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REVIEW

REVISED A review on the phytochemistry and biological activities of *Curculigo latifolia* Dryand ex. W.Aiton

[version 2; peer review: 1 approved, 1 approved with reservations, 1 not approved]

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Abstract

Curculigo latifolia Dryand. ex W. T. Aiton, from the genus Curculigo, is a medicinal plant traditionally used to treat numerous illnesses such as fever, stomach aches, jaundice, wounds, and inflammation. *C. latifolia* is a perennial herb that is widely found in tropical and subtropical regions, such as Southeast Asia, Southern China, Bangladesh, Australia, and the Andaman Islands. This review collates the reported studies on the different aspects of *C. latifolia* from its plant description, nutritional value, phytochemistry, chemical composition, and pharmacological properties. This review aims to identify gaps in the literature and provide useful references for future work on this plant. Previous studies have shown that *C. latifolia* contains high mineral contents of calcium, iron, and magnesium, which are essential components of human health. Moreover, the plant is rich in phytochemicals, which play a prominent role in various pharmacological activities. The most common compounds identified included curculigoside, crassifoside I, nyasicoside, and curculigine. *C. latifolia* demonstrated high antioxidant activity through its ability to scavenge superoxide anions, 1,1–diphenyl–2–picrylhydrazyl (DPPH) and 2,2'-azino–bis(3–ethylbenzthiazoline–6–sulfonic acid) (ABTS) radicals, reducing ferric ions to ferrous complexes, iron chelation, and β –carotene bleaching. It was also shown that the roots, stems, and leaves of *C. latifolia* were effective in exerting antimicrobial activity against several microbial strains, including *Bacillus cereus, Bacillus subtillis, Enterobacter aerogenes, Erwinia* sp., *Klebsiella* sp., *Pseudomonas*

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sp., *Candida albicans, Salmonella choleraesuis* and *Staphylococcus aureus.* Moreover, the root, fruit, leaf, petiole, and rhizome extracts were found to improve glucose uptake and insulin secretion in diabetic rats, suggesting their antidiabetic potential. *C. latifolia* presents a wide range of medicinal properties that could make it a promising functional food or source of food supplements to prevent nutrition–related or chronic diseases.

Keywords
Curculigo latifolia, antioxidant, anti–diabetic, curculin, medicinal, functional food

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REVISED **Amendments from Version 1**

We have revised the manuscript following the comments made by the reviewer. All detected typographical and grammar errors were corrected. Additionally, some sentences were amended based on the recommendations from the reviewer which enhanced their clarity and comprehension while maintaining the original meaning.

Any further responses from the reviewers can be found at the end of the article

1. Introduction

The genus Curculigo of the Hypoxidaceae family consists of 20 species of perennial herbs that are typically distributed in tropical and subtropical regions such as India, China, Southeast Asia, and Australia. Some species in this genus are known for their medicinal properties and have often been used in traditional therapeutic remedies.[1] *Curculigo orchioides* is a species native to India and China and is known to have a long–standing tradition of medicinal use, including the treatment of jaundice, limb limpness, knee joints, and diarrhea.[2] Additionally, the rhizomes of *C. orchioides* have been suggested to be favorable for maintaining the health of the liver and kidneys.[3] Curculigo species, which are widely known for their medicinal properties and a variety of health benefits, are called *Curculigo capitulata.* This plant is generally found in China, South Asia, Southeast Asia, Australia, Taiwan, and the Pacific Islands, and is traditionally used for the treatment of chronic bronchitis, nephritis, hemorrhoids, gonorrhea, and asthma.[2,4] In Africa, an indigenous species of Curculigo, known as *Curculigo pilosa* is recognized as a useful remedy for infertility, leukemia, coughs, diabetes, genital infections, and sterility.[2,5]

Furthermore, previous studies have reported that these Curculigo species are composed of phytochemical constituents, such as phenols, phenolic glycosides, norlignans, and terpenoids, which are known to promote various biological activities.[2] Many studies have revealed that these compounds have anti–osteoporotic,[6] nephroprotective,[7] antioxidant,[8] antibacterial,[9] anti-diabetic,[10] and anti-inflammatory activities.[11]

Curculigo latifolia Dryand. ex W. T. Aiton is a Curculigo species found in Brunei Darussalam, and is more recognizable by its local name, Lemba. This plant is also synonymous with *Molineria latifolia, Curculigo villosa* and *Aurota.*[12] In Malaysia, the species is known as Kelapa Puyuh, Lumbah Puyuh, Pinang Puyuh, and Nyiur Lember, whereas in Indonesia, it is identified as Marasi, Keliangau, Prakuwang, Lumpa, Doyo, and Kehoang.[13] Additionally, in Thailand, *C. latifolia* is known as Chaa Laan, Ma Phraao Nok Khum and Phraa Nok, whereas in Vietnam, it is called Cồ Nốc Lá Rộng, Sâm Cau Lá Rộng.[13]

C. latifolia is widely distributed in most Southeast Asian regions, such as Myanmar, the Philippines, Thailand, Vietnam, and Cambodia, as well as Borneo Island, which includes Malaysia, Brunei, and Indonesia.[13] This plant has also been reported in Southern China, Bangladesh, Australia, and Andaman Islands.[14] Lim[13] suggested that this species of Curculigo is predominantly susceptible to growth in warm temperate regions and humid tropical and subtropical areas. Moreover, the plant is mostly widespread on slopes and forests, as well as in highland areas with an altitude of 1500 – 2000 m.[15] A previous study has investigated the effects of light and soil media on the growth of *C. latifolia.*[16] In the present study, the plant showed the most prominent growth progression at 50% light intensity, indicating that *C. latifolia* generally prefers moderate shading.[16] The plant was also found to grow in the wild in fertile, well–drained soils rich in organic matter. Additionally, the study suggested that soil media comprising topsoil, organic manure, and sand in a ratio of 2:3:1 showed the best results in terms of plant growth.[16]

C. latifolia is claimed to have medicinal value in the treatment of asthma, hemorrhoids, jaundice, skin disease, and diabetes.[17] Moreover, several studies on *C. latifolia* have shown the presence of phenols and flavonoids that could counteract free radicals and thus assist in a broad spectrum of pharmacological activities, such as anti–diabetic, antioxidant, and antimicrobial activities.[10,18,19] Each part of the *Curculigo latifolia* plant plays a role in promoting certain biological activities. In traditional medicine, the rhizome of *C. latifolia* is used to treat jaundice, menorrhagia, and fever.[18,20] It can also be boiled with *Areca catechu* and *Hibiscus rosa–sinensis* which helps in regulating menstrual bleeding and healing ophthalmia.[13] Moreover, the flowers and roots have been used for treating stomach or urinary disorders, and in Malaysia, the leaves and roots are usually used for inflammation and wounds.[18,21] In Brunei Darussalam, the root is utilized to cure headaches and mouth thrush, while the mixture of roots and rhizomes can help with diarrhea.[22] Additionally, traditional Thai medicine claims that the root can be used as a tonic to regulate blood circulation.[23] It is also known to have several other medicinal properties, such as hemorrhoids and asthma.[24] Additionally, previous findings have also suggested that the phytochemicals found in *C. latifolia* exhibit hepatitis B virus inhibitor, anti–diabetic, anti–arthritic, anti–tumor, anti-inflammatory, estrogenic, and sexual behavior-modifying activities.[18,25]

Additionally, *C. latifolia* has also been shown to be used for taste modifying activities and as an alternative to low–calorie sweeteners owing to its composition of sweet proteins known as curculin or neoculin.[26] This protein is isolated from the fruits of the *C. latifolia* plant and can produce a strong sweet taste when mixed with an acidic solution.[27] It was found that curculin in its heterodimeric form (also known as neoculin) can interact with T1R2–T1R3 sweet–taste receptors, which resembles the sweettasting activity of sugar and aspartame.[28] Additionally, the large cluster found in the basic subunit (NBS) of the sweet proteins, which is composed of six basic residues on its surface, was suggested to contribute to the sweetness and taste–modifying activities.[29]

In addition, *C. latifolia* has other practical uses: the sturdy, durable, and lightweight fibers of its leaves have been utilized for making fishing nets, strings, and food wrappings.[30] It was also revealed that the fibers showed characteristics similar to those of cotton fibers, making them an alternative material in clothing production. In Eastern Kalimantan, *C. latifolia* fibers have traditionally been used for weaving fabrics and handbags.[31,32] Additionally, the plant was considered for its potential as a natural dye, and Shaari[30] found that the leaves and flowers produced promising colors ranging from dark green to yellow, which can act as dyes.

This review presents several reported findings that demonstrate the different aspects of *C. latifolia* such as its morphology, nutritional value, phytochemistry, chemical composition, and biological activity. To the best of our knowledge, there are limited publications on this plant, and no reported paper has summarized the studies carried out. The aim of this study was to determine the gaps in the literature and provide baseline information that may be useful for future studies on this plant.

2. Method

Scientific literature was collected using web search engines, including Scopus, PubMed, Science Direct, Google Scholar, and Taylor and Francis, from inception until August 2023. The search was conducted using keywords such as '*Curculigo latifolia', 'Molineria latifolia', 'Curculigo species',' Curculigo latifolia OR Molineria latifolia',' C. latifolia* AND phytochemistry, "'*C. latifolia* AND pharmacological activities', and"'*C. latifolia* medicinal values'. Online resources such as botanical websites were also considered to determine the geographic distribution, description, and synonyms of the plant. The author attempted to document the relevant literature that primarily focused on the phytochemistry and biological activities of *C. latifolia.*

3. Morphology of *Curculigo latifolia*

Curculigo latifolia is a perennial herbaceous monocotyledon that has an erect rhizome of about 9.5 cm long and forms a cluster of green leaves up to 1 m tall, as seen in Figure 1.[33] The leaves of this plant are generally thin, broad, and elliptical, making them suitable for use as wrappings, fishing nets, and strings.[30] They are also mainly subglabrous or pubescent and

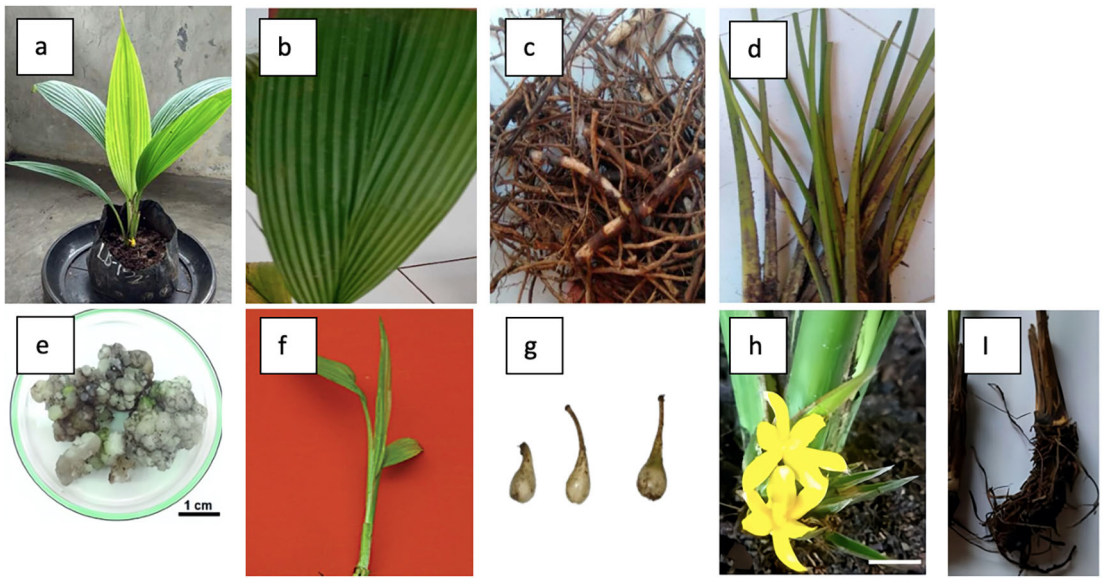


Figure 1. Different parts of *Curculigo latifolia.* (a) whole plant, (b) leaves, (c) roots, (d) petiole/stem, (e) callus, (f) plantlet leaves, (g) fruits, (h) flowers, (i) rhizomes (Images retrieved from Babaei et al. (2014),[34] Haryanto et al. (2023),[35] Nur, Setiawan, et al. (2023a),[36] Umar et al. (2023),[37] Umar et al. (2021a)[38], and Umar et al. (2021b)[39]).

Table 1. Summary of the nutritional value of *C. latifolia* reported by Briliani et al.[4]

Nutrients	Units	Values stated in literature (per 100 g)	Reference
Fructose	mg	1.08	Briliani et al.[4]
Sucrose	mg	1.08	
Vitamin C	mg	5.61	
Potassium	mg	0.41	
Calcium	mg	3452.01	
Iron	mg	872.93	
Magnesium	mg	117.6	

have entire margins, followed by an acuminate tip.[26,31] Additionally, they commonly have leafstalks that are approximately one–third of the length of the leaves, which are generally 30 – 100 cm long and 5 – 10 cm wide.[26] The inflorescences are compact and ovoid or cylindrical, with a length of 1 – 6 cm. The flowers are yellow and have lanceolate, hairy bracts and stamens of 1.5 cm long that are slightly shorter than the slender style.[13] The fruits of *C. latifolia* are white to green and have been found to be 10 – 25 mm wide and sweet. They are usually ovoid and long-beaked, with small black seeds.[13,33]

4. Nutritional value

C. latifolia fruits have been reported to contain various nutritional content such as 1.08 mg/100 g of fructose, 1.08 mg/100 g sucrose, 5.61 mg/100 g vitamin C and 0.41 mg/100 g potassium (Table 1).[4] These mineral nutrients are crucial for the development of strong bones and teeth, management of body fluids, and transmission of nerve signals, all of which are essential for sustaining optimal functions of the body.[40]

Their magnesium, calcium, and iron contents were shown to be abundant compared to other fruits. For instance, the magnesium content of *C. latifolia* (117.6 mg/100 g)[4] was richer than figs (67.90 mg/100 g)[41] and banana (29.39 mg/100 g).[42] Magnesium is an important component in the formation of proteins, muscle function, and immune system support, and low levels of magnesium can lead to diabetes, cardiovascular disease, and neurological disorders.[40,43] This shows *C. latifolia* fruits contain a desirable amount of magnesium that could potentially serve as a supplement for improving overall human health, specifically in areas where magnesium deficiency is prevalent.

Furthermore, *C. latifolia* fruits (3452.01 mg/100 g)[4] exhibited higher calcium content compared to figs (154.55 mg/100 g)[41] and mulberry (1493.22 mg/100 g),[44] which enhances their suitability for maintaining strong bones, supporting muscle and nerve function, and regulation of blood pressure.[45] Calcium is one of the micronutrients essential to the human body to maintain optimal health, and the recommended dietary intake of calcium ranges from 1000 to 1300 mg/day.[46,47] The calcium content of *C. latifolia* fruits could support individuals with insufficient calcium levels, subsequently mitigating the chances of osteoporosis, hypertension, and cardiac arrhythmias.[45]

Iron is another major mineral in the body that plays an important role in metabolic functions, such as deoxyribonucleic acid (DNA) synthesis, oxygen, and electron transport.[48] The iron content of *C. latifolia* was 872. 93 mg/100 g,[4] which is higher than dried apricots at 6.97 mg/100 g dried weight basis,[49] and Tunisian dates at 7.2 mg/100 g.[50] Generally, the daily iron intake from foods and supplements is recommended to be 19.7–20.5 mg/day for men and 17.0–18.9 mg/day for women aged above19 years old.[51] Excessive amounts of iron can generate oxygen free radicals, which can lead to tissue damage and organ failure.[52] Therefore, maintaining a balanced consumption of minerals is important for the proper functioning of organs, metabolic and homeostatic processes in the body, and protection against illnesses such as cancer, diabetes, and heart disease.[53]

The above literature suggests *C. latifolia* fruit is a viable food source for providing essential nutrients, making it a potential ingredient in functional food applications. However, very few studies have reported the mineral content of *C. latifolia* fruits and plants as a whole. Therefore, more investigations, such as fatty acid profile, vitamin analysis, amino acid analysis, and clinical trials, are needed to provide more information about its nutritional value.

Moreover, the relatively low sugar content could potentially make it suitable for low–calorie diets, which are suggested for obese and diabetic patients.[54] Further studies exploring the glycemic index and cholesterol levels of this plant could provide an understanding of the blood sugar response and overall effects on the body. Nevertheless, *C. latifolia* fruits have promising nutritional content and can be a valuable supplement for a healthy body.

Table 2. Types of phytochemicals detected in the fruits, leaves, petiole, rhizome, the underground and aerial parts of *C. latifolia* from compiled previous studies. (+) denotes the presence of phytochemicals, while (–) indicates that the absence of phytochemical and (NR) suggests that the presence of phytochemical was not reported.

Plant part	Solvent used	Alkaloids	Tannins	Saponin	Steroid	Terpenoids	Glycoside	Reference
Fruits	96% (v/v) Ethanol	+	+	+	–	–	–	Lumbangaol[55]
Underground parts	Water	+	+	NR	+	+	+	Akkarasiritharattana and Chamutpong[18]
	Ethyl acetate							
	Ethanol							
Aerial parts	Water	+	+	NR	+	+	+	Akkarasiritharattana and Chamutpong[18]
	Ethyl acetate							
	Ethanol							
Rhizome	70% (v/v)	+	NR	NR	+	+	+	Umar et al.[56]
	ethanol							
Petiole	70% (v/v) ethanol	+	NR	NR	+	+	+	Umar et al.[56]
Leaves	70% (v/v) ethanol	NR	NR	NR	+	+	+	Umar et al.[56]
Callus	70% (v/v) ethanol	NR	NR	NR	+	+	+	Umar et al.[37]
Plantlet leaves	70% (v/v) ethanol	+	NR	NR	+	+	+	Umar et al.[37]

5. Phytochemistry

Previous studies have revealed the phytochemicals detected in different parts of *C. latifolia* (Table 2). Lumbangaol[55] found that the fruits of this plant contain alkaloids, tannins, saponins, and flavonoids. This study also observed a tannin concentration of 35.6 ppm in the fruit, potentially contributing to a range of pharmacological activities. Akkarasirithar-attana and Chamutpong[18] also showed similar results for the underground and aerial parts of *C. latifolia*, detecting the presence of flavonoids, tannins, steroids, terpenoids, alkaloids, and glycoside*s* using high-performance thin-layer chromatography (HPTLC). Other findings by Umar et al.[56] and Umar et al.[37] examined the calluses, plantlet leaves, rhizomes, leaves, and petioles of *C. latifolia* and found that these parts contain alkaloids, norlignan, phenolic glycosides, steroids, and terpenoids. Research has indicated that these constituents are responsible for numerous biological activities, such as antioxidant and anti-inflammatory activities, which are valuable properties for the production of functional foods.[57] Additionally, these bioactive compounds generally exert a significant positive impact on human health and bodily functions while also regulating, preventing, and reducing the severity of chronic diseases.[57] However, systematic investigations of these isolated compounds and the biological effects of *C. latifolia* should be conducted to validate these findings further.

6. Chemical composition

A literature search of the chemical composition of *C. latifolia* yielded various studies that showed presence of different chemical groups depending on the different parts of the plant, where Table 3 outlines some of the common compounds identified. *C. latifolia* roots, fruits, rhizomes, leaves, petioles, calluses, and plantlet leaves contain constituents from different classes of secondary metabolites, such as phenolics, glycosides, flavonoids, flavones, triterpene lignans, cycloartane, alkaloids, sisterols, and proteins. These active compounds play a key role in the interaction with other molecules, receptors, enzymes, or proteins in the body, leading to various health benefits, such as improvements in digestion and cardiovascular health, and a reduction in the risk of chronic diseases.[57] Therefore, *C. latifolia* is a potential source of functional food ingredients owing to its health–promoting bioactive compounds. In the next section (**Section 7. Biological activities**) elaborates on the biological activities that have been carried out on different parts of *C. latifolia* which could be associated with their active compounds.

6.1 Roots

Zabidi et al.[58] identified the chemical compounds in the root extract of *C. latifolia* using liquid chromatography–mass spectrometry (LC–MS) analysis, which was found to contain phenolic compounds such as monobenzone, phloridzin, mundulone, scandenin, pomiferin, dimethyl caffeic acid, hordatine A, ubiquinone, hydroquinone, frangulin B, rubratoxin B, and emmotin A. These phytochemicals have a diverse range of bioactive attributes that can play a significant role in exerting pharmacological activities such as anti–diabetic, antimicrobial, anti–inflammatory, antioxidant, and anti–cancer.[59] For instance, hydroquinone is known to exhibit antioxidant activity by preventing oxidative damage in human cells,[60] whereas ubiquinone plays a key role in cellular metabolism and protection against lipid peroxidation.[61]

Furthermore, Maliwong et al.[23] used high-resolution electrospray mass spectrometry (HR–ESI–MS), which revealed phenolic glycosides, such as molineriosides A–C, curculigoside, curculigoside H, 3–hydroxy–5– methylphenyl 1–*O*–β–D–glucopyranosyl–(1→6)–β–D–glucopyranoside, nyasicoside, crassifoside B, 1–*O*–methyl– curculigine, 1–*O*–methyisolcurculigine, capituloside, and curcapicycloside. Curculigoside is reported as one of the major bioactive compounds in another Curculigo species, *Curculigo orchioides*, where it was found to promote neuroprotection, anti–arthritic, anti–osteoporosis, and anti–tumor activities.[2] Curculigoside has also been suggested to exert significant antioxidant activity, which ameliorates learning performance and bone loss in mutated transgenic mice with Alzheimer's disease.[20]

A more recent study by Nur et al.[62] reported the presence of methyl–3–hydroxy–4–methoxybenzoate, sugiol (diterpene), stigmastan–3,6–dione (steroid), aviprin (flavonoid), lucialdehyde B (sesquiterpene), guaiacol (phenol), and smilaxin (saponin). Avipirin is a bioactive compound that exhibits antibacterial, antifungal, and phytotoxic activities.[63] Guaiacol has been reported to effectively inhibit human carbonic anhydrase isoenzymes,[64] and the compound smilaxin has demonstrated immunostimulatory, antiproliferative, and human immunodeficiency virus (HIV) –1–reverse transcriptase inhibitory activities.[65]

6.2 Fruit

Curculin, a sweet protein, is found in the fruit extract of *C. latifolia.* This protein has sweet–tasting and taste–modifying properties that can enhance the sweetness of acidic or tasteless substances.[26] Moreover, its sweet properties make it a promising option for low–calorie sweeteners, which may be beneficial for individuals aiming to reduce their sugar or calorie consumption.[34]

Table 3. Common compounds isolated from different parts of *C. latifolia*.

Plant parts	Solvent system	Name	Formula	Reference
a. Phenolics				
Root and Fruit	Distilled water	Pomiferin	$C_{25}H_{24}O_6$	Zabidi et al.[10]
Petiole, plantlet leaves, callus, rhizome and leaves	70% (v/v) ethanol	1,1–Bis(3,4–dihydroxyphenyl–1–(2–furan)–methane	$C_{17}H_{14}O_5$	Umar et al.[56] Umar et al.[37]
Plantlet leaves, callus, rhizome and leaves		Vanillin	$C_8H_8O_3$	
Callus, rhizome, leaves and petiole		Crassifoside I	$C_8H_8Cl_2O_2$	
Rhizome, leaves, petiole, and plantlet leaves		2,4–Dichloro–5–methoxy–3–methylphenol	$C_{23}H_{24}O_{11}$	
b. Phenolic glycosides				
Root and Fruit	Distilled water	Frangulin B	$C_{20}H_{18}O_9$	Zabidi et al.[10]
	70% (v/v) ethanol	Orchioside A	$C_{16}H_{17}NO_4$	Umar et al.[56] Umar et al.[37]
Callus and plantlet leaves		Orchioside B	$C_{23}H_{26}O_{10}$	
		Curculigoside B	$C_{21}H_{24}O_{11}$	
Rhizome, leaves, and petiole		Curculigoside C	$C_{22}H_{26}O_{12}$	
		(1S,2R)–O–Methylnyasicoside	$C_{24}H_{28}O_{11}$	
	Methanol	Curculigine M	$C_{13}H_{16}Cl_2O_7$	Mad Nasir et al.[74]
Rhizome and root	Ethyl acetate Methanol	Curculigoside	$C_{22}H_{26}O_{11}$	Ooi et al.[20] Maliwong et al.[23]
Root and leaves	70% (v/v) ethanol Methanol	Nyasicoside	$C_{23}H_{26}O_{11}$	Umar et al.[56] Maliwong et al.[23]
Callus, petiole and plantlet leaves	70% (v/v) ethanol			Umar et al.[56] Umar et al.[37]
c. Cycloartane				
Rhizome, leaves and petiole	70% (v/v) ethanol	Curculigosaponin G	$C_{42}H_{70}O_{13}$	Umar et al.[56]
		Curculigosaponin H	$C_{41}H_{68}O_{13}$	
		Curculigosaponin C	$C_{47}H_{78}O_{17}$	
Callus and plantlet leaves		Curculigosaponin C	$C_{47}H_{78}O_{17}$	Umar et al.[37]
d. Alkaloid				
Rhizome, petiole, leaves and plantlet leaves	70% (v/v) ethanol	Lycorine	$C_{16}H_{17}NO_4$	Umar et al.[56] Umar et al.[37]
e. Sisterol				
Rhizome, leaves and petiole	70% (v/v) ethanol	3–O–B–D–Glucopyranosyl sitosterol	$C_{35}H_{60}O_6$	Umar et al.[56]
f. Glucuronidated flavonoid				
Petiole, callus, plantlet leaves	70% (v/v) ethanol	Breviscapin	$C_{21}H_{18}O_{12}$	Umar et al.[37]

Moreover, several phytochemicals such as berberine, hordatine A, robustine (alkaloids), frangulin B (anthraquinone), pomiferin (flavonoid), and monobenzone (aromatic hydrocarbons) have been identified.[10] These chemical compounds generally exhibit pharmacological effects. For example, berberine and frangulin B have anti–inflammatory properties,[66,67] pomiferin has high antioxidant activities,[68] and monobenzone can inhibit the growth of acute myeloid leukemia.[69]

The edible fruit of *C. Latifolia* could be a promising functional food that can provide health–promoting and taste–enhancing effects owing to the presence of phytochemicals and sweet proteins. However, there are still limited studies on the unique compounds of *C. latifolia* and curculin; therefore, further investigations into its glycemic index, cholesterol level, and anti-diabetic, anti-inflammatory, and anti–cancer activities will provide more information about it.

6.3 Rhizome

In a previous study by Ooi et al.,[20] the phenolic composition of the rhizome extract of *C. latifolia* was determined using high-performance liquid chromatography with diode–array detection (HPLC–DAD). Several active components have been identified, including cinnamic acid, curculigoside, syringic acid, ferulic acid, and protocatechuic acid. The findings also highlighted the efficacy of ethyl acetate solvent in extracting a higher amount of curculigoside and cinnamic acid compared to methanolic rhizome extract.[20]

In recent studies by Umar et al.[56] and Umar et al.,[37] the chemical composition of the ethanolic rhizome extract of *C. latifolia* was determined using ultra-high-performance liquid chromatography–Q Exactive hybrid quadrupole–Orbitrap high-resolution accurate mass spectrometry (UHPLC–Q–Orbitrap HRMS). This sensitive and accurate method detected the presence of active components such as lycorine, vanillin, nyasicoside, 4–hydroxy–phenol, and curculigoside B.[39,56] Additionally, the study also identified some isolates that were previously extracted from other Curculigo species such as orchioside B, orcinol glycoside, curculigine C, curculigosaponin G and C, from *Curculigo orchiosides*,[1,70] capituloside and crassifoside I from *Curculigo capitulata*,[71,72] and (1S,2R)–*O*–methylnyasicoside from *Curculigo sinensis.*[73]

Mad Nasir et al.[74] also found Curculigo isolates in methanolic rhizome extracts using ultra–high performance liquid chromatography mass spectrometry (UHPLC–MS). These included curculigine, curculigine M and G, curcupicycloside, sinensigenin A, 1–*O*–methylisocurculigine, brevicaside B, crassifoside C and D, curculigenin, sinenside B, and orchioside J.[74]

C. latifolia is rich in chemical diversity, some of which can potentially exert various physiological effects. Some of the isolates of Curculigo species that have been reported for their promising biological effects include orcinol glucoside and crassifoside H, which improve depressive behaviors (antidepressant–like effects) in chronic unpredictable mild stress rat models.[75,76] However, many of these compounds have not yet been fully investigated for their biological activity. Therefore, extensive studies on these unique isolates are needed to understand the mechanisms underlying their biological activities, such as antioxidant, anti–diabetic, and antimicrobial activities.

6.4 Leaves

Umar et al.[56] detected chemical components in the leaves of *C. latifolia,* where some of the compounds were similar to those found in the rhizome extract. This study identified nyasicoside, vanillin, lycorine, orcinol glycoside, crassifogenin A, behenic acid, pothobanoside C, daucosterol, stigmasterol, curculigine C, curculigosaponin C, E, G, H, and I; crassifoside C, E, and I; curculigoside B and C; and orchioside A and B.[39,56,74] Some of these compounds have been reported to exhibit anti-estrogenic and anti-allergic activities against estrogen–responsive human breast cancer cell lines.[77] Plant–derived sterols, such as daucosterol and stigmasterol, effectively inhibit cell proliferation and reduce tumor size in patients with prostate, colorectal, and breast cancers.[78] Additionally, behenic acid showed significant antibacterial activity against *Agrobacterium tumefaciens* T–37 and *Erwinia carotovora* EC–1.[79]

Furthermore, in a study by Mad Nasir et al.,[74] numerous compounds were also detected in the methanolic leaf extract, including orcinoside E, orcinol gentiobioside, sinensigenin B, curculigine M, and (*Z*)-resveratrol 3,4′-diglucoside. Most of these compounds are derived from glycosides and stilbene groups; however, few studies have investigated their biological effects. Generally, glycosides possess a wide variety of biological attributes, such as anti–inflammatory, antiseptic, anti-rheumatic, and analgesic effects,[80] whereas stilbenes exhibit cardioprotective, neuroprotective, anti–diabetic, and cancer treatment and prevention activities.[81]

Phytochemical screening using liquid chromatography–electrospray ionization mass spectrometry (LC–ESI–MS) by Nur et al.[62] identified compounds including digiprolactone, 3–tert–butyl–4–methoxyphenol, axedarachin C and 4–*O*–caffeoylquinic acid–1, and quercetin. Quercetin is regarded as one of the most effective antioxidants that can scavenge

free radicals and mitigate diseases associated with oxidative stress such as diabetes, cancer, allergies, inflammation, and gastrointestinal and cardiovascular diseases.[82]

6.5 Other parts

Umar et al.[37] identified the chemical compounds in *C. latifolia* callus and plantlet leaves, which consist of ecdysterone, a natural anabolic agent that can inhibit the proliferation of breast cancer cells,[83] and emodin dianthrone,[37] which possesses antidiabetic properties.[84] Moreover, the petiole, callus, and plantlet leaves showed the presence of breviscapin, a bioactive compound that was previously extracted from *Erigeron breviscapus* with the ability to enhance cerebral blood flow and microcirculation and resist platelet aggregation.[85] *C. latifolia* callus also contained the compound salidroside, which has effective properties in ameliorating memory and emotional behavior in adult mice,[37,86] and theanaphthoquinone, which has been shown to induce cell death in breast cancer cells.[37,87]

These bioactive compounds are important for managing various diseases and should be included in the human diet because of their ability to provide energy and nutrients and contribute to overall well–being.[57] Therefore, it is worthwhile to further study the bioactivities of the isolated chemical compounds of *C. latifolia* to validate the findings for potential use in pharmaceuticals or food supplements.

7. Biological activities

C. latifolia has been involved in several *in vitro* and *in vivo* investigations, where the plant was shown to exhibit bioactivities such as antioxidant, antimicrobial, anti–diabetic, anti–aging, ultraviolet protection activities and reported to improve sperm quality (summarised in Table 4). The diverse range of bioactivities of plants may be attributed to the different types of bioactive compounds. An overview of the biological evaluations carried out on *C. latifolia* is described in this section.

7.1 Antioxidant activity

Different types of assays have been employed to investigate the antioxidant activity of *C. latifolia,* and each assay generally involves different chemical reactions and mechanisms.[88] Some common antioxidant assays that were involved can be seen in Table 5, which include 1,1–diphenyl–2–picrylhydrazyl (DPPH), 2,2'-azino–bis(3–ethylbenzthiazoline–6–sulfonic acid) (ABTS) radical cation scavenging, and ferric reducing antioxidant power (FRAP) assays. In a previous study by Ooi et al.,[20] it was reported that *C. latifolia* rhizome extract exhibited promising scavenging activity for both DPPH and ABTS radicals, with a Trolox–comparable capability. This study suggested that these antioxidant activities were significantly correlated with the bioactive compounds in the extract, such as phenolics and flavonoids.[20] The unique features of these compounds, such as their functional groups, configuration, substitution, and amount of hydroxyl groups, essentially facilitate protection against oxidative damage by radical neutralization, iron binding, and reducing power capacities.[89] The report by Ishak and Zabidi[24] is consistent with Ooi et al.,[20] where high contents of flavonoids and phenolics in the extracts also corresponded to antioxidant activities. The study demonstrated that the root extract of *C. latifolia* with high phenolic and flavonoid contents under subcritical water extraction showed DPPH radical scavenging activities of 128.70 mg Trolox equivalents/g sample and ABTS scavenging activity of 66.78 mg Trolox equivalents/g sample.[24]

Moreover, in the findings of Nur et al.,[62] different extracts of *C. latifolia* roots, stems, and leaves reported varying antioxidant capacities, in ABTS study, ethanol and ethyl acetate extracts of *C. latifolia* exerted the most significant activity by contributing proton radicals to free radical compounds. Meanwhile, β-carotene bleaching assay demonstrated that ethyl acetate extracts of *C. latifolia* roots, stems, and leaves could effectively prevent β-carotene decomposition upon oxidation of linoleic acid to hydroperoxide compared to the other extracts. In the FRAP assay, the root extracts (ethyl acetate and ethanol) showed the strongest antioxidant activity for reducing Fe^{3+} to Fe^{2+} complexes. Nur et al.[62] suggested that the hydroxyl groups in the phenolic compounds in the extracts were highly effective in the chelation of iron and subsequently reduced it via a redox reaction.

A recent study by Umar et al.[56] also suggested that the rhizome extract of *C. latifolia* showed higher antioxidant activity than the leaf and petiole extracts. In this study, the active components that significantly contributed to the antioxidant activity were evaluated using Fourier transform infrared (FTIR) spectroscopy and UHPLC–Q–Orbitrap HRMS combined with partial least squares (PLS) assay. Based on this analysis, a chemical compound identified as unknown (185) with chemical formula $C_{47}H_{59}O_7$ was found to be a major contributor to the activity, whereas phenolics (curculigoside B, 2,4– dichloro–5–methoxy–3–methylphenol, orchioside B), cycloartane triterpene (curculigosaponin G), and norlignan compounds (1,1–bis (3,4–dihydroxyphenyl)–1–(2–furan)–methane and (1S,2R)–*O*–methylnyasicoside) showed only a minor contribution.[62] Moreover, the presence of phenolics, norlignan, and alkaloid compounds, such as vanillin, crassifoside A, and lycorine, in *C. latifolia* extracts exhibited antioxidant properties.[39] Regarding the functional groups,

Table 4. Reported biological activities of the different parts of *Curculigo latifolia* extracts from compiled studies. DPPH refers to 1,1–diphenyl–2–picrylhydrazyl, ABTS is 2,2'–azino–bis(3–ethylbenzthiazoline–6–sulphonic acid radical cation scavenging, FRAP is ferric reducing antioxidant power, SOD is superoxide dismutase, and NR indicates that the information was not reported.

Biological activities	Plant parts	Solvent used	Model	Concentration range	Author
Antioxidant activities.	Roots, stems leaves	n–hexane, ethyl acetate, 70% (v/v) ethanol	ABTS method, β–carotene bleaching assay, and FRAP	9.79 –549.52 µg/mL, 6.25–200 µg/mL, 0.1% (w/v)	Nur et al.[97]
	Fruits, leaves, rhizomes	70% (v/v) methanol and 100% (v/v) methanol	DPPH radical scavenging, β–carotene bleaching assay	26.99–547.29 µg/mL	Mad Nasir et al.[74]
	Rhizome, leaves, petiole	70% (v/v) ethanol	DPPH radical scavenging assay	47.08–473.04 mg/mL	Umar et al.[56]
	Root	Distilled water	ABTS and DPPH radical scavenging assays	NR	Zabidi et al.[58]
	Roots, fruits, leaves	Distilled water	DPPH radical scavenging assay	1.0–2.0 mg/mL	Ishak and Zabidi[24]
	Aerial and underground parts	Distilled water, ethanol and ethyl acetate	DPPH radical scavenging assay and FRAP	NR	Akkarasiritharattana and Chamutpong[18]
	Callus induction/ explants leaf, seed, tuber	70% (v/v) ethanol	DPPH radical scavenging assay and SOD	10 g/L	Farzinebrahimi et al.[15]
	Rhizome	80% (v/v) methanol, distilled water, hexane, ethyl acetate and n–butanol	DPPH and ABTS radical scavenging assays, β–carotene bleaching assay, FRAP, Iron chelating assay	NR	Ooi et al.[20]
Antimicrobial activity	Fruits, leaves, rhizomes	70% (v/v) methanol and 100% (v/v) methanol	*Salmonella choleraesuis, Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus*	1 mg/mL	Mad Nasir et al.[74]
	Callus induction/ explants leaf, seed, tuber	70% (v/v) ethanol	*Staphylococcus aureus*, *Bacillus cereus, Pseudomonas aeruginosa* and *Klebsiella* sp.	10 g/L	Farzinebrahimi et al.[15]
	Root	Methanol	*Candida albicans*	100 mg/mL	Lim and Ibrahim[91]
	Root, stems, leaves	Methanol	*Bacillus cereus*, *Bacillus subtilis*, *Enterobacter aerogenes*, *Erwinia* sp., *Klebsiella* sp., *Pseudomonas* sp., *Staphylococcus aureus*, *Candida albicans*, *Cryptococcus neoformans, Aspergillus flavus, Apergillus niger, Microsporum canis, Trichyton mentagrophytes*	1–100 mg/mL	Lim and Ibrahim[19]

Table 4. *Continued*

Biological activities	Plant parts	Solvent used	Model	Concentration range	Author
Anti–diabetic activity	Roots, fruits	Distilled water	α–glucosidase inhibitory activity, DPP (IV) enzyme, glucose uptake and insulin secretion assay	0.3–2.5 mg/mL, 250–3000 µg/mL, 47–1000 µg/mL, 125–1000 µg/mL	Zabidi et al.[10]
	Roots, fruits, leaves	Distilled water	Insulin secreting activity, glucose uptake activity in 3T3–L1 adipocyte and L6 myotube cell line	0.01–0.1 mg/mL	Ishak and Zabidi[24]
	Rhizome	Ethyl acetate	Glucose uptake stimulatory activity using 3T3–L1 adipocyte model	50, 100 and 200 µg/mL	Ooi et al.[93]
	Rhizome	Ethyl acetate	Glucose tolerance and body weight changes on male Sprague–Drawley rats, and gene expressions in adipose tissue	100 and 200 mg/kg bodyweight	Ooi et al.[94]
	Roots, fruits	Distilled water	Treatment on STZ–induced male Sprague–Dawley rats, analysis of blood and gene expression in glucose metabolism	50, 100 and 200 mg/kg bodyweight	Ishak et al.[24]
Adipogenesis	Rhizome	Ethyl acetate	Lipid profile analysis	100 and 200 mg/kg bodyweight	Ooi et al.[94]
	Roots, fruits	Distilled water	Lipid profile analysis	50, 100 and 200 mg/kg bodyweight	Ishak et al.[24]
Antiaging	*C. latifolia* ligands		Molecular docking stimulation		Nur et al.[62]
Elastase inhibition activity	Root, Stems, leaves	n–hexane, ethyl acetate, and 70% (v/v) ethanol	*In vitro* and *in silico* anti–elastase activity	10–1000 µg/mL	Nur et al.[97]
Ultraviolet protection	Roots, stems and rhizomes	n–hexane, ethyl acetate, and 70% (v/v) ethanol	Sunscreen profile in UVA and UVB ranges	250 mg/L	Nur et al.[98]
Spermatogenic activity	Root and leaves	80% (v/v) ethanol	Male mice Mus musculus	500 mg/kg bodyweight	Jaafar et al.[95]

Table 5. Different assays used to investigate the antioxidant activity of the different parts of *C. latifolia* from compiled studies. (DPPH (1,1–diphenyl–2–picrylhydrazyl), ABTS (2,2'–azino–bis(3–ethylbenzthiazoline–6–sulphonic acid) radical cation scavenging, FRAP (ferric reducing antioxidant power), and SOD (superoxide dismutase)).

Plant part	Solvent used	DPPH	ABTS	FRAP	Iron chelating	β–Carotene bleaching	SOD
Aerial part							
Aerial part	Water Ethanol Ethyl acetate	Akkarasiritharattana and Chamutpong[18]		Akkarasiritharattana and Chamutpong[18]			
Leaves	70% (v/v) ethanol[15,56] Distilled water[24] Methanol[74]	Umar et al.[56] Ishak and Zabidi[24] Farzinebrahimi et al.[15]				[c]Mad Nasir et al.[74] [a]Farzinebrahimi et al.[15]	
Fruit	Distilled water[24] Methanol[74]	Ishak and Zabidi[24]				[c]Mad Nasir et al.[74]	
Petiole	70% (v/v) ethanol	Umar et al.[56]					
Leaf explant	70% (v/v) ethanol	Farzinebrahimi et al.[15]					Farzinebrahimi et al.[15]
Underground part							
Underground part	Water Ethanol Ethyl acetate	Akkarasiritharattana and Chamutpong[18]		Akkarasiritharattana and Chamutpong[18]			
Root	Distilled water	Zabidi et al.[58] Ishak and Zabidi[24]	Zabidi et al.[58]				
	Hexane Ethyl acetate 70% (v/v) ethanol		Nur et al.[62]	Nur et al.[62]		Nur et al.[62]	
Rhizome	80% (v/v) methanol[20] 70% (v/v) ethanol[56] Methanol[74]	Ooi et al.[20] Umar et al.[56]	Ooi et al.[20]	Ooi et al.[20]	Ooi et al.[20]	Ooi et al.[20] [c]Mad Nasir et al.[74]	
Tuber	70% (v/v) ethanol	Farzinebrahimi et al.[15]					Farzinebrahimi et al.[15]
Tuber explant	70% (v/v) ethanol	Farzinebrahimi et al.[15]					Farzinebrahimi et al.[15]

Umar et al.[56] determined that compounds with –OH, C=O, C–O, –C–H, C–C, and C–OH groups strongly influenced the antioxidant capacity. This result agrees with the study by Mad Nasir et al.,[74] which suggested a positive correlation between phenolics and DPPH antioxidant activity of *C. latifolia* extracts. The report showed that the rhizome extract produced a high DPPH radical scavenging activity having an IC_{50} value of 18.10 ± 0.91 μg/mL, which is comparable to that of standard ascorbic acid, which has an IC_{50} value of 11.49 ± 0.071 μg/mL. In contrast, the fruit and leaf extracts displayed a lower antioxidant activity against DPPH assay, with IC_{50} values of 26.99 ± 1.58 and 547.29 ± 5.09 μg/mL respectively.[74]

In addition, an interesting finding by Farzinebrahimi et al.[15] indicated that the free radical scavenging abilities of tuber and leaf extracts of *C. latifolia* reached 80% and 60%, respectively. The same study also evaluated a considerable antioxidant activity of 70% and 65% in the callus of tuber and leaf extracts, respectively, suggesting that the plant can be considered to have antioxidant effects.[15] Akkarasiritharattana and Chamutpong[18] found that the aqueous extract of the underground part of *C. latifolia*, assessed using DPPH and FRAP assays, also showed favorable radical scavenging activity and reducing power ability. However, the ethyl acetate extract of *C. latifolia* underground part of *C. latifolia* in the same study resulted in a lower potential. This may be due to the discrepancy in the solvents used, where more polar phenolic and flavonoid compounds possessing antioxidant properties may have been extracted in greater quantities using water than ethyl acetate.[18]

With its high antioxidant activity comparable to ascorbic acid, *C. latifolia* effectively scavenges free radicals, chelates metal iron, and reduces ferric (III) iron to ferrous (II) iron. The antioxidant properties of the plant can protect cells and tissues in the human body from oxidative stress, which is linked to chronic diseases such as diabetes, cancer, and heart disease.[90] This makes *C. latifolia* a valuable source of functional foods that can help supplement the daily diet with antioxidants, subsequently preventing the body from harmful free radicals. Nonetheless, investigations of the antioxidant effects of different extracts of various parts of the plant and isolated components are still warranted. Further detailed studies are needed to explore the bioactivities of *C. latifolia* which will support its medicinal value.

7.2 Antimicrobial activity

Previous studies have reported that different parts of *C. latifolia* such as the root, stem, and leaf, exert antimicrobial activities against seven different bacterial strains, including *Bacillus cereus, Bacillus subtillis, Enterobacter aerogenes, Erwinia* sp., *Klebsiella* sp., *Pseudomonas* sp. and *Staphylococcus aureus.*[19] It was demonstrated that by increasing the concentration of all the extracts, with the highest concentration being 100 mg/mL, the elimination and restraint of the microorganisms were gradually more effective.[19] A similar observation was made by Lim and Ibrahim[91] where the root extract was seen to have the ability to inhibit the growth of *Candida albicans,* with the lowest minimum inhibitory concentration of the extract being 1.56 mg/mL. In another study, the leaves and tubers from intact *C. latifolia* plant (*in vitro*) and callus (*in vivo*) extracts showed considerable antibacterial activity against *Pseudomonas aeruginosa* and *Klebsiella sp.*[15] However, the most prominent activity was observed in the tuber extract, which was suggested to contain phytochemicals with antibiotic properties.[15] Furthermore, a study by Mad Nasir et al.[74] revealed that the methanolic leaf extract had promising antibacterial properties against *Staphylococcus aureus* (gram-positive bacteria) and *Salmonella choleraesuis* (gram-negative bacteria), with mean (n=3) inhibition zones of 15.33 mm and 8 mm, respectively. The active phenolic compounds, such as tetrahydromethylmononya– sine, (*2R,4S,5S,6R*)–2–ethyl–6–(4–methylphenoxy)oxane–3,4,5–triol, and (*Z*)–resveratrol 3,4′-diglucoside, in the leaf extracts were found to predominantly react with the enzymes and proteins of the microbial cell membrane.[15]

Given the antibacterial effects of this plant, additional investigations, such as in–depth research on the chemical constituents of *C. latifolia* responsible for its antimicrobial activity, are needed. Additionally, since there are limited studies related to the antimicrobial activities of this plant and its different parts, further detailed investigations are required.

7.3 Anti–diabetic activity

The antidiabetic properties of *C. latifolia* have been investigated in multiple studies, both through chemical assays and animal model experiments. In a report by Zabidi et al.[10], *C. latifolia* root extract was found to exhibit a considerably significant inhibition of *α*– glucosidase and dipeptidyl peptidase–4 (DPP (IV)) enzymes, where its percentage inhibition was in close proximity to that of acarbose, a marketed anti–diabetic drug. In addition, it was found that through the synergistic interaction of phytochemicals in the extracts, such as berberine, flavonoid glycoside (phlorizin), isoflavonoid (mundulone and scandenin), and cinnamic acid derivative (dimethyl caffeic acid), insulin secretion and glucose uptake activity were greatly enhanced.[15] The study also suggested that the fruit extract of *C. latifolia* demonstrated antidiabetic activity, although it was less effective than the root extract. This was possibly because some bioactive compounds in the root extract were absent from the fruit extract, which lowered the efficacy level where fewer synergistic interactions

occurred.[15] A similar result was also seen in the study by Ishak and Zabidi,[24] where the fruit and root extracts displayed promising antidiabetic effects. However, in this study, the leaf extract of *C. latifolia* showed a lower potential in activity, which may be due to the lack of some active components.

Furthermore, a study by Umar et al.[56] found that the rhizome extract exhibited a more significant α– glucosidase inhibition than the leaf and petiole extracts. The study suggested that the isolated compound, unknown–85 ($C_{42}H_{51}O_6$), primarily influenced inhibition, whereas phenolics (orcinol glucoside), cycloartane triterpene (curculigosaponin G, H, and I), and norlignan compounds (1,1–bis (3,4–dihydroxyphenyl)–1–(2–furan)–methane) contributed slightly. Moreover, the fruit of the plant contains a sweet protein known as curculin.[34] This protein was suggested to be 500 to 9000 times sweeter than sucrose by weight, and is known for its use as a sugar substitute and taste modifier. Curculin is also recognized as a low–calorie sweetener; thus, it is considered to have a potential in having antidiabetic properties.[34] Despite this, there have been no studies to confirm this postulation; therefore, further studies are needed to investigate the glucose uptake, insulin secretion, and α–glucosidase and α–amylase inhibitory effects of curculin.

Moreover, in an *in vivo* study, *C. latifolia* fruit:root extract at a 1:1 ratio was found to decrease glucose and lipid levels, as well as increase insulin and adiponectin levels in streptozotocin (STZ)–induced diabetic rats.[92] The extract demonstrated its efficiency in inhibiting the disruption of pancreatic β–cells, which is usually induced by STZ in diabetic rats. This indicates that the fruit and root extract of this plant was capable of scavenging radicals that could cause oxidative stress in cells, suggesting its antioxidant properties.[92] Another previous study reported the potential for diabetes management linked to an isolated compound from the rhizome extract of *C. latifolia* known as curculigoside.[93] In response to this, it was observed that glucose uptake was improved by the increased availability of glucose transporter type 4 (GLUT4) at the plasma membrane of differentiated 3t3–L1 adipocytes in male Sprague–Dawley rats.[93]

Based on the reported improvements in glucose uptake, insulin secretion, and the significant α–glucosidase and α–amylase inhibition effects, it can be deduced that *C. latifolia* possesses promising anti–diabetic properties. Despite this, the reported studies carried out so far revealed that only aqueous and ethyl acetate extracts of the roots, rhizomes, fruits, and leaves were used. Therefore, various other plant extracts can also be considered for the investigation of their anti–diabetic properties.

7.4 Other bioactivities

Ooi et al.[94] investigated the lipid profile of *C. latifolia* rhizome extract and reported improvements in total cholesterol levels and increased high–density lipoprotein (HDL) levels in obese diabetic rats. Additionally, the lipoprotein cholesterol ratio of HDL and low–density lipoprotein (LDL) (HDL:LDL) was ameliorated by treatment with 200 mg/kg body weight rhizome extract. This indicated that the extract could potentially help reduce the risk of cardiovascular disease, especially in obese patients.[94] Similarly, Ishak et al.[92] found that treatment with 50, 100, and 200 mg/kg body weight of fruit improved the lipid profile of obese diabetic rats. The findings demonstrated a significant decrease in total cholesterol, triglycerides, and LDL and an increase in HDL. These findings suggest that *C. latifolia* is a promising plant for controlling cholesterol levels in the body, which is important for reducing the risk of heart disease and stroke, which are more prevalent in individuals with obesity.

C. latifolia root and leaf extracts have also been demonstrated to improve sperm quality in mice (*Mus musculus*). According to a study by Jaafar et al.,[95] mice fed with *C. latifolia* root extract showed a greater increase in sperm motility when compared to the control group, whereas the mice fed with *C. latifolia* leaf extract showed a higher sperm count and viability.

In addition, a cytotoxicity test was carried out on the root extract of this plant, and Lim and Ibrahim[91] suggested that the extract demonstrated no toxicity against brine shrimp eggs, with a lethal concentration (LC_{50}) of 2.25 mg/mL. This finding indicated that the extract had a minimal negative impact on living cells and was less likely to cause a reduction in cell viability or cell death.[96] Moreover, a cell viability assessment, which measures the proportion of healthy functional cells, was conducted by Zabidi et al.[10] via the MTT (3-[4,5–dimethylthiazol–2–yl] –2,5 diphenyl tetrazolium bromide) assay. The study showed the ability of 3T3–L1 cells to survive at IC_{20} (153.21 $\pm$ 9.65 µg/ml) and IC_{50} (561.42 $\pm$ 6.22 µg/ml) of *C. latifolia* root extract and IC_{20} (295.67 $\pm$ 7.43µg/ml) and IC_{50} (495.67 $\pm$ 11.31 µg/ml) of fruits extract. Meanwhile, MTT assay by Ooi et al.[93] found the IC_{20} and IC_{50} values for ethyl acetate fraction of rhizome extract were 111.73 $\pm$ 9.57 and 509.59 $\pm$ 49.75 mg/mL, respectively. These findings suggest that *C. latifolia* does not have toxic effects on cells, suggesting that it is safe for use or consumption.

Previous reports have suggested that *C. latifolia* compounds have anti–aging and ultraviolet protection properties. An *in silico* anti–elastase study was conducted by Nur et al.[62] through molecular docking to predict the interactions between

ligands (*C. latifolia* compounds) and the elastase target protein (1B0F). From the study, sugiol, aviprin, 4–*O*–caffeoyl-quinic acid–1, quercetin and 5,7,3,5–tetrahydroxyflavanone compounds of *C. latifolia* demonstrated the best interaction against the target protein, where the binding free energies of the compounds were <–6 kcal/mol. This indicated that the compounds of the plant have promising potential to exert anti–elastase activity, which could promote anti–aging effects. In another study by Nur et al.,[97] *C. latifolia* compounds, pomiferin, scandenin, mundulon, and rubratoxin were found to have a negative binding affinity energy against matrix metalloproteinases, MMP–1 (collagenase) and MMP–9 (gelatinase), while 1,1,6–trimethyl–1,2–dihydronaphthalene, orcinol glucoside, and sugiol compounds effectively inhibited the target proteins hyaluronidase. The ability to inhibit target proteins is mainly attributed to the functional groups in the chemical structures of the active compounds, which can readily interact with the amino acid residues of the target proteins.[97]

Furthermore, Nur et al.[98] revealed that hexane, ethyl acetate, and ethanol extracts of *Curculigo latifolia* leaves, roots, and stems have promising bioactivity in ultraviolet protection against UVA and UVB rays. The study found that the hexane leaf extract demonstrated the highest intensity in absorbing UVA and UVB radiation, with absorption values of 1.192 and 1.804, respectively. Additionally, it was also indicated that leaf hexane, root ethyl acetate, stem ethyl acetate and leaf ethyl acetate extracts at concentration 250 ppm showed the most prominent ultra–protective effect with sun protection factor (SPF) values of 23.65, 16.5, 22.5 and 23.03 respectively. Based on the reported findings, it can be suggested that *C. latifolia* plants have properties that could be used to make sunscreen products and protect the skin against erythema, pigmentation, and harmful UV rays.[98]

8. Conclusion

This review provides information on the distribution, species description, traditional uses, nutritional value, phytochemistry, chemical composition, and pharmacological activities of *Curculigo latifolia.* Previous studies have described the plant as a good source of phytochemical compounds, such as alkaloids, tannins, saponins, flavonoids, glycosides, steroids, terpenoids, and norlignans. Several common compounds, such as curculigoside, crassifoside I, nyasicoside, and curculigine, were also detected, which could play a significant role in the biological activities of *C. latifolia.* Furthermore, the plant has been investigated for several pharmacological activities such as antioxidant, antimicrobial, anti–diabetic, cholesterol, anti–elastase, ultraviolet protection and spermatogenic activities.

Considering the promising biological studies outlined, *C. latifolia* could mitigate some diseases and therefore have potential medicinal value that could be used as dietary food supplements. However, the underlying potential of *C. latifolia* is not yet fully understood, and merits further research. Further investigations could include studies of other bioactivities, such as anti–cancer, anti–viral, wound healing, and anti–inflammatory activities. Isolation and characterization of the phytochemicals in the different parts of *C. latifolia* with varying extraction solvents should also be undertaken to identify bioactive compounds and further understand their mechanisms of action and biological activities. Moreover, human clinical trials could provide more information on the plant as a functional food for improving human health.

Declaration

Ethics approval and consent to participate

Not applicable – review paper.

Consent for publication

Not applicable - does not contain data from any individual person.

Authors' contributions

AT, HY, NA, MA, and FJ have made substantial contributions to the conception and design of the manuscript; have drafted the work and substantively revised it; have approved the submitted version (and any substantially modified version that involves the author's contribution to the study); have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even those in which the author was not personally involved, are appropriately investigated and resolved, and the resolution documented in the literature.

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Reviewer report
Manuscript Title: "A review on the phytochemistry and biological activities of *Curculigo latifolia* Dryand ex. W. Aiton"
General assessment
This manuscript aims to provide an overview of the phytochemical composition and biological activities of Curculigo latifolia. While the topic is of potential scientific and industrial interest, the review does not currently meet the rigor and critical depth expected for a high-quality review article. The manuscript is predominantly descriptive, lacks conceptual integration, and contains several instances of overinterpretation and questionable data reliability. In its present form, the work provides limited added scientific value beyond a narrative compilation of existing studies and would not be suitable for publication in high-impact journals without substantial revision.
Major critical issues
1. Serious concerns regarding the reliability and quality of referenced literature
The manuscript relies heavily on in vitro chemical assays, in silico molecular docking, and rodent models to support claims of antioxidant, antimicrobial, anti-diabetic, anti-aging, and UV-protective activities. However, the authors frequently extrapolate these preliminary findings to functional food, nutraceutical, and medicinal applications without citing any clinical or human intervention studies. Such extrapolation constitutes overinterpretation of preclinical data, which is not acceptable in high-impact journals.
Furthermore, the cited literature is heavily clustered within a limited number of research groups (e.g., Umar et al., Nur et al., Ishak et al., Zabidi et al.), raising concerns about limited independent validation and potential self-citation clustering. A critical review should assess reproducibility across independent laboratories, but this aspect is not addressed.
The manuscript also exhibits species misattribution, where phytochemicals and biological activities reported for other Curculigo species (e.g., C. orchioides and C. capitulata) are discussed without clear taxonomic differentiation. This undermines the accuracy of the phytochemical profile attributed to C. latifolia.
Additionally, several quantitative values appear questionable, including extremely high mineral contents (e.g., Ca and Fe) and unusually low IC_{50} values comparable to standard antioxidants. The

authors do not clarify whether these values are expressed on a dry or fresh weight basis, nor do they discuss analytical validation, matrix interference, or contamination risks. Without such contextualization, the reliability and comparability of these data remain uncertain.

2. Lack of critical synthesis and conceptual integration

The manuscript is largely descriptive and narrative, resembling a literature compilation rather than a critical integrative review. In the Biological Activities section, the authors primarily list assays, IC_{50} values, and identified compounds without discussing:

- Structure–activity relationships
- Correlations between extraction methods and bioactivity
- Mechanistic insights
- Comparative synthesis among different plant parts or extraction strategies

Moreover, the review lacks a conceptual framework linking phytochemical composition to biological activity. For example, phenolic compounds are mentioned in relation to antioxidant and metabolic effects, but no mechanistic pathways (e.g., ROS modulation, insulin signaling pathways) are discussed. The narrative is fragmented and repetitive, with antioxidant-related content reiterated across sections without higher-level synthesis or integrative conclusions.

3. Overstated translational and functional claims

Several statements imply that C. latifolia compounds should be included in the human diet, that the plant is a valuable functional food source, or that it could mitigate diseases. These claims are not supported by clinical evidence, pharmacokinetic data, or regulatory context and therefore represent inappropriate translational overclaims. High-impact journals require cautious language and a clear distinction between preliminary bioactivity evidence and clinical applicability.

Scientific red flags

Several aspects raise concerns regarding scientific rigor and data reliability, including unusually high mineral contents, IC_{50} values comparable to standard antioxidants, extensive compound lists without clear structural confirmation (e.g., NMR validation), overreliance on molecular docking studies, and unsupported functional food and medicinal claims. These issues may lead to serious concerns during peer review and could result in desk rejection in high-impact journals.

Recommendation

In its current form, the manuscript lacks critical synthesis, methodological rigor, and scientific caution in interpretation. Substantial restructuring, inclusion of systematic review methodology, critical integration of data, clarification of quantitative values, and removal of unsupported translational claims are required.

Overall recommendation: Not approved

Is the topic of the review discussed comprehensively in the context of the current literature?

Partly

Are all factual statements correct and adequately supported by citations?

Partly

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Food chemistry, natural product extraction, polysaccharides and bioactive compounds, functional foods and nutraceuticals, biomaterials (chitosan-based films), and food preservation.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 25 February 2025

https://doi.org/10.5256/f1000research.169407.r365036

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?

Srinivasan Prabhu
Department of Biosciences, Rajagiri College of Social Sciences, Cochin, Kerala, India

1. There is no any detail about the taxonomic treatment of this plant
2. Authors can incorporate the structure of some key chemical constituents of this species
3. Authors can include the biosynthesis of unique chemical constituent of this plant
4. Authors can show the unexplored chemical constituents of this plant with molecular docking if anything found in this plant

Is the topic of the review discussed comprehensively in the context of the current literature?
Partly

Are all factual statements correct and adequately supported by citations?
No

Is the review written in accessible language?
Partly

Are the conclusions drawn appropriate in the context of the current research literature?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Ethnobotany and Computer aided drug design

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 30 July 2024

https://doi.org/10.5256/f1000research.169407.r306186

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Azlini Ismail
International Islamic University Malaysia, Kuala Lumpur, Federal Territory of Kuala Lumpur, Malaysia

The authors have revised the manuscript accordingly as per commented.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Antihypertensive, antioxidant, anti-inflammatory, pharmacognosy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 24 June 2024

https://doi.org/10.5256/f1000research.163349.r281841

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Azlini Ismail
International Islamic University Malaysia, Kuala Lumpur, Federal Territory of Kuala Lumpur, Malaysia

Overall, this review article summarizes the phytochemicals, nutritional, and biological properties of *Curculigo latifolia* and highlights the gap of studies required for future research.

There are a few amendments required for further improvement:

1. Introduction – Please correct the typographical error for some words (i.e. ome)

2. Figure 1 (I) should be standardized using small letter (i). The labels (c) and (d) for roots and petioles/stem are switched. Please double-check.
3. Please double-check grammar for the following: *regulation blood pressure.*
4. To re-confirm the following sentence: *.....the plant was shown to exhibit bioactivities such as antioxidant, antimicrobial, anti–diabetic, sperm quality, cytotoxicity, anti–aging and ultraviolet protection activities.* Sperm quality is not a type of bioactivity, kindly choose other suitable words. The findings using the brine shrimp test and MTT assay indicate that the plant was not cytotoxic, thus it is better to omit the cytotoxic effect in this sentence and wherever applicable in this review, unless some findings suggest so.
5. Please revise the following sentence as the diverse range of bioactivities is attributed to the presence of different types of bioactive compounds that the plant has, not because of the high content of any chemical compounds: *The diverse range of bioactivities of plants may be attributed to their high content of chemical compounds.*
6. Please correct the sentence (IC50 11.49 ± 0.071 µg/mL).
7. Please double-check the value in the following sentence: *Furthermore, a study by Mad Nasir et al.74 revealed that the methanolic leaf extract had promising antibacterial properties against Staphylococcus aureus (gram-positive bacteria) and Salmonella choleraesuis (gram-negative bacteria), with inhibition zones of ±15.33 mm and ±8 mm, respectively.*
8. Please revise the typographical error in the following sentence: *The study found that The hexane leaf extract demonstrated the highest intensity in absorbing UVA and UVB radiation, with absorption values of 1.192 and 1.804, respectively.*

Is the topic of the review discussed comprehensively in the context of the current literature?

Yes

Are all factual statements correct and adequately supported by citations?

Yes

Is the review written in accessible language?

Yes

Are the conclusions drawn appropriate in the context of the current research literature?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Antihypertensive, antioxidant, anti-inflammatory, pharmacognosy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 19 Jul 2024

Amanina Taufik

Dear Reviewer,

We appreciate your thoughtful and thorough review of our manuscript. We have carefully considered your feedback and made the following revisions (please see below):

Comment 1: Introduction – Please correct the typographical error for some words (i.e. ome)
Response 1: Thank you for noting the error. The typo has been corrected: "Some species in this genus are known for their medicinal properties and have often been used in traditional therapeutic remedies."

Comment 2: Figure 1 (I) should be standardized using small letter (i). The labels (c) and (d) for roots and petioles/stem are switched. Please double-check.
Response 2: Thank you for your comment. (I) has been changed to small letter (i) and the labels for (c) and (d) have been switched.

Comment 3: Please double-check grammar for the following: regulation blood pressure.
Response 3: Thank you for pointing out the error. The sentence has been corrected to: "regulation of blood pressure."

Comment 4: To re-confirm the following sentence: .....the plant was shown to exhibit bioactivities such as antioxidant, antimicrobial, anti–diabetic, sperm quality, cytotoxicity, anti–aging and ultraviolet protection activities. Sperm quality is not a type of bioactivity, kindly choose other suitable words. The findings using the brine shrimp test and MTT assay indicate that the plant was not cytotoxic, thus it is better to omit the cytotoxic effect in this sentence and wherever applicable in this review, unless some findings suggest so.
Response 4: Thank you for your comment. We agree that sperm quality is not a type of bioactivity and therefore, this sentence has been rewritten to, "*C. latifolia* has been involved in several *in vitro* and *in vivo* investigations, where the plant was shown to exhibit bioactivities such as antioxidant, antimicrobial, anti–diabetic, anti–aging, ultraviolet protection activities and reported to improve sperm quality (summarised in Table 4)." Additionally, we have replaced the term "sperm quality" in Table 4 which listed the reported biological activities to "spermatogenic activity." We have also removed cytotoxic effect from the sentence.

Comment 5: Please revise the following sentence as the diverse range of bioactivities is attributed to the presence of different types of bioactive compounds that the plant has, not because of the high content of any chemical compounds: The diverse range of bioactivities of plants may be attributed to their high content of chemical compounds.
Response 5: Thank you for your comment. The sentence has been revised to: "The diverse range of bioactivities of plants may be attributed to the different types of bioactive compounds."

Comment 6: Please correct the sentence (IC50 11.49 ± 0.071 µg/mL).
Response 6: Thank you for your comment. The sentence has been revised to: "The report showed that the rhizome extract produced a high DPPH radical scavenging activity having an IC_{50} value of 18.10 ± 0.91 µg/mL, which is comparable to that of standard ascorbic acid, which has an IC_{50} value of 11.49 ± 0.071 µg/mL)."

Comment 7: Please double-check the value in the following sentence: Furthermore, a study by Mad Nasir et al.74 revealed that the methanolic leaf extract had promising antibacterial properties against Staphylococcus aureus (gram-positive bacteria) and Salmonella choleraesuis (gram-negative bacteria), with inhibition zones of ±15.33 mm and ±8 mm, respectively.
Response 7: Thank you for your comment. The values were changed and revised to: "Furthermore, a study by Mad Nasir et al. [74] revealed that the methanolic leaf extract had promising antibacterial properties against *Staphylococcus aureus* (gram-positive bacteria) and *Salmonella choleraesuis* (gram-negative bacteria), with mean (n=3) inhibition zones of 15.33 mm and 8 mm, respectively."

Comment 8: Please revise the typographical error in the following sentence: The study found that The hexane leaf extract demonstrated the highest intensity in absorbing UVA and UVB radiation, with absorption values of 1.192 and 1.804, respectively.
Response 8: Thank you for pointing out the error. The typo has been corrected: "The study found that the hexane leaf extract demonstrated the highest intensity in absorbing UVA and UVB radiation, with absorption values of 1.192 and 1.804, respectively."

Competing Interests: No competing interests were disclosed.

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