipes do not include the plant currently [10]. Furthermore, volatile oil is also used in the aromatization of candies and tobacco [1, 7, 11]. The plant is considered to be a functional food and nutraceutical preparations are also being prepared with the volatile oil of the plant [12, 13]. With all these different usages, it is no surprise that anise seed is listed in various pharmacopoeia such as British, German and European Pharmacopoeia [14, 15], and is also approved by Herbal Medicinal Products Committee (HMPC) of European Medicines Agency (EMA) as a traditional herbal medicinal product [16].

The plant can be up to 30-50 cm in height, peak height is reported to be 50-60 cm; leaves are heterophyllous, petiolate basal leaves are simple, 2-5 cm long, reniform/ovate shaped with dentate margins; lower cauline leaves are pinnate having ovate/obovate segments and upper cauline leaves are 2-3 pinnate with linear-lanceolate lobes and sheathing petioles. The plant has white flowers, umbels 7-15 rayed, has 1 bract or none, and bracteoles also none or few, very narrow if present. Approximately 10 white flowers are present per umbellule and has greenish-grey to brown colored schizocarp fruits of 2-5 mm with a conical stylopodium. The flowering period of the plant is June and fruits are harvested in August [17 - 19]. The general appearances of the plant and the fruits are given in Fig. (**1**).

The plant is known by different names in various countries, some examples are listed in Table **1**.



(a) (b) (c)

Fig. (1). (**a**) *Pimpinella anisum* field; (**b**) General appearance of *P. anisum* (Photos by A.M. Gençler Özkan); (**c**) *P. anisum* fruits (Photo by C.S. Kılıç).

Table 1. Vernacular names of *P. anisum* in different countries.

Vernacular Name	Country	Refs.
Habathlawa, Nafaa	Algeria	[20, 21]
Andres huaylla, anisa, anis	Bolivia	[22, 23]
Erva-doce,	Brazil	[24, 25]
Anis	Ecuador	[26]
Anise	England	[27]
Anise vert	France	[27]
Anisa, Badian, Kuppi, Muhuri, Saunf, Sop	India	[27]
Anison, Badian rami, Vaveshing	Iran	[28 - 30]
Yansun, Razyane	Iraq	[31, 32]
Annesella, Matafaluga, Anice, Anici, Anesc	Italy	[27, 33, 34]

CHAPTER 2

Sinapis alba L. Seeds: Taxonomic and Ethnobotanical Aspects

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Abstract: This chapter concisely presents the state of knowledge about the taxonomical and ethnobotanical aspects of the seeds of *Sinapis alba* L. (*S. alba*), known as white or yellow mustard, belonging to the famous *Cruciferaceae* (or *Brassicaceae*) family. It starts with an introduction to medicinal plants, the seeds of *S. alba*, and their benefits for humans. This is followed by the systematics and taxonomy of the seeds, which are very important for the identification and reconstruction of the phylogeny of spices. In addition, the physical description of the plant and seeds has also been explained in detail in this section. The main part of this chapter is devoted to the extraction methods used to prepare essential oils and/or crude extracts from *S. alba* seeds for chemical and biological valorization. The last part deals with the history and the ethnomedical uses of the seeds.

Keywords: *Sinapis alba*, White mustard, Essential oil, Seeds, Biological activities.

INTRODUCTION

Spices and herbs have been used since the dawn of time. Since then, people have used these medicinal plants in the form of teas, tinctures, powders, and other herbal preparations to prevent or cure various diseases [1]. However, the methods of the use of a particular plant to cure a specific disease were transmitted from generation to generation *via* oral history [2]. According to the World Health Organization (WHO), around 80% of the population still depends on traditional medicine, where most of them use plant extracts or their bioactive compounds instead of synthetic components [3]. Nowadays, the consumption of medicinal plants is rapidly increasing due to their safety and curative effectiveness against many diseases [4]. Furthermore, it must be noted that these plants play a main role in the medication, manufacturing, and development of numerous drugs [5].

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Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

Brassicaceae is one of the biggest plant families with hundreds of genera and thousands of spices, including herbs, food crops, weeds, ornamentals, *etc.* In addition, it is also called the mustard family of flowering plants. Currently, three commercial mustard species are commonly grown. These include *Brassica juncea* (oriental mustard), *S. alba* (yellow or white mustard), and *Brassica nigra* (black mustard) [6].

One of the most economically important plants belonging to this family is *S. alba* [7]. This oilseed is cultivated all over the world. It can grow on poor soils, even in drought, humidity, heat, and frost [8]. For this reason, this plant could be found worldwide. It has the potential to extract Pb, Zn, and Cd from the soil [9]. *S. alba* seeds are rich in protein (28-36% w/w), oil (28-45% w/w) and low in starch [10, 11]. In addition, it was reported that the seeds contain different classes of secondary metabolites, most importantly glucosinolates, isothiocyanates, and phenolic compounds. These components are recognized for their numerous biological activities, especially against microorganisms and oxidative stress, making these seeds a valuable source of bioactive compounds [12].

Systematics and Taxonomy of *S. alba*

Systematics is a science enclosing the synthesis, analysis, and the acquirement of details about organisms or plants and their different parts (roots, stems, leaves, flowers, fruits, and seeds) [13]. It has many objectives, where the major ones are the discovery and the reconstruction of the phylogeny of a group of organisms. Systematics could also be named as an interrogative and central science; this is because it could use data from a large range of fields such as chemistry, biology, geography, ecology, embryology, anatomy, molecular biology, and morphology. Thus, researchers working on it have the opportunity to understand many aspects of the above-mentioned fields.

Taxonomy can be defined as the main part of systematics, which itself is constituted by four parts (DINC): description, identification, nomenclature, and classification. These form the basis for the most intellectual endeavors of a wide range of fields, and they are not restricted to a study of formal systematics [14]. We cannot talk about the systematics and taxonomy without introducing the French botanist Joseph Pitton de Tournefort (1656-1708) and the Swedish naturalist Carl's von Linné (1707-1778), the latter being known as the father of systematics and taxonomy. The French botanist has reported that it is mandatory to separate plants into groups from those they resemble, and this classification should be deduced from the plants' parts, the medicinal virtues, and the place where these plants originate from [15]. In addition, the Swedish naturalist was the first to classify organisms into domain, kingdom, phylum, class, order, family, genus, and species.

The *Brassicaceae* family constitutes around 75 genera and about 3200 species [16], including mustard, cauliflower, cabbage, and broccoli. The genus mustard comprises 150 spices of biennial and/or annual herbs. Their seeds are known as one of the oldest recorded species, and their cultivation and use date back to over 5000 years [17 - 19]. Among this very wide number of plants we mention,*S. alba Syn. Brassica alba* L. or *Brassica hirta* Moench, commonly named white or yellow mustard. It is classified as follows, from kingdom to species:Domain: *Eukaryota*

Kingdom: *Plantae*

Phylum: *Spermatophyta*

Subphylum: *Angiospermae*

Class: *Dicotyledonae*

Order: *Capparidales*

Family: *Brassicaceae*

Genus: *Sinapis* L.

Species: *S. alba*

This plant is widely cultivated in North Africa, Chile, Netherlands, United Kingdom, Japan, Canada, China, USA, Australia, and Italy [20].

S. alba is an annual herbaceous plant with irregularly serrated leaves that are alternating, stretched, and hairy on both sides. Its flowers are pistil bi-carpel, stamens tetradynamous with four cruciform yellowish petals, with a characteristic fragrance of honey. In addition, its fruits are ribbed and rounded, having swollen seeds with a uniform long beak and pods that are spread throughout the raceme. In early summer, *S. alba* grows rapidly and reaches a full height of 1.5 to 2 m. Besides that, the flowers become paler, and the fruits appear (Fig. **1**).

The seeds of *S. alba* are universal and called alkhurdal al abyad (Arabic), moutarde jaune ou blanche (French), Bai Jie Zi (Chinese), mostaza blanca (Spanish), senape biancha (Italian), sufedrai (Hindi) and bi ji sawi (Malaysian, Indonesian). They are prickly and globular in shape (Fig. **2**), with a length of 1.5 to 3 mm and no characteristic odour.

CHAPTER 3

An Updated Literature-based Mechanistic Review: Phytochemistry, Pharmacology and Therapeutic Promises of Cinnamon *(Cinnamomum verum)*

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Abstract: Cinnamon, also known as *Cinnamomum verum,* has long been recognized for its therapeutic benefits. The inner bark of trees, known as Cinnamomum, is used to make the spice cinnamon. It has been used as a component since the dawn of time, possibly as early as Ancient Egypt. It was once considered a blessing fit for a lord and was unusual and remarkable. These days, cinnamon is inexpensive, available at every general store and used as an ingredient in a variety of dishes and recipes. Cinnamon comes in two primary varieties: *Ceylon cinnamon*, also called "true" cinnamon, and *Cassia cinnamon*, which is the more widely available variety and what most people call "Cinnamon" nowadays. Cutting the stems of cinnamon trees yields cinnamon. After that, the woody portions are released, and the inner bark is split apart. When it dries, it becomes cinnamon sticks, which are strips that twist into rolls, and these sticks can be ground to make cinnamon powder. The major component of cinnamon is cinnamaldehyde. Cinnamaldehyde is concentrated in the slick section of the plant, which gives cinnamon its unique flavours and fragrance. In addition, it is also responsible for the majority of cinnamon's health benefits, including its anti-inflammatory, anti-cancer, anti-infective, and anti-diabetic properties. Furthermore, it can bring down glucose levels, decrease coronary illness chance factors and has plenty of other great medical advantages. The cinnamon variant has significant amounts of coumarin, a substance that is known to be harmful in high concentrations. While all cinnamon should offer health benefits, Cinnamon's high coumarin level may cause major problems with large doses. In this way, Ceylon, often known as "true" cinnamon, is greatly enhanced, and research indicates that it has far less coumarin than cinnamon. In the end, one of the world's tastiest and healthiest flavors is cinnamon.

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Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

Keywords: Cinnamon, Ceylon, Coumarin, Phytochemicals, Remedies.

INTRODUCTION

The evergreen tree species of the *Lauraceae* family, *Cinnamomum zeylanicum L.* and *Cinnamon cassia L.*, are native to the tropics and are utilized for a variety of purposes worldwide, including medicinal purposes. The word was borrowed from the Old French word “Cinnamon” and adopted by the English around the end of the 14th century. This phrase must originate in Semitic languages; it is derived from Latin through the Phoenician-Greek word “Kinnamomon” (See Hebrew “Qinamon”). The term “Printed word” first appears in print in John Lydgate's “Fall of the Princes” in 1430. Dietary fiber, iron, calcium, and manganese are all found in cinnamon [1, 2]. It contains a variety of compounds, including cinnamic acid, cinnamaldehyde and cinnamate, as well as a host of other naturally occurring antioxidants and polyphenols with anti-inflammatory, anti-cancer, and anti-microbial qualities. Numerous studies on cinnamon in the form of bark and bark powder have revealed a variety of benefits. Cinnamon's phenolic components and essential oils are beneficial to human health. Recent research has shown that cinnamon is beneficial in the treatment of diabetes, atherosclerosis, arthritis, and Alzheimer's disease [3 - 5].

HISTORY

For the past hundreds of years, cinnamon has been recognized as one of the valuable spices having many culinary uses. In Ayurveda, cinnamon is used as a stimulant, carminative, antiemetic and antidiarrheal. In addition, the ancient Egyptians used it for embalming. The Portuguese conquerors found *C. zeylanicum* rising extensively in Sri Lanka in the 16th century. They also imported the spice into countries of European origin in the 16th and 17th centuries. The cultivation of cinnamon in the 17th century began in Java during the Dutch occupation. The main exporter of cinnamon to European countries was The East India Company [6, 7]. Although the cultivation of *Ceylon cinnamon* has declined,, Sri Lanka still remains the key cultivator of cinnamon oil, while the oil of *Ceylon cinnamon* from Sri Lanka is widely used in the food as well as pharmaceutical industries. The history of cinnamon is tracedback to hundreds of years, and cinnamon is recognized as one of the greatest spices, along with many culinary uses [8 - 10]. Different types of cinnamon are presented in Table **1** [11 - 14].

Table 1. Types of cinnamon.

S. No.	Type	Origin	Color	Taste	Others
1.	*Cinnamomum loureiroi*	Vietnam	Dark reddish brown	Spicy and sweet	Strong aroma, spicy, high coumarin
2.	*Cinnamomum aromaticum*	China	Dark reddish brown	Spicy but bitter	High coumarin, verystrong taste
3.	*Cinnamomum zeylanicum*	Sri Lanka	Light to medium reddish brown	Slightly sweet	Lowest coumarin content
4.	*Cinnamomum burmanni*	Indonesia	Dark reddish brown	Spicy	High coumarin, strong aroma

PHARMACOGNOSTIC CHARACTERISTICS

The leaves of the *C. verum* tree are lanceolate to ovate, have sharp points and are 11 to 16 cm long. The tree can grow to a height of around 10 m. The tubular, pale yellow flowers have six lobes and develop in panicles that are the same length as the leaves. When ripe, the little fruit, about 1 to 1.5 cm in length, turns black.

CHEMICAL COMPOSITION

Numerous essential oils, as well as resinous substances including cinnamic acid, cinnamaldehyde and cinnamate, are present in cinnamon. Because of the absorption of oxygen, cinnamon acquires its spicy flavor and scent from the presence of cinnamaldehyde [15]. Cinnamon's color darkens with age, enhancing the resinous components. Table **2** lists the different physiochemical characteristics of cinnamon [16]. A variety of essential oils have also been claimed to be present, including trans-cinnamaldehyde, cinnamyl acetate, eugenol, L-borneol, caryophyllene oxide, β-caryophyllene, L-bornyl acetate, E-nerolidol, α-cubebene, α-terpineol, terpinolene, and α-thujene. Resinous substances are found in varying amounts in the leaves, bark, root bark, and fruits of the cinnamon plant (Table **3**) [17 - 21].

Table 2. Physicochemical properties of cinnamon oil.

S. No.	Parameter	Bark Oil	Leaf Oil
1.	Refractive index (20^{0}C)	1.573–1.591	1.529–1.537
2.	Solubility characteristics	Soluble in 2–3 volumes of 70% alcohol	Soluble in 1.5 volumes of 70% alcohol
3.	Specific gravity (20^{0}C)	1.010–1.030	1.030–1.050
4.	Eugenol content	4.0-10.0%	4%

CHAPTER 4

Tamarindus indica L. Its Phytochemicals and Health Related Issues

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Abstract: *Tamarindus indica* L. is a multifunctional plant native to Madagascar that may now be found in most tropical and subtropical climates from Africa through South Asia, northern Australia, Southeast Asia, and China. Almost every part of the tree is used in the food, chemical, pharmaceutical, or textile industries, as well as for fodder, wood, and fuel. It has been connected to a variety of therapeutic uses, including inflammation, diabetes, constipation, indigestion, flatulence, and more. The purpose of this chapter is to review research subjects on phytochemical elements in tamarind and their relationship to health that have recently been published in peer-reviewed journals. We gathered data from original peer-reviewed studies that focused on *Tamarindus indica* L., its phytochemicals, and health/medicinal-related issues. We used four NIH Library-registered databases to perform our literature search. We included open access research and review publications in English (2010 to 2021). A total of 124 articles were used to form the basis of the discussion. Among the phytochemical components found in tamarind stem bark aqueous extract were saponin, catechin, iristectorin A, proanthocyanidin B1, procyanidin tetramer, and procyanidin trimer (bergenin, catechin, iristectorin A, proanthocyanidin B1, procyanidin tetramer, and procyanidin trimer). The essential oil (limonene, linalool anthranilate, p-cymene), 3-eicosyne, cryptopinone, free and conjugated fatty acids (malic, tartaric, phthalic, palmitic, 10-octadecenoic, and n-nonadecanoic), flavones (luteolin 7-o-glucoside, luteolin, apigenin, isorientin (caffeic acid) were most identified in tamarind leaf. Diphenyl-ether, longifolene, caryophyllene, and 6, 10, 14-trimethylpentadeca-5, 9, 13-trien-2-one were among the new chemicals discovered in the leaf extract. 2-furancarboxaldehyde, 2, 3-butanediol, and 2-furancarboxaldehyde, 5-methyl were the most common phytochemicals found in pulp extracts. These chemicals are known for their antioxidant properties, treatment of allergic rhinitis, anti-inflammatory and analgesic properties, antidiabetic and antibacterial activity, *etc*. Because this versatile plant has been widely utilised as herbal medicine, the findings of this review could be used as a database for future phytochemicals and clinical studies of this plant. Considering the plant's uses and benefits, it can be recommended as a valuable multifunctional medicinal plant for both animals and humans.

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Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

Keywords: Health Benefits, Medicinal Effects, Phytochemicals, *Tamarindus indica* L.

INTRODUCTION

Tamarindus indica L., also known as *Tamarindus occidentalis* Gaertn, *T. officinalis* Hook, and *T. umbrosa* Salisb, is a member of the Leguminaceae (Fabaceae) and the subfamily of Caesalpinaceae [1]. *Tamarindus indica* L. is commonly known as a tamarind in English, 'asam jawa' in Malay, 'puli or pulian' in Tamil, 'khaam or mak kham' in Sino-Tibetan, China, 'makham' in Thai, 'sampalok' in Tagalog, Philippines and 'ambli, amli or imli' in Hindi and 'ardeib' or 'tamarhindi' in Arabic [2]. Theophrastus recorded the tamarind tree between 370 and 287 BC, but it had already been documented in the Indian Brahmasamhita scriptures between 1200 and 200 BC, including mention of its cultivation in Egypt in 400 BC [3]. Tamarind is supposed to be an East African native that was brought to Southeast Asia by Arab and Persian traders in the first millennium BC [4]. Tamarind trees can be found in various regions of the world, and they are farmed in eighteen of their native countries, as well as thirty-six others. India, Thailand, Bangladesh, Sri Lanka, and Indonesia are among Asia's leading tamarind growers [5], with India and Thailand being the two largest producers, producing from 300 thousand to 140 thousand tons per year [6]. On the other hand, Mexico and Costa Rica are the biggest producers of the American continent [5].

This tree grows slowly but can reach a height of 25 metres and a diameter of 1-2 metres. Tamarind trees have a lengthy life expectancy of 80 to 200 years and can produce fruit for decades [7]. The tamarind fruit pulps are contained in a pod; a hard shell, sub-cylindrical straight or curve shape with rounded ends and brown in colour. When the fruits began to ripe, the shells became softer, brittle, and breakable. The fruit pulps have a soft and mushy texture, brown in colour when raw, but turn to blackish-brown after ripening. They are surrounded by strong fibrous threads and there are up to 12 seeded fruit pulps in a pod [8]. The tamarind seeds are small, firm, glossy, irregularly rhomboid or orbicular in shape, a little flattened, and typically brownish-black in colour, measuring 3-10 cm x 1.3 cm [5]. Apart from the fruit pulps, the leaves are also edible. The leaflets are bright green in colour, tiny, slender, oval or oblong in shape, rounded, stipule-free, and 1.2–3.2 cm long. They are arranged in 10–18 pairs and are 1.2–3.2 cm long [9]. The blossoms of the tamarind are small, elongated, and yellow with orange or red streaks. Flowers are 2.5 cm in diameter (one inch) and come in little racemes with five petals (two of which have been reduced to bristles). The flower bud is protected and supported by four pink sepals, which fall off when the flower blooms [10]. The tamarind tree's bark is brownish-grey in colour with a rough, scaly texture [4]. Hard, dark-red heartwood and softer, yellowish sapwood make up tamarind wood [11].

The edible component of the plant, the fruits, is widely used in cooking and as a beverage, particularly in Asia [12]. Sweet and sour tamarind cultivars exist, with the latter being the most prevalent [1]. The sweet tamarind fruits are typically consumed unprocessed. Sour fruits can be eaten raw or processed into a variety of items before being consumed [13]. The sour fruits are normally ground into a paste, with or without seeds, and put in a container before being marketed as a food flavouring. It is used as a condiment in a variety of dishes, including curries, sauces, and dips. It adds a sour note to a dish or balances off the sweetness and saltiness, resulting in a well-balanced flavour profile [13]. Tamarind paste is also often used to prepare juice in hot climate countries, which is excellent for decreasing body temperature. In addition, drinking sweet-sour tamarind juice can help to reduce or eliminate nausea and vomiting. The salted and roasted seeds are consumed as a snack [14, 15]. Sweets, ice cream, alcoholic beverages, soft drinks, and juice concentrate were all made using the sweet-sour fibrous pulp in Africa [16]. In-store items such as chutneys and Worcestershire sauce [15] contain the fruit as a component.

The health advantages of *Tamarindus indica* L. have attracted a lot of attention and interest, as evidenced by surveys of traditional claims or scientific studies and discoveries. In the local community, all portions of *T. indica* L. have been claimed and reported to have enormous health effects, and this indigenous knowledge is being brought into the scientific context to support the valuable local practitioners and users' assertions on its advantages. The herb is used in traditional African medicine to treat wounds, stomach aches, and parasite infection. In some tropical cultures, it is also used to induce bowel movement and as a libido-booster [17]. The fruit pulp is used to make a drink called 'kunu zaki' in Nigeria [18]. In addition to the extensively utilised portions of *T. indica* L. of fruits and leaves in traditional practises, the Ivory Coast population employed stem bark to cure haemorrhoids and chronic bowel problems [19]. Snakebites, diabetes, eye problems, ulcers, intestinal inflammation, jaundice, and diarrhoea are all treated with tamarind seeds [14, 20]. The seeds are also utilised in the culinary and pharmaceutical industries to make seed gum, which is used as a thickening and stabilising agent [15]. *T. indica* L. was also employed as an antimicrobial agent in India to cure microorganism sickness. Amenorrhea, lotions and pustules, ulcers, boils, asthma, and diarrhoea were all treated with the entire plant [21].

CHAPTER 5

Synthetic Analogues of Curcumin: The Search for Anticancer and Antioxidant Activities

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Abstract: Curcumin, a key component of *Curcuma longa* L.'s rhizome, has a wide range of biological activities, as evidenced by intensive research over the last five decades. Curcumin has recently been utilized as an alternative medical ingredient in Southeast Asia to cure a variety of diseases, including stomach trouble, flatulence, jaundice, arthritis, sprains, wounds, skin infections, *etc*. Curcumin has also been shown to have antioxidant, anti-inflammatory, antiviral, antibacterial, antifungal, and anticancer properties. Medicinal chemists employ rational structural modifications to improve the pharmacokinetic properties of a potential candidate to make them a therapeutically useful candidate. The objective of the chapter is to summarise the various modifications that have been carried out in curcumin's structural framework concerning its medicinal property. An elaborate discussion will be presented on antioxidant and anticancer activities.

Keywords: Anticancer activity, Antioxidant activity, Curcumin and its analogues.

INTRODUCTION

Curcumin is a natural polyphenolic compound found in turmeric (*Curcuma longa*,

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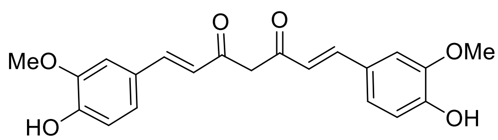
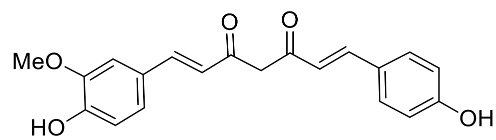
Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

Family: Zingiberaceae). In Indian and Chinese health systems, it has been used to heal wounds, sprains, as well as gastrointestinal, lung, and liver problems.

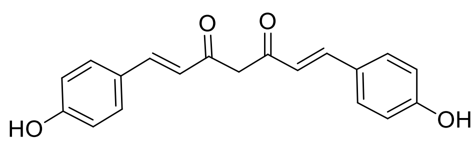
Curcuminoids, such as curcumin, dimethoxy curcumin, bisdemethoxycurcumin, and cyclo-curcumin, are responsible for turmeric's distinctive yellow colour. Turmeric contains 3–5% curcuminoids, the most active of which is curcumin (1,7-bis(4-hydroxy-3-methoxy phenyl)-1,6-heptadiene-3,5-dione or diferuloy lmethane). It is water-insoluble but soluble in ethanol and acetone [1]. Curcumin was first isolated in the year 1815, and the crystalline form was achieved in 1870. Later, its chemical structure was revealed in 1910 [2]. According to Payton *et al.*, the enol form is more stable, and curcumin is available in this form [3].



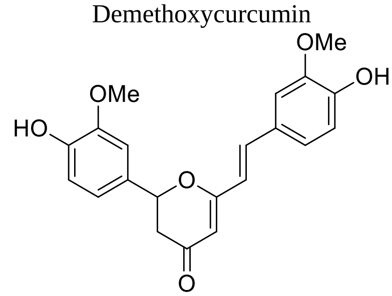
Curcumin



Demethoxycurcumin



Bisdemethoxycurcumin



Cyclocurcumin

Curcumin's therapeutic properties have been well documented in reviews by numerous researchers [4 - 9]. For the past few years, there has been an exponential development in the trend of research into the efficacy of curcumin [10] in animal models of serious depression [11]. Ferulic acid amide derivatives containing one-half curcumin, *i.e.*, an aryl-, -unsaturated carbonyl group, are partially attached with amines [12] and curcumin-based pyrazolines [13 - 16] for MAO inhibitory activity. As curcumin has poor bioavailability [17] and metabolic stability [18]; it is not yet recognised as a good antidepressant. Informed by these facts, medicinal chemists employ rational structural modifications carried out in curcumin's structural framework with reference to its medicinal properties to improve the pharmacokinetic properties [19] in an effort to make them a therapeutically useful candidate. The literature review was carried out from 1970 to 2020 and is regularly updated. The basic knowledge for an elaborate discussion will be presented on anticancer and antioxidant activities.

ANTICANCER ACTIVITY OF CURCUMIN

Cancer is one of the world's most dreadful diseases, characterised by the shutting down of regulatory mechanisms of normal cells, a property of uncontrolled cell division, and the migration of proliferating cells to other organs of the body from the original site [20]. For the last couple of decades, curcumin has been a promising molecule in the field of cancer research as its structure has such chemical groups (*e.g*., phenols), which play an essential role in inhibiting cancer, mainly by inducing the apoptosis phase of the cell cycle. It has been observed from previous research and *in-vitro* studies that curcumin has a high degree of selectivity for cancer cells [21, 22].

There are many mechanisms that define the action of curcumin in inhibiting cancer, but some of them are really prominent and hard to accept [21]. Curcumin is attracting the attention of cancer research worldwide because of its powerful inhibitory capabilities against human malignancies. According to Pal *et al*., curcumin has been proven *in vitro* to have anti-tumour promoting anti-proliferative properties against tumour cells in research in recent years [23 - 26]. Curcumin has a strong cytotoxic effect on a variety of cancer cells. In human promyelocytic leukaemia HL-60 cells and human oral squamous carcinoma HSC-4 cells, it causes apoptosis. Curcumin also has anticarcinogenic properties against a variety of cancers, including skin cancer, stomach cancer, duodenal cancer, and colon cancer [27 - 32].

Curcumin inhibits NF-κB (Nuclear factor), which results in ubiquitination and degradation of the phosphorylated IκBα and the release of NF-κB from its stationary location in the cytoplasm. IκBα, TNF-α, cyclooxygenase-2 (COX-2), ICAM-1, Bcl2, MMP-9, c-myc, interleukins including IL-6 and IL-8, MMP-9, and inducible nitric oxide synthase (iNOS) are all regulated by NF-B [33]. NF-κB, is also involved in the progression of cancer, including the production of anti-apoptotic genes, tumour promotion, angiogenesis, and metastasis [34]. The unbound NF-κB enters the nucleus, where it binds to DNA and activates transcription. Curcumin blocks the IκK-mediated phosphorylation and degradation of IκBα. Yet, NF-κB remains bound to IκBα in the cytoplasm and is not able to enter the nucleus to activate transcription [35 - 37]. Curcumin activates the glutathione-S-transferase (GST) enzyme, which helps to prevent glutathione depletion in cells (GSH). The cystinylthiol group of GSH has been shown to be a key location for thiocarbamoylation by the cytotoxic drug phenethylisoth iocyanate during apoptosis induction, leading to cellular GSH depletion *via* efflux of the GSH conjugate [38, 39].

CHAPTER 6

Licorice: Evaluation of Phytochemical-Neuropharmacological Profile and Drug Interactions with a Focus on Gut Microbiota

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Abstract: Licorice, derived from the dried roots and rhizomes of *Glycyrrhiza uralensis* Fisch., *Glycyrrhiza inflata* Bat. or *Glycyrrhiza glabra* L., has been utilized in Traditional Chinese Medicine for centuries. Licorice serves not only as a sweetener, but also as a remedy for various ailments, including cough, fever, pain, heartburn, kidney stones, and skin ulcers. Glycyrrhizin is a major compound of licorice that contains high amounts of flavonoids, saponins, triterpenes, isoflavonoids, and chalcones. The gut microbiota contains trillions of microorganisms in the gastrointestinal system, and the balance/imbalance of gut microbiota composition is related to healthy state and disease susceptibility. Moreover, gut microbiota plays a pivotal role in the metabolism of herbal medicines. Following ingestion, glycyrrhizin undergoes conversion by gut microbiota, resulting in the formation of 18β-glycyrrhetinic acid (GA). Notably, GA represents a bioactive form of glycyrrhizin, responsible for both the pharmacological effects and adverse reactions associated with licorice. Conversely, oral administration of herbal medicines, including licorice, may impact the gut microbiota composition. Licorice and its metabolites possess the potential to modulate the abundance of gut microbiota members. This chapter aims to explore the intricate relationship between licorice and gut microbiota while specifically evaluating the effects of licorice and gut microbiota on neurodegenerative diseases such as Parkinson's and Alzheimer's diseases. Additionally, we provide a comprehensive summary of the adverse effects of licorice and its potential interactions with other drugs. Further studies focused on elucidating the interplay between licorice

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Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

and gut microbiota will improve our understanding of the neuropharmacological profile and adverse effects of licorice, thus facilitating the development of novel treatment approaches using licorice.

Keywords: Alzheimer's disease, glycyrrhetinic acid, glycyrrhizin, glycyrrhizinic acid, gut-brain axis, isoliquiritigenin, licochalcone, liquiritigenin, Parkinson's disease, pseudohyperaldosteronism.

INTRODUCTION

Licorice is a commonly prescribed herbal remedy in Traditional Chinese Medicine formulas [1]. Licorice has been used medicinally since 500 BC and is often referred to as the "grandfather of plants". Licorice was mentioned in early medical texts such as the Ebers Papyrus (1552 BC), Codex Hammurabi (2100 BC), De Materia Medica (50-70 AD), De Historia Plantarum, and De Causis Plantarum (371–286 BC) of Theophrastus [2]. Licorice is derived from the roots of the *Glycyrrhiza uralensis* Fisch., *Glycyrrhiza inflata* Bat. or *Glycyrrhiza glabra* L., which belong to the Fabaceae family and the genus Glycyrrhiza [3]. Licorice is native to warm climate countries, including North Africa, China, West and East Asia, Southwest and Southeast Europe, and is widely cultivated in different regions [4].

Glycyrrhizin, also known as glycyrrhizic acid or glycyrrhizinic acid, is a major bioactive compound of licorice. It is a sweet-tasting triterpenoid saponin that contains high amounts of phenolic compounds [5]. Additionally, licorice contains yellow-colored flavonoids, such as liquiritin, isoliquiritin, licochalcones, glabridin, and licoricidin, which are also important for its pharmacological activity [6]. Licorice has been traditionally used for the treatment of gastric ulcers, wound healing, cystitis, cough, diabetes, and tuberculosis [2]. Studies have shown that the active compounds of licorice exhibit a wide range of activities, including anti-inflammatory, antiviral, antimicrobial, antitumor, and immunomodulatory [7]. Due to its promising pharmacological profile, licorice could potentially be considered for the treatment of liver diseases, depression, Alzheimer's and Parkinson's disease [7 - 10].

The components of herbal medicines are usually metabolized in the gastrointestinal tract since most herbal medicines are administered orally. In addition to low stomach pH and digestive enzymes, gut microbiota also plays a role in this metabolism [11]. Bioactive molecules of herbal medicines eventually come into contact with gut microbiota members, which may enhance or decrease their activity through bacterial metabolism [12]. For example, glycyrrhizin is transformed by the gut microbiota into 18β-glycyrrhetinic acid (GA), an active metabolite responsible for the pharmacological activity of glycyrrhizin [11]. Similarly, the flavone compound liquiritin is metabolized into liquiritigenin and isoliquiritigenin, which exhibit similar pharmacological effects [13]. Although herbal remedies are easily accessible as over-the-counter products, their misuse can lead to serious life-threatening complications [14], such as licorice-induced pseudohyperaldosteronism. Therefore, the use of licorice in patients receiving concomitant medication should be carefully monitored for potential drug interactions.

In this chapter, our objective is to review the pharmacological profile of licorice and its metabolites, with a specific focus on neurodegenerative diseases. We aim to enhance our understanding of the bidirectional relationship between licorice and gut microbiota by analyzing data from preclinical and clinical studies. We provide a clear and well-organized summary of the phytochemical and neuropharmacological properties of licorice. In addition, the reported adverse effects of licorice and the potential herb-drug interactions between licorice and medications will help healthcare professionals and patients to be cautious when using licorice with other therapies.

BOTANICAL DESCRIPTIONS

The medicinal parts of licorice consist of unpeeled, dried roots and runners, as well as peeled dried roots and rhizomes [15]. Glycyrrhiza belongs to the Fabaceae family. It is a herbaceous perennial plant, typically reaching approximately 1-2 meters long. The pinnate leaves are 7 to 15 cm long [15, 16] and composed of 3 to 8 pairs of leaflets. The flowers, which are pale blue to purple, are approximately 1 to 1.5 cm long and have short-pedicled [16]. The fruit is a pod measuring 1.5 - 2.5 cm in length and 4-6 mm in width, containing 3-5 reniform brown seeds [15]. The tap root is approximately 15 cm long and is divided into 3-5 subsidiary roots [15]. In addition, the plant produces horizontal woody stolons that can reach up to 8 meters, and new stems emerge annually [15].

Glycyrrhiza species are distributed across different regions. *G. glanulifera* is found in Western Asia and Southeast Europe, *G. pallida* in Iraq. *G. typica* is native to southern Europe and southwestern Asia [15]. *G. uralensis* is native to Central Asia, Mongolia, and Northwest and Northeast China. *G. glabra* is found in South Europe, Türkiye, Iran, Iraq, Central Asia, and the north-western part of China. Finally, *G. inflata* is exclusively found in the Xinjiang Uygur Autonomous Region of China [17].

SUBJECT INDEX

A

Atta-ur-Rahman, M. Iqbal Choudhary & Sammer Yousuf (Eds.)

B

C

D

E

F

G

H

I

K

L

M

R

S

T

U

V

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