

Review

Traditional Knowledge, Phytochemistry, and Biological Properties of *Vachellia tortilis*

Douae Taha ^{1,2}, Souad El Hajjaji ¹, Yassine Mourabit ¹, Abdelhakim Bouyahya ², Learn-Han Lee ^{3,*}, Naoual El Menyiy ⁴, Aanniz Tarik ⁵, Taoufiq Benali ⁶, Hamza El Moudden ⁷, Monica Gallo ^{8,*}, Naima Iba ² and Ilhame Bourais ^{2,*}

- ¹ Laboratory of Spectroscopy, Molecular Modeling Materials, Nanomaterials Water and Environment—CERNE2D, Faculty of Sciences, Mohammed V University in Rabat, Rabat 10100, Morocco
 - ² Laboratory of Human Pathologies Biology, Department of Biology, Faculty of Sciences, Genomic Center of Human Pathologies, Mohammed V University in Rabat, Rabat 10106, Morocco
 - ³ Novel Bacteria and Drug Discovery Research Group (NBDD), Microbiome and Bioresource Research Strength (MBRS), Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Bandar Sunway 47500, Malaysia
 - ⁴ Laboratory of Pharmacology, National Agency of Medicinal and Aromatic Plants, Taounate 34025, Morocco
 - ⁵ Medical Biotechnology Laboratory (MedBiotech), Rabat Medical & Pharmacy School, Mohammed V University in Rabat, Rabat 10100, Morocco
 - ⁶ Laboratory of Natural Resources and Environment, Polydisciplinary Faculty of Taza, Sidi Mohamed Ben Abdellah University of Fez, Taza-Gare, Taza 30050, Morocco
 - ⁷ Higher School of Technology of El Kelaa Des Sraghna, Cadi Ayyad University, El Kelaa Des Sraghna BP 104, Marrakesh 40001, Morocco
 - ⁸ Department of Molecular Medicine and Medical Biotechnology, University of Naples Federico II, Via Pansini 5, 80131 Naples, Italy
- * Correspondence: lee.learn.han@monash.edu (L.-H.L.); mongallo@unina.it (M.G.); i.bourais@um5r.ac.ma (I.B.)



Citation: Taha, D.; El Hajjaji, S.; Mourabit, Y.; Bouyahya, A.; Lee, L.-H.; El Menyiy, N.; Tarik, A.; Benali, T.; El Moudden, H.; Gallo, M.; et al. Traditional Knowledge, Phytochemistry, and Biological Properties of *Vachellia tortilis*. *Plants* **2022**, *11*, 3348. <https://doi.org/10.3390/plants11233348>

Academic Editor: Reneta Gevrenova

Received: 20 October 2022

Accepted: 24 November 2022

Published: 2 December 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Abstract: *Vachellia tortilis* is a medicinal plant of the Fabaceae family, widely distributed in arid and semi-arid regions of North, East and Southern Africa, the Middle East and the Arabian Peninsula. In traditional medicine. It's commonly used to treat certain ailments, including diabetes, asthma, hepatitis and burns. Different scientific search databases were used to obtain data on *V. tortilis*, notably Google Scholar, Scopus, Wiley Online, Scifinder, Web of Science, ScienceDirect, SpringerLink, and PubMed. The knowledge of *V. tortilis* was organized based on ethnomedicinal use, phytochemistry, and pharmacological investigations. Phytochemical studies revealed the presence of a variety of phytocompounds, including fatty acids, monosaccharides, flavonoids, chalcones, and alcohols. Essential oils and organic extracts prepared from *V. tortilis* showed several biological properties, specifically antibacterial, antifungal, antiparasitic, antioxidant, antiproliferative, anti-diabetic, and anti-inflammatory effects. Antimicrobial and antiparasitic activities are due to the disturbance of cellular membranes and ultra-structural changes triggered by *V. tortilis* phytochemicals. While physiological and molecular processes such as apoptosis induction, preventing cell proliferation, and inflammatory mediators are responsible for the anti-diabetic, anti-cancer, and anti-inflammatory activities. However, further investigations concerning pharmacodynamics and pharmacokinetics should be carried out to validate their clinical applications.

Keywords: *Vachellia tortilis*; Fabaceae family; bioactive compounds; medicinal use; antimicrobial activities; pharmacological effects

1. Introduction

Fabaceae family contains several medicinal plants that have been recognized for their therapeutic potential in the treatment of a variety of ailments. Among these medicinal species, *V. tortilis* is a medicinal plant that is extensively employed in traditional pharmacopeia for its therapeutic properties [1]. This species distribution includes arid and

semi-arid regions of northern, eastern, and southern Africa (Mauritania, Senegal, Mali, Niger, Chad and Sudan) and the Middle East (Palestine and the Arabian Peninsula) [2].

Biochemical and pharmacological studies have shown that *V. tortilis* exerts multiple biological properties, including antimicrobial, antidiabetic, anti-inflammatory and anticancer activities. Extracts and essential oils may, in fact, have antibacterial properties against a variety of bacteria, including multi-resistant strains (such as *Proteus mirabilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*) to conventional antibiotics [3,4]. The antibacterial action of *V. tortilis* extracts has not been well addressed and appears to be linked to cell membrane disruption and structural changes. Furthermore, *V. tortilis* has been shown to have other antimicrobial properties against fungi such as *Candida albicans* and *Candida maltose* linked to human pathologies [5,6].

Oxidative stress produces free radicals, which are involved in the pathogenesis of complicated diseases such as chronic inflammation, diabetes, and cancer. *V. tortilis* extracts have shown an important capacity in the elimination of free radicals used in in vitro tests which supports their potential use in traditional therapies against these stress-related diseases [7].

In addition, *V. tortilis* extracts have been demonstrated to have anti-diabetic, anti-inflammatory, and antiproliferative properties in vitro and in vivo experiments. Although the mechanisms were not really completely understood, studies reveal that the plants' major components have cellular and molecular effects.

Indeed, *V. tortilis* extracts and essential oils are known for their high concentration of bioactive components such as flavonoids, chalcone and fatty acids with a remarkable variability depending on the region of collection, the parts used and the extraction methods used [4,8].

In this review, we explore studies performed on *V. tortilis* with respect to its taxonomy, medicinal properties, phytochemicals, and pharmacological properties. We will thus discuss the perspectives of applications of bioactive substances isolated from this plant.

2. Research Methodology

In this review, several scientific research databases were used to acquire data on the taxonomy, botanical description, ethnobotany, phytochemistry, and pharmacology of *V. tortilis*, including Google Scholar, Web of Science, Scopus, ScienceDirect, SpringerLink, Wiley Online, SciFinder, and PubMed. The obtained data were summarized according to each studied theme. Different keywords relating to *V. tortilis*, seed oil, extracts, biological effects, and chemical composition were used in this bibliometric survey. The reported phytochemical structures were established using ChemDraw Pro 8.0 and verified using the Pub Chemdatabase.

3. Results and Discussion

3.1. Taxonomy and Geographic Distribution

There are around 1200 species in the *Acacia* genus [9], endemic to the arid and semi-arid regions of northern and eastern Africa (Egypt, Libya, Tunisia, Algeria, and Morocco) and southern Africa (Mauritania, Senegal, Mali, Niger, Chad, and Sudan), as well as the Arabian Peninsula and the Middle East (Palestine; Figure 1) [2].

3.2. Botanical Description and Ecological Factors

In extremely dry conditions, a medium tree that is 4–15 m tall and has multiple trunks and an umbrella shape is reduced to a little wiry shrub (1 m tall maximum).

V. tortilis (Figure 2) bears little brownish hooked thorns and straight white thorns [10].

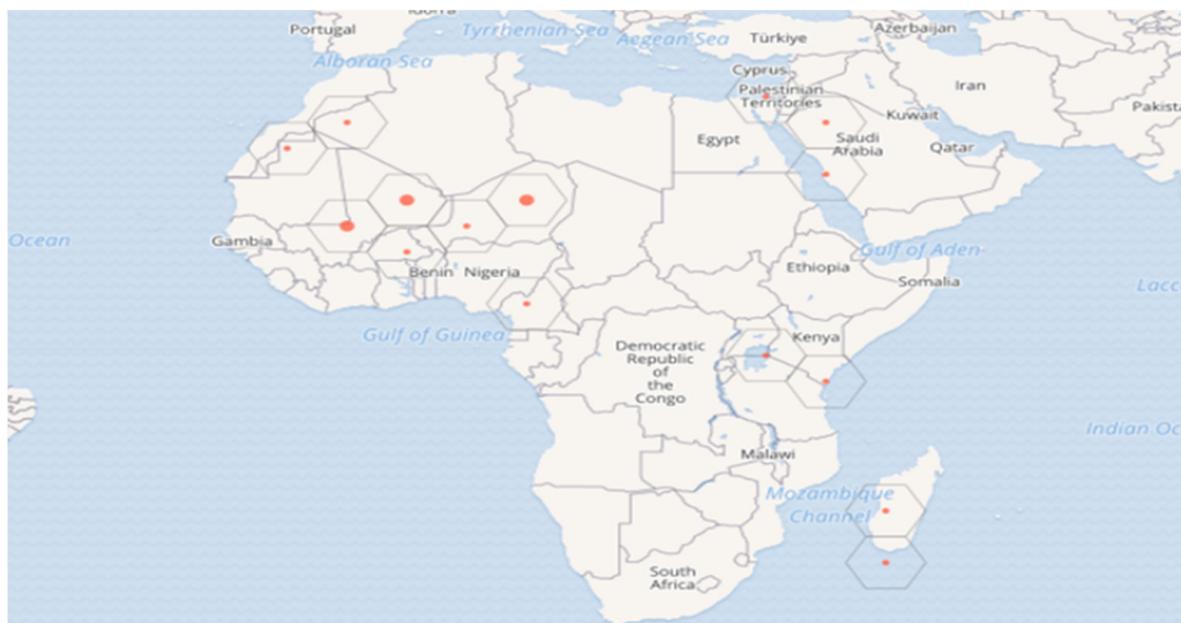


Figure 1. Geographic distribution of *V. tortilis*. The red dots in the figure legend illustrate the species intensity of distribution.

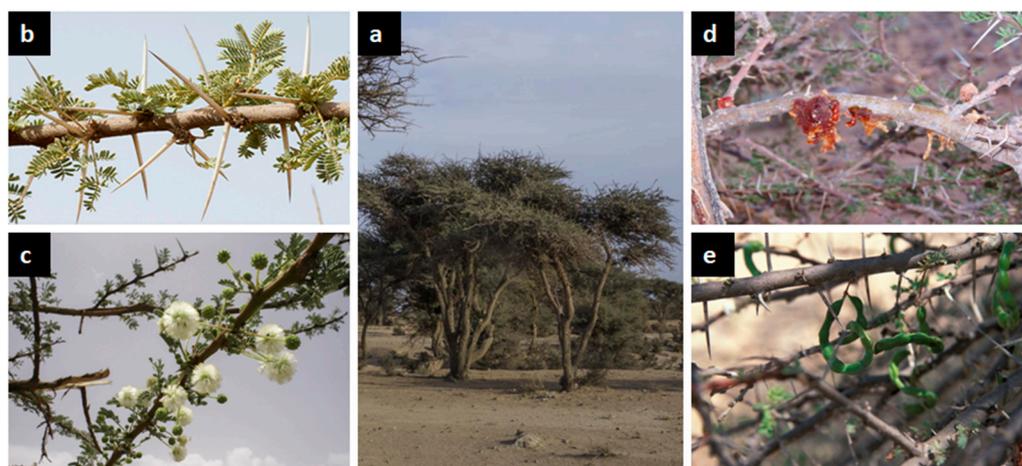


Figure 2. *V. tortilis* tree general aspect (a), leaves (b), flowers (c), gum (d) and pods (e) (<https://www.telinde.fr>, accessed on 10 August 2022).

The immature stems and branches are reddish brown with grey lenticel stems, which transform to dark brown when mature, and the bark is a strong, fissured grey-brown-black color [11].

The pairs of spines are organized, with some spines being short and hooked (up to 5 mm long) and others being long and straight (up to 10 cm long). Having 4–10 pinnae and a maximum length of 2.5 cm, leaves can actually be large (15 leaflets pairs each). White, fragrant flowers are paired with flat, twisted, coil-like pods that resemble springtime. They blossom from May to June, bear fruit in July, and reach maturity from November to February. With longitudinal veins slightly constricted between the seeds, post-floral yellow-brown pods measuring 5–15 cm long and containing 5–18 seeds are present [9–11].

The *V. tortilis* tree can be found in a wide variety of environments, from subtropical deserts to tropical deserts to very dry forests. With an estimated minimum annual precipitation requirement of 10 mm and a maximum of over 100 mm, an expected annual temperature of 18–28 °C, and a pH of 6.5–8.5, it can withstand a wide range of precipitation. This species can withstand temperatures of up to 50 °C in hot, arid conditions. The um-

brella tree thrives in the lowlands. It develops in regions where the annual rainfall exceeds 1000 mm. It is also drought tolerant, surviving in climates with an annual rainfall of less than 100 mm and a long and erratic dry season. The tree thrives in soils with a neutral pH. It develops lengthy roots in soils that are at least 0.25 m deep. The plant remains shade tolerant in shallow soil and must be spaced widely to allow for the growth and proliferation of its lateral roots [10].

3.3. Ethnomedicinal Use

V. tortilis is one of the most useful medicinal plants in Morocco, particularly in the southern area. Plant parts are employed in folk medicine for a variety of medicinal benefits. Different traditional uses of *A. tortilis* in different countries to treat different pathologies are shown in Table 1.

The pharmacological effects of the leaves of *V. tortilis* include antibacterial, antidiabetic, antiparasitic, cytotoxic, and anti-inflammatory characteristics [12–14]. In traditional medicine, root extracts are applied as cytotoxic and antiparasitic medicines [14]. Similarly, fruits exhibit cytotoxic and antimicrobial properties [15]. However, the gum serves as an antibacterial agent [3].

Table 1. Traditional uses of different parts of *V. tortilis*.

Study of Area	Used Part	Mode of Preparation	Traditional Use	References
Morocco (Al Haouz Rhamna region)	Root, fruit and leaf	Decoction and powder	Diabetes	[12]
Moroccan Sahara (Tan Tan)	Plant pod	Powder	Diabetes	[16]
Morocco (Tata Province)	Gum	Infusion	Neuralgia, asthma, hepatitis, jaundice	[1]
	Bark	Infusion	Astringent, demulcent, haemostatic, expectorant, angina	
	Fruit	Decoction	Kidney stones	
Morocco (Agadir Ida Outanane)	Leaves	Powder	Diarrhea, stomach diseases, burns	[17]
	Leaves	Poutine of powder mixed with olive oil		
Northern Kenya (Samburu)	Roots	Not reported	Minimize bloating	[18]
Southern Algerian Sahara (Tassili N'ajjer)	Fruit	Powder	Stomach diseases, diarrhoeaaches	[19]
Central Sudan (Soba area, Khartoum State)	No reported	Not reported	Malaria, swollen joint problems, skin allergies	[20]
Eastern Desert of Egypt (Wadi El-Gemal National Park)	Gum	Not reported	Stomach acidity, ocular affections, jaundice	[21]
Yemen	Fruits	Not reported	Stomach aches, digestive disorders	[15]
Some regions of Africa	Leaves, trunk bark	Not reported	Jaundice, bilious fevers, skin allergies, diabetes, hypertension, diuretic properties	[13]
			Urogenital and pulmonary	
Northern Burkina Fasso	No reported	Not reported	Infectious, schistosomiasis, ulcers, malaria, yellow fever, dysentery	[22]

V. tortilis materials are prepared according to various methods to treat a variety of disorders (Table 1). Infusion, decoction and powdered materials are used in traditional medicinal preparations.

In Moroccan pharmacopeia, stomach disorders and diabetes were the most common medical applications of *V. tortilis* [1,12]. In fact, roots, fruits, and leaves were used as both decoctions and powders by the population of the Al Haouz Rhamna region to treat

diabetes [12]. However, plant pod powder is used by the Moroccan Sahara population in Tan Tan [16].

Digestive problems are relieved with powdered leaves [17]. The bark of *V. tortilis* has been used in traditional medicine as an astringent, demulcent, detergent, hemostatic, and expectorant for angina, neuralgia, asthma, hepatitis, and jaundice [1]. Furthermore, the Tata province's inhabitants (Morocco) used fruit to manage kidney stones using a decoction [1]. They are also used, by mixing the powder with olive oil as a poultice, for burns treatment [17].

In the Southern Algerian Sahara (Tassili N'ajjer), Hammiche and Maizahave reported that powdered fruit and seeds exert an effect against stomach diseases, diarrhea, and aches [19]. However, in Yemen, only *V. tortilis* fruits are used for digestive problems and similar purposes [15]. In addition, roots reduce bloating in the population of Samburu in Northern Kenya [18]. In Central Sudan (Soba area), *V. tortilis* is known to be used for malaria, swollen joints and skin disorders [20]. The local population of the Eastern Desert of Egypt (Wadi El-Gemal National Park) uses *V. tortilis* gum against jaundice, stomach acidity and ocular affections [21].

In Northern Burkina Faso, *V. tortilis* is used in traditional medicine for tropical infectious diseases such as schistosomiasis and malaria, as well as other illnesses (pulmonary and urogenital) [23]. Additionally, people in many parts of Africa use the trunk bark, which has diuretic and hypotensive qualities [13].

3.4. Phytochemical Compounds

The main compounds included in *V. tortilis* vegetable oil, essential oils, and extracts are listed in Table 2. The materials used, the type of extract, the chemical compounds found, and the corresponding chemical classes are all stated in this table for each nation.

Table 2. Chemical composition of different *V. tortilis* plant parts extracts.

Part Used	Origin	Type of Extract/ Seed Oil	Chemical Composition	Compounds Class	References
Leaves	Saudi Arabia	Methanolic Extract	2',6'-dihydroxy, Chalcone-4'-O-glucoside, 4-methoxy chalcone Vitexin	Flavonoids (chalcone glycosides) Flavonoids (flavones)	[11]
Leaves	Algerian Sahara	Ethanol extract	Epigallocatechin-3,7,3',4',5'-penta-Ogallate; Epigallocatechin-3,5,4',5'-tetra-Ogallate; (Epi)gallocatechin-3,5'di-O-gallate; Epigallocatechin-3,5,3'-tri-O-gallate; Trigalloylquinic acid; (Epi)gallocatechin-5,7-di-O-gallate; Epigallocatechin-3,5,5'-tri-O-gallate; Epigallocatechin-5,7,4'-tri-O-gallate; Epigallocatechin-3,7,5'-tri-O-gallate; Epigallocatechin-3,5,4'-tri-O-gallate. Myricetin 3-O-rutinoside;	Flavonoids (flavanol)	[4]
Leaves	Egypt	Ethanol extract	Rutin (Quercetin 3-O-rutinoside); Kaempferol 3-O-rutinoside	Flavonol glycoside	[24]
Leaves	Yemen	Methanol extract	5,7-dihydroxy-4-p-methyl benzyl isoflavone Apigenin Luteolin Quercetin	Flavonoids (isoflavone) Flavonoids (flavone) Flavonoids (flavanols)	[25]
Gum exudates	India	Aqueous extract	L-arabinose, D-galactose, L-rhamnose, D-mannose, D-glucose, D-galacturonic acid, and D-glucuronic acid	Monosaccharides and derivatives	[26]
Stem bark (with gum)	Somalia	Aqueous extract	Quracol A and Quracol B	Alcohols	[27]
Seeds	Israel	Seed oil	Linolenic acid, linoleic acid, palmitic acid, oleic acid, and stearic acid	Fatty acids	[28]
	Egypt		Linoleic acid, palmitic acid, stearic acid, oleic acid, and arachidic acids	Fatty acids	[8]

According to the literature, chromatographic and spectroscopic techniques were used to identify the phytochemicals of *V. tortilis*. Chemical compositions reported in the literature are different due to the plant parts utilized and the countries from which they were procured (Table 2). The phytochemicals of *V. tortilis* are listed below according to the corresponding chemical classes.

3.4.1. Fatty Acids

The chemical properties of *V. tortilis* seed oil showed a significant proportion of fatty acids. Linoleic acid was found to be the most abundant (381.3 ± 3.7 – 685.8 ± 5.3 g kg⁻¹), oleic acid (190.0 ± 3.4 – 386.2 ± 4.06 g kg⁻¹), has been followed by palmitic acid (74.2 ± 2.1 – 192.5 ± 1.5 g kg⁻¹), stearic acid (16.8 ± 1.6 – 104.0 ± 6.6 g kg⁻¹), and linolenic acid (7.9 ± 0.5 – 15.9 ± 0.6 g kg⁻¹) [29].

Fatty acids are mainly extracted from seed oil with petroleum ether (40–60 °C) using a soxhlet. Linolenic acid was found to be the most abundant, then palmitic acid, oleic acid, and stearic acid [28]. However, in Egypt (South and North Sinai) fatty acid profile was different, and linoleic acid was the main component [8].

3.4.2. Monosaccharides

The monosaccharide compounds were identified in the gum exudates of *A. tortilis*. The carbohydrate composition has only been documented through one research from India. It includes mostly L-arabinose, D-galactose, L-rhamnose, D-mannose, and D-glucose [26].

3.4.3. Flavonoids and Chalcone

Flavonoids are a type of secondary metabolite found mostly in plant pigments and are responsible for flowers' and fruits' coloring. They could be used to treat a wide range of disorders. In *V. tortilis* preparations, the analytical analysis revealed a considerable group of flavonoid components (Table 2, Figure 3). The ethanolic extract of leaves collected in Algerian Sahara revealed the presence of flavonoids, including flavanol, epigallocatechin-3,7,3',4',5'-penta-Ogallate, epigallocatechin-3,5,4',5'-tetra-Ogallate, (epi)gallocatechin-3,5'-di-O-gallate, epigallocatechin-3,5,3'-tri-O-gallate, tri galloylquinic acid, (epi)gallocatechin-5,7-di-O-gallate, epigallocatechin-3,5,5'-tri-O-gallate, epigallocatechin-5,7,4'-tri-O-gallate, epigallocatechin-3,7,5'-tri-O-gallate, epigallocatechin-3,5,4'-tri-O-gallate [4].

The flavonol glycoside content of an ethanolic extract of *V. tortilis* leaves from Egypt is considerable. Myricetin 3-o-rutinoside, rutin (quercetin 3-o-rutinoside), kaempferol 3-o-rutinoside were listed [24]. In addition, flavonoids such as isoflavone, flavones, and flavanols, 5,7-dihydroxy-4-p-methyl benzyl isoflavone, apigenin, luteolin and quercetin are mainly encountered in the methanolic extract of Yemen's leaves [25].

Chalcone glycosides (Figure 4) were detected in the methanolic extract obtained by maceration. *V. tortilis* tested was collected from Alwadeha, Saudi Arabia. 2',6'-dihydroxy, chalcone-4'-O-glucoside, and 4-methoxy chalcone were identified. Flavones, including vitexin, were also detected [25].

3.4.4. Alcohols

A study conducted on Acacia (Figure 5) collected in Somalia showed that an aqueous extract of stem bark covered with gum (decoction) contains alcohols. Uracol A [(2,4-dihydroxyphenyl)-3-(3-hydroxyphenyl)-propan-2-ol] and quracol B [1-(2,4-dihydroxyphenyl)-3-(3,4-dihydroxyphenyl)-propan-2-ol] were also identified [27].

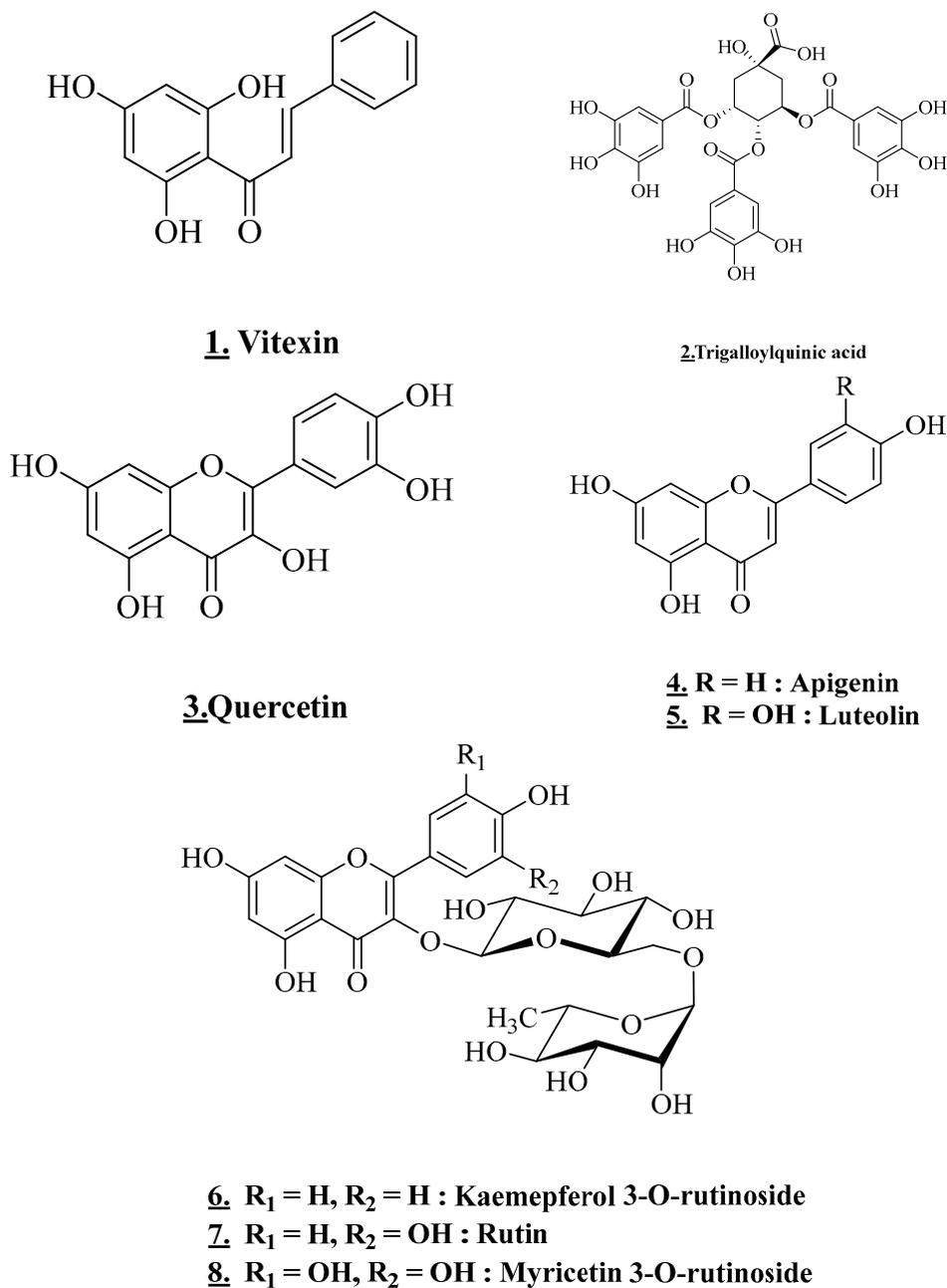


Figure 3. Structures of the main flavonoids, (1), (2), (3), (4), (5), (6), (7), (8).

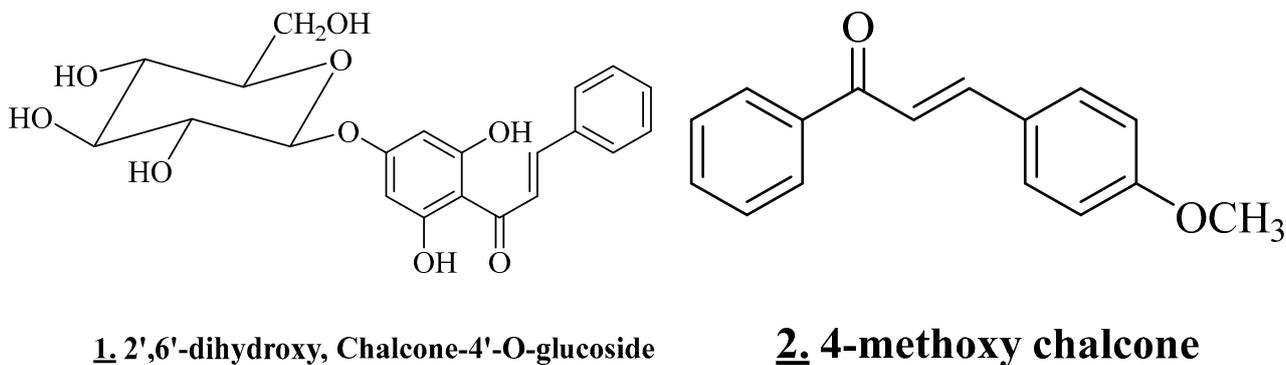
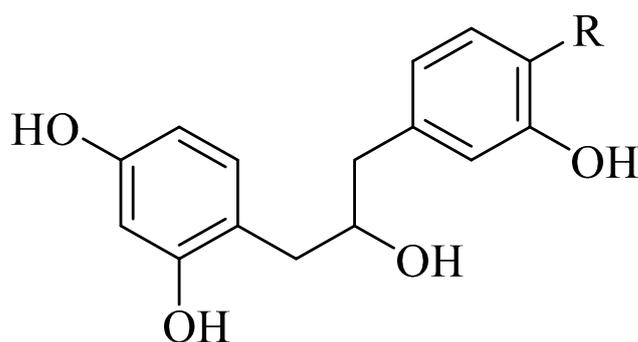


Figure 4. Structures of the main chalcone (1), (2).



1. R = H : Quracol A

2. R = OH : Quracol B

Figure 5. Structures of the main alcohols in *V. tortilis* (1), (2).

Plants have grown in popularity as functional food ingredients. Phytochemical profiles vary depending on the season, growth conditions, location, and environmental changes. The chemical composition of *V. tortilis* extracts differs qualitatively and quantitatively depending on the plant part used, the plants' growing area, and the period of the vegetative phase.

3.5. Biological Properties

3.5.1. Antibacterial Activity

Previous investigations reveal the antibacterial effects of this medicinal plant against Gram-positive and Gram-negative bacteria species. Table 3 summarizes antibacterial investigations conducted on extracts of various *V. tortilis* parts. Inhibition zone diameters (\emptyset) and minimum inhibitory and bactericidal concentrations (MIC and MBC) data are mentioned.

Table 3. Antibacterial activity of *V. tortilis*.

Use Part	Extract	Bacterial Strain	Key Results	References
Aerial part	Ethanollic extract	<i>Staphylococcus aureus</i> (ATCC25923)	$\emptyset = 20$ mm Control not reported	[5]
		<i>Pseudomonas aeruginosa</i> (ATCC27853)	$\emptyset = 20$ mm Control not reported	
	Chloroform extract	<i>Staphylococcus aureus</i> (ATCC25923)	nd	
		<i>Pseudomonas aeruginosa</i> (ATCC 27853)	nd	
	Acetonic extract	<i>Staphylococcus aureus</i> (ATCC 25923)	$\emptyset = 23$ mm Control not reported	
		<i>Pseudomonas aeruginosa</i> (ATCC 27853)	$\emptyset = 18$ mm Control not reported	
Aerial part	Ethanollic extract	<i>Staphylococcus aureus</i>	$\emptyset = 17 \pm 0.9$ mm MIC = 0.4 mg/mL Ampicillin $\emptyset = 21 \pm 1.9$ mm	[30]
		<i>Escherichia coli</i>	$\emptyset = 19 \pm 0.8$ mm MIC = 0.8 mg/mL Doxycycline $\emptyset = 25 \pm 1.2$ mm	
		<i>Pseudomonas aeruginosa</i>	$\emptyset = 16 \pm 1.5$ mm MIC = 0.8 mg/mL Doxycycline $\emptyset = 24 \pm 1.7$ mm	

Table 3. Cont.

Use Part	Extract	Bacterial Strain	Key Results	References
Fruit	Dichloromethanic extract	<i>Staphylococcus aureus</i> ATCC 29213	Ø = 20 mm Ampicillin Ø = 26 mm	[15]
		<i>Bacillus subtilis</i> ATCC 6059	Ø = 20 mm Ampicillin Ø = 28 mm	
	Methanolic extract	<i>Micrococcus flavus</i> SBUG	Ø = 15 mm Ampicillin Ø = 31 mm	
		<i>Staphylococcus aureus</i> ATCC 29213	Ø = 10 mm Ampicillin Ø = 26 mm	
		<i>Bacillus subtilis</i> ATCC 6059	Ø = 8 mm Ampicillin Ø = 28 mm	
		<i>Micrococcus flavus</i> SBUG	Ø = 8 mm Ampicillin Ø = 31 mm	
		<i>Pseudomonas aeruginosa</i> ATCC 27853	Ø = 10 mm Gentamicin Ø = 18 mm	
	Aqueous extract	<i>Staphylococcus aureus</i> ATCC 29213	Ø = 10 mm Ampicillin Ø = 26 mm	
		<i>Micrococcus flavus</i> SBUG	Ø = 8 mm Ampicillin Ø = 31 mm	
	Dichloromethanic extract	<i>Pseudomonas aeruginosa</i> ATCC 27853	Ø = 8 mm Gentamicin Ø = 18 mm	
<i>Staphylococcus aureus</i> ATCC 29213		MIC = 500 µg/mL Ampicillin = 0.05 µg/mL		
<i>Bacillus subtilis</i> ATCC 6059		MIC = 500 µg/mL Control not tested		
Methanolic extract	<i>Micrococcus flavus</i> SBUG	MIC = 1000 µg/mL Ampicillin = 0.25 µg/mL		
	<i>Staphylococcus aureus</i> ATCC 29213	MIC = 500 µg/mL Ampicillin = 0.05 µg/mL		
Aqueous extract	<i>Pseudomonas aeruginosa</i> ATCC 27853	MIC = 1000 µg/mL Control not tested		
Gum	Aqueous extract	<i>Staphylococcus aureus</i> ATCC 29213	MIC = 1000 µg/mL Ampicillin = 0.05 µg/mL	
		<i>Salmonella typhi</i>	Ø = 19 ± 0.5 mm Control not tested	
		<i>Escherichia coli</i>	Ø = 17 ± 0.4 mm Control not tested	
		<i>Staphylococcus aureus</i>	Ø = 24 ± 0.6 mm Control not tested	
Fresh leaves	Chloroform extract	<i>Bacillus subtilis</i>	Ø = 23 ± 0.1 mm Control not tested	
		<i>Klebsiella oxytoca</i>	Ø = 10.0 ± 0.57 mm Control not reported	
		<i>Staphylococcus aureus</i>	Ø = 10.6 ± 0.66 mm Control not reported	
		<i>Proteus mirabilis</i>	Ø = 10.0 ± 0.57 mm Control not reported	
		<i>Klebsiella pneumoniae</i>	Ø = 14.3 ± 0.88 mm Control not reported	
		<i>Pseudomonas aeruginosa</i>	Ø = 9.3 ± 0.33 mm Control not reported	

Table 3. Cont.

Use Part	Extract	Bacterial Strain	Key Results	References
Fresh leaves	Alcoholic extract	<i>Klebsiella oxytoca</i>	$\varnothing = 12.0 \pm 1.15$ mm Control not reported	[6]
		<i>Staphylococcus aureus</i>	$\varnothing = 9.3 \pm 0.33$ mm Control not reported	
		<i>Proteus mirabilis</i>	$\varnothing = 8.6 \pm 0.66$ mm Control not reported	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 15.0 \pm 0.57$ mm Control not reported	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 11.0 \pm 0.00$ mm Control not reported	
	Petroleum ether extract	<i>Klebsiella oxytoca</i>	$\varnothing = 10.6 \pm 0.66$ mm	
		<i>Staphylococcus aureus</i>	$\varnothing = 9.0 \pm 1.00$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 8.3 \pm 0.88$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 14.3 \pm 0.33$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 8.6 \pm 0.33$ mm Control not reported	
	Methanolic extract	<i>Klebsiella oxytoca</i>	$\varnothing = 13.0 \pm 0.58$ mm	
		<i>Staphylococcus aureus</i>	$\varnothing = 11.3 \pm 0.33$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 9.6 \pm 1.30$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 15.3 \pm 0.33$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 11.3 \pm 0.33$ mm Control not reported	
Petroleum Benzin extract	<i>Klebsiella oxytoca</i>	$\varnothing = 9.3 \pm 0.88$ mm		
	<i>Staphylococcus aureus</i>	$\varnothing = 8.6 \pm 0.33$ mm		
	<i>Proteus mirabilis</i>	$\varnothing = 9.6 \pm 1.45$ mm Control not reported		
	<i>Klebsiella pneumoniae</i>	$\varnothing = 16.0 \pm 0.00$ mm		
	<i>Pseudomonas aeruginosa</i>	$\varnothing = 8.6 \pm 0.88$ mm Control not reported		
Dry Bark	Chloroform extract	<i>Klebsiella oxytoca</i>	$\varnothing = 7.3 \pm 0.33$ mm	
		<i>Staphylococcus aureus</i>	$\varnothing = 7.6 \pm 0.66$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 12.0 \pm 0.00$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 11.3 \pm 0.33$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 7.0 \pm 0.00$ mm Control not reported	
	Alcoholic extract	<i>Klebsiella oxytoca</i>	$\varnothing = 9.0 \pm 0.57$ mm	
		<i>Staphylococcus aureus</i>	$\varnothing = 7.3 \pm 0.33$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 13.3 \pm 0.33$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 13.6 \pm 0.88$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 7.0 \pm 0.00$ mm Control not reported	
	Petroleum ether extract	<i>Klebsiella oxytoca</i>	$\varnothing = 7.6 \pm 0.33$ mm	
		<i>Staphylococcus aureus</i>	$\varnothing = 8.3 \pm 0.88$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 12.3 \pm 0.33$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 12.3 \pm 0.88$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 7.6 \pm 0.33$ mm	
Methanolic extract	<i>Klebsiella oxytoca</i>	$\varnothing = 7.6 \pm 0.67$ mm		
	<i>Staphylococcus aureus</i>	$\varnothing = 7.0 \pm 0.00$ mm		
	<i>Proteus mirabilis</i>	$\varnothing = 11.3 \pm 0.88$ mm		
	<i>Klebsiella pneumoniae</i>	$\varnothing = 13.0 \pm 0.58$ mm		
	<i>Pseudomonas aeruginosa</i>	$\varnothing = 7.0 \pm 0.00$ mm		

Table 3. Cont.

Use Part	Extract	Bacterial Strain	Key Results	References
Dry Bark	Petroleum benzin extract	<i>Klebsiella oxytoca</i>	$\varnothing = 7.0 \pm 0.00$ mm	[6]
		<i>Staphylococcus aureus</i>	$\varnothing = 8.6 \pm 0.67$ mm	
		<i>Proteus mirabilis</i>	$\varnothing = 12.0 \pm 0.00$ mm	
		<i>Klebsiella pneumoniae</i>	$\varnothing = 13.3 \pm 0.33$ mm	
		<i>Pseudomonas aeruginosa</i>	$\varnothing = 7.3 \pm 0.33$ mm	
Fresh leaves	Aqueous extract	<i>Escherichia coli</i>	MIC = 1.25 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	[4]
		<i>Klebsiella pneumoniae</i>	MIC = 2.5 mg/mL Ampicillin (20 mg/mL) = 10 MBC = 20 mg/mL Ampicillin (20 mg/mL) = 20	
		<i>Morganella morganii</i>	MIC = 1.25 mg/mL Ampicillin (20 mg/mL) = 20 MBC = 20 mg/mL Ampicillin (20 mg/mL) > 20	
		<i>Proteus mirabilis</i>	MIC = 2.5 mg/mL ; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Pseudomonas aeruginosa</i>	MIC = 2.5 mg/mL ; MBC = 20 mg/mL Ampicillin (20 mg/mL) > 20	
		<i>Enterococcus faecalis</i>	MIC = 5 mg/mL ; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Listeria monocytogenes</i>	MIC = 1.25 mg/mL ; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Escherichia coli</i>	MIC = 1.25 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Klebsiella pneumoniae</i>	MIC = 1.25 mg/mL Ampicillin (20 mg/mL) = 10 MBC = 20 mg/mL Ampicillin (20 mg/mL) = 20	
		<i>Morganella morganii</i>	MIC = 1.25 mg/mL Ampicillin (20 mg/mL) = 20 MBC = 20 mg/mL Ampicillin (20 mg/mL) > 20	
Fresh leaves	Ethanollic extract	<i>Proteus mirabilis</i>	MIC = 1.25 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Pseudomonas aeruginosa</i>	MIC = 1.25 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) > 20	
		<i>Enterococcus faecalis</i>	MIC = 2.5 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	
		<i>Listeria monocytogenes</i>	MIC = 1.25 mg/mL; MBC = 20 mg/mL Ampicillin (20 mg/mL) < 0.15	

Ethanol, chloroform, and acetic extracts obtained from the aerial segment of *V. tortilis* antimicrobial properties were studied against *Staphylococcus aureus* (ATCC25923) and *Pseudomonas aeruginosa* (ATCC 27853) in vitro by Abdllha and collaborators [5]. The strains were sensitive to ethanol and acetic extracts with diameter zones of inhibition ranging from 18 to 23 mm. Whereas no activity was found with the chloroform extract. The antibacterial property of extracts from the aerial section of *V. tortilis* was also investigated by the Alajmi team. The results revealed that ethanol extract inhibited the proliferation of *Escherichia coli* ($\text{Ø} = 19 \pm 0.8$ mm; MIC = 0.8 mg/mL), *Staphylococcus aureus* ($\text{Ø} = 17 \pm 0.9$ mm; MIC = 0.4 mg/mL), and *Pseudomonas aeruginosa* germs ($\text{Ø} = 16 \pm 1.5$ mm; MIC = 0.8 mg/mL) [30]. These differences in inhibition activities are certainly due to the difference in the plant parts used, the extraction technique, and edaphic factors. In another study, chloroform, alcoholic, petroleum ether, methanolic, and petroleum Benzoin extracts of *V. tortilis* extracts, prepared from dry bark and fresh leaves were tested against *Klebsiella oxytoca*, *Staphylococcus aureus*, *Proteus mirabilis*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The diameter of the inhibition zone in this research ranged between 7–16 mm, with *Klebsiella pneumoniae* being the most sensitive bacteria, including all extracts [6]. Another study showed the antibacterial action of an aqueous extract generated from plant gum by using the disk diffusion method. *Salmonella typhi*, *Escherichia coli*, *Staphylococcus aureus*, and *Bacillus subtilis* have antibacterial activity with inhibition zone diameters of 19 ± 0.5 , 17 ± 0.4 , 24 ± 0.6 , and 23 ± 0.1 mm, respectively [3].

Aqueous and ethanol extracts produced from fresh leaves were tested for antibacterial activity using MIC and MBC against *Escherichia coli*, *Morganella morganii*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, and *Listeria monocytogenes*. The MIC and MBC values varied from 1.25 to 5 mg/mL and 20 mg/mL, according to the results of [4].

Al-Fatimi and company investigated the antibacterial activity of dichloromethane, methanolic, and aqueous extracts collected from the plant's fruit using disc diffusion and minimum inhibitory concentrations methods. When compared to other extracts tested, dichloromethane has a significant antimicrobial effect against *Staphylococcus aureus* ($\text{Ø} = 20$ mm; MIC = 500 µg/mL), *Bacillus subtilis* ($\text{Ø} = 20$ mm; MIC = 500 µg/mL), and *Micrococcus flavus* ($\text{Ø} = 15$ mm; MIC = 1000 µg/mL) [15].

Chloroform, petroleum ether, and methanol extracts inhibited more strains such as *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Pseudomonas aeruginosa* compared to other types of extracts such as an ethanol extract and an aqueous extract [6]. The results of the experiments with dried bark, which have higher inhibitory diameters than the experiments with leaves, were reversed [6]. Leaves inhibit more *Klebsiella pneumoniae* than dry bark, later inhibits *Proteus mirabilis* more than *Staphylococcus aureus* [6]. The gum component inhibits Gram-positive bacteria, such as *Staphylococcus aureus* and *Bacillus subtilis*, as well as Gram-negative bacteria, including *Salmonella typhi* and *Escherichia coli* [3]. Gram-negative bacteria resistance to *V. tortilis* extracts is due to the enveloping outer membrane encircling the cell wall, which prevents hydrophobic chemicals from diffusing through the lipopolysaccharide. The main and synergistic effects of the major and minor chemical components, notably flavonoids (chalcone glycosides, flavones, flavanol, flavonol glycoside, isoflavone, flavone, and flavanols), monosaccharides, alcohols, and fatty acids, are frequently attributed to extracts antibacterial action (linolenic, linoleic, palmitic, oleic, stearic acids) [4,8,24–28,31].

Although plant extracts have been proven effective against these strains, the mode of action has yet to be discovered, necessitating more investigation into their mechanism of action.

3.5.2. Antifungal Activity

V. tortilis antifungal activity was previously described in the literature against only three fungal strains [5,6,29]. Table 4 lists the data of previous studies on antifungal investigations from various parts of *V. tortilis* extracts.

Table 4. Antifungal activity of *V. tortilis* (none of the references cited below reported control data).

Use Part	Type of Extract	Tested Microorganisms	Key Results	References
Aerial part	Ethanol extract	<i>Candida albicans</i> (ATCC90028)	Ø = 23 mm	[5]
	Chloroform extract		nd	
	Acetonic extract		Ø = 25 mm	
Aerial part	Ethanol extract	<i>Candida albicans</i>	Ø = 15 ± 1.0 mm MIC = 0.8 mg/mL	[30]
Fruit	Methanol extract	<i>Candida maltosa</i>	Ø = 8 mm	[15]
	Chloroform extract		Ø = 16.0 ± 0.00 mm	
	Alcoholic extract		Ø = 16.6 ± 0.33 mm	
Aerial part	Petroleum ether extract	<i>Candida albicans</i>	Ø = 15.3 ± 0.33 mm	[6]
	Methanol extract		Ø = 16.6 ± 0.67 mm	
	Petroleum benzoin extract		Ø = 15.6 ± 0.33 mm	
	Chloroform extract		Ø = 12.3 ± 1.20 mm	
Dry Bark	Alcoholic extract	<i>Candida albicans</i>	Ø = 10.3 ± 1.76 mm	[6]
	Petroleum ether extract		Ø = 11.0 ± 1.52 mm	
	Methanol extract		Ø = 12.3 ± 0.33 mm	
	Petroleum benzoin extract		Ø = 12.3 ± 0.33 mm	

Using the agar-plate well diffusion method, Abdllha and his associates tested the antifungal activity of aerial part extracts against *Candida albicans* (ATCC90028). The acetonic extract (25 mm) and the ethanolic extract (23 mm) had the most activity against yeast, whereas the chloroform extract showed no inhibition [5].

Agar well diffusion method was also used [30] to determine the antifungal effect property of the aerial parts ethanolic extract against *Candida albicans*. Minimal inhibition concentration was also determined (0.8 mg/mL), which is of the same value as *Acacia salicina* (0.8 mg/mL), lower than *Acacia laeta* (1.6 mg/mL) and *Acacia hamulosa* (3.2 mg/mL).

Using the agar diffusion method, Al-Fatimi and colleagues found that the methanolic extract of fruit from *V. tortilis* had antifungal activity against *Candida maltosa*. The extract effectively suppressed proliferation, with an inhibition zone equal to 8 mm [15].

Ref. [6] and co-workers carried out the agar well diffusion method to evaluate the antifungal properties of methanolic extract, chloroform extract, petroleum benzoin extract, and petroleum ether extract from *V. tortilis* aerial parts and dry bark against *Candida albicans* [6]. According to the experimental fungal growth, five extracts from the aerial parts exhibited inhibitory effects differently. As a result, the highest activity against *Candida albicans* was found using the methanolic and alcoholic extracts (Ø = 16.6 ± 0.67 and 16.6 ± 0.33 mm, respectively), subsequently the chloroform extract (Ø = 16.0 mm). The zones of inhibition for petroleum benzoin and petroleum ether extracts, respectively, were 15.6 ± 0.33 mm and 15.3 ± 0.33 mm. Furthermore, similar *Candida albicans* inhibition activities were obtained using methanolic, petroleum benzoin, and chloroform extracts from the dry bark of *V. tortilis* (Ø = 12.3 mm). Petroleum ether and alcohol exhibited a slight difference in this antifungal activity (Ø = 11.0 ± 1.52 and 10.3 ± 1.76 mm, respectively [6]).

As previously stated, the differences in the results are related to genetic variability, environmental influences, and chemical composition. Thus, the antifungal activity is mainly due to the bioactive phytochemicals of *V. tortilis* (fatty acids, monosaccharides, flavonoids, and alcohols). Polyphenols are a significant class of natural compounds that includes flavonoids [32].

3.5.3. Antiparasitic Effects

Malaria is a serious tropical disease caused by protozoa of the Plasmodium genus. The anti-plasmodial activity of *V. tortilis* chloroform extract against chloroquine (CQ)-resistant plasmodium was investigated in vitro (D6 clone). In comparison to chloroquine (IC₅₀ = 0.004 g/mL), the results showed an IC₅₀ equal to or higher than 10.0 µg/mL [14]. Another analysis revealed that methanolic extract exhibited anti-plasmodial potential in vitro, with an IC₅₀ value of 85.73 ± 3.36 µg/mL [33]. The anti-leishmanial activity of

aqueous and methanol extracts from the leaves of *V. tortilis* appears promising against *Leishmania major* (IDU/KE/83 NLB-144 strain) [33].

3.5.4. Antioxidant Activity

Using all plant parts and processes, such as the DPPH, ABTS, FRAP, and carotene-linoleic acid approaches, several researchers have evaluated the antioxidant activity of various *V. tortilis* preparations (Table 5).

Table 5. Antioxidant activity of *V. tortilis*.

Use Part	Extracts/Method Extraction	Used Method	Key Results	References
Aerial parts	Ethanol extract/maceration	DPPH	RSA = $83 \pm 0.02\%$ Control not reported	[5]
	Chloroform extract/maceration	DPPH	RSA = $42 \pm 0.7\%$ Control not reported	
Leaves	Acetonic extract/maceration	DPPH	RSA = $82 \pm 0.04\%$ Control not reported	[7]
	Ethanol extract/ultrasound	DPPH	IC ₅₀ = 250.13 µg/mL Rutin IC ₅₀ = 250.13 µg/mL	
Leaves	n-Butanol extract/maceration	DPPH	RSA = 89.8% Control not tested	[34]
Leaves	Methanolic extract/infusion	DPPH	84.3 ± 9.7 mg/g DW (Chlorogenic acid equivalent) Control not tested	[35]
Leaves	Methanolic extract/maceration	DPPH	IC ₅₀ = 0.03 ± 0.01 µg/mL Trolox = 0.01 ± 0.00 µg/mL	[23].
Trunk bark	Methanolic extract/maceration	DPPH	IC ₅₀ = 0.01 ± 0.01 µg/mL Trolox = 0.01 ± 0.00 µg/mL	[23].
Fruit	Methanolic extract/maceration	DPPH	RSA = 26.17% (at 100 µg/mL) Ascorbic acid RSA = 96.9% (at 100 µg/mL)	[15]
Fruit	Aqueous extract/maceration	ABTS	RSA = 80.62 ± 0.14% Control not tested	[36]
		DPPH	RSA = 19.12 ± 1.34% Control not tested	
Seeds	Methanolic extract/maceration	DPPH	RSA = 0.84 ± 0.03 (TEAC mM) Control not tested	[37]
		ABTS	RSA = 2.22 ± 0.20 (TEAC mM) Control not tested	
Gum	Aqueous extract/maceration	DPPH	RSA = 92.13 ± 0.13% (at 20 mg/mL) Control not tested	[3]

The antioxidant properties of *V. tortilis* ethanolic extract were measured by Alam and coworkers using the DPPH test [7]. The results were expressed as IC₅₀ values, which were equal to 250.13 and 747.50 µg/mL, respectively.

According to the literature, at 500 µg/mL, the DPPH scavenging activity was in the following order: *A. salicina* > *A. laeta* > *A. tortilis* > *A. hamulosa* [7]. Surprisingly, the antioxidant activity of *Acacia salicina* was similar to that of the antioxidant standard rutin at amounts higher than 250 µg/mL. *Acacia* extracts' activities were dose-dependent, according to the results of the DPPH radical scavenging assay.

In another work, a methanolic extract of *V. tortilis* leaves obtained by infusion and maceration exhibited considerable DPPH radical scavenging activity [23,35]. Results obtained were expressed as 84.3 ± 9.7 mg/g dry weight equivalent of chlorogenic acid.

The acetonic and ethanolic extracts of the aerial parts had the highest radical scavenging activity, with values of 82.04 and 83.02%, respectively [5]. However, the chloroform extract exhibits the lowest scavenging activity, with an RSA equal to 42.7%.

Using testing methods, including the ABTS test, Habib and colleagues demonstrated that aqueous extract by maceration of fruit *V. tortilis* exhibited an antiradical effect (80.62 ± 0.14%),

by the DPPH antioxidant ($19.12 \pm 1.34\%$) [36]. According to the DPPH test, a methanolic extract from Acacia fruit maceration has a radical trapping activity of 26.17% (concentration = 100 $\mu\text{g}/\text{mL}$) in a study by Al-Fatimi and colleagues [15].

The antioxidant effect of maceration-based methanolic extract of Acacia seeds was studied using the DPPH and ABTS assays in another study. Data indicates that extract has the lowest activity, with EC_{50} values of 0.84 ± 0.03 and 2.22 ± 0.20 mM (TEAC), respectively [37].

Another investigation evaluated the antioxidant activity of *V. tortilis* gum aqueous extract obtained by maceration using the DPPH assay. As a result, 20 mg/mL gum extract exhibited a scavenging potential of $92.13 \pm 0.13\%$ [3].

The methods conducted to evaluate antioxidant activity have a specific mechanism, which explains the diversity in the results listed in Table 5. These approaches are, in effect, mutually beneficial. Thus, in order to confirm and validate the results presented in the table of extracts from *A. tortilis*, in vivo antioxidant activity tests should be performed.

3.5.5. Antiproliferative Activity

Different analytical methods highlighted the cytotoxic activity of *V. tortilis*, as shown in Table 6. *V. tortilis* leaves revealed potential in vitro cytotoxic effect, according to Ziani and colleagues. The sulforhodamine B colorimetric assay was used to determine the capacity of extracts to inhibit cell proliferation in four human tumor cell lines: NCI-H460 (non-small cell lung cancer), HeLa (cervical carcinoma), HepG2 (hepatocellular carcinoma), and MCF-7 (breast carcinoma). Ellipticine was used as a positive control, and the results were expressed as Growth Inhibition values (GI_{50} , $\mu\text{g}/\text{mL}$). The growth of non-tumor liver cells (PLP2) was indeed tested using different amounts of *V. tortilis* extracts under the same conditions as tumor cell lines. Ethanolic extract expressed a low GI_{50} on the four tumor cell lines (from 33.3 to 53.0 $\mu\text{g}/\text{mL}$) [4]. Compared to the cytotoxicity data obtained by the ethanolic extract of aerial parts [30], ethanolic leaf extracts seem to have a high cytotoxic effect on HepG2 cells (IC_{50} 42.3 and 33 $\mu\text{g}/\text{mL}$, respectively).

Table 6. Antiproliferative activity of *V. tortilis*.

Activities	Use Part	Extracts	Experimental Approach	Key Results	References
Cytotoxic activity	Aerial part	Ethanolic extract	HepG2, HEK-293, MCF-7, and MDA-MB-231 cancer cells were tested in vitro for anticancer efficacy.	The estimated IC_{50} ($\mu\text{g}\cdot\text{mL}^{-1} \pm \text{SD}$): HepG2 (Liver) = 42.3 ± 1.78 5-Flurourasil = 3.1 ± 0.07 HEK-293 (Kidney) = 49.1 ± 1.92 5-Flurourasil = 2.5 ± 0.05 MCF-7 (Breast) = 65.7 ± 2.49 5-Flurourasil = 3.7 ± 0.07 MDA-MB-231 (Breast) = 52.2 ± 1 . 995-Flurourasil = 3.9 ± 0.09	[30]
Cytotoxic activity	Fruit	Methanolic extract	FL-cells, a human amniotic epithelial cell line	$\text{IC}_{50}\%$ ($\mu\text{g}/\text{mL}$) against FL-cells > 1000	[15]
Cytotoxic activity	Root bark	Chloroform extract	One human cancer cell line was used to test cytotoxic activity (KB, a human oral epidermoid cancer cell line)	Cytotoxicity assay; KB IC_{50} ($\mu\text{g}/\text{mL}$) > 20 Chloroquine = 17.4 $\mu\text{g}/\text{mL}$	[14]
Cytotoxic activity	Leaves	Ethanolic extract	Cytotoxicity, Growth inhibition values (GI_{50} , $\mu\text{g}/\text{mL}$)	Cell lung cancer (NCI-H460) = 52 ± 1 . Ellipticine = 1.0 ± 0.1 Cervical carcinoma (HeLa) = 48.2 ± 0.1 . Ellipticine = 1.9 ± 0.1 Hepatocellular carcinoma (HepG2) = 33 ± 1 ($p < 0.05$) Ellipticine = 1.1 ± 0.2 Breast carcinoma (MCF-7) = 52 ± 1 ($p < 0.05$). Ellipticine = 0.91 ± 0.04 PLP2 = 259 ± 0.1 Ellipticine = 3.2 ± 0.7	[4]

Acacia species have been demonstrated to have a cytotoxic effect on a variety of tumor cell lines (HepG2, MCF-7, HEK-293) ([38]. A high GI_{50} ($259 \pm 0.05 \mu\text{g/mL}$) was recorded on the PLP2 cell line using the ethanolic leaves extract [4]. The lower cytotoxicity of *V. tortilis* extracts in the normal PLP2 cell line might be due to the specific molecular mechanisms involved in tumor cells that are not present or active in normal cell lines.

Furthermore, tumor cells that were exposed to *V. tortilis* extracts had a higher response than non-tumor cells, implying that they were more reactive to the phenolic chemicals present in the extracts. These substances tend to be interfering with the cell cycle, apoptosis, and cell death pathways, all of which are implicated in tumor proliferation [39,40]. According to [41], the cytotoxic effect could be attributed to epigallocatechin derivatives, which are prevalent in *V. tortilis* extracts, as well as a possible synergistic interaction with different *Acacia* active components that approach epigallocatechin derivatives. As previously reported by [42], *V. tortilis* contains a significant amount of esterified gallic acid and epicatechin galloyled with a significant level of hydroxyl ring substitutions, which have also been shown to inhibit the proliferation of many tumor cell lines directly. This provides a coherent explanation for cytotoxicity on human tumor cells [4].

3.5.6. Antidiabetic Effect

Investigations conducted on *V. tortilis*' anti-diabetic properties are limited. Table 7 reports the in vivo research data realized with different *Acacia* extracts.

Table 7. In vivo antidiabetic effects of *V. tortilis*.

Part Used	Extract Tested	Dose	Model	Keys Results	References
Seed	Aqueous extract	100 and 200 mg/kg body weight	Normoglycaemic and Alloxan-induced diabetic rats	Decreases blood glucose levels, fluid intake by 34.49%, and food intake	[43]
Leaves	Aqueous extract	800 mg/kg	Normoglycaemic rats	Reduces blood glucose, serum total cholesterol and LDL level, and body weight Increase serum HDL-cholesterol	[44]
Stem and branches	Aqueous extract	250–1000 mg/kg	Streptozotocin-Nicotinamide Induced diabetic rats	Minimizes fasting blood glucose level, glycated hemoglobin level, total cholesterol, triglyceride, LDL, VLDL, SGOT, and SGPT levels, and improved HDL level	[45]

Because diabetes is always related to body weight loss due to muscle wasting and tissue protein catabolism, the effect of the administration of AEATP on body weight was followed [46,47]. Indeed, AEATP markedly increased body weight on the 14th day of administration and balanced the effect of STZ approximately close to the glimepiride-treated group.

Kumar and Singh assessed the anti-diabetic activity of aqueous extract of *V. tortilis* polysaccharide from gum exudates on streptozotocin-nicotinamide-induced diabetic rats. Dosages of 250, 500, and 1000 mg/kg were administered to male albino Wistar rats for 28 days, with all necessary controls. AEATP reduces current weight, fasting blood glucose, total cholesterol, triglyceride, LDL, VLDL, SGOT, and SGPT levels while improving HDL levels [48].

Treatments were completed on the 21st and 28th days, and body weight was almost the same, and statistically, no significant difference was found between the glimepiride and polysaccharide tests [48]. This could be ascribed to the protective effect of polysaccharides in the control of muscle wasting, contrary to neoglucogenesis, as well as increased insulin secretion and enhanced glycemic control.

After administering polysaccharide, glycated hemoglobin was also substantially reduced (250–1000 mg/kg) as compared to the STZ-induced diabetic group with close value

to those of glimepiride after 28 days of treatment [48]. Flavonoids abundant in *V. tortilis* are known for their ability to attenuate hyperglycemia and reduce the nonenzymatic glycation of proteins in animals [25,49,50]. Nutritional flavonoids or extracts rich in flavonoids may prevent and treat T2DM, as well as reduce diabetes complications, according to significant variables from cell and animal models. Flavonoids in the diet lower blood glucose levels by protecting pancreatic cells, stimulating insulin signaling, inducing the pancreas to release insulin, inhibiting glycogenolysis, and inhibiting neoglucogenesis, digestive enzymes, and carbohydrate metabolizing enzymes, as well as inhibiting neoglucogenesis, digestion enzymes, and carbohydrate metabolizing enzymes [51].

Certain flavonoids aglycones and their O-glycosides/C-glycosides exhibited anti-diabetic effects in animal models, namely apigenin, baicalein, quercetin, kaempferol, myricetin, daidzein, luteolin, and naringenin. Leading to a shortage of data and varied animal models, determining the structure-activity interaction of flavonoids and antidiabetic effects remains difficult [51].

Lipids are well-known for their role in the pathophysiology of diabetic complications and the resulting hyperlipidemia. Diabetics have a higher risk of developing atherosclerosis than non-diabetics [52]. Interestingly, polysaccharides have shown a considerable reduction in TG and LDL-C, implying additional hypolipidemic activity that could protect against the development of cardiovascular disease and diabetes. Cholesterol levels in serum significantly decreased from 206.1 ± 3.7 mg/dL (STZ-induced diabetic group), and both 500 and 1000 mg/kg of polysaccharide normalized the elevated cholesterol to levels similar to that of glimepiride (134.2 ± 3.52 mg/dL) [48]. In the same study, Bhateja and Singh also showed that levels of total triglyceride (TG), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels were significantly reduced after administration (Figure 6). The same effectiveness was reported for VLDL levels. Otherwise, HDL levels were significantly reduced in the diabetic control group, which was close to that of glimepiride (24.44 ± 1.3 mg/kg) [48].

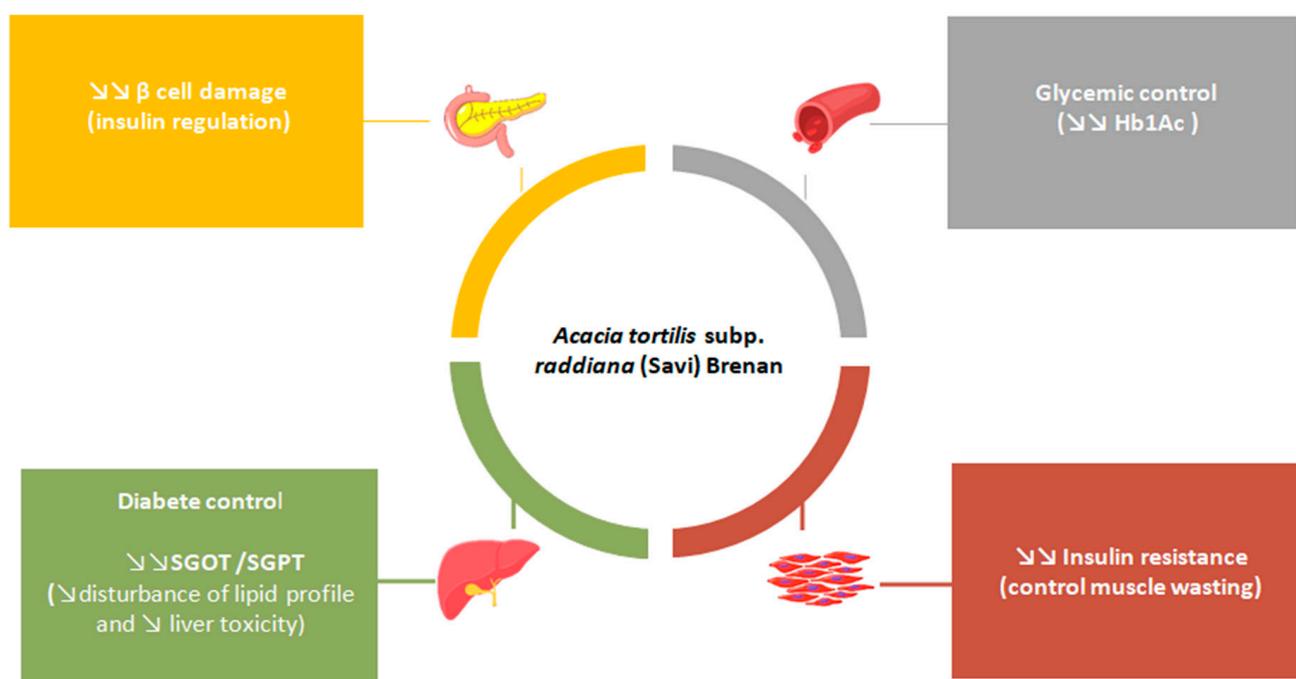


Figure 6. In vivo antidiabetic mechanism effects of *V. tortilis*.

Regarding the effect of polysaccharides on liver enzymes, high levels of SGOT (284.5 ± 10.21) and SGPT (161.9 ± 5.21 unit/L) in the serum of diabetic rats were lowered after administration of AEATP [48]. Normalized serum SGPT and SGOT levels are responsible for normal liver function in reversing diabetes-related organ damage.

Decreased fasting insulin levels (0.373 ± 0.026 ng/mL) and the insulin content of the pancreas (56.0 ± 2.81 ng/mg pancreas) in STZ-induced diabetic rats were also improved by AEATP [48]. Polysaccharides may improve insulin secretion by membrane depolarization, inhibiting K^+ -ATP channels and stimulating Ca^{2+} influx. Since altered content of gut incretin is associated with type 2 diabetes in animal models, polysaccharides may stimulate incretin secretion and thus probably induce glucagon-like peptide-1 (GLP-1) increase or dipeptidyl peptidase-4 (DPP-4) inhibition [53]. Moreover, it shows that the polysaccharide effect, similar to STZ treatment, may include a reduction in oxidative stress and, consequently, oxidative damage and dyslipidemia prevention.

3.5.7. Anti-Inflammatory Effect

A murine macrophage-like cell line was used to study the anti-inflammatory properties of ethanolic and aqueous extracts of *V. tortilis* leaves collected in the Algerian Sahara [4]. RAW 264.7 cell model was stimulated by lipopolysaccharide (LPS). The anti-inflammatory activities could be explained by the presence of phenolic compounds, particularly (epi)-gallocatechin derivatives. Phenolic compounds have been shown to inhibit inflammatory responses in activated Raw 264.7 cells through NO production reduction as well as inhibition of proinflammatory mediators and cytokines, including TNF- α , IL-1, IL-6, and IL-12. The use of (epi)-catechin to reduce NO production in the studied cell model has been previously reported in the literature [54,55]. In addition, a gallate ester substitution is involved in the anti-inflammatory properties of (epi)-catechins and gallic acid enhancement [56]. Epigallocatechin-3-gallate is an efficient scavenger ROS and RNS such as NO and peroxynitrite involved in the nucleus translocation of NF- κ B nuclear factor from the cytoplasm [57]. Moreover, it has been previously reported that the suppression of iNOS and COX-2 enzymes and TNF- α expression is due to the reduction of NO production by acetone extract of *Acacia* stem bark [58].

In the study conducted by [24], ethanolic extract of *V. tortilis* leaves exhibited significant inhibition of COX-1 and COX-2. These enzymes are often targeted in the inflammatory response [59]. The observed effect is certainly ascribed to the richness of *V. tortilis* extract with rutin and catechin.

4. Conclusions and Perspectives

This review covered the taxonomy, medical applications, phytochemistry, and pharmacological characteristics of *V. tortilis*. According to published data, the biological activities of *V. tortilis*, as supported by conventional medical uses, are implicated by bioactive substances of plant sections cited (fruit, seeds, gum, leaves, and roots). These phytochemicals, which are involved in biological processes, include fatty acids, flavonoids, and chalcones. The fact that other compounds have not yet been recognized and classified as terpenoids makes a significant recommendation for additional phytochemical research.

Additionally, *V. tortilis* extracts show exceptional pharmacological qualities, such as anti-inflammatory, anti-microbial, antioxidant, and anti-diabetic action. These characteristics include cellular and molecular activities on many pathology-causing sites. Researched works revealed that the primary bioactive components of *V. tortilis* are the mediators of these pathways.

To confirm their effectiveness, additional research into the pharmacodynamic activities of these key bioactive chemicals needs to be done. Additionally, studies on the pharmacokinetics of the primary bioactive chemicals in *V. tortilis* should be conducted to demonstrate their safety.

This study provides a conventional analysis using pharmacological justifications on the functional advantages of the various *V. tortilis* plant parts that could be used, on the one hand, in in vivo studies for the creation and innovation of therapeutic strategies to prevent and manage type 2 diabetes, and, on the other hand, in the pharmaceutical industry, use of nanoparticles and the formulation based on non-toxic natural resources.

Author Contributions: Conceptualization: S.E.H., I.B. and A.B.; Data curation: D.T., I.B., Y.M., A.T., T.B. and N.E.M.; Formal analysis: H.E.M. and A.B.; Investigation: I.B., S.E.H. and N.I.; Project administration: I.B., S.E.H. and N.I.; Software: A.B. and H.E.M.; Supervision: I.B., S.E.H. and N.I.; Validation: L.-H.L., A.B. and M.G.; Visualization: A.B., L.-H.L. and M.G.; Writing—original draft: D.T., Y.M., A.T., T.B. and N.E.M.; Writing—review & editing: N.I., S.E.H., I.B., A.B., M.G. and L.-H.L. All authors have read and agreed to the published version of the manuscript.

Funding: No specific funding support from governmental, private, or non-profit funding bodies was allowed for this research.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

ABTS	2,2'-Azino-bis (3-ethylBenzoThiazoline-6-Sulphonic)acid
ATCC	American Type Culture Collection
COX-2	Cyclooxygenase-2
DPPH	2,2-Diphenyl-1-picryl hydrazyl radical
DW	Dry Weight
EC₅₀	Effective Concentration of 50%
FRAP	Ferric Reducing Antioxidant Power
GA	Gallic Acid
HDL	High-Density Lipoprotein
IC₅₀	Inhibition Concentration of 50%
iNOS	Inducible Nitric Oxide Synthase
IZD	Inhibition Zone Diameter
LD	Lethal Dose
LDL	Low-Density Lipoprotein
MBC	Minimum Bactericidal Concentration
MIC	Minimum Inhibitory Concentration
RNS	Reactive Nitrogen Species
ROS	Reactive Oxygen Species
SGOT	Glutamooxaloacetate Transferase Serum
SGPT	Glutamate Pyruvate Transaminase Serum
STZ	Streptozotocin-Induced Diabetic
TG	Triglyceride
TNF-α	Tumor Necrosis Factor
VLDL	Very Low-Density Lipoprotein

References

- Abouri, M.; Mousadik, A.E.; Msanda, F.; Boubaker, H.; Saadi, B.; Cherifi, K. An ethnobotanical survey of medicinal plants used in the Tata Province, Morocco. *Int. J. Med. Plants Res.* **2012**, *27*, 99–123.
- Jaouadi, W.; Mechergui, K.; Ammari, Y.; Hamrouni, L.; Hanana, M.; Khouja, M.L. Étude ethnobotanique et ethnopharmacologique d'*Acacia tortilis* (Forssk) Hayne subsp. *raddiana* (Savi) de la steppe arborée du Nord de l'Afrique. *Phytothérapie* **2016**, *14*, 285–292. [[CrossRef](#)]
- Ali, M.R.; EL Said, R.M. Assessment of the potential of *Arabic* gum as an antimicrobial and antioxidant agent in developing vegan “egg-free” mayonnaise. *J. Food Saf.* **2020**, *40*, e12771. [[CrossRef](#)]
- Ziani, B.E.C.; Carochi, M.; Abreu, R.M.V.; Bachari, K.; Alves, M.J.; Calhelha, R.C.; Talhi, O.; Barros, L.; Ferreira, I.C.F.R. Phenolic profiling, biological activities and in silico studies of *Acacia tortilis* (Forssk.) Hayne ssp. *raddiana* extracts. *Food Biosci.* **2020**, *36*, 100616. [[CrossRef](#)]
- Abdlla, H.B.; Mohamed, A.I.; Almoniem, K.A.; Adam, N.I.; Alhaadi, W.; Elshikh, A.A.; Ali, A.J.; Makuar, I.G.; Elnazeer, A.M.; Elrofaei, N.A.; et al. Evolution of Antimicrobial, Antioxidant Potentials and Phytochemical Studies of Three Solvent Extracts of Five Species from Acacia Used in Sudanese Ethnomedicine. *AiM* **2016**, *6*, 691–698. [[CrossRef](#)]
- Sulayli, A.I.; Moustafa, M.F.; Eid, E.M. Genetic Variability, Antimicrobial Activity And Natural Water-Soluble Vitamins Contents Of Five Acacia Species Growing In Jazan Region, Saudi Arabia. *Pak. J. Agric. Sci.* **2019**, *56*, 289–300.
- Alam, P.; Alajmi, M.F.; Arbab, A.H.; Parvez, M.K.; Siddiqui, N.A.; Alqasoumi, S.I.; Al-Rehaily, A.J.; Al-Dosari, M.S.; Basudan, O.A. Comparative study of antioxidant activity and validated RP-HPTLC analysis of rutin in the leaves of different Acacia species grown in Saudi Arabia. *Saudi Pharm. J.* **2017**, *25*, 715–723. [[CrossRef](#)]

8. Embaby, H.E.; Rayan, A.M. Chemical composition and nutritional evaluation of the seeds of *Acacia tortilis* (Forssk.) Hayne ssp. *raddiana*. *Food Chem.* **2016**, *200*, 62–68. [[CrossRef](#)]
9. Verma, S. A Review Study on *Acacia tortillis* Sunita Verma. *Int. J. Life Sci. Pharma Res.* **2016**, *6*, 22–24.
10. *A Guide to Medicinal Plants in North Africa*; IUCN: Grand, Switzerland, 2009; Volume 14.
11. Muhaisen, H.M.H. A Review on Chemical Constituents of *Acacia tortilis* (Leguminosae). *J. Pharm.* **2021**, *11*, 10–21.
12. Benkhiguel, O.; Akka, F.B.; Salhi, S.; Fadli, M.; Zidane, L. Catalogue des plantes médicinales utilisées dans le traitement du diabète dans la région d'Al Haouz-Rhamna (Maroc). *J. Anim. Plant Sci.* **2014**, *30*, 3539–3568.
13. Bouyahya, A.; El Omari, N.; Elmeniyi, N.; Guaouguaou, F.E.; Balahbib, A.; Belmehdi, O.; Bakri, Y. Moroccan antidiabetic medicinal plants: Ethnobotanical studies, phytochemical bioactive compounds, preclinical investigations, toxicological validations and clinical evidences; challenges, guidance and perspectives for future management of diabetes worldwide. *Trends Food Sci. Technol.* **2021**, *115*, 147–254.
14. Koch, A.; Tamez, P.; Pezzuto, J.; Soejarto, D. Evaluation of plants used for antimalarial treatment by the Maasai of Kenya. *J. Ethnopharmacol.* **2005**, *101*, 95–99. [[CrossRef](#)] [[PubMed](#)]
15. Al-Fatimi, M.; Wurster, M.; Schröder, G.; Lindequist, U. Antioxidant, antimicrobial and cytotoxic activities of selected medicinal plants from Yemen. *J. Ethnopharmacol.* **2007**, *111*, 657–666. [[CrossRef](#)]
16. Ghourri, M.; Zidane, L.; Douira, A. Usage des plantes médicinales dans le traitement du Diabète Au Sahara marocain (Tan-Tan). *J. Anim. Plant Sci.* **2013**, *17*, 2388–2411.
17. El Hafian, M.; Benlandini, N.; Elyacoubi, H.; Zidane, L.; Rochdi, A. Étude floristique et ethnobotanique des plantes médicinales utilisées au niveau de la préfecture d'Agadir-Ida-Outanane (Maroc). *J. App. Bioscience.* **2014**, *81*, 7198. [[CrossRef](#)]
18. Roué, M.; Molnar, Z. *Knowing Our Lands and Resources: Indigenous and Local Knowledge of Biodiversity and Ecosystem Services in Europe and Central Asia*; UNESCO Publishing: Paris, France, 2017; Volume 9.
19. Hammiche, V.; Maiza, K. Traditional medicine in Central Sahara: Pharmacopoeia of Tassili N'ajjer. *J. Ethnopharmacol.* **2006**, *105*, 358–367. [[CrossRef](#)] [[PubMed](#)]
20. Jada, E.K.M. Taxonomic Study on Woody Plants in Soba Area Khartoum State Sudan. Ph.D. Thesis, Sudan University of Science and Technology, Khartoum, Sudan, 2007.
21. Mahmoud, T.; Gairola, S. Traditional knowledge and use of medicinal plants in the Eastern Desert of Egypt: A case study from Wadi El-Gemal National Park. *J. Med. Plants* **2013**, *1*, 10–17.
22. Ramde-Tiendrebeogo, A.; Zerbo, R.; Ouattara, B.; Doulikom, A.; Guissou, I.P. Plantes sahéliennes adaptées dans la récupération des terres dégradées et leurs usages pour la santé: Cas de la province du Soum au Nord du Burkina Faso. *J. Anim. Plant Sci.* **2019**, *41*, 6767–6783.
23. Alphonsine, R.-T.; Moumouni, K.; Nabere, O.; Marius, L.; Innocent, P.G. A comparative study of phytochemical profile and antioxidant activity of Sahelian plants used in the treatment of infectious diseases in northern part of Burkina Faso: *Acacia seyal* Delile and *Acacia tortilis* (Forssk.) Hayne subsp. *raddiana* (Savi). *J. Pharmacogn. Phytother.* **2019**, *11*, 74–79. [[CrossRef](#)]
24. Gabr, S.; Nikles, S.; Pferschy Wenzig, E.M.; Ardjomand-Woelkart, K.; Hathout, R.M.; El-Ahmady, S.; Motaal, A.A.; Singab, A.; Bauer, R. Characterization and optimization of phenolics extracts from *Acacia* species in relevance to their anti-inflammatory activity. *Biochem. Syst. Ecol.* **2018**, *78*, 21–30. [[CrossRef](#)]
25. Muhaisen, H.M.H.; Ilyas, M.; Mushfiq, M.; Parveen, M.; Basudan, O.A. Flavonoids from *Acacia Tortilis*. *J. Chem. Res.* **2002**, *2002*, 276–278. [[CrossRef](#)]
26. Lakhera, A.K.; Kumar, V. Monosaccharide composition of acidic gum exudates from Indian *Acacia tortilis* ssp. *raddiana* (Savi) Brenan. *Int. J. Biol. Macromol.* **2017**, *94*, 45–50. [[CrossRef](#)] [[PubMed](#)]
27. Hagos, M.; Samuelsson, G.; Kenne, L.; Modawi, B.M. Isolation of smooth muscle relaxing 1, 3-diarylpropan-2-ol derivatives from *Acacia tortilis*. *Planta Med.* **1987**, *53*, 27–31. [[CrossRef](#)]
28. Srivastava, M.; Kumar, S. Fatty Acid Compositional Studies of Lesser Known *Acacia tortilis* Seed Oil. *FNS* **2013**, *4*, 59–62. [[CrossRef](#)]
29. Khan, R.; Srivastava, R.; Khan, M.A.; Alam, P.; Abdin, M.Z. Mahmooduzzafr Variation in oil content and fatty acid composition of the seed oil of *Acacia* species collected from the northwest zone of India. *J. Sci. Food Agric.* **2012**, *92*, 2310–2315. [[CrossRef](#)] [[PubMed](#)]
30. Alajmi, M.F.; Alam, P.; Alqasoumi, S.I.; Ali Siddiqui, N.; Basudan, O.A.; Hussain, A.; Mabood Husain, F.; Ali Khan, A. Comparative anticancer and antimicrobial activity of aerial parts of *Acacia salicina*, *Acacia laeta*, *Acacia hamulosa* and *Acacia tortilis* grown in Saudi Arabia. *Saudi Pharm. J.* **2017**, *25*, 1248–1252. [[CrossRef](#)]
31. Muhaisen, H.M. Flavonoid Glycosides from *Acacia tortilis*. *Merit Res. J. Med. Med. Sci.* **2020**, *8*, 575–580.
32. Taveira, M.; Silva, L.R.; Vale-Silva, L.A.; Pinto, E.; Valentao, P.; Ferreres, F.; Guedes de Pinho, P.; Andrade, P.B. Lycopersicon esculentum seeds: An industrial byproduct as an antimicrobial agent. *J. Agric. Food Chem.* **2010**, *58*, 9529–9536. [[CrossRef](#)]
33. Kigonda, E.V.M.; Rukunga, G.M.; Keriko, J.M.; Tonui, W.K.; Gathirwa, J.W.; Kirira, P.G.; Irungu, B.; Ingonga, J.M.; Ndiege, I.O. Anti-parasitic activity and cytotoxicity of selected medicinal plants from Kenya. *J. Ethnopharmacol.* **2009**, *123*, 504–509. [[CrossRef](#)]
34. Al-Busafi, S.; Al-Riyami, M.; Al-Ouwaisi, K.; Hisham, A. Screening of Antioxidant and Radical Scavenging Activities of Some Omani Medicinal Plants. *SQU J. Sci.* **2007**, *12*, 1. [[CrossRef](#)]
35. Dudai, N.; Raz, A.; Hofesh, N.; Rozenzweig, N.; Aharon, R.; Fischer, R.; Chaimovitsh, D.; Segev, D. Antioxidant activity and phenol content of plant germplasm originating in the Dead Sea area. *Isr. J. Plant Sci.* **2008**, *56*, 227–232. [[CrossRef](#)]

36. Habib, H.M.; Al Meqbali, F.T.; Kamal, H.; Souka, U.D.; Ibrahim, W.H. Bioactive components, antioxidant and DNA damage inhibitory activities of honeys from arid regions. *Food Chemistry* **2014**, *153*, 28–34. [[CrossRef](#)]
37. Hédia Hannachi Chemicals profiling and antioxidants activities of Acacia seeds. *J. Med. Plants Res.* **2011**, *5*, 6869–6875. [[CrossRef](#)]
38. Sakthive, K.M.; Kannan, N.; Angeline, A.; Guruvayoorappan, C. Anticancer activity of *Acacia nilotica* (L.) Wild. Ex. Delile subsp. indica against Dalton's ascitic lymphoma induced solid and ascitic tumor model. *Asian Pac. J. Cancer Prev.* **2012**, *13*, 3989–3995. [[CrossRef](#)] [[PubMed](#)]
39. Carocho, M.; CFR Ferreira, I. The role of phenolic compounds in the fight against cancer—a review. *Anti-Cancer Agents Med. Chem.* **2013**, *13*, 1236–1258. [[CrossRef](#)]
40. Elsadig Karar, M.G.; Quiet, L.; Rezk, A.; Jaiswal, R.; Rehders, M. Phenolic Profile and In Vitro Assessment of Cytotoxicity and Antibacterial Activity of *Ziziphus spina-christi* Leaf Extracts. *Med. Chem.* **2016**, *6*, 143–156. [[CrossRef](#)]
41. Padmaharish, V.; Lakshmi, T. Anticancer activities of medicinal plants—an update. *J. Pharm. Sci. Res.* **2017**, *9*, 432.
42. Guimarães, R.; Barros, L.; Calhella, R.C.; Carvalho, A.M.; Queiroz, M.J.R.; Ferreira, I.C. Bioactivity of different enriched phenolic extracts of wild fruits from Northeastern Portugal: A comparative study. *Plant Foods Hum. Nutr.* **2014**, *69*, 37–42. [[CrossRef](#)]
43. Agrawal, N.K.; Gupta, U.; Misra, P.; Singh, S.P.; Verma, R.C. Antidiabetic Effects of *Acacia Tortilis* Seed Extract in Normal and Alloxan-Induced Diabetic Rats. *IJPSR* **2013**, *4*, 1392–1397.
44. Alharbi, W.D.M.; Azmat, A. Hypoglycemic and hypocholesterolemic effects of *Acacia tortilis* (fabaceae) growing in makkah. *Pak. J. Pharmacol.* **2011**, *28*, 1–8.
45. Kumar Bhateja, P.; Singh, R. Antidiabetic Activity of *Acacia tortilis* (Forsk.) Hayne ssp. raddiana Polysaccharide on Streptozotocin-Nicotinamide Induced Diabetic Rats. *BioMed Res. Int.* **2014**, *2014*, e572013. [[CrossRef](#)] [[PubMed](#)]
46. Kumar, N.J.; Loganathan, P. Hypoglycemic effect of *Spinacia oleracea* in alloxan induced diabetic rat. *Glob. J. Biotechnol. Biochem.* **2010**, *5*, 87–91.
47. Hossain, M.S.; Ahmed, M.; Islam, A. Hypolipidemic and hepatoprotective effects of different fractions of ethanolic extract of immature leaves of *Mangifera indica* (Linn.) in alloxan induced diabetic rats. *Int. J. Pharm. Sci. Res.* **2010**, *1*, 132.
48. Pi-Sunyer, F.X. Weight loss in type 2 diabetic patients. *Diabetes Care* **2005**, *28*, 1526–1527. [[CrossRef](#)]
49. Niwa, A.; Tajiri, T.; Higashino, H. Ipomoea batatas and Agaricus blazei ameliorate diabetic disorders with therapeutic antioxidant potential in streptozotocin-induced diabetic rats. *J. Clin. Biochem. Nutr.* **2011**, *48*, 1101050064. [[CrossRef](#)]
50. Anjaneyulu, M.; Chopra, K. Quercetin, an anti-oxidant bioflavonoid, attenuates diabetic nephropathy in rats. *Clin. Exp. Pharmacol. Physiol.* **2004**, *31*, 244–248. [[CrossRef](#)]
51. Xiao, M.; Jia, X.; Wang, N.; Kang, J.; Hu, X.; Goff, H.D.; Cui, S.W.; Ding, H.; Guo, Q. Therapeutic potential of non-starch polysaccharides on type 2 diabetes: From hypoglycemic mechanism to clinical trials. *Crit. Rev. Food Sci. Nutr.* **2022**, 1–34. [[CrossRef](#)]
52. Khosla, P.; Gupta, D.D.; Nagpal, R.K. Effect of *Trigonella foenum graecum* (Fenugreek) on serum lipids in normal and diabetic rats. *Indian J. Pharmacol.* **1995**, *27*, 89.
53. Moritoh, Y.; Takeuchi, K.; Hazama, M. Chronic administration of voglibose, an α -glucosidase inhibitor, increases active glucagon-like peptide-1 levels by increasing its secretion and decreasing dipeptidyl peptidase-4 activity in ob/ob mice. *J. Pharmacol. Exp. Ther.* **2009**, *329*, 669–676. [[CrossRef](#)]
54. Khalatbary, A.R.; Ahmadvand, H. Anti-inflammatory effect of the epigallocatechin gallate following spinal cord trauma in rat. *Iran. Biomed. J.* **2011**, *15*, 31. [[PubMed](#)]
55. Wu, Y.R.; Choi, H.J.; Kang, Y.G.; Kim, J.K.; Shin, J.-W. In vitro study on anti-inflammatory effects of epigallocatechin-3-gallate-loaded nano-and microscale particles. *Int. J. Nanomed.* **2017**, *12*, 7007. [[CrossRef](#)] [[PubMed](#)]
56. Locatelli, C.; Filippin-Monteiro, F.B.; Centa, A.; Creczinsky-Pasa, T.B. *Antioxidant, Antitumoral and Anti-Inflammatory Activities of Gallic Acid. Handbook on Gallic Acid: Natural Occurrences, Antioxidant Properties and Health Implications*, 4th ed.; Nova Publishers: New York, NY, USA, 2013; pp. 1–23.
57. Chu, C.; Deng, J.; Man, Y.; Qu, Y. Green tea extracts epigallocatechin-3-gallate for different treatments. *BioMed Res. Int.* **2017**, *2017*, 5615647. [[CrossRef](#)] [[PubMed](#)]
58. Sowndhararajan, K.; Santhanam, R.; Hong, S.; Jhoo, J.-W.; Kim, S. Suppressive effects of acetone extract from the stem bark of three *Acacia* species on nitric oxide production in lipopolysaccharide-stimulated RAW 264.7 macrophage cells. *Asian Pac. J. Trop. Biomed.* **2016**, *6*, 658–664. [[CrossRef](#)]
59. Ricciotti, E.; FitzGerald, G.A. Prostaglandins and inflammation. *Arterioscler. Thromb. Vasc. Biol.* **2011**, *31*, 986–1000. [[CrossRef](#)]