

## PAPER DETAILS

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## The botanical study, phytochemical composition, and biological activities of *Laurus nobilis* L. leaves: A review

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**Abstract:** *Laurus nobilis* is native to the southern Mediterranean region. It is a small tree from the Lauraceae family. The leaves of *L. nobilis* are the most exploited part of the plant due not only to the high produced quantity but to the large benefits and extensive use in different fields including culinary, cosmetic, therapeutic, and pharmacologic. The various beneficial health properties attributed to bay leaves are related to the presence of various bioactive compounds. Chemically, they contain numerous essential elements, some vitamins, and many secondary metabolites such as essential oils (cineole, linalool, and eugenol), phenolic compounds, particularly phenolic acids (ferulic, protocatechuic, and caffeic acids, etc.) and flavonoids (such as catechin, kaempferol, apigenin, quercetin, and their derivatives), and alkaloids (noraporphins and aporphins). Laurel leaves are not only used to flavor dishes, but present several beneficial properties that justified their traditional use against numerous illnesses, particularly for rheumatism, indigestion, and diarrhea. Bay leaves are an essential component of several industrial applications including agrifoods, cosmetics, and pharmaceuticals. Due to the presence of cited chemical constituents in bay leaves, various biological and pharmacological properties have been reported such as antioxidant, antibacterial, fungicidal, antiviral, insecticidal, wound healing, antimutagen, anticonvulsant, analgesic, anti-inflammatory, and immunostimulatory activities. This review provides an overview of *L. nobilis* leaves, beginning with botanical aspects, including its preparation and composition, followed by a discussion about the most abundant bioactive compounds, and finally the traditional uses and therapeutic effects.

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## 1. INTRODUCTION

The use of plants for therapeutic purposes is a growing practice. Although the use of medicinal plants is continuously increasing, there the use of plants for therapeutic purposes is a growing practice. Despite the large number of investigations on medicinal plants, there are still many aspects to explore in this area (Ahmad *et al.*, 2022; Barroso *et al.*, 2018; Elefe, 2021). Besides their content of important nutrients, plants also synthesize bioactive compounds that have preventive properties against various diseases. These plants are now industrially transformed into various products for pharmaceutical, food, perfume, and cosmetic uses (Ambrose *et al.*, 2016; Yasin *et al.*, 2020).

Condiments are used to add flavor to foods and for preservation purposes due to their antioxidant and antibacterial properties. Condiments such as bay laurel are widely used in various products (Morais *et al.*, 2009). The noble laurel, much appreciated for the condiment benefit of its leaves, is one of the aromatic plant species, which is experiencing a resurgence of interest for its use in traditional medicine and the pharmaceutical, agrifood, and cosmetic industries. The increased demand for products resulting from the use of bay leaves has significantly increased its global production (Chaaben *et al.*, 2015).

Laurel (*L. nobilis*, family Lauraceae) is an evergreen tree that has been used for 1000 years and is an essential ingredient in cooking and many traditional uses (Hanif *et al.*, 2020). The leaves are used in fresh or dried form to flavor culinary preparations and scented and aromatic essential oil in perfumery. Laurel has been traditionally used for years in traditional medicine, due to its various pharmacological activities, including antimicrobial, antioxidant, anticancer, insecticide, and antifungal (Bendjersi *et al.*, 2016; Nabila *et al.*, 2022; Zibi *et al.*, 2022). This tree is native to the southern Mediterranean region. It is cultivated commercially for its aromatic leaves in Algeria, Türkiye, Morocco, Portugal, Spain, Italy, France, and Mexico. It is widely cultivated in Europe and the United States as ornamental (Guenane *et al.*, 2016).

*L. nobilis* is a widely studied medicinal plant that is the subject of numerous studies concerning its phytochemical compounds (Caputo *et al.*, 2017; Chahal *et al.*, 2017; Khaled Khodja *et al.*, 2021) and its therapeutic virtues such as the treatment of several neurological pathologies, dermatological and urological as well as gastrointestinal diseases such as epigastric bloating, impaired digestion, gas and belching (Khaled Khodja *et al.*, 2020). To gather recent knowledge concerning *L. nobilis*, this review is devoted to the phytochemical composition and traditional uses of bay leaves.

## 2. BOTANICAL STUDY

### 2.1. Origin

*L. nobilis* is native to the Mediterranean region (Buto *et al.*, 1990). The ancient Greeks and Romans used it as a condiment and medicine. In Greek mythology, it was considered sacred, which is why in ancient Greece, receiving a wreath made of bay leaves was considered an honor. Olympic winners, poets, victors, and heroes received the crown to wear on their heads. This habit was also accepted by the Romans (Ballabio & Goetz, 2010).

The name *Laurus* was derived from the Latin word “*laureola*”, which means laurel wreath. The word “*baccalaureate*”, whose Latin root comes from *bacca lauri* meaning bay of laurel, refers to the laurel wreath offered to heroes in antiquity. The Romans spread the species to parts of Europe; the first settlers introduced it to the New World. Today, the species is cultivated in the Mediterranean region, Russia, Central America, and, the southern United States (Elzebroek & Wind, 2008).

## 2.2. Botanical Classification

The laurel, *L. nobilis* L., belongs to the Lauraceae family. It is also known as the laurel sauce or the laurel of Apollo. The Laurales constitute a large order which brings together 9 families and about 3000 species. The main families of this order are Calycanthaceae, Lauraceae, and Monimiaceae. The Lauraceae family comprises more than 55 genera and 2500-3500 species (Trofimov *et al.*, 2022). The genus *Laurus* includes three major species: *Laurus azorica*, also called *Laurus canariensis*, growing in the forests of the Azores islands; *L. nobilis*, in the Mediterranean region and *Laurus novocanariensis*, present on the island of Madeira, the Canaries and Morocco (Ballabio & Goetz, 2010). The botanical classification of *L. nobilis* L. is reported in Table 1.

**Table 1.** Botanical classification of *L. nobilis* L. (Quézel & Santa, 1962).

Kingdom	Plantae
Under the reign	Vascular plants
Branch	Spermaphytes
Sub-Branch	Angiosperms
Class	Dicotyledonous
Subclass	Magnolideae
Order	Laurales
Family	Lauraceae
Genus	<i>Laurus</i>
Species	<i>L. nobilis</i> L.

## 2.3. Botanical Description

Laurel is an evergreen shrub or tree up to 12 m tall in the wild and cultivation is usually pruned to 2-3 m tall. The species naturally has several trunks. The bark of the stem and branches is dark brown to almost black (Elzebroek & Wind, 2008). The foliage of *L. nobilis* is evergreen with a dark green color above and lighter below. The leaf shape is elongated, even lanceolate, with pointed tips and a short petiole. The blade has a slightly thickened, wavy edge that curves inward. The leaves are approximately 3 to 5 cm wide by 10 cm long. Hairy at first, they then take on a shiny and hairless appearance (Geerts *et al.*, 2002) (Figure 1).

Laurel is a dioecious plant, that is, the male and female flowers are on separate feet. Flowering takes place from March to May. The inflorescence is made up of small umbels of four or five axillary flowers. It is creamy-white to greenish-white in color, unlike other Lauraceae which are trimers, the flower of the genus *Laurus* is a dimer, which can be seen more easily on a floral diagram. As a bud, the flowers are enclosed in an involucre of bracts. Since the petals and sepals are not distinct, we will speak of tepals. The tepals are arranged in two whorls, with a slightly smaller size for those located internally (Figure 1).

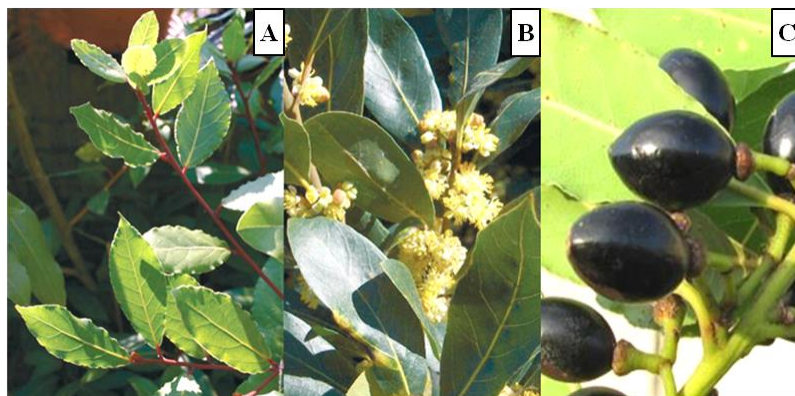
The fruit is a fleshy aromatic drupe, 10-15 mm long, ovoid, bright green at first and purplish black when ripe in autumn. It is made up, from the outside to the inside of the pericarp, mesocarp, and endocarp and contains a single seed, formed by two cotyledons rich in fat. The first two parts are dark, a few millimeters thick and makeup about 36% of the weight of the fresh fruit, the remainder, 64%, being made up of the endocarp and the seed. The berries remain on the plant all winter, sometimes until spring, which may coexist with the new flowering (Ballabio & Goetz, 2010) (Figure 1).

## 2.4. Geographical Distribution

Laurel is cultivated in different ecological and climatic conditions. Well-drained, moist soil with a pH ranging from 4.5 to 8.2 and humid atmospheric conditions near the sea are better

conditions for rapid growth (Kemp, 1983; Patrakar *et al.*, 2012). The cultivation of laurel grows in the following countries: Türkiye, Algeria, Morocco, Portugal, France, Spain, Greece, India, Pakistan, other Southeast Asian countries, some Pacific Islands, Australia, America Central, Mexico, southern United States, and Canary Islands (Parthasarathy *et al.*, 2008).

**Figure 1.** Morphological appearance of the different organs of *L. nobilis*: branch (A), flowers (B), fruits (C) (Chaaben *et al.*, 2015; Elzebroek & Wind, 2008).



## 2.5. Leaf Treatment

### 2.5.1. Harvesting of leaves

Laurel leaves can be harvested all year round thanks to the fact that the plant is evergreen. In the Mediterranean region, the optimum time for harvesting is in the autumn season. For example, in Türkiye, Greece, and the former Yugoslavia, bay leaves are harvested from August to October, for Morocco and Portugal the recommended harvest period is July to August. Harvesting should be done in optimal conditions avoiding dew, humidity, and heavy rains, as these can accelerate deterioration and discoloration and thus result in a poor quality product. The collection of bay leaves is usually done by hand or using small agricultural tools such as rakes (Ambrose *et al.*, 2016).

### 2.5.2. Drying of leaves

Drying is the oldest method used for preserving food. By definition, drying is the operation aimed at evaporating free water from a foodstuff to minimize microbial growth and chemical and enzymatic reactions (Cantín *et al.*, 2011). Drying is a process that can bypass the seasonal overproduction of crops and spread their availability throughout the year. In addition, the fresh plant cannot be cost-effectively supplied to all places in the world, due to the high water content, it suffers deterioration caused by the growth of microorganisms and biochemical changes. The elimination of water by dehydration reduces this growth and keeps the organoleptic characteristics of the plant (Ouafi *et al.*, 2015).

Small farmers and large producers of bay leaves wash the leaves after harvest and then proceed to drying. Leaf moisture levels are reduced to less than 10% using drying to improve the stability of their quality in storage (Ambrose *et al.*, 2016; Díaz-Maroto *et al.*, 2002). Drying of bay leaves is carried out by several methods such as sun drying, in shade, artificial process using dryers, or in hot air. Sun drying is an easy and inexpensive method, but direct sunlight can cause leaf discoloration and the use of high temperatures in other drying methods can cause a loss of volatiles. Drying in the shade or artificial drying is particularly recommended to achieve better quality (Ambrose *et al.*, 2016; Cakmak *et al.*, 2013; Sellami *et al.*, 2011).

Hot air drying is a method applicable when air drying cannot be practiced due to atmospheric conditions. This method also allows a considerable reduction in drying time. In addition to these traditional methods, new drying methods have recently been introduced, such as oven and

microwave drying; these can both comply with microbiological safety and food quality regulations and reduce the energy costs of drying (Cakmak *et al.*, 2013; Díaz-Maroto *et al.*, 2002; Kuzgunkaya & Hepbasli, 2007; Sellami *et al.*, 2011).

## 2.6. Composition and Nutritional Value

A bay leaf has a sharp, bitter taste. The difference in fragrance and aroma is due to the presence of essential oils in the leaves (Sumono & Sd, 2008). Fresh leaves have a water content of around 50% (Cakmak *et al.*, 2013), on the other hand, dry leaves contain 5-10% water, 65% carbohydrate, 8-11% protein, 5-9% fat, and 4% ash. The oil contains over 140 different components (Elzebroek & Wind, 2008).

Four sugars (fructose, sucrose, glucose, and trehalose), three polysaccharides (alginate, fucoidan, and laminaran), and three organic acids (oxalic, malic, and ascorbic acids) were detected in bay leaves. As they also contain several fatty acids; palmitic acid being the main one, followed by linoleic acid (Alejo-Armijo *et al.*, 2017).

Four tocopherols ( $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$ ) are detected in bay leaves and seeds. The  $\alpha$  and  $\gamma$ -tocopherols are the most abundant in the leaves, while  $\beta$ -tocopherol predominates in the seeds. In both bay organs (leaves and seeds),  $\delta$ -tocopherol is the least abundant component (Chahal *et al.*, 2017). The nutritional composition of the leaves of *L. nobilis* is presented in Table 2.

**Table 2.** Composition and nutritional value of *L. nobilis* leaves (Ambrose *et al.*, 2016).

Constituent	Value per 100g of dry matter
Water (g)	5.44
Energy (kcal)	313
Protein (g)	7.61
Carbohydrates (g)	74.96
Ash (g)	3.62
Fat (g)	8.36
Total saturated fatty acids (g)	2.28
Total monosaturated fatty acids (g)	1.64
Total polyunsaturated fatty acids (g)	2.29
Calcium (mg)	834
Iron (mg)	43
Magnesium (mg)	120
Phosphate (mg)	113
Potassium (mg)	529
Sodium (mg)	23
Zinc (mg)	3.70
Folate ( $\mu$ g)	180
Niacin (mg)	2.005
Riboflavin (mg)	0.421
Thiamine (mg)	0.009
Vitamin A, IU (IU)	6185
Vitamin A ( $\mu$ g)	309
Vitamin B (mg)	1.740
Vitamin C (mg)	46.5
Vitamin E (mg)	139



### 3. Bioactive Compounds of *L. nobilis* Leaves

An antioxidant is any substance present at a low concentration compared to that of the oxidizable substrate, significantly delays or prevents the oxidation of this substrate. Antioxidants are substances that can have an endogenous origin such as enzymes (superoxide dismutase, catalase, and glutathione peroxidase) and transition metal chelating proteins (transferrin, ferritin, and ceruloplasmin) and an exogenous origin (molecules antioxidants including phenolic compounds, carotenoids, vitamin C, and certain trace elements such as copper, zinc, selenium which are essential for the activity of antioxidant enzymes). These different antioxidants can neutralize or reduce the oxidation caused by reactive oxygen species (Pincemail *et al.*, 2002; Ghulam Yasin *et al.*, 2020).

Reactive oxygen species can have an endogenous origin following their generation by metabolic reactions in the cytosol, membranes, and mitochondria or exogenous such as pollution, ozone, tobacco, radiation, pesticides, and drugs (Pincemail *et al.*, 1998). These reactive species cause a direct action on biological molecules (lipids, proteins, DNA, and carbohydrates), but also secondary damage due to the cytotoxic and mutagenic properties of the metabolites released in particular during the oxidation of lipids (Deby-Dupont *et al.*, 2002).

#### 3.1. Essential Oils

Over 150 components have been identified in bay leaf essential oil by GC-MS, with 1,8-cineole generally being the major component. The other main compounds are  $\alpha$ -pinene,  $\beta$ -pinene, sabinene, limonene, and linalool (Figure 2) (Chahal *et al.*, 2017). Other parts of the plant, other than leaves, have also been explored regarding their volatile composition. Thus, the essential oils of bay fruits (Abu-Dahab *et al.*, 2014), seeds (Zolfaghari *et al.*, 2013), flowers (Moghtader & Salari, 2012), stems, and bark have also been studied repeatedly, although to a lesser extent than leaves. 1,8-cineol (26 to 51%),  $\alpha$ -terpinyl acetate (5% to 14%), and  $\alpha$ -pinene (4 to 6%) were the main components of the essential oil of the stem and fruits (Chalchat *et al.*, 2011).

Compounds like eugenol (11 to 12%), methyl-eugenol (9% to 12%), and elemicin (1% to 12%) are important for the spicy aroma of noble bay leaves and they are used as important indicators in determining the quality of these leaves (Hanif *et al.*, 2020). This essential oil can also be used as a conservator of many foodstuffs such as table oils (Ordoudi *et al.*, 2022).

#### 3.2. Phenolic Compounds

Polyphenols or phenolic compounds group together a vast set of more than 8000 molecules, divided into ten chemical classes, which all have one point in common: an aromatic ring with 6 carbon atoms that carry a variable number of hydroxyl functions (Harborne & Baxter, 1999). Many compounds such as flavones and flavonol found in bay leaves exhibit antioxidant activity (Hanif *et al.*, 2020).

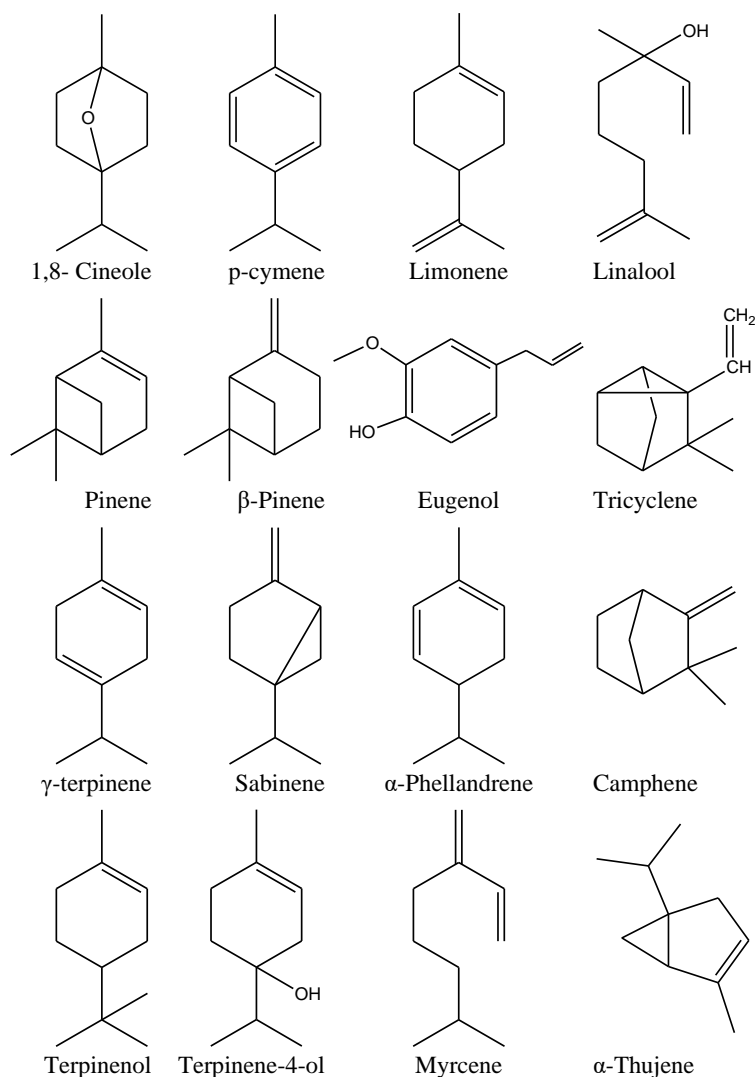
Phenolic compounds in plants are also very important, as their hydroxyl groups confer scavenging capacity (Naczki & Shahidi, 2004). Plant materials rich in phenolic compounds are increasingly used in the food industry, as they delay the oxidative degradation of lipids and improve the quality and nutritional value of food as well as for antimicrobial activity (Nithya *et al.*, 2016; Zerrouki & Riazi, 2021). *L. nobilis* present all phenolic classes including flavonoids, phenolic acids, tannins (proanthocyanidins), and lignans (Dobrosłavić *et al.*, 2022). Phenolic compounds of *L. nobilis* leaves are subjected to quantitative and qualitative variations depending on the region of harvesting, method of extraction, and solvent used for phenolics recovery (Table 3).

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**Figure 2.** Compounds are identified in the essential oil of the leaves of *L. nobilis* (Chahal *et al.*, 2017).



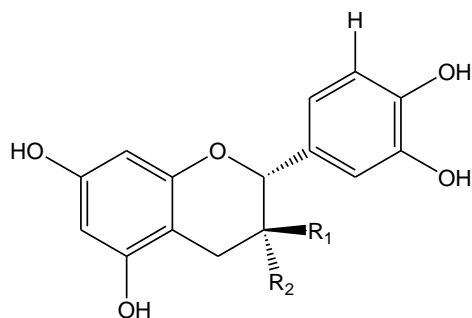
### 3.2.1. Flavonoids

Flavonoids are a group of more than 6000 naturally occurring compounds that are nearly universal in vascular plants (Erlund, 2004). They are pigments responsible for the yellow, orange, and red colorings of different plant organs (Havsteen, 2002). Flavonoids are polyphenols, and therefore, their antioxidant activity depends on the reactivity of hydroxyl substituents in hydrogen atom transfer reactions.



Flavonoids are very effective scavengers of the most oxidizing molecules, including singlet oxygen and various free radicals involved in several diseases (Bravo, 1998). Flavonoids have positive effects on human health. Studies on flavonoid derivatives have shown a wide range of antibacterial, antiviral, anti-inflammatory, anticancer, and antiallergic activities (Di Carlo *et al.*, 1999; Hossain *et al.*, 2012; Montoro *et al.*, 2005). Flavonoids are the main phenolic constituents in extracts of noble bay leaves. Flavones and flavonols are the main flavonoids in leaf extracts. Apigenin, kaempferol, quercetin, and their glycosides are also frequently present in leaves (Alejo-Armijo *et al.*, 2017) (Figure 3).

**Figure 3.** Some flavonoids of *L. nobilis* leaves (Konovalov & Alieva, 2019).

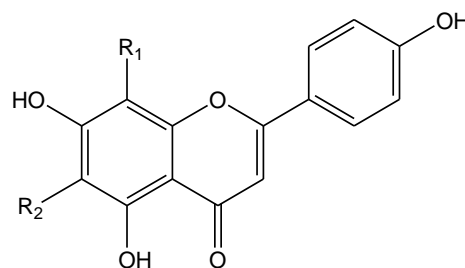


(-)-Epicatechin:  $R_1=H$ ,  $R_2=OH$ ,  $R_3=H$

(-)-Epigallocatechin:  $R_1=H$ ,  $R_2=OH$ ,  $R_3=OH$

(+)-Catechin:  $R_1=OH$ ,  $R_2=H$ ,  $R_3=H$

(+)-Gallocatechin:  $R_1=OH$ ,  $R_2=H$ ,  $R_3=OH$

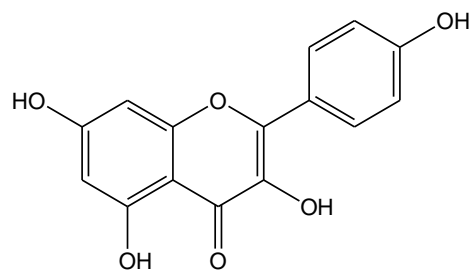


Apigenin:  $R_1=H$ ,  $R_2=H$

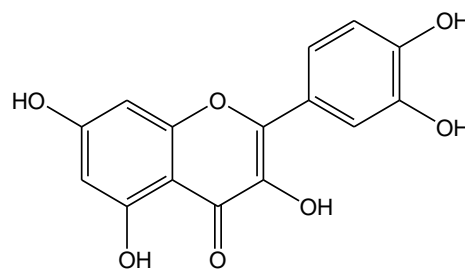
Apigenin 8-C-glucoside:  $R_1=\text{glucoside}$ ,  $R_2=H$

Apigenin-6,8-di-C-hexoside:  $R_1=\text{hexoside}$ ,  $R_2=\text{hexoside}$

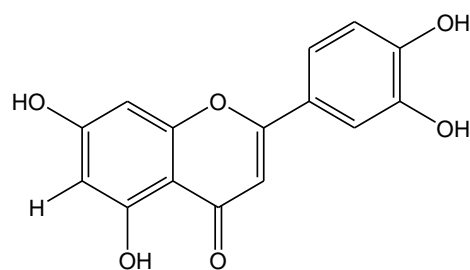
Apigenin-6-C-glucoside:  $R_1=H$ ,  $R_2=\text{glucoside}$



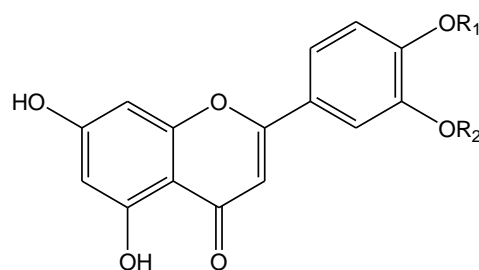
Kaempferol



Quercetin and derivatives (Q-3-O-rutinoside, Q-3-O-rhamnopyranoside, Q-3-O-glucopyranoside, ...)



Luteolin



Hesperetin:  $R_1=CH_3$ ,  $R_2=OH$

Naringenin:  $R_1=H$ ,  $R_2=H$

**Table 3.** Phenolic compounds of *L. nobilis* leaves.

Compound	Content	Extraction method	Collection
Phenolic acids			
Gallic acid	24.8 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	4.5 / 10.5 / 4.8 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	1.4 mg/g	Maceration (50% ethanol)	
	1420 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al
Rosmarinic acid	47.5 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	5.3 / 12.5 / 14.4 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	0.1-0.2 mg/g	Maceration (50% ethanol)	
Chlorogenic acid	243.9 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	3.8 / 3.8 / 3.9 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	210 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al
Caffeic acid	586.1 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	25.5 / 343.1 / 207.3 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
<i>p</i> -Coumaric acid	151.1 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste

	14 / 8.3 / 8.2 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Ferulic acid	300.1 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	94.4 / 7.8 / 11 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Syringic acid	242 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	0.3 / 0.4 / 0.6 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Sinapic acid	607.7 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg
Cinnamic acid	135 mg/g		Monaste
3,4-dihydroxybenzoic acid hexoside	17.5 / 28.9 / 24.9 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Protocatehuic acid	28 / 35.4 / 20.4 µg/g		
<i>p</i> -hydroxybenzoic acid	7.2 / 10.2 / 13 µg/g	Maceration (50% ethanol)	
Hydroxybenzoic acid	0.45-5 mg/g		
Vanillic acid	0.45-5 mg/g		
Dicaffeoylquinic acid	160 µg/g		
3-5-Dicaffeoylquinic acid	110 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al
Flavonoids			
Myricetin	124.5 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	6.5 / 7.3 / 7.8 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Quercetin	48.9 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	30 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al
Luteolin	4.8 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste

	38 / 71.7 / 113.6 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	0.2-4.5 mg/g	/	Macerat eth
	268.6 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
Apigenin	6.5 / 37.4 / 85.2 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Kaempferol	122.2 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
	217.4 mg/g		
Rutin	280.7 / 982.1 / 231.4 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	929.4 mg/g	Maceration (50% ethanol)	
Hyperoside	141.8 mg/g	Maceration (0.5g/70% ethanol at 70 °C for 15 min)	Bulg Monaste
(Epi)catechin-hexoside	3.92 mg/g	Maceration (1 g/30 mL methanol for 1h)	Castro Por
(+)-Gallocatechin	5.97 mg/g		
	0.76 mg/g		
	0.58 mg/g		
	330 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al
Catechin	723.7 / 126.2 / 198.8 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
	22.9 mg/g	Infusion (25g/200ml boiling water)	Sardin
	15.69 mg/g	Maceration (1 g/30 mL methanol for 1h)	Castro Por
(-)-Epicatechin	3.44 mg/g	Maceration (50% ethanol)	
	9510 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Al

	711.7 / 136.5 / 139 µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Luteolin 6-C-glucoside	1.35 mg/g	Maceration (1 g/30 mL methanol for 1h)	Castro Por
Apigenin 8-C-glucoside	0.99 mg/g		
2"-O-Rhamnosyl-C-hexosyl-apigenin	0.56 mg/g		
Quercetin 3-O-rutinoside	1.58 mg/g		
Apigenin 6-C-glucoside	1.61 mg/g		
Quercetin 3-O-glucoside	4.32 mg/g		
Quercetin O-hexoside	4.99 mg/g		
Kaempferol 3-O-rutinoside	1.63 mg/g		
Quercetin O-pentoside	1.56 mg/g		
Kaempferol 3-O-glucoside	1.89 mg/g		
Isorhamnetin O-rutinoside	3.13 mg/g		
Quercetin O-rhamnoside	4.62 mg/g		
Isorhamnetin O-hexoside	1.29 mg/g		
Kaempferol O-pentoside	0.67 mg/g		
Isorhamnetin O-pentoside	0.22 mg/g		
Kaempferol O-hexoside	1.83 mg/g		
Isorhamnetin O-rhamnoside	0.03 mg/g		
kaempferol-3-O-glucopyranoside	23 mg/g	Infusion (25g/200ml boiling water)	Sardin
kaempferol-3-O-rhamnopyranoside	28 mg/g		
kaempferol-3-O-(2'',4''-di-E-p-coumaroyl)-rhamnoside	22.9 mg/g		
kaempferol-3-Oarabinopyranoside	16 mg/g		
kaempferol-3-O-[6-O-(rhamnopyranosyl)glucopyranoside]	2.8 mg/g		

Quercetin-3- <i>O</i> -glucopyranoside	38 mg/g
Quercetin-3- <i>O</i> -rhamnopyranoside	21 mg/g
Quercetin-3- <i>O</i> -[6- <i>O</i> -(rhamnopyranosyl)glucopyranoside]	15.5 mg/g
3'-methoxyquercetin-3- <i>O</i> -[6- <i>O</i> -(rhamnopyranosyl)glucopyranoside]	12.2 mg/g
3'-methoxyquercetin-3- <i>O</i> -glucopyranoside	20 mg/g
2''-Rhamnosylisovitexin	13.4 mg/g
Kaempferol-3- <i>O</i> -deoxyhexoside	1.4 / 0.6 / 1 µg/g
Quercetin-3-glucoside	513.4 / 1027.4 / 918.3 µg/g
Kaempferol-3-rutinoside	241.7 / 57.8 / 75.2 µg/g
Quercetin-3-pentoside	283.2 / 86.2 / 54.3 µg/g
Kaempferol-3- <i>O</i> -hexoside	1116.3 / 187.3 / 142.5 µg/g
Isorhamnetin-3-hexoside	405.6 / 251 / 216.2 µg/g
Quercetin-3-rhamnoside	127.4 / 143.4 / 399.6 µg/g
Kaempferol-3- <i>O</i> -pentoside	439 / 83.7 / 79.2 µg/g
Epicatechin gallate	1 / 4.5 / 2.6 µg/g
Epigallocatechin gallate	4.9 / 2.2 / 0.8 µg/g
Luteolin-6- <i>C</i> -glucoside	21 / 52.3 / 40.4 µg/g
Apigenin-6- <i>C</i> -( <i>O</i> -deoxyhexosyl)-hexoside	0.9 / 1.3 / 1 µg/g

CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min;  
MAE: 50% ethanol, 80 °C, for 10 min and 400 W;  
UAE: (70% ethanol, 50% amplitude for 10 min)

Zagreb



Gallocatechin		900 µg/g		
Quercetagetin ether/isomer	dimethyl	40 µg/g		
Quercetagetin ether/isomer	trimethyl	50 µg/g		
Kaempferol rutinoside/isomer		1450 µg/g	Ultra-Turrax extraction (30g/300 ethanol at 10 000 rpm for 4 min)	Semi-ar Alq
Quercetin ether/isomer	methyl	30 µg/g		
Quercetin ether/isomer	dimethyl	80 µg/g		
Procyanidin dimer		1.92 mg/g	Maceration (1 g/30 mL methanol for 1h)	Castro Por
		16.97 mg/g	Maceration (50% ethanol)	
Cinnamtannin B-1		2.3 mg/g	Infusion (25g/200ml boiling water)	Sardin
		1.25 mg/g		Castro Por
		1.29 mg/g	Maceration (1 g/30 mL methanol for 1h)	
Procyanidin trimer		203.3 / 77.2 / - µg/g	CRE / MAE / UAE (CRE: 40ml 50% ethanol for 30min; MAE: 50% ethanol, 80 °C, for 10 min and 400 W; UAE: (70% ethanol, 50% amplitude for 10 min)	Zagreb
Trimeric proanthocyanidins 1		1.24 mg/g		
Trimeric proanthocyanidins 2		5.05 mg/g	Maceration (50% ethanol)	
Procyanidin tetramer		3.54 mg/g	Maceration (1 g/30 mL methanol for 1h)	Castro Por
		1.16 mg/g	Maceration (50% ethanol)	

CRE: conventional heat-reflux extraction, MAE: microwave-assisted extraction, UAE: ultrasound-assisted extraction.

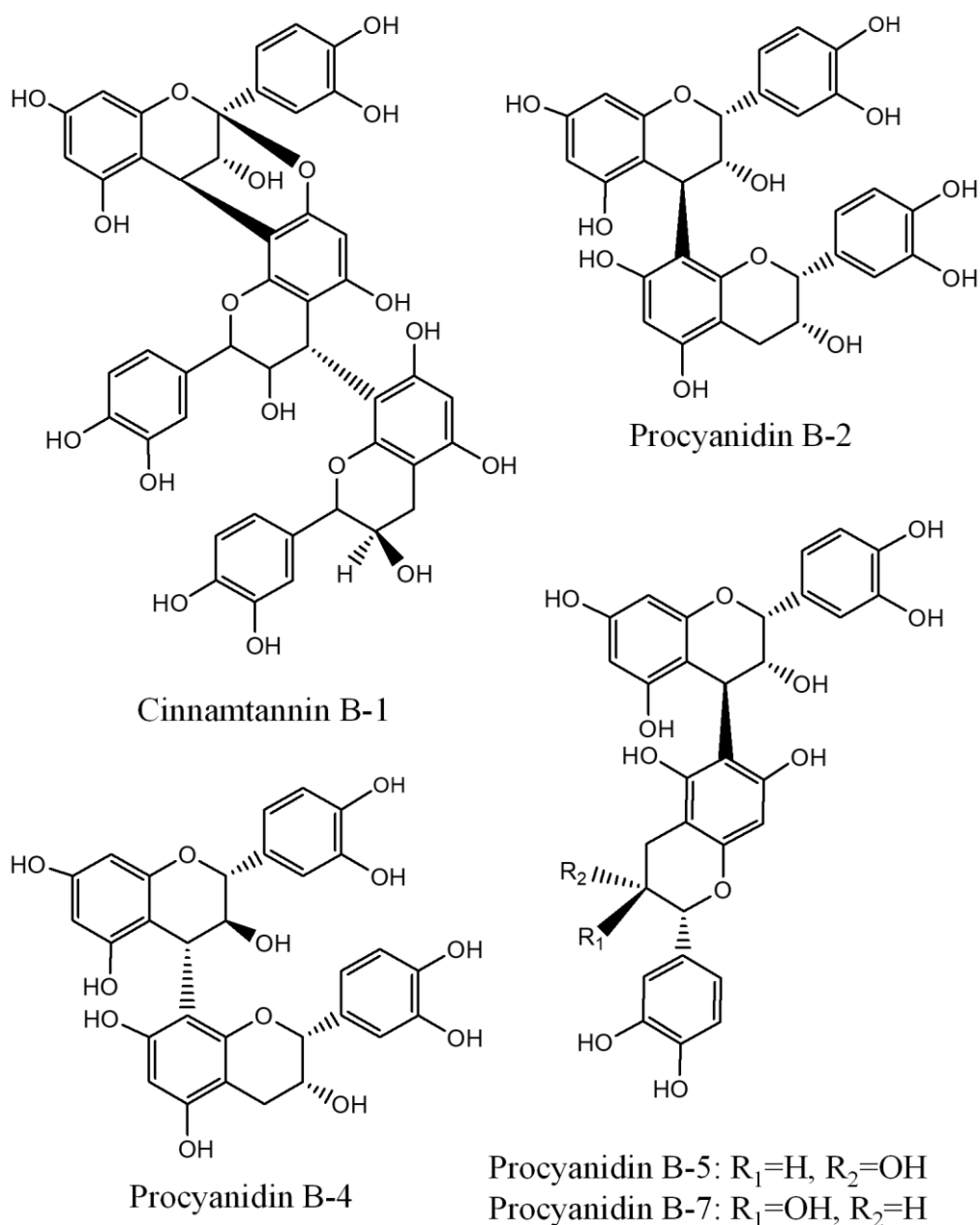
### 3.2.2. Proanthocyanidins

Proanthocyanidins, also called condensed tannins, are oligomers and polymers of flavans linked by specific bonds. These secondary metabolites have significant antioxidant activity. They are widespread in some foods and dietary supplements. The proanthocyanidin composition of bay leaves was studied by Vinha *et al.* (2015). They reported that dimeric proanthocyanidins were most abundant in this part (Figure 4).

### 3.2.3. Other phenolic compounds

Other phenolic compounds detected in bay leaves are structural derivatives of caffeic and coumaric acids. Frequently, these compounds are esters of these acids with quinic or 3,4-dihydroxy phenyl lactic acids. Four lignans could also be isolated from a hydroalcoholic extract of bay leaves (Alejo-Armijo *et al.*, 2017).

**Figure 4.** Some proanthocyanidins of *L. nobilis* leaves (Konovalov & Alieva, 2019).

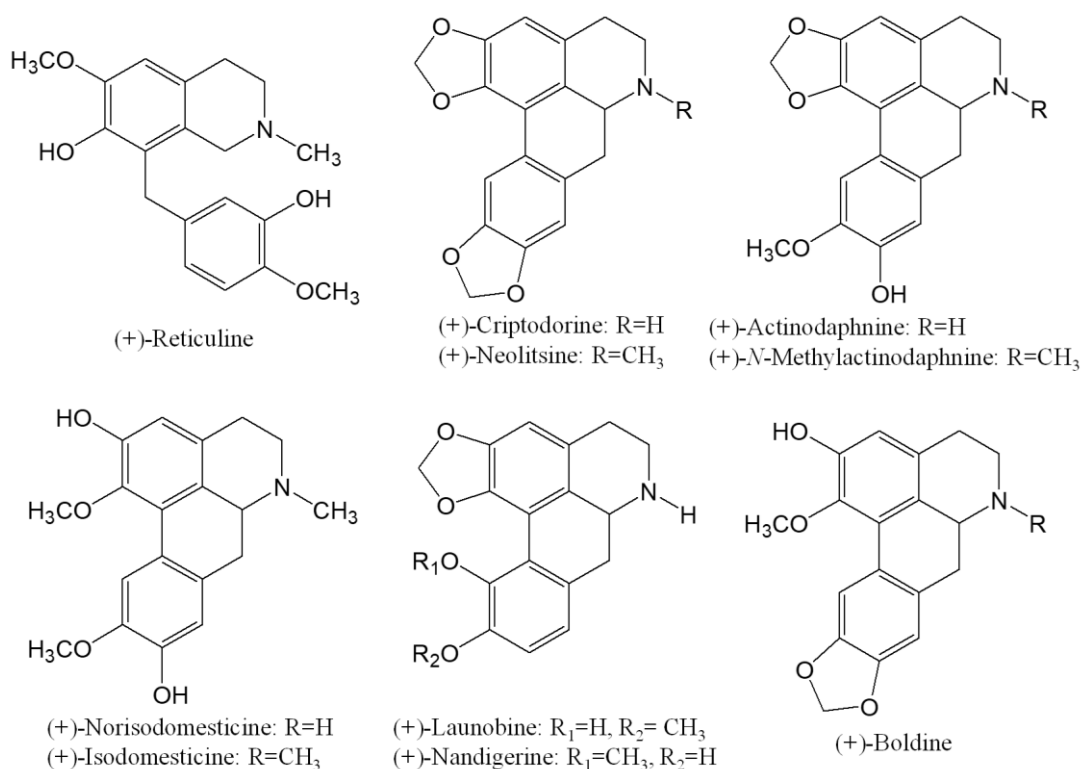


### 3.3. Alkaloids

Alkaloids are a group of secondary metabolites, overwhelmingly of plant origin. Chemically, alkaloids are nitrogen-based molecules, most often heterocyclic. Over ten thousand alkaloids have been isolated from plants. Alkaloids have a wide range of biological activities, including antioxidant, antibacterial, and anticancer activities (Hassan *et al.*, 2013; Nithya *et al.*, 2016).

Ten alkaloids (1-10) have been isolated from noble bay leaves, of which five are noraporphins (2, 4, 6, 8, 9), four are aporphins (3, 5, 7, 10), and one only (1) is an alkaloid of the benzyl-tetrahydro-isoquinoline type (Figure 5). Compound 9 has also been isolated from roots, and is found 1, 4, and 8 in the bark of stems and roots (Pech & Bruneton, 1982). Launobin (8) has also been obtained from noble laurel wood. Noraporphin 4 is the major alkaloid of bay leaves (Pech & Bruneton, 1982).

**Figure 5.** Alkaloids of *L. nobilis* leaves (Alejo-Armijo *et al.*, 2017).



## 4. TRADITIONAL USES and THERAPEUTIC EFFECTS

In addition to its well-known culinary virtues, noble laurel also exhibits medicinal properties, known since ancient times. The leaf is traded internationally and its production is estimated at over 2,000 tonnes per year. Türkiye is the world's largest producer and exporter with around two-thirds of international trade. The leaf is used in many food products as well as in toiletries and medicines (Ravindran, 2017).

### 4.1. Medicinal Uses

Traditionally, bay leaves have been used in herbal medicine against several diseases such as rheumatism, sprains, indigestion, and earaches. The leaves having anti-diarrheal, anti-inflammatory, and anti-diabetic activity are used for improving the response of the immune system. These leaves contain numerous molecules, which are responsible for anti-inflammatory activity, inhibiting alcohol absorption, and which can enhance the activity of glutathione S-transferase in the liver (Fang *et al.*, 2005).

Many components of the essential oil of noble laurels such as eugenol, methyl eugenol, and pinene have anticonvulsant activity (Sayyah *et al.*, 2002). The essential oil of this leaf also has analgesic activities (Barla *et al.*, 2007). Different research has revealed that bay leaves can also be used to treat diabetes and migraine (Aljamal, 2010; Fang *et al.*, 2005; Mirbadal Zadeh & Shirdel, 2011). Fresh leaves are used to treat blood dysentery, inflammation, and congestion of the kidneys. They are also used to treat arthritis, headaches, fungal diseases, anorexia, colds, cataracts, diarrhea, and colonic ulcer (Parthasarathy *et al.*, 2008).

Laurel leaves are effective against many infections caused by fungi, viruses, bacteria, and protozoa. They are also useful for inhibiting the growth of cancer cells and for fevers, coughs, flu, colds, bronchitis, and asthma. Laurel juice is an effective drug for soothing sore eyes and night blindness, usually caused by vitamin A deficiency (Hanif *et al.*, 2020).

#### 4.2. Culinary Uses

Different parts of plants can be eaten as spices, including bark, flowers, leaves, roots, stems, and seeds. Spices can also be consumed in fresh, dried, and powdered forms (Raghavan & Orsat, 2007; Schweiggert *et al.*, 2007). Laurel leaves are mainly used to flavor several dishes, stews, soups, sauces, fish, meats, and drinks. As the fresh leaves are bitter, the leaves are usually dried before use. The dried and powdered leaves are used industrially in the manufacture of various foods (Elzebroek & Wind, 2008).

#### 4.3. Cosmetic Uses

Laurel contains essential oil which can be obtained from the leaves by steam distillation; the oil is used in industry to scent candles, perfumes, creams, and soaps (Elzebroek & Wind, 2008). In Syria, it is a main component of the traditional and very old Aleppo soap, which also contains olive oil and caustic soda, and Salicornia ashes (Ballabio & Goetz, 2010).

#### 4.4. Pharmacological Uses

Due to the presence of various antioxidant molecules in bay laurel, several biological and pharmacological activities have been reported by researchers, such as antioxidant, antibacterial, antifungal, antiviral, and insecticidal activities (Chahal *et al.*, 2017).

##### 4.4.1. Antioxidant activity

*L. nobilis* leaves demonstrated strong antioxidant properties. Elmastaş *et al.* (2006) showed that freeze-dried extracts (water and ethanol) of bay leaves showed strong total antioxidant activity in the linoleic acid emulsion. The concentrations of 20, 40, and 60 µg/ml showed inhibition of 84.9, 95.7, 96.8 and 94.2, 97.7 and 98.6% of the lipid peroxidation of the emulsion of linoleic acid, respectively for aqueous and ethanolic extracts. The findings are comparable to 60 µg/ml of standard antioxidants including butylated hydroxyanisole, butylated hydroxytoluene, and  $\alpha$ -tocopherol with 96.6, 99.1, and 76.9% inhibition of lipid peroxidation, respectively. The alkaloid extract obtained from bay leaves expressed a high antioxidant activity with an IC<sub>50</sub> of 63.28 µg/ml higher than gallic acid (143.18 µg/ml) used as standard. The phenolic extract exhibited an antioxidant power with an IC<sub>50</sub> of 317.57 µg/ml, less than that of alkaloids extract (Khaled Khodja *et al.*, 2021).

##### 4.4.2. Antidiabetic activity

*L. nobilis* leaves are very beneficial to diabetic people; their extract can improve the blood glucose level and prevent the apparition of diabetes complications. The study carried out by Khan *et al.* (2009) on forty people with type 2 diabetes, given capsules containing 1, 2, or 3 g of ground bay leaves, showed a significant decrease in serum glucose level by 21-26% after 30 days of treatment. Another study realized *in vitro* showed that *L. nobilis* ethanolic extract improves insulin sensitivity by increasing insulin receptor substrate expression, and reduces

considerably the intracellular oxidative stress induced by chronic hyperglycemia. These biological activities are attributed to phenolic compounds, mainly gallic acid (Bourebaba *et al.*, 2021).

Some experiences realized *in vivo* reported also the possible ameliorative effect of bay leaves extracts on diabetic people; for example, the study conducted by Mohammed *et al.* (2021) on streptozotocin-induced diabetic rats showed that leaves extract of *L. nobilis*, 200 mg/kg of bay extract administered every day orally using the intragastric tube for 28 days, decreases significantly the blood glucose level and improves the regeneration of the pancreatic islets. Al Chalabi *et al.* (2020) reported that the polyphenols contained in the alcoholic extract of *L. nobilis* decrease significantly the fasting blood glucose level and improve insulin secretion in alloxan-induced diabetic rats.

On the other hand, the bioactive molecules contained in bay leaves can enhance significantly the post-prandial glucose level in diabetic patients. In this regard, the terpenes found in the aqueous and the methanol/acetone extract of bay leaves exert a potent protective effect against high-fat diet-induced type 2 diabetes in rats. These compounds can probably act via the inhibition of carbohydrate hydrolyzing enzymes such as  $\alpha$ -amylase and  $\alpha$ -glucosidase (Daher *et al.*, 2021). In addition, an *in vitro* study carried out by Duletić-Laušević *et al.* (2019) showed that the phenolic compounds extract of *L. nobilis* leaves inhibit significantly the  $\alpha$ -glucosidase activity at levels ranging from 11-93% depending on the extraction solvent (acetone and methanol) and origin of leaves (commercial and cultivated), which can probably reduce the postprandial glycemia in diabetic people.

#### 4.4.3. Antihyperlipidemic activity

Several experimental studies demonstrated the possible curative effect of bay leaf extracts and their isolated molecules on dyslipidemia. The daily oral administration for female rabbits of 100 mg/ml/kg of bay leaf crude, 50 mg/ml/kg of isolated flavonoids extract, or 12.5 mg/ml/kg of isolated glycosides extracts during 30 days demonstrated a significant decrease of total cholesterol, LDL-Cholesterol, and triglycerides levels AL-Samarrai *et al.* (2017). Another study showed that polyphenols contained in the alcoholic extract of *L. nobilis* decrease significantly the level of total cholesterol, LDL-Cholesterol, and triglycerides as well as increase the level of HDL-cholesterol in alloxan-induced diabetic rats using a dose of 200mg/kg administered orally during one month (Al Chalabi *et al.*, 2020).

The investigation conducted by Chbili *et al.* (2020) on 30 healthy volunteers showed that the consumption of *L. nobilis* tea (one intake a day for 10 days of the infusion of 5 g of dried bay leaves in 100 ml water) increases significantly the concentration of HDL cholesterol. Another investigation realized on 56 people with type 1 diabetes demonstrated that the consumption of bay leaves decreases risk factors for diabetes and reduced total cholesterol, LDL, and triglycerides but increases HDL levels (Aljamal, 2010).

#### 4.4.4. Hepatoprotective activity

The crude extract of *L. nobilis* leaves showed good hepatoprotective activity against paracetamol's toxic effects on rat hepatocytes at a concentration of 40  $\mu$ g/ml (Ayoub *et al.*, 2013). Similarly, an experimental study performed on rats showed that the methanol extract of *L. nobilis* at 400 mg/kg acts on the liver as a potent scavenger of free radicals to prevent the hepatotoxicity induced by paracetamol (Ravindran *et al.*, 2013). Another *in vivo* study carried out by Gasparyan *et al.* (2015) revealed that some phenolic compounds such as flavonoids and eugenol of *L. nobilis* protect hepatocytes of rats against metabolic and histological abnormalities induced by tetrachloromethane.

#### 4.4.5. Antimutagenic activity

The noble laurel contains the antimutagen *p*-coumarate 3-kaempferol at a level of 20mg/100g. This compound acts against the dietary carcinogen 3-amino-1-methyl-5H-pyrido[4,3-b]indole (Trp-P-2) with an IC<sub>50</sub> of 1.9µg. This value is close to those found for strong antimutagens like flavonols and flavones. The mutagenicity is due to a desmutagenic action that converts the metabolically activated form of Trp-P-2 to its carcinogenic form. The antimutagenicity effect of *p*-coumarate 3-kaempferol is due to the inhibition of metabolic activation of Trp-P-2 to its ultimate carcinogenic form and the kaempferyl moiety contributes particularly to this activity (Samejima *et al.*, 1998).

#### 4.4.6. Anticonvulsant activity

The leaf essential oil of *L. nobilis*, which has been used as an antiepileptic remedy in Iranian traditional medicine, was evaluated for anticonvulsant activity against experimental seizures. The essential oil protected mice against tonic convulsions induced by maximal electroshock and especially by pentylenetetrazole. Components responsible for this effect may be methyleugenol, eugenol, and pinene present in the essential oil. At anticonvulsant doses (1.22–1.71 ml/kg), the essential oil produced sedation and motor impairment. This effect seems to be related in part to cineol, eugenol, and methyleugenol (Sayyah *et al.*, 2002).

#### 4.4.7. Immunostimulatory activity

The immunostimulatory effects of noble laurel powder have been demonstrated on rainbow trout. Three groups of rainbow trout were fed experimental diets. After 21 days, nonspecific immune parameters such as phagocytosis in blood leukocytes, lysozymes, and protein levels were examined and showed immunostimulatory activity. The phagocytic activity of fish fed with a diet supplemented by 0.5 and % 1 laurel was significantly higher than other groups (Bilen & Bulut, 2010).

#### 4.4.8. Analgesic and anti-inflammatory activities

The essential oil of bay laurel has shown analgesic and anti-inflammatory activities in mice and rats. The essential oil exhibited a significant analgesic effect in the tail-flick and formalin tests, a dose-dependent anti-inflammatory effect in the formalin-induced edema, and a moderate sedative effect at the anti-inflammatory doses. The analgesic and anti-inflammatory effect of the essential oil was comparable to reference analgesics and non-steroid anti-inflammatory drugs: morphine and piroxicam (Sayyah *et al.*, 2003).

#### 4.4.9. Wound healing activity

Many healing models have been used to estimate the healing activity of bay laurel, and many factors have been studied to assess wound healing. It revealed that the animals treated with *L. nobilis* had moderately higher rates of wound contraction and weight of the granulation tissue and significantly more hydroxyproline content than the control group. The histological study of the granulation tissue of treated animals with *L. nobilis* showed a larger number of inflammatory cells, and lesser collagen when compared with the control group of animals (Nayak *et al.*, 2006).

#### 4.4.10. Antibacterial activity

Bay leaves expressed good antimicrobial activities that have been related to the presence of many classes of bioactive compounds. Indeed, the methanolic extract of bay laurel essential oil showed significant antibacterial activity *in vitro* against *Staphylococcus aureus*, *Enterococcus gallinarum*, *Haemophilus influenzae* and *Pseudomonas aeruginosa* strains, with respective minimum inhibitory concentrations (MIC) of 10, 6.5, 6, and 6 mg/ml (Ozcan *et al.*, 2010). Similarly, in another study, the extract of essential oils from *L. nobilis* leaves showed highly



effective antibactericidal activity against *Staphylococcus aureus*, *Staphylococcus intermedius*, and *Klebsiella pneumonia*, with minimum inhibitory concentrations ranging from 0.01 to 1 mg/ml (Derwich *et al.*, 2009).

*L. nobilis* essential oil expressed a significant antibactericidal and antistaphylococcal activity (MIC values ranging from 3.9 to 15.6 mg/m) and a strong biofilm inhibition effect of more than 70% obtained by a low sub-inhibitory concentration (1/16 MIC). The MTT (3- (4, 5-dimethyl-thiazol-2-yl)- 2,5-diphenyl-tetrazolium bromide) test reveals that these essential oils exhibited excellent antibiofilm activity with eradication percentages ranging from 79.6 to 95.2%. This oil could have a promising role in preventing oral infections (Merghni *et al.*, 2016).

Khaled Khodja *et al.* (2021) showed that the alkaloid extract (1 mg/ml) of bay leaves had strong antibacterial activity against the staphylococcal strains responsible for food poisoning with inhibition zones ranging from 12 to 22 mm. However, the extract of phenolic compounds (1 mg/ml) showed better activity against phytopathogenic strains associated with potato soft rot with inhibition zones varying from 12 to 17 mm. The experiments conducted by Berendika *et al.* (2022) demonstrated that the phenolic extract of laurel at 50 and 100 mg/kg positively affects the health of rats after intragastric treatment by increasing the number of colonies of lactobacilli and bifidobacteria and reducing the growth of pathogenic bacteria such as Enterobacteriaceae strains providing thus better health status for animals.

#### 4.4.11. Fungicidal activity

Peixoto *et al.* (2017) demonstrated the antifungal potential of the chemically characterized essential oil of *L. nobilis* against *Candida spp.* The MIC and MFC (minimum fungicidal concentrations) values of the essential oil ranged from 250 to 500 mg/ml. MIC values increased in the presence of sorbitol (osmotic protector) and ergosterol, indicating that the essential oil may affect cell wall biosynthesis and membrane ion permeability. At 2 MIC, essential oil disrupted the initial adhesion of *C. albicans* biofilms and affected biofilm formation without difference compared to nystatin. The phytochemical analysis identified isoeugenol as the main compound (53.49%) in the sample. The antifungal activity of *L. nobilis* essential oil is probably due to the monoterpenes and sesquiterpenes present in its composition.

Most of the aromatic molecules that are active (phenols, geraniol) on bacteria are also active on micromycetes, but with longer treatment times. The antifungal activity of bay laurel was examined *in vitro* on seven strains of phytopathogenic fungi at different concentrations such as 50, 125, and 250 mg/mL. The greatest antifungal activity was obtained against the fungus *Botrytis cinerea* at a concentration of 250 mg/mL (Patrakar *et al.*, 2012).

#### 4.4.12. Antiviral activity

The combination of 1,8-cineole and monoterpenol, present in the essential oil of *L. nobilis*, is very effective in treating low pathologies of viral origin. *L. nobilis* essential oil containing the constituents  $\beta$ -ocimene, 1,8-cineol,  $\alpha$ -pinene, and  $\beta$ -pinene has been reported for its inhibitory activity *in vitro* against the replication of the SARS-CoV coronavirus and the HSV-1 virus by visually scoring of the virus-induced cytopathogenic effect post-infection. *L. nobilis* oil demonstrated good activity against SARS-CoV with an IC<sub>50</sub> value of 120  $\mu$ g/ml and a selectivity index (SI) of 4,16 (Patrakar *et al.*, 2012). Roviello and Roviello (2021) examined over forty compounds found in bay laurel and found that nine of them had significantly high affinity for the major SARS-CoV-2 protease Mpro. One of the most important targets in anti-COVID-19 therapeutic strategies. Among these ligands derived from laurel, lauruside 5 is considered to be the most promising candidate as a potentially effective inhibitor of Mpro. The combination of 1,8-cineole and monoterpenol, present in the essential oil of *L. nobilis*, is very effective in treating low ENT (ear, nose, throat) pathologies of viral origin (Franchomme *et al.*, 2001).

#### 4.4.13. Insecticidal activity

*L. nobilis* leaf essential oil was tested for its insecticidal activity against *Tribolium castaneum* using five different concentrations ranging from 4-12 mg/g and the results showed that the polar fraction of essential oil was more active as compared to the non-polar fraction, and the insecticidal potential was found to be both concentration and time-dependent (Chahal *et al.*, 2016).

Jemâa *et al.* (2012) evaluated the essential oils of *L. nobilis* for their repellent and toxic activities against two major stored product pests: *Rhyzopertha dominica* and *Tribolium castaneum*. The results showed that *L. nobilis* essential oils were repellent and toxic for both pests. *L. nobilis* essential oil was effective and expressed a half repulsive dose (RD50) of 0.013 ml/cm<sup>2</sup> for *R. dominica* versus 0.045 ml/cm<sup>2</sup> for *T. castaneum*. The corresponding half lethal dose (LC50) of 68 ml/l of air and 172 ml/l of air, respectively, and this clearly justifies the interest in the effectiveness of noble laurel essential oils both as insecticides and repellents against stored product pests. Likewise, Erler *et al.* (2006) reported that the essential oils of noble laurel would have a repellent activity against the insects of the species *Culex pipiens*.

### 5. CONCLUSION

*L. nobilis* is an aromatic herb with relevant medicinal properties due to its important chemical composition and its potential therapeutic effects. Due to its wide use, the chemical composition and biological activity of the plant have been widely studied. Several pharmacological studies have scientifically demonstrated some of the known activities of traditional medicine, including overall antimicrobial and antioxidant properties. Screening of literature on bay showed that essential oil possesses a wide range of biologically active compounds. Bay leaf essential oil finds application with a lot of pharmacological activities such as antimicrobial, insecticidal, antioxidant, anticonvulsant, etc. The presence of diverse constituents in bay leaf essential oil may be responsible for wide spectrum of biological activities.

Laurel leaves, due to a wide range of structurally diverse bioactive molecules and their antioxidant, antimicrobial, anti-inflammatory, and other health beneficial properties, are an excellent base for the production of high-quality extracts with potential applications in the food, pharmaceutical, and cosmetic industries. Insights into the biopotential of laurel require new approaches in the production of plant extracts, and consequently, the use of advanced green techniques that allow the development of formulations and high value-added products with improved biological properties and actions.

Since *L. nobilis* leaves are rich in phenolic compounds, future research should focus on various techniques that would result in better extraction of these compounds. Studying the biological activities of bay polyphenols for application in functional foods and supplements is extremely important. The pharmacological activities mentioned in the present study present prospects for the future and open up new areas for the multidisciplinary research and development of sustainable, effective, and economical procedures that would make it possible to exploit to the maximum the great potential of the leaves of *L. nobilis* and their bioactive molecules.

From this study, we can conclude that the results examined in the review article will be useful to researchers looking for new bioactive molecules and therapeutic interests extracted from the leaves of *L. nobilis*. The isolated compounds will be considered in the future for more clinical evaluations. Considering the pharmacological potential of *L. nobilis* leaves, this condiment will certainly attract more attention in the future.

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## Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research and publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the authors.

## Authorship Contribution Statement

**Yazid Khaled Khodja:** Writing - original draft. **Mostapha Bachir-bey:** Writing - review & editing. **Messaoud Belmouhoub:** Writing the manuscript. **Rachid Ladjouzi:** Editing. **Farid Dahmoune:** Resources. **Bachra Khettal:** Supervision.

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