plants

MDPI

Review

Antidiabetic Potential of *Silybum marianum* (L.) Gaertn. and *Brachylaena discolor* DC (Asteraceae) in the Management of Type 2 Diabetes Mellitus

Emmanuel A. Ayeni and Anthony J. Afolayan *

Department of Biotechnology and Biological Science, University of Fort Hare, Alice 5700, South Africa; ayeniemmanuel91@yahoo.com

* Correspondence: aafolayan@ufh.ac.za; Tel.: +27-40-602-2323

Abstract

Silybum marianum and *Brachylaena discolor* were identified from the ethnobotanical pool of medicinal plants used in managing type 2 diabetes mellitus in South Africa. These two plants were selected based on their strength of evidence from our preliminary investigation and frequency of ethnomedicinal use. An extensive literature review was performed using major scientific databases. *Silybum marianum* and *Brachylaena discolor* have shown potential activity in decreasing blood glucose levels. Previously isolated chemical compounds validated their anti-diabetic properties, thus confirming their importance and utilization from an ethnobotanical perspective for drug discovery in the development of type 2 diabetes drugs. The traditional use of *Brachylaena discolor* involved infusion and decoction methods, and the isolation of target-based compounds will be required for anti-diabetic activities. However, the existing toxicity profile remains insufficient, especially for *B. discolor*. The findings suggest that these plants would be beneficial to the populace as an add-on dietary vegetable in lowering blood sugar levels for the treatment of type 2 diabetes. Further comprehensive studies are needed to fully establish their safety profile, particularly with long-term use or when consumed.

Keywords: *Silybum marianum*; *Brachylaena discolor*; diabetes; medicinal plants; Asteraceae

check for updates

Academic Editors: Juei-Tang Cheng, Eduardo Luis Konrath and Mara Rejane Ritter

Received: 12 August 2025
Revised: 19 October 2025
Accepted: 20 October 2025
Published: 26 October 2025

Citation: Ayeni, E.A.; Afolayan, A.J. Antidiabetic Potential of *Silybum marianum* (L.) Gaertn. and *Brachylaena discolor* DC (Asteraceae) in the Management of Type 2 Diabetes Mellitus. *Plants* **2025**, *14*, 3267. https://doi.org/10.3390/plants14213267

Copyright: © 2025 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/).

1. Introduction

Type 2 diabetes (T2DM) is a metabolic condition characterized by insulin resistance and hyperglycaemia [1]. It involves impairment of carbohydrate metabolism as a result of insufficient insulin production or a decrease in the responsiveness of peripheral tissues to insulin signaling [2]. Type 2 diabetes mellitus is a global burden disease that affects approximately 537 million adults worldwide and is estimated to increase to 783 million by the year 2045 [3,4]. For instance, in South Africa, diabetes has steadily increased, especially among low-income communities [5]. Medicinal plants are widely known to complement conventional medicines, and their utilization is linked to various cultural and community groups, particularly those that demonstrate efficacy in the treatment of chronic diseases such as diabetes [6,7]. Several studies have documented the strength of medicinal plants in treating and managing various diseases [8–10]. However, several limitations have been identified, as they often present long-term side effects, toxicity, and unknown adverse effects, thus impeding their wider acceptability [11–13]. Yet, medicinal plants contain several different biologically active compounds that provide healthy benefits [14–16]. The World Health

Organisation (WHO) states that about 70–80% of the global population still relies solely on medicinal plants for healthcare management, promoting the sustainable health and well-being of individuals [6]. Since time immemorial, medicinal plants have been involved in a plethora of complex biochemical, metabolic, and physiological mechanisms [10]. Several studies have identified that many rural communities in South Africa still rely on medicinal plants to manage diabetes because they are highly trusted among communities and affordable [10,16–20]. Therefore, scientific investigation of medicinal plants will continue to be a veritable and valuable source of ethnobotanical knowledge, preserving cultural diversity, facilitating co-integration into evidence-based healthcare and contributing to drug discovery and development. In this review, we documented the phytochemical, pharmacological, and toxicological profiles of *Silybum marianum* and *Brachylaena discolor* in managing type 2 diabetes. The study showed that both plants offered several promising potential benefits that could be explored when combined as an herbal formulation and consumed as an add-on dietary vegetable for people living with type 2 diabetes.

1.1. Asteraceae Family in the Management of T2DM

Silybum marianum and *Brachylaena discolor* belong to the Asteraceae family and are taxonomical groups that comprise approximately 32,000 plant species and are unique for their flowering characteristics [21–23]. Several ethnobotanical studies have reported that the Asteraceae family has nutritional and medicinal properties and is often used for food and medicinal purposes [18,21–24]. Some of the plant species in this family include chamomile, marigolds, sunflowers, dandelions, *Silybum marianum* (thistles), and *Brachylaena discolor* (coast silver oak), among others. They are rich in medicinal components and are highly nutritionally functional foods when consumed [25–28]. Many plant species in Asteraceae have been investigated for their pharmacological potential, including their antioxidant, anti-inflammatory, antimicrobial, and cytotoxic effects due to the presence of multiple secondary metabolites [29,30]. A hallmark phytochemical group within this family is the sesquiterpene lactones, which are significant for their bitter characteristic, an organoleptic diagnostic feature that is recognized for their significant role in modulating various biochemical and cellular pathways [25,31,32].

1.2. Origin, Morphology, and Biology of Silybum marianum

Silybum marianum (L.) Garten, commonly known as milk thistle, is a spiny herbaceous plant that belongs to the family of Asteraceae [33,34]. *Silybum marianum* is originally native to Mediterranean areas, Asia, Southern Europe, Australia, South America, Africa, and some parts of Russia, and it migrated to other countries worldwide due to its medicinal properties [35]. *Silybum marianum* cultivation varies based on different sowing times [36]. For instance, it is a biennial crop when it grows in the wild and might be regarded as an annual crop when cultivated [36]. The seeds germinate in autumn and flower in summer, reaching a vegetative cycle of 8–9 months when grown in the wild [37]. The morphological features of the plants show a glabrous or slightly downy stem that is erect and branched in the upper part [38]. The young leaves of *S. marianum* are tender, juicy, crisp, and refreshing, thus making it a tender vegetable for consumption [39]. The stem leaves are smaller than those of the rosette, between 50 and 60 cm in length and 20 and 30 cm in width, and their leaves are broad, lanceolate, and include purple tubular petals (Figure 1). Their height ranges between 40 and 200 cm and the leaves show notable white veins along the top side as a unique feature that aids in taxonomical identification [40].



Figure 1. Morphology of *S. marianum*.

1.3. Ethnopharmacological Utilization of S. marianum

All parts of *S. marianum*, including the roots, aerial parts, leaves, and seeds, are used for medicinal purposes, such as treating liver disorders and gallbladder disease, protecting from snake bites, cardiac disorders, fevers, rheumatism, liver cirrhosis, and controlling blood sugar levels and gastroenteritis [33,38,41]. The seeds, roots, bark, leaves and immature fruits have been used to treat gastrointestinal, type 2 diabetes, and diarrhea, while the leaves are applied to sores and manage hemorrhoid pain [36].

1.4. Chemical Components of Silybum marianum and Their Role in Anti-Diabetic Activity

Several chemical compounds have been isolated from *S. marianum*, which include silymarin, silibinin, isosilychristin, isosilybin A and isosilybin B, silybin A and silybin B, silychristin, silydianin and taxifolin, apigenin 7-*O*-*β*-(2″-*O*-*α*-rhamnosyl) galacturonide, kaempferol 3-*O*-*α*-rhamnoside-7-*O*-*β*-galacturonide, apigenin 7-*O*-*β*-glucuronide, apigenin 7-*O*-*β*-glucoside, apigenin 7-*O*-*β*-galactoside, kaempferol-3-*O*-*α*-rhamnoside, kaempferol and quercetin [42–44], linoleic (35–55%), oleic (24–30%) acids, together with palmitic (8–12%), behenic (3–9%), and other fatty acids and oils (Figure 2 and Table 1). *Silybum marianum* produces edible oils, protein powder, and forage. It exhibits excellent antioxidant effects, making it very suitable for use in cosmetics to protect the skin [38]. Specifically, silymarin, a major component in the plant, possesses free radical scavenging properties and inhibits lipid peroxidation. It was noted that these properties are likely due to the presence of the *β*-ring catechol group as well as the donation of hydrogen electrons, which prevents the depletion of free radicals [38,45,46]. Silibinin also showed significant protection by improving the level of superoxide dismutase and reducing the high triglyceride levels in the hepatic system, thereby impeding oxidative damage [47]. Awla et al. [48] reported that silydianin and silychristin in the extract of *S. marianum* reduced serum triglyceride levels and decreased glucose levels significantly ($p < 0.001$). These compounds prevented weight gain and normalized blood pressure in a high-fat/high-fructose diet compared to the control group [49]. The oils from *S. marianum* have the potential to improve the nutritional value of food by providing additional vitamins, proteins, and linoleic acid, as well as low-fat content and low cholesterol levels [38,50,51].

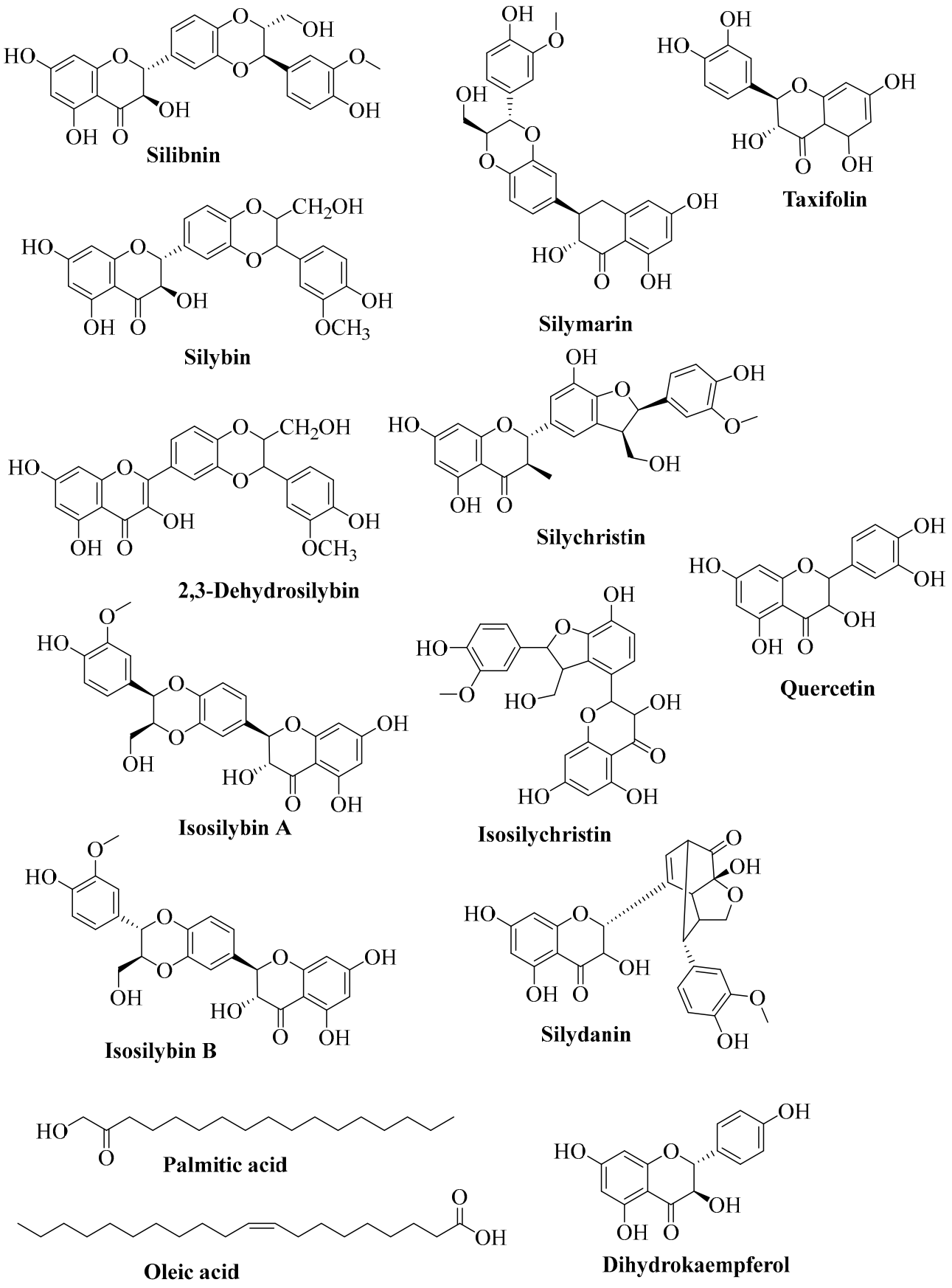


Figure 2. Chemical components of *S. marianum*.

1.5. Toxicity

Silybum marianum is considered safe for both human and veterinary use when administered in liquid or solid dosage forms. Clinical studies have reported that silymarin is well tolerated at 700–1500 mg three times daily for 24 weeks [52]. According to the European Medicines Agency (EMA), some side effects of *S. marianum* include dry mouth, nausea, upset stomach, stomach irritation, diarrhea, headache, and allergic reactions (including skin inflammation, itching, rash, sudden severe allergic reaction, and asthma [53]. The ethylacetate extract of *S. marianum* showed normal neurological, behavioral, and autonomic profiles at 2000 mg/kg, and no mortality was recorded during the 48 h of oral administration [48]. Other compounds, such as silybin, silydianin, and silychristin, showed no cytotoxic and genotoxic effects at a 100 µM concentration. It was found that silymarin showed mutagenic activity in *S. typhii* strains in the presence of metabolic enzymes [52,54]. However, some gastrointestinal symptoms might occur, which include nausea and laxative effects, due to increased bile secretion and diarrhea [52]. *S. marianum* is affected by some mycotoxin-based dietary supplements, which are toxigenic and have the potential to reduce the beneficial effect of silymarin when consumed [53]. Many European countries, such as Austria, Belgium, Croatia, the Czech Republic, Estonia, France, and Germany, have established the use of *Silybum marianum* capsules in tablets and pharmacopeia standards [55]. Comprehensive toxicological studies will be helpful to understand pathways and multi-target disease conditions in our future studies. Maaliah et al. reported that the extract of *S. marianum* is hepatotoxic and could lead to acute and chronic liver diseases [56]. Kazazis et al. [57] stated that silymarin is safe at 13 g/day and could be tolerated in chemotherapeutic agents. However, it was suggested that doses as high as 20 g/day could cause asymptomatic liver toxicity [57]. In an in silico study, it was evaluated that the extract of *S. marianum* showed high absorption, favorable metabolism, and minimal toxicity with no hERG channel inhibition or hepatotoxicity [58]. Soleimani et al. suggested that silymarin is considered safe during pregnancy [52]. However, there is a need for caution when taken during pregnancy, as it might interfere with other drugs, leading to drug–drug interactions. Rysava et al. [59] reported that silymarin and its polyphenols affect the Nrf2 signaling pathway in human skin cells, but their effect after repeated long-term application to the whole skin was not ascertained. Silibinin, another potential chemical component, increased the expression of glucagon-like peptide-1 receptor (GLP1R) in the duodenum, and the activation of neurons in the nucleus of the solitary tract decreased hepatic glucose production at 100–300 mg/kg in rats when fed with a high-fat diet, alongside alleviating streptozotocin-induced diabetes [60]. The in vivo activity of silibinin alleviated non-alcoholic fatty liver diseases and insulin resistance by modulating the IRS-1/PI3K/Akt pathway [61]. In addition, silymarin has been reported to ameliorate insulin resistance, dyslipidemia, and inflammation and reconstitute the bile acid pool in the liver of experimental animals with diet-induced obesity [62]. Also, it was noted that silymarin showed significant overall health performance on the lens even in type 1 diabetic experimental rats [63]. Wang et al. stated that silymarin reduced liver and pancreatic protein damage and creatinine levels in some animal studies [64–66]. Silymarin supplementation reduced fasting blood sugar, serum insulin, and homeostasis, and there was a significant increase in high-density lipoprotein cholesterol levels and the quantitative insulin sensitivity check index [67]. Tuorkey and colleagues reported that silymarin extracted from the seeds significantly normalized the enzyme levels and decreased the serum glucose level, cholesterol, and triglycerides compared to the negative control group [68]. Silymarin enhanced the antioxidant capacity and normalized liver and renal function enzymes [68].

1.6. Anti-Diabetic Activity of S. marianum

Silybum marianum has received considerable scientific attention due to its anti-diabetic, antioxidant, and anti-inflammatory properties [69]. The oral administration of *S. marianum* extract to alloxan-induced diabetic rats reduced their MDA levels and validated its antioxidant properties. For instance, at 75 mg/kg, there was a significant decrease in MDA levels and lipid peroxidation and the half-maximal inhibitory value was found to be 13.88 ± 0.25 mg/kg. Methanolic leaf extracts of *S. marianum* demonstrated significant reducing power for some metabolic enzymes, with β-carotene bleaching inhibition at doses as low as 0.02 mg/mL in lipid peroxidation assays [70]. *Silybum marianum* extract at 400 mg/kg decreased the blood glucose levels significantly ($p < 0.05$) and revealed a significant effect on the cholesterol, liver enzymes, and kidney functions of diabetic rats compared with those that received 200 mg/kg [71]. The findings above suggest dose-dependent therapeutic potential, and higher doses show better efficacy of the extract. Furthermore, in an experimental animal study on the extract, there was a significant improvement in some of the pancreatic enzymes and plasma glutathione, which thus confirmed protection against lipid peroxidation and enhanced plasma glucose induced by alloxan in mice [72,73]. Maaliah et al. [56] reported that the ethanol extract of *S. marianum* decreased serum glucose, triglyceride, total cholesterol, low-density lipoprotein, very-low-density lipoprotein, and malondialdehyde (MDA) levels. The methanol extract demonstrated an inhibitory concentration, IC_{50}, of 5.2 ± 0.07 µg/mL [74]. The aqueous extract of *S. marianum* from the aerial parts revealed a decrease in blood glucose levels [75]. In an in vivo study conducted by Villiger and co-authors on ethanol fruit extract [76], it was observed that 80% of α-glucosidase inhibitory activity was reported at 100 µg/mL compared to that of acarbose (1–1500 µM). Some major chemical components of *S. marianum* are used as a single therapy to lower blood glucose levels; however, when combined with other drugs such as phosphatidylcholine, simvastatin, and vitamin E, they can lower blood glucose even more significantly [77–79]. The hypoglycemic and antihyperlipidemic effects of the extract were beneficial in BSA glycation and α-amylase activity studies [56]. Its antioxidant activity has been extensively studied, alongside how it contributes to the antioxidant potential [80,81]. *Silybum marianum* displays potent antioxidant capabilities, which are principally attributed to the presence of polyphenolic components, particularly flavonolignans such as silymarin and silibinin [81]. The extract of *S. marianum* possessed a strong antioxidant profile, measured using a microwave-enhanced technique, and the extract contained 251.2 ± 1.2 mg GAE/g of total phenolics and 125.1 ± 1.6 mg QE/g of total flavonoids, while strong antioxidant activity was observed through half-maximal inhibitory concentration (IC_{50}) values of 19.2 ± 2.3 µg/mL for DPPH, 7.2 ± 1.7 µg/mL (ABTS), 22.2 ± 1.2 µg/mL (CUPRAC), 35.2 ± 1.8 µg/mL (Phenanthroline), and 24.1 ± 1.2 µg/mL (FRAP) [58]. The anti-diabetic effects were significant at 18.1 ± 1.7 µg/mL (α-glucosidase) and 26.5 ± 1.3 µg/mL (α-amylase), respectively [58]. The aerial part of *S. marianum* showed significant free radical scavenging and ferric-reducing antioxidant power (FRAP), with an IC_{50} value of 1.73 mg/mL. In contrast, the methanolic extracts obtained during the flowering stage showed the highest activity in both DPPH and ABTS assays, with IC_{50} values ranging from 3.45 to 4.08 mmol compared with Trolox equivalents per 100 g dry weight [82]. Some of the isolated compounds have been reported to reduce oxidative stress, which is significant in the management of type 2 diabetes [83]. Co-morbid diseases contribute to excessive ROS formation and worsen diabetic conditions when not controlled [84]. Thus, silymarin reduced oxidative stress and inflammation in streptozotocin-induced diabetes mice [85].

In a synergistic study conducted by Nasir et al. [86] on dilute acetic acid extracts of *N. sativa* and *S. marianum* seeds, they showed the potential of various fractions to have different inhibitory α-amylase activities. Moreover, subfraction (F5) demonstrated the strongest

inhibitory α-amylase activity due to the presence of various phytochemical components. These findings also revealed that when anti-diabetic medicinal plants are combined in herbal formulations, they significantly decrease blood glucose levels, increase pancreatic secretions, and maintain good antioxidant status with little or no side effects in the body tissues or systems. The seeds were found to be richer in antioxidants than other parts of the plant and a rich source of protein, potassium, calcium, and magnesium [32]. In a clinical trial conducted by Wang et al., some of the health benefits of phytochemical compounds found in *S. marianum* showed that patients who received silymarin extract had a significant improvement in their glycemic indices, lipid profiles, and antioxidant indices, while the hs-CRP levels in patients decreased [67]. Huseini et al. reported the effect of antioxidant nutrients on the glycemic control of diabetic patients in experimental and clinical studies [20]. It was stated that the average fasting blood glucose level in the silymarin group decreased significantly ($p < 0.001$) after 4 months of silymarin treatment, while the average fasting blood glucose level in the placebo group at the beginning of the study was increased significantly ($p < 0.0001$) after 4 months of placebo treatment [87]. The isolation of mariamides A and mariamides B revealed the potential of the compounds to regulate the insulin signaling pathway by increasing protein tyrosine phosphatase 1B (PTP1B) inhibition [88]. Silybin (A and B) acted as a non-competitive PTP1B inhibitor, and IC_{50} values of 1.54–1.37 μM were recorded [89]. Silibinin exhibited a hyperglycemia-reducing effect and decreased the elevation of ALT, which prevented the decrease in insulin in a streptozotocin (STZ)-induced diabetic rat model [42]. In a study conducted on obese db/db mice, silibinin reduced insulin resistance and prevented myocardial and hepatic damage [90]. Silibinin significantly suppressed H_2O_2 production in rat macrophages in a dose-dependent manner and outperformed standard antioxidant control at comparable concentrations. Further analyses showed strong antioxidant potential in ethanolic and aqueous extracts of *S. marianum* (IC_{50} = 36 and 44 μg/mL, respectively) [91]. It was noted that silibinin inhibited hIAPP fibrillization by suppressing the toxic oligomerization of hIAPP and enhancing the viability of pancreatic β-cells; therefore, silibinin may serve as a potential therapeutic agent for T2DM [92]. Other pharmacological activities also include hepatoprotectivity against ischemia/reperfusion injury, renal protectivity, cardioprotectivity, neuroprotectivity, and antinociceptive, analgesic, antimicrobial, anti-ulcerative, and immunomodulatory effects [30,93–95].

Table 1. Phytochemical components present in *S. marianum*.

Plant Sources	Compound Class	Compound Name	Molecular Weight (g/mol)	Chemical Formula	CAS Number	Biological Activity	References
	Flavonolignans						
Seeds Leaves Root		silymarin	482.4	$C_{25}H_{22}O_{10}$	22888-70-6	anti-diabetic, anti-inflammatory properties, anti-diarrhea, and antioxidant activity.	[27,46]
Seeds Leaves Root		silybin A	482.4	$C_{25}H_{22}O_{10}$	22888-70-6	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective, and anti-diabetic activity.	[52,54]
Seeds Leaves Root		silybin B	482.4	$C_{25}H_{22}O_{10}$	142797-34-0	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective, and anti-diabetic activity.	[52,54]
Seeds Leaves Root		silydianin	482.4	$C_{25}H_{22}O_{10}$	29782-68-1	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective, and anti-diabetic activity.	[64,85]
Seeds Leaves Root		isosilybin A	482.4	$C_{25}H_{22}O_{10}$	142796-21-2	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective, and anti-diabetic activity.	[52,54]
Seeds Leaves Root		isosilybin B	482.4	$C_{25}H_{22}O_{10}$	142796-22-3	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective, and anti-diabetic activity.	[52,54]
Seeds Leaves Root		silychristin	482.4	$C_{25}H_{22}O_{10}$	33889-69-9	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective effects, and anti-diabetic activity	[89,96]
stem		2,3-dehydrosilybin	480	$C_{25}H_{22}O_{10}$	25166-14-7	shows potential cardioprotective effects, strong antioxidant, anticancer, anti-lipid peroxidation, and cell damage attenuation properties.	[97,98]
	Phenylpropanoids						
Seeds Leaves Root		mariamide A	756.3	$C_{42}H_{46}N_4O_{10}$	Not known	antioxidant and anti-diabetic activities.	[88]
Seeds Leaves Root		mariamide B	407.2	$C_{21}H_{24}N_2O_5$	Not known	antioxidant and anti-diabetic activities.	[88]

Table 1. *Cont.*

Plant Sources	Compound Class	Compound Name	Molecular Weight (g/mol)	Chemical Formula	CAS Number	Biological Activity	References
	Flavonoids						
Seeds		3, 3′, 5, 5′, 7-pentahydroxyflavanone	305.1	$C_{15}H_{12}O_7$	215257-15-1	anticancer and antioxidant activities	[99]
Stem		taxifolin	304.3	$C_{15}H_{12}O_7$	480-18-2	antioxidant, anti-inflammatory, and anticancer effects, neuroprotective activity, benefits for Alzheimer's disease, cardioprotectivity, anti-diabetic activity by improving insulin sensitivity, and liver protection.	[100]
Seeds Leaves Root		quercetin	302.23	$C_{15}H_{10}O_7$	117-39-5	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective effects and anti-diabetic, antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective and anti-diabetic activities.	[42–44]
Seeds Leaves Root		kaempferol	286.24	$C_{15}H_{10}O_6$	520-18-3	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective effects and anti-diabetic activity.	[42–44]
	Flavonoid glycosides						
Seeds Leaves Root		apigenin 7-*O*-*β*-(2″-*O*-*α*-rhamnosyl) galacturonide	592.5	$C_{27}H_{28}O_{15}$	124167-97-1	anti-inflammatory and antioxidant effects, cardiovascular disease management, neuroprotection, and anti-diabetic properties by reducing oxidative stress and insulin resistance.	[101]
Seeds Leaves Root		kaempferol 3-*O*-*α*-rhamnoside-7-*O*-*β*-galacturonide	608.1	$C_{27}H_{30}O_{16}$	124167-98-2	antioxidant, anti-inflammatory, and potential anticancer activity.	[27,46]
Seeds Leaves Root		apigenin 7-*O*-*β*-glucuronide	446.36	$C_{21}H_{18}O_{11}$	29741-09-1	anti-diabetic and antioxidant activities	[42–44]
Seeds Leaves Root		apigenin 7-O-*β*-galactoside	432.4	$C_{21}H_{20}O_{10}$	578-74-5	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective effects, and anti-diabetic activity.	[42–44]
Seeds Leaves Root		kaempferol-3-*O*-*α*-rhamnoside	432.4	$C_{21}H_{20}O_{10}$	482-39-3	antioxidant, anti-inflammatory, anti-fibrotic, hepatoprotective effects, and anti-diabetic activity	[42–44]
	Fatty acids						
Seeds		oleic acid	282.5	$C_{18}H_{34}O_2$	112-80-1	anti-inflammatory and antioxidant effects, and cardiovascular disease and obesity treatment	[42–44]
Seeds		linoleic acid	280.4	$C_{18}H_{32}O_2$	60-33-3	potential anti-neoplastic and pro-apoptotic effects against certain cancers and anti-inflammatory activity	[42–44]
Seeds		palmitic acid	256.4	$C_{16}H_{32}O_2$	57-10-3	anti-inflammatory, anticancer, and anti-viral agent by modulating immune signaling pathways like NF-κB and inducing apoptosis in cancer cells	[42–44]

1.7. Origin, Morphology, and Biology of Brachylaena discolor

Brachylaena discolor DC. is popularly known as the coast silver oak. This plant is a shrubby plant indigenous to South Africa and belongs to the family Asteraceae [102]. The Genus name *Brachylaena* is derived from the Greek brachys (short) and klaina (cloak), referring to the disproportion between the relatively long florets and the shorter involucral bracts [10,103]. The specific epithet discolor reflects the bicolor foliage, which is dark greenish on the adaxial (upper) surface and pale, silver-gray on the abaxial (lower) surface (Figure 3). This feature informs the species' common name "coastal silver oak" [103]. The plant is variably evergreen or deciduous and may attain a height of up to 30 m [104,105]. Its bark ranges in coloration from dark gray to reddish-brown and is lenticellate and fissured, while the branches are characteristically rough. The leaves are lanceolate to ovate, with entire or slightly serrated margins, and display dual coloration. Inflorescences are borne in axillary panicles, comprising numerous creamy-white florets. The fruit is a cypsela (achene) and is capped by a pappus of cream to brown bristles, facilitating anemochory [106]. The plant generally prefers dunes and coastal places as habitats and can grow to about 10 m high, depending on environmental factors, so it might be a bushy shrub or a small tree of about 10 m high [107]. Among Afrikaans people, it is called *Kusvaalbos*, *Muakawura*, and *Mupasa* in *Shona* and *Iphahla/Umpahla* in *IsiZulu* in Southern Africa. *Brachylaena discolor* is distributed across Southern Africa, including Zimbabwe, Botswana, Eswatini, Zambia, Mozambique, and South Africa. It occurs in varied ecological niches such as termite mounds, sandy soils, secondary woodlands, evergreen forests, forest margins, rocky slopes, and hillsides, at elevations ranging from sea level to approximately 1900 m above sea level [105,108].



Figure 3. Morphology of *Brachylaena discolor*.

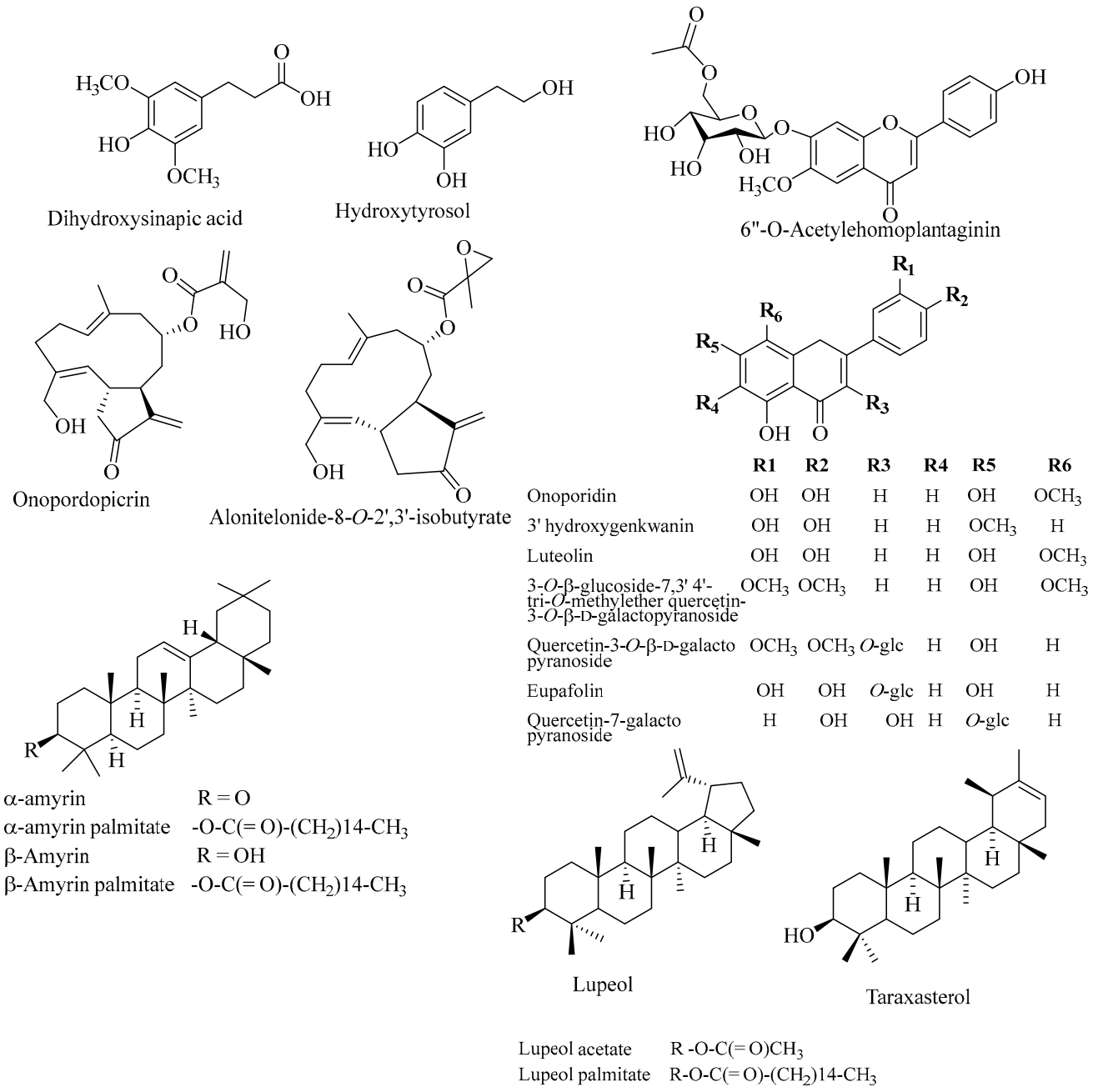
1.8. Ethnopharmacological Utilization of Brachylaena discolor

Brachylaena discolor is widely used among traditional healers across Southern African countries in Botswana, Eswatini, Mozambique, South Africa, Zambia, and Zimbabwe [19]. The roots and leaves are frequently traded in herbal markets within KwaZulu-Natal and Gauteng provinces of South Africa [109]. Traditional remedies use aqueous extractions (infusions or decoctions) of the plant twigs, stems, bark, roots, or leaves. For instance, the leaves are boiled and the infusion is taken orally [110]. *B. discolor* is commonly mixed with other herbs to treat many illnesses [111]. Several ethnomedicinal uses include anti-helmintics, general tonics, treatments for ailments such as female infertility; dermatological conditions; renal disorders; anticancer, anthelmintic, and antihyperglycemic effects; gas-

trointestinal disturbances; and respiratory tract infections [112]. In South Africa, *Brachylaena discolor* is among the species commonly used to manage diabetes, alongside *B. ilicifolia* and *B. elliptica* [113–115]. Topical preparations incorporating *B. discolor* twigs with species such as *Euphorbia tirucalli*, *Hypoxis hemerocallidea*, *Ozoroa engleri*, and *Senecio serratuloides* are traditionally used to manage sores and cutaneous infections, thus making it ideal to treat diabetes [115]. Ethnopharmacological studies revealed that these compounds contribute to other biological activities such as antibacterial, cytotoxic, antifungal, and anti-leishmanial effects [16].

1.9. Chemical Components of *Brachylaena discolor* and Their Role in Anti-Diabetic Activity

Several chemical compounds have been identified from *B. discolor*, including alkaloids, flavonoids, phenolic acids, phlobotannins, saponins, sesquiterpene lactones, steroids, tannins and terpenoids, α-amyrin acetate, β-amyrin acetate, ψ-taraxasterol acetate, taraxasterol acetate, lupeol, α-amyrin palmitate, β-amyrin palmitate and lupeol palmitate, α-amyrin, β-amyrin, and taraxasterol, as shown in Figure 4 and Table 2 [103]. Other reported isolated compounds include lupeol acetate, β-sitosteryl linolenate, α-tocopherol, genkwanin 5-*O*-β-D-glucopyranoside, onopordopicrin, and its epoxide derivatives such as alonitelonide-8-*O*-2′,3′-isobutyrate, hydroxytyrosol, dihydroxysinapic acid, 6″-*O*-acetyl 3′-hydroxygenkwanin, 6″-*O*-acetyl-homoplantaginin, dihydroxysinapic acid, quercetin3-*O*-glucoside-7, 3′, 4′-trimethyl ether, onoporidin, quercetin-7-galactopyranoside, luteolin, homoplantaginin, onoporidin, 3′-hydroxygenkwanin, luteolin, quercetin 3-*O*-glucoside-7, 3′, 4′-trimethyl ether, quercetin 3-*O*-β-D-galactopyranoside, eupafolin, quercetin-7-galactopyranoside-15-Dihydrodehydrozaluzanin C, 3-acetoxy-12-lupene, dehydrobrachylaenolide, di-hydrodehydrocostuslactone, brachylaenolide, dehydrocostuslactone, germacrene D, costunolide, dehydrozaluzanin C, furanoheliangolide, germacranolide, genkwanin-5-*O*-D-glucopyranoside, germacronolide epoxide, hydroxytyrosol, lupeol acetate, onopordopicrin, salonitenolide, 9-oxo-nerolidol, salonitenolide-8-*O*-2,3-epoxyisobutyrate, and linolenic acid [103,114,116–118]. It was stated that the daily administration of β-amyrin palmitate showed strong anti-diabetic activity in alloxan-induced diabetic and streptozotocin-induced diabetic rats at 50 mg/kg body weight [119]. β-amyrin showed significant protection of β-cell integrity in streptozotocin-challenged mice [120]. Xu et al. [121] also found that β-amyrin improved kidney injury in diabetic nephropathy mice and suppressed the inflammatory response and apoptosis of HG-stimulated HK-2 cells. The oral administration of α- and β-amyrins compounds showed significant reductions in blood glucose levels, total cholesterol, and serum triglyceride [122]. It was stated that at a dose of 100 mg/kg, there was a significant reduction in blood glucose and a strong lipid-lowering effect [122]. These findings revealed the potential of α- and β-amyrins to enhance glucose metabolism and preserve pancreatic functions. β-amyrin also has significant antibacterial and anti-diabetic properties through its enzymatic inhibitory activity, notably achieving an inhibition rate of between 49.8 ± 0.3% and 69.3 ± 1.0% at a concentration of 10 µg/mL in α-amylase inhibitory activity studies [123]. It was reported that β-amyrin at doses of 10 and 50 mg/kg did not exhibit a significant decrease in food and water consumption in 4 weeks of treatment. Still, noticeable signs of toxicity were observed at doses greater than 30 mg/kg administered orally. The toxicity signs included tremor, ataxia, increased respiration, and decreased activity [124]. β-amyrin palmitate possibly blocked the entry of glucose from the intestine. This resulted in a significant decrease ($p < 0.001$) in the non-fasting levels of blood glucose without interfering with the body weight and liver weight. From our findings, toxicological information on *B. discolor* was limited, and the extract exhibited activities with a half-maximal lethal dose (LD_{50}) value of 0.004 mg/mL [125].



	R1	R2	R3	R4	R5	R6
Onoporidin	OH	OH	H	H	OH	OCH_3
3' hydroxygenkwanin	OH	OH	H	H	OCH_3	H
Luteolin	OH	OH	H	H	OH	OCH_3
3-*O*-β-glucoside-7,3' 4'-tri-*O*-methylether quercetin-3-*O*-β-D-galactopyranoside	OCH_3	OCH_3	H	H	OH	OCH_3
Quercetin-3-*O*-β-D-galacto pyranoside	OCH_3	OCH_3	*O*-glc	H	OH	H
Eupafolin	OH	OH	*O*-glc	H	OH	H
Quercetin-7-galacto pyranoside	H	OH	OH	H	*O*-glc	H

Figure 4. Chemical components from *Brachylaena discolor*.

1.10. Anti-Diabetic Activity of Brachylaena discolor

Brachylaena discolor is a major plant used in managing type 2 diabetes in the Eastern Cape of South Africa [112]. The biological relevance of the crude extract was reported using dichloromethane–methanol extraction for its ability to inhibit α-glucosidase activity [126–128]. The findings demonstrated that the extract showed superior inhibitory activity compared to acarbose, a standard pharmaceutical agent. However, attempts to evaluate the enzyme inhibitory potential of the isolated pure compounds were unsuccessful due to their poor solubility in the assay medium [128]. Given the diverse traditional applications and promising preliminary pharmacological evidence, further chemical studies should focus on elucidating other active components of *B. discolor* (Table 2). The effects of organic and aqueous extracts derived from the leaves, roots, and stems of *B. discolor* on glucose uptake in 3T3-L1 adipocytes and liver cells improved glucose utilization across many cell lines, thus indicating promising anti-diabetic activity [129]. The methanolic leaf

extracts of *B. discolor* administered to streptozotocin-induced diabetic rats at 50 mg/kg and 150 mg/kg resulted in a significant reduction in blood glucose levels [113]. Further alterations in body weight and key biochemical parameters such as total bilirubin, creatinine, and alkaline phosphatase confirmed the potential of the extract to have anti-diabetic efficacy. The inhibitory effects of aqueous and methanolic leaf extracts on the digestive enzymes α-amylase and α-glucosidase can be used to manage postprandial hyperglycemia. In a study conducted by Mellem and colleagues [126] on the antioxidant activity of aqueous and methanolic extracts, it was found that methanol and aqueous extracts exhibit IC_{50} values of 92.3 µg/mL and 82.8 µg/mL, respectively, and a moderate free radical scavenging activity was shown [126]. The *B. discolor* extracts demonstrated notable inhibitory activity, with IC_{50} values ranging from 1.8 to 11.0 mg/mL, in comparison to the control, with IC_{50} values of 0.03–1.2 mg/mL [113]. Adamu et al. reported that the acetone extracts revealed moderate antioxidant capacity, with a Trolox Equivalent Antioxidant Capacity (TEAC) value of 0.2 in the ABTS assay and an EC_{50} of 2.6 mg/mL in the DPPH assay. Dikhoba et al. further stated the effects of the acetone leaf extract of *B. discolor* on ABTS and DPPH, and IC_{50} values of 0.03 mg/mL and 0.2 mg/mL were reported, benchmarked against ascorbic acid (0.5 mg/mL). As a result, it was found that *B. discolor* is a rich source of antioxidant compounds [127]. However, it was stated that the *Brachylaena discolor* plant is still underutilized in managing diabetes and that the anti-diabetic potential of *Brachylaena discolor* should be elucidated to uncover the active ingredients and other pharmacological activities [20,129].

Table 2. Phytochemical components present in *Brachylaena discolor*.

Plant Sources	Compound Class	Compound Name	Molecular Weight (g/mol)	Chemical Formula	CAS Number	Biological Activity	References
	Triterpene						
Stems Fruits Leaves		α-amyrin	456.7	$C_{30}H_{48}O_3$	638-95-9	enhances periodontal inflammation, anti-diabetic effects, neutrophil infiltration, and oxidative stress management	[130,131]
Stems Fruits Leaves		β-amyrin	426.0	$C_{30}H_{50}O$	559-70-6	anti-inflammatory, antibacterial, antinociceptive (pain-relieving), hepatoprotective (liver-protective), and anti-diabetic effects, neuroprotective agent, antifungal agent, and antioxidant properties.	[131]
Stems Fruits Leaves		α-amyrin palmitate	665.1	$C_{46}H_{80}O_2$	22255-10-3	anti-inflammatory activity, improves brain neuronal hormones, anti-diabetic activity, neutrophil infiltration, and helps in managing oxidative stress	[131]
Stems Fruits Leaves		β-amyrin palmitate	665.1	$C_{46}H_{80}O_2$	5973-06-8	antidepressant, hypoactive, anti-diabetic, and hypolipidemic activities	[122]
Stems Fruits Leaves		α-amyrin acetate	468.0	$C_{32}H_{52}O_2$	863-76-3.	anti-inflammatory, antihyperglycemic, hepatoprotective, and antifungal effects	[131]
Stems Fruits Leaves		ψ-taraxasterol acetate	469.4	$C_{32}H_{53}O_2$	4586-65-6	neuroprotective, anticancer, and anti-diabetic properties, inhibiting pro-inflammatory cytokines and reducing oxidative stress	[132,133]
Stems Fruits Leaves		taraxasterol acetate	468.8	$C_{32}H_{52}O_2$	6426-43-3	anti-inflammatory, anticancer, antioxidant, and neuroprotective activities.	[132,133]
Stems Fruits Leaves		taraxasterol	426.7	$C_{30}H_{50}O$	1059-14-9	anti-inflammatory, anticancer, antioxidant, and neuroprotective activities.	[132,133]
Stems Fruits Leaves		lupeol acetate	468	$C_{32}H_{53}O_2$	1617-68-1	acts as an anti-inflammatory agent, has anti-diabetic activity, suppresses pro-inflammatory cytokines, has antioxidant and neutralizing anti-venom components and improves antioxidant status of cells.	[128]
Stems Fruits Leaves		lupeol palmitate	663.6	$C_{46}H_{80}O_2$	32214-80-5	reduces blood glucose levels, improves antioxidant levels, and reduces inflammatory markers.	[134]
Stems Fruits Leaves		lupeol	409.4	$C_{30}H_{49}$	545-47-1	reduces blood glucose levels, improves antioxidant levels, and reduces inflammatory markers	[134]
Stems Fruits Leaves		luteolin	286.2	$C_{15}H_{10}O_6$	491-70-3	improves glucose and lipid metabolism by reducing insulin resistance, enhancing glucose uptake, inhibiting inflammatory pathways, and scavenging free radicals.	[135]
	Sesquiterpene						
Leaves Stem Fruits		onopordopicrin	349.1651	$C_{19}H_{24}O_6$	19889-00-0	antioxidant, anti-inflammatory, and cytotoxic activities.	[103,114,136]

Table 2. *Cont.*

Plant Sources	Compound Class	Compound Name	Molecular Weight (g/mol)	Chemical Formula	CAS Number	Biological Activity	References
	Organic acids						
Stems Fruits Leaves		dihydroxysinapic acid	180.2	C_9H_8O	331-39-5	potent antioxidant, anti-inflammatory, and anticancer properties, along with antiviral, anti-diabetic, antimicrobial, cardioprotective, immune-stimulatory, and neuroprotective effects.	[137,138]
Stems Fruits Leaves		salonitelonide-8-*O*-,3-isobutyrate	348.1570	$C_{19}H_{24}O_6$	Not known	anti-leishmanicidal activity and treats stomach pain, tuberculosis, and diabetes.	[103,114,136]
	Flavonoids						
Stems Fruits Leaves		hydroxytyrosol	154.2	$C_8H_{10}O_3$	10597-60-1	strong antioxidant and anti-inflammatory effects and neuroprotective, cardioprotective, and anticancer properties by inhibiting tumor cell growth, inducing apoptosis, and improving cardiovascular health markers.	[137,139]
Stems Fruits Leaves		eupafolin	316.3	$C_{16}H_{12}O_7$	520-11-6	increases glucose metabolism and antioxidant and anti-inflammatory activity.	[140]
Stems Fruits Leaves		3′-hydroxygenkwanin	300.3	$C_{16}H_{12}O_6$	20243-59-8	offers cardiovascular protection, inhibits cancer cell growth, and reverses drug-induced DNA damage repair inhibition in liver cancer cells	[141]
	Flavonoid glycosides						
Stems Fruits Leaves		quercetin 3-*O*-glucoside-7,3′,4′-trimethyl ether	622.5	$C_{27}H_{30}O_{17}$	Not known	anti-diabetic, antibacterial, anti-inflammatory, and antioxidant effects	[142]
Stems Fruits Leaves		quercetin-3-*O*-*β*-D-galactopyranoside	464.4	$C_{21}H_{20}O_{12}$	482-36-0	anti-diabetic, antibacterial, anti-inflammatory, and antioxidant effects	[143]
Stems Fruits Leaves		quercetin-7-galactopyranoside	464.4	$C_{21}H_{20}O_{12}$	482-36-0	antioxidant, anti-inflammatory, anti-diabetic, and cytoprotective effects and manages oxidative stress.	[143]

2. Conclusions

This study documented the anti-diabetic potential of *Silybum marianum* and *Brachylaena discolor* from the Asteraceae family to manage type 2 diabetes mellitus. Knowledge of their ethnobotanical utilization justified their pharmacological investigation as anti-diabetic plants. Several chemical components isolated from these plants have been shown to have the potential to lower blood glucose levels in many experimental studies. However, toxicological information on their long-term effects is limited, and safe dosages are a major concern. Commercialization of these plants is encouraged to provide economic benefits, and they are recommended as an add-on vegetable to dietary meals to lower blood sugar levels.

Author Contributions: Conceptualization, E.A.A. and A.J.A.; validation, A.J.A. and E.A.A.; formal analysis, E.A.A.; investigation, E.A.A.; writing—original draft preparation, E.A.A.; writing—review and editing, E.A.A. and A.J.A.; supervision, A.J.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding and the APC was funded by the University of Fort Hare, South Africa.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflicts of Interest: The authors declare that there are no conflicts of interest.

References

1. Galicia-Garcia, U.; Benito-Vicente, A.; Jebari, S.; Larrea-Sebal, A.; Siddiqi, H.; Uribe, K.B.; Ostolaza, H.; Martín, C. Pathophysiology of Type 2 Diabetes Mellitus. *Int. J. Mol. Sci.* **2020**, *21*, 6275. [CrossRef] [PubMed]
2. Ojo, O.A.; Ibrahim, H.S.; Rotimi, D.E.; Ogunlakin, A.D.; Ojo, A.B. Diabetes Mellitus: From Molecular Mechanism to Pathophysiology and Pharmacology. *Med. Nov. Technol. Devices* **2023**, *19*, 100247. [CrossRef]
3. International Diabetes Federation. *IDF Diabetes Atlas*; International Diabetes Federation: Brussels, Belgium, 2025.
4. Saeedi, P.; Petersohn, I.; Salpea, P.; Malanda, B.; Karuranga, S.; Unwin, N.; Colagiuri, S.; Guariguata, L.; Motala, A.A.; Ogurtsova, K.; et al. Global and Regional Diabetes Prevalence Estimates for 2019 and Projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th Edition. *Diabetes Res. Clin. Pract.* **2019**, *157*, 107843. [CrossRef] [PubMed]
5. Nyakudya, T.T.; Tshabalala, T.; Dangarembizi, R.; Erlwanger, K.H.; Ndhlala, A.R. The Potential Therapeutic Value of Medicinal Plants in the Management of Metabolic Disorders. *Molecules* **2020**, *25*, 2669. [CrossRef] [PubMed]
6. Newman, D.J.; Cragg, G.M. Natural Products as Sources of New Drugs from 1981 to 2014. *J. Nat. Prod.* **2016**, *79*, 629–661. [CrossRef]
7. Baharvand-Ahmadi, B.; Bahmani, M.; Tajeddini, P.; Naghdi, N.; Rafieian-Kopaei, M. An Ethno-Medicinal Study of Medicinal Plants Used for the Treatment of Diabetes. *J. Nephropathol.* **2015**, *5*, 44–50. [CrossRef]
8. Sriraman, S.; Sreejith, D.; Andrew, E.; Okello, I.; Willcox, M. Use of Herbal Medicines for the Management of Type 2 Diabetes: A Systematic Review of Qualitative Studies. *Complement. Ther. Clin. Pract.* **2023**, *53*, 101808. [CrossRef]
9. Nurcahyanti, A.D.R.; Jap, A.; Lady, J.; Prismawan, D.; Sharopov, F.; Daoud, R.; Wink, M.; Sobeh, M. Function of Selected Natural Antidiabetic Compounds with Potential against Cancer via Modulation of the PI3K/AKT/MTOR Cascade. *Biomed. Pharmacother.* **2021**, *144*, 112138. [CrossRef]
10. Sagbo, I.J.; Van De Venter, M.; Koekemoer, T.; Bradley, G. In Vitro Antidiabetic Activity and Mechanism of Action of Brachylaena Elliptica (Thunb.) DC. *Evid.-Based Complement. Altern. Med.* **2018**, *2018*, 4170372. [CrossRef]
11. McGaw, L.J.; Eloff, J.N. Ethnoveterinary Use of Southern African Plants and Scientific Evaluation of Their Medicinal Properties. *J. Ethnopharmacol.* **2008**, *119*, 559–574. [CrossRef]
12. Liu, C.; Fan, H.; Li, Y.; Xiao, X. Research Advances on Hepatotoxicity of Herbal Medicines in China. *BioMed Res. Int.* **2016**, *2016*, 7150391. [CrossRef]
13. World Health Organization. *WHO Global Report on Traditional and Complementary Medicine 2019*; World Health Organization: Geneva, Switzerland, 2019; ISBN 9789241515436.
14. Banwo, K.; Olojede, A.O.; Adesulu-Dahunsi, A.T.; Verma, D.K.; Thakur, M.; Tripathy, S.; Singh, S.; Patel, A.R.; Gupta, A.K.; Aguilar, C.N.; et al. Functional Importance of Bioactive Compounds of Foods with Potential Health Benefits: A Review on Recent Trends. *Food Biosci.* **2021**, *43*, 101320. [CrossRef]

15. Goyal, S.N.; Prajapati, C.P.; Gore, P.R.; Patil, C.R.; Mahajan, U.B.; Sharma, C.; Talla, S.P.; Ojha, S.K. Therapeutic Potential and Pharmaceutical Development of Thymoquinone: A Multitargeted Molecule of Natural Origin. *Front. Pharmacol.* **2017**, *8*, 656. [CrossRef] [PubMed]
16. Erasto, P.; Adebola, P.O.; Grierson, D.S.; Afolayan, A.J. An Ethnobotanical Study of Plants Used for the Treatment of Diabetes in the Eastern Cape Province, South Africa. *Afr. J. Biotechnol.* **2005**, *4*, 1458–1460.
17. Afolayan, A.J.; Sunmonu, T.O. In Vivo Studies on Antidiabetic Plants Used in South African Herbal Medicine. *J. Clin. Biochem. Nutr.* **2010**, *47*, 98–106. [CrossRef] [PubMed]
18. Deutschlnder, M.S.; Lall, N.; Van De Venter, M. Plant Species Used in the Treatment of Diabetes by South African Traditional Healers: An Inventory. *Pharm. Biol.* **2009**, *47*, 348–365. [CrossRef]
19. Japhet, M.; Mlungisi, N.; Exnevia, G. Mechanisms of Action of Traditional Herbal Medicines Used in the Management of Diabetes Mellitus: A Review of the Literature. *Afr. J. Tradit. Complement. Altern. Med.* **2017**, *14*, 156–165. [CrossRef]
20. Sagbo, I.J.; Hussein, A.A. Antidiabetic Medicinal Plants Used in the Eastern Cape Province of South Africa: An Updated Review. *Processes* **2022**, *10*, 1817. [CrossRef]
21. Mohanta, Y.K.; Mishra, A.K.; Nongbet, A.; Chakrabartty, I.; Mahanta, S.; Sarma, B.; Panda, J.; Panda, S.K. Potential Use of the Asteraceae Family as a Cure for Diabetes: A Review of Ethnopharmacology to Modern Day Drug and Nutraceuticals Developments. *Front. Pharmacol.* **2023**, *14*, 1153600. [CrossRef]
22. Ghazal, E.M.A.A. Taxonomic Studies on the Family Asteraceae (Compositae) of Hajjah Governorate, West of Yemen. *J. Med. Plants Stud.* **2019**, *7*, 90–100.
23. Hussain, A. Potential Medicinal Uses of Plants From the Asteraceae (Compositae) Family in Pakistan: A Literature Review Based Meta-Analysis. *J. Herb. Med.* **2024**, *45*, 100871. [CrossRef]
24. Wallace, C.E.; Elston, D.M. Asteraceae Dermatitis: Everyday Plants With Allergenic Potential. *Cutis* **2024**, *114*, E18–E21. [CrossRef] [PubMed]
25. Maroyi, A. Review of Phytochemistry, Biological Activities and Therapeutic Potential of Brachylaena Discolor. *Int. J. Res. Pharm. Sci.* **2020**, *11*, 5626–5633. [CrossRef]
26. Rolnik, A.; Olas, B. The Plants of the Asteraceae Family as Agents in the Protection of Human Health. *Int. J. Mol. Sci.* **2021**, *22*, 3009. [CrossRef]
27. Maaloul, S.; Mahmoudi, M.; Mighri, H.; Ghzaiel, I.; Bouhamda, T.; Boughalleb, F.; El Midaoui, A.; Vejux, A.; Lizard, G.; Abdellaoui, R. Tunisian Silybum Species: Important Sources of Polyphenols, Organic Acids, Minerals, and Proteins across Various Plant Organs. *Plants* **2024**, *13*, 989. [CrossRef]
28. Mahmoud, N.N.; Selim, M.T. Phytochemical Analysis and Antimicrobial Activity of *Silybum marianum* L. via Multi-Solvent Extraction. *AMB Express* **2025**, *15*, 122. [CrossRef] [PubMed]
29. Javeed, A.; Ahmed, M.; Sajid, A.R.; Sikandar, A.; Aslam, M.; Ul Hassan, T.; Samiullah; Nazir, Z.; Ji, M.; Li, C. Comparative Assessment of Phytoconstituents, Antioxidant Activity and Chemical Analysis of Different Parts of Milk Thistle *Silybum marianum* L. *Molecules* **2022**, *27*, 2641. [CrossRef]
30. Krystyjan, M.; Gumul, D.; Adamczyk, G. The Effect of Milk Thistle (*Silybum marianum* L.) Fortification, Rich in Dietary Fibre and Antioxidants, on Structure and Physicochemical Properties of Biscuits. *Appl. Sci.* **2022**, *12*, 12501. [CrossRef]
31. Iraqi, O.; Aouji, M.; Oubihi, A.; Imtara, H.; Noman, O.M.; Mothana, R.A.; Tarayrah, M.; Taboz, Y.; Habsaoui, A. Exploring the Chemical Composition, Antioxidant, and Antibacterial Properties of Milk Thistle (*Silybum marianum* L.). *Front. Sustain. Food Syst.* **2025**, *9*, 1551584. [CrossRef]
32. Djellouli, M.; Moussaoui, A.; Benmehdi, H.; Belabbes, A.; Badraoui, M.; Slimani, N.; Hamidi, N. Ethnopharmacological Study and Phytochemical Screening of Three Plants (Asteraceae Family) from the Region of South West Algeria. *Asian J. Nat. Appl. Sci.* **2013**, *2*, 59–65.
33. Maaloul, S.; Ghzaiel, I.; Mahmoudi, M.; Mighri, H.; Pires, V.; Vejux, A.; Martine, L.; de Barros, J.P.P.; Prost-Camus, E.; Boughalleb, F.; et al. Characterization of *Silybum marianum* and *Silybum eburneum* Seed Oils: Phytochemical Profiles and Antioxidant Properties Supporting Important Nutritional Interests. *PLoS ONE* **2024**, *19*, e0304021. [CrossRef] [PubMed]
34. Porwal, O.; Mohammed Ameen, M.S.; Anwer, E.T.; Uthirapathy, S.; Ahamad, J.; Tahsin, A. *Silybum marianum* (Milk Thistle): Review on Its Chemistry, Morphology, Ethno Medical Uses, Phytochemistry and Pharmacological Activities. *J. Drug Deliv. Ther.* **2019**, *9*, 199–206. [CrossRef]
35. Arshad, A.; Pervaiz, S.; Errum, A.; Mahmood, A.; Asghar, H.; Maqsood, S.; Shamim, S. Evaluation of Antidiabetic Effect of *Silybum marianum* and Cichorium Intybus Extracts. *Pak. J. Med. Health Sci.* **2022**, *16*, 820–823. [CrossRef]
36. Amjadi, E.; Ganjeali, A.; Shakeri, A.; Lahouti, M.; Tavakoli, S. Ecophysiological and Phytochemical Insights in to *Silybum marianum*: Geographic Variations in Antioxidant Activity and Silybin Content. *Russ. J. Plant Physiol.* **2025**, *72*, 45. [CrossRef]
37. Marceddu, R.; Dinolfo, L.; Carrubba, A.; Sarno, M.; Di Miceli, G. Milk Thistle (*Silybum marianum* L.) as a Novel Multipurpose Crop for Agriculture in Marginal Environments: A Review. *Agronomy* **2022**, *12*, 729. [CrossRef]

38. Eldalawy, R.; Al-Ani, W.M.K.; Abdul Kareem, W. Phenotypic, Anatomical and Phytochemical Investigation of Iraqi *Silybum marianum*. *J. Phys. Conf. Ser.* **2021**, *1879*, 022029. [CrossRef]
39. Zhang, X.; Liu, M.; Wang, Z.; Wang, P.; Kong, L.; Wu, J.; Wu, W.; Ma, L.; Jiang, S.; Ren, W.; et al. A Review of the Botany, Phytochemistry, Pharmacology, Synthetic Biology and Comprehensive Utilization of *Silybum marianum*. *Front. Pharmacol.* **2024**, *15*, 1417655. [CrossRef]
40. Liu, Y.; Liu, Z.; Zheng, Y. Research Progress of Milk Thistle. *J. Ginseng Res.* **2016**, *28*, 55–58.
41. Bijak, M. Silybin, a Major Bioactive Component of Milk Thistle (*Silybum marianum* L. Gaernt.)—Chemistry, Bioavailability, and Metabolism. *Molecules* **2017**, *22*, 1942. [CrossRef]
42. Dagli Gul, A.S.; Boyuk Ozcan, G.; Arihan, O. Silibinin as a Promising Treatment for Diabetes: Insights into Behavioral and Metabolic Changes in an Animal Model. *Food Sci. Nutr.* **2024**, *12*, 3336–3345. [CrossRef] [PubMed]
43. Ferysiuk, K.; Wójciak, K.M.; Materska, M. Phytochemical Profile of *Silybum marianum* (L.) Gaertn. and Graminis Rhizoma and Its Influence on the Bioactivity and Shelf Life of Industrially Produced Pâté. *Int. J. Food Sci. Technol.* **2020**, *55*, 1586–1598. [CrossRef]
44. Marmouzi, I.; Bouyahya, A.; Ezzat, S.M.; El Jemli, M.; Kharbach, M. The Food Plant *Silybum marianum* (L.) Gaertn.: Phytochemistry, Ethnopharmacology and Clinical Evidence. *J. Ethnopharmacol.* **2021**, *265*, 113303. [CrossRef]
45. Vahabzadeh, M.; Amiri, N.; Karimi, G. Effects of Silymarin on Metabolic Syndrome: A Review. *J. Sci. Food Agric.* **2018**, *98*, 4816–4823. [CrossRef]
46. Tileshova, M.; Yessimsiitova, Z.; Alseitova, F.; Chunetova, Z.; Pravin, N.; Tileubayeva, Z.; Ryskali, T.; Yeltay, G. Phytochemical Study of Milk Thistle, *Silybum marianum* (L.) Gaertn. *Casp. J. Environ. Sci.* **2024**, *22*, 1293–1299. [CrossRef]
47. Bouderba, S.; Sanchez-Martin, C.; Villanueva, G.R.; Detaille, D.; Koceïr, E.A. Beneficial Effects of Silibinin against the Progression of Metabolic Syndrome, Increased Oxidative Stress, and Liver Steatosis in *Psammomys obesus*, a Relevant Animal Model of Human Obesity and Diabetes. *J. Diabetes* **2014**, *6*, 184–192. [CrossRef]
48. Awla, N.J.; Naqishbandi, A.M.; Baqi, Y. Preventive and Therapeutic Effects of *Silybum marianum* Seed Extract Rich in Silydianin and Silychristin in a Rat Model of Metabolic Syndrome. *ACS Pharmacol. Transl. Sci.* **2023**, *6*, 1715–1723. [CrossRef] [PubMed]
49. Abdullaev, A.A.; Inamjanov, D.R.; Abduazimova, D.S.; Omonturdiyev, S.Z.; Gayibov, U.G.; Gayibova, S.N.; Aripov, T.F. Sílybum Mariánum's Impact On Physiological Alterations and Oxidative Stress In Diabetic Rats. *Biomed. Pharmacol. J.* **2024**, *17*, 1291–1300. [CrossRef]
50. Krepkova, L.V.; Babenko, A.N.; Saybel', O.L.; Lupanova, I.A.; Kuzina, O.S.; Job, K.M.; Sherwin, C.M.; Enioutina, E.Y. Valuable Hepatoprotective Plants-How Can We Optimize Waste Free Uses of Such Highly Versatile Resources? *Front. Pharmacol.* **2021**, *12*, 738504. [CrossRef] [PubMed]
51. Liu, C. Study on Extraction Technology of Milk Thistle Protein Functional Evaluation and Preparation of Bread. Master's Thesis, Harbin University of Commerce, Harbin, China, 2021.
52. Soleimani, V.; Delghandi, P.S.; Moallem, S.A.; Karimi, G. Safety and Toxicity of Silymarin, the Major Constituent of Milk Thistle Extract: An Updated Review. *Phyther. Res.* **2019**, *33*, 1627–1638. [CrossRef]
53. European Medicines Agency (EMA); Committee on Herbal Medicinal Products (HMPC). *Final Assessment Report on Silybum marianum (L.) Gaertn., Fructus*; Doc. Ref. EMA/HMPC/294188/2013; European Medicines Agency: Amsterdam, The Netherlands, 2018; Available online: https://www.ema.europa.eu/en/documents/herbal-report/final-assessment-report-silybum-marianum-l-gaertn-fructus_en.pdf (accessed on 19 October 2025).
54. Bijak, M.; Synowiec, E.; Sitarek, P.; Sliwiński, T.; Saluk-Bijak, J. Evaluation of the Cytotoxicity and Genotoxicity of Flavonolignans in Different Cellular Models. *Nutrients* **2017**, *9*, 1356. [CrossRef]
55. Pickova, D.; Ostry, V.; Toman, J.; Malir, F. Presence of Mycotoxins in Milk Thistle (*Silybum marianum*) Food Supplements: A Review. *Toxins* **2020**, *12*, 782. [CrossRef]
56. Maaliah, M.S.; Haddadin, M.; Abdalla, S. Hypolipidemic and Hypoglycemic Effects of *Silybum marianum* (L.) Gaertn. (Milk Thistle) Ethanol Seed Extract in Streptozotocin-Induced Diabetes in Rats. *Pharmacogn. Mag.* **2024**, *20*, 841–852. [CrossRef]
57. Kazazis, C.E.; Evangelopoulos, A.A.; Kollas, A.; Vallianou, N.G. The Therapeutic Potential of Milk Thistle in Diabetes. *Rev. Diabet. Stud.* **2014**, *11*, 167–174. [CrossRef]
58. Lekmine, S.; Benslama, O.; Ola, M.S.; Touzout, N.; Moussa, H.; Tahraoui, H.; Hafsa, H.; Zhang, J.; Amrane, A. Preliminary Data on *Silybum marianum* Metabolites: Comprehensive Characterization, Antioxidant, Antidiabetic, Antimicrobial Activities, LC-MS/MS Profiling, and Predicted ADMET Analysis. *Metabolites* **2025**, *15*, 13. [CrossRef] [PubMed]
59. Rysava, A.; Valentova, K.; Cizkova, K.; Vostalova, J.; Zalesak, B.; Rajnochova Svobodova, A. Potential of Silymarin and Its Polyphenols to Affect Nrf2 Signalling Pathway in Human Skin Cells. *Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub.* **2025**, *169*, 1–10. [CrossRef] [PubMed]
60. Xu, F.; Yang, J.; Negishi, H.; Sun, Y.; Li, D.; Zhang, X.; Hayashi, T.; Gao, M.; Ikeda, K.; Ikejima, T. Silibinin Decreases Hepatic Glucose Production through the Activation of Gut-Brain-Liver Axis in Diabetic Rats. *Food Funct.* **2018**, *9*, 4926–4935. [CrossRef] [PubMed]

61. Zhang, Y.; Hai, J.; Cao, M.; Zhang, Y.; Pei, S.; Wang, J.; Zhang, Q. Silibinin Ameliorates Steatosis and Insulin Resistance during Non-Alcoholic Fatty Liver Disease Development Partly through Targeting IRS-1/PI3K/Akt Pathway. *Int. Immunopharmacol.* **2013**, *17*, 714–720. [CrossRef]
62. Gu, M.; Zhao, P.; Huang, J.; Zhao, Y.; Wang, Y.; Li, Y.; Li, Y.; Fan, S.; Ma, Y.M.; Tong, Q.; et al. Silymarin Ameliorates Metabolic Dysfunction Associated with Diet-Induced Obesity via Activation of Farnesyl X Receptor. *Front. Pharmacol.* **2016**, *7*, 345. [CrossRef]
63. Borymska, W.; Zych, M.; Dudek, S.; Kaczmarczyk-Sedlak, I. Silymarin from Milk Thistle Fruits Counteracts Selected Pathological Changes in the Lenses of Type 1 Diabetic Rats. *Nutrients* **2022**, *14*, 1450. [CrossRef]
64. Miranda, L.M.; Agostini, L.; Lima, W.; Camini, F.; Costa, D. Silymarin Attenuates Hepatic and Pancreatic Redox Imbalance Independent of Glycemic Regulation in the Alloxan-Induced Diabetic Rat Model. *Biomed. Environ. Sci.* **2020**, *33*, 690–700. [CrossRef]
65. Wang, Y.; Yuan, A.J.; Wu, Y.J.; Wu, L.M.; Zhang, L. Silymarin in Cancer Therapy: Mechanisms of Action, Protective Roles in Chemotherapy-Induced Toxicity, and Nanoformulations. *J. Funct. Foods* **2023**, *100*, 105384. [CrossRef]
66. Wang, X.; Zhang, Z.; Wu, S.C. Health Benefits of *Silybum marianum*: Phytochemistry, Pharmacology, and Applications. *J. Agric. Food Chem.* **2020**, *68*, 11644–11664. [CrossRef]
67. Ebrahimpour-koujan, S.; Gargari, B.P.; Mobasseri, M.; Valizadeh, H.; Asghari-Jafarabadi, M. Lower Glycemic Indices and Lipid Profile among Type 2 Diabetes Mellitus Patients Who Received Novel Dose of *Silybum marianum* (L.) Gaertn. (Silymarin) Extract Supplement: A Triple-Blinded Randomized Controlled Clinical Trial. *Phytomedicine* **2018**, *44*, 39–44. [CrossRef]
68. Tuorkey, M.J.; El-Desouki, N.I.; Kamel, R.A. Cytoprotective Effect of Silymarin against Diabetes-Induced Cardiomyocyte Apoptosis in Diabetic Rats. *Biomed. Environ. Sci.* **2015**, *28*, 36–43. [CrossRef] [PubMed]
69. Rizzo, M.; Colletti, A.; Penson, P.E.; Katsiki, N.; Mikhailidis, D.P.; Toth, P.P.; Gouni-Berthold, I.; Mancini, J.; Marais, D.; Moriarty, P.; et al. Nutraceutical Approaches to Non-Alcoholic Fatty Liver Disease (NAFLD): A Position Paper from the International Lipid Expert Panel (ILEP). *Pharmacol. Res.* **2023**, *189*, 106679. [CrossRef] [PubMed]
70. López-pérez, S.J.; Morales-villagrán, A.; Medina-ceja, L. Effect of Perinatal Asphyxia and Carbamazepine Treatment on Cortical Dopamine and DOPAC Levels. *J. Biomed. Sci.* **2015**, *22*, 14. [CrossRef]
71. Abu-zaiton, A.S. Evaluating the Effect of *Silybum marianum* Extract on Blood Glucose, Liver and Kidney Functions in Diabetic Rats. *Adv. Stud. Biol.* **2013**, *5*, 447–454. [CrossRef]
72. Lazebnik, L.B.; Golovanova, E.V.; Tarasova, L.V.; Krivosheev, A.B.; Sas, E.I.; Eremina, E.Y.; Trukhan, D.I.; Hlynova, O.V.; Tsyganova, Y.V.; Lazebnik, L.B.; et al. Adult Alcoholic Liver Disease. *Exp. Clin. Gastroenterol.* **2020**, *174*, 4–28. [CrossRef]
73. Aghemo, A.; Alekseeva, O.P.; Angelico, F.; Bakulin, I.G.; Bakulina, N.V.; Bordin, D.; Bueverov, A.O.; Drapkina, O.M.; Gillessen, A.; Kagarmanova, E.M.; et al. Role of Silymarin as Antioxidant in Clinical Management of Chronic Liver Diseases: A Narrative Review. *Ann. Med.* **2022**, *54*, 1548–1560. [CrossRef]
74. Iqbal, T.; Aslam, T.; Zulfiqar, S.; Faisal, N.; Rehman, A.U.; Aslam, S.; Rehman, R. Exploring *Silybum marianum* L. Seeds from Pakistan for Its Antibacterial, Antioxidant, Antidiabetic Activities, and Phytochemical Analysis. *Nat. Prod. Res.* **2025**, 1–7. [CrossRef]
75. Maghrani, M.; Zeggwagh, N.-A.; Lemhadri, A.; El Amraoui, M.; Michel, J.-B.; Eddouks, M. Study of the Hypoglycaemic Activity of Fraxinus Excelsior and *Silybum marianum* in an Animal Model of Type 1 Diabetes Mellitus. *J. Ethnopharmacol.* **2004**, *91*, 309–316. [CrossRef]
76. Villiger, A.; Sala, F.; Suter, A.; Butterweck, V. In Vitro Inhibitory Potential of *Cynara scolymus*, *Silybum marianum*, *Taraxacum officinale*, and *Peumus boldus* on Key Enzymes Relevant to Metabolic Syndrome. *Phytomedicine* **2015**, *22*, 138–144. [CrossRef]
77. Vessal, G.; Akmali, M.; Najafi, P.; Moein, M.; Sagheb, M. Silymarin and Milk Thistle Extract May Prevent the Progression of Diabetic Nephropathy in Streptozotocin-Induced Diabetic Rats. *Ren. Fail.* **2010**, *32*, 733–739. [CrossRef]
78. Mohammadi, S.M.; Kianbakht, S.; Rezazadeh, S.; Ziaee, M.; Huseini, H.F. Clinical Efficacy of *Silybum marianum* Seed Extract in Treatment of Type 2 Diabetes Mellitus and Non-Alcoholic Fatty Liver Disease: A Narrative Review. *J. Med. Plants* **2020**, *19*, 12–26. [CrossRef]
79. Khalili, N.; Fereydoonzadeh, R.; Mohtashami, R.; Mehrzadi, S.; Heydari, M.; Huseini, H.F. Silymarin, Olibanum, and Nettle, A Mixed Herbal Formulation in the Treatment of Type II Diabetes: A Randomized, Double-Blind, Placebo-Controlled, Clinical Trial. *J. Evid.-Based Complement. Altern. Med.* **2017**, *22*, 603–608. [CrossRef]
80. Kasote, D.M.; Katyare, S.S.; Hegde, M.V.; Bae, H. Significance of Antioxidant Potential of Plants and Its Relevance to Therapeutic Applications. *Int. J. Biol. Sci.* **2015**, *11*, 982–991. [CrossRef] [PubMed]
81. Surai, P.F. Silymarin as a Natural Antioxidant: An Overview of the Current Evidence and Perspectives. *Antioxidants* **2015**, *4*, 204–247. [CrossRef]
82. Martinelli, T.; Andrzejewska, J.; Salis, M.; Sulas, L. Phenological Growth Stages of *Silybum marianum* According to the Extended BBCH Scale. *Ann. Appl. Biol.* **2015**, *166*, 53–66. [CrossRef]

83. Oguntibeju, O.O. Type 2 Diabetes Mellitus, Oxidative Stress and Inflammation: Examining the Links. *Int. J. Physiol. Pathophysiol. Pharmacol.* **2019**, *11*, 45–63. [PubMed]
84. Caturano, A.; D'Angelo, M.; Mormone, A.; Russo, V.; Mollica, M.P.; Salvatore, T.; Galiero, R.; Rinaldi, L.; Vetrano, E.; Marfella, R.; et al. Oxidative Stress in Type 2 Diabetes: Impacts from Pathogenesis to Lifestyle Modifications. *Curr. Issues Mol. Biol.* **2023**, *45*, 6651–6666. [CrossRef]
85. Stolf, A.M.; Cardoso, C.C.; Acco, A. Effects of Silymarin on Diabetes Mellitus Complications: A Review. *Phyther. Res.* **2017**, *31*, 366–374. [CrossRef]
86. Nasir, K.; Rubab, S.L.; Fatima, H.; Shamim, F.; Tawab, A.; Arshad, I.; Iqbal, R.; Parveen, S.; Saadia, M.; Abbasi, B.B.K.; et al. Exploring Antidiabetic Potential of Nigella Sativa and *Silybum marianum* Seed Extracts through Bioassay-Guided Alpha-Amylase Inhibition Activity and Characterization of Bioactive Fractions. *Results Chem.* **2025**, *15*, 102183. [CrossRef]
87. Kumar, J.; Park, K.-C.; Awasthi, A.; Prasad, B. Silymarin Extends Lifespan and Reduces Proteotoxicity in C. Elegans Alzheimer's Model. *CNS Neurol. Disord.-Drug Targets* **2015**, *14*, 295–302. [CrossRef]
88. Qin, N.-B.; Jia, C.-C.; Xu, J.; Li, D.-H.; Xu, F.-X.; Bai, J.; Li, Z.-L.; Hua, H.-M. New Amides from Seeds of *Silybum marianum* with Potential Antioxidant and Antidiabetic Activities. *Fitoterapia* **2017**, *119*, 83–89. [CrossRef]
89. Qin, N.; Sasaki, T.; Li, W.; Wang, J.; Zhang, X.; Li, D.; Li, Z.; Cheng, M.; Hua, H.; Koike, K. Identification of Flavonolignans from *Silybum marianum* Seeds as Allosteric Protein Tyrosine Phosphatase 1B Inhibitors. *J. Enzym. Inhib. Med. Chem.* **2018**, *33*, 1283–1291. [CrossRef]
90. Salamone, F.; Galvano, F.; Marino, A.; Paternostro, C.; Tibullo, D.; Bucchieri, F.; Mangiameli, A.; Parola, M.; Bugianesi, E.; Li Volti, G. Silibinin Improves Hepatic and Myocardial Injury in Mice with Nonalcoholic Steatohepatitis. *Dig. Liver Dis.* **2012**, *44*, 334–342. [CrossRef] [PubMed]
91. Taha, M.N.; Krawinkel, M.B.; Morlock, G.E. High-Performance Thin-Layer Chromatography Linked with (Bio)Assays and Mass Spectrometry-A Suited Method for Discovery and Quantification of Bioactive Components? Exemplarily Shown for Turmeric and Milk Thistle Extracts. *J. Chromatogr. A* **2015**, *1394*, 137–147. [CrossRef] [PubMed]
92. Cheng, B.; Gong, H.; Li, X.; Sun, Y.; Zhang, X.; Chen, H.; Liu, X.; Zheng, L.; Huang, K. Silibinin Inhibits the Toxic Aggregation of Human Islet Amyloid Polypeptide. *Biochem. Biophys. Res. Commun.* **2012**, *419*, 495–499. [CrossRef] [PubMed]
93. El-Sapagh, S.; Allam, N.G.; El-Sayed, M.N.E.D.; El-Hefnawy, A.A.; Korbecka-Glinka, G.; Shala, A.Y. Effects of *Silybum marianum* L. Seed Extracts on Multi Drug Resistant (MDR) Bacteria. *Molecules* **2024**, *29*, 64. [CrossRef]
94. Amirghofran, Z.; Azadbakht, M.; Karimi, M. Evaluation of the Immunomodulatory Effect of Five Herbal Plants. *J. Ethnopharmacol.* **2000**, *72*, 167–172. [CrossRef]
95. Wilasrusmee, C.; Kittur, S.; Shah, G.; Siddiqui, J.; Bruch, D.; Wilasrusmee, S.; Kittur, D.S. Immunostimulatory Effect of *Silybum marianum* (Milk Thistle) Extract. *Med. Sci. Monit. Int. Med. J. Exp. Clin. Res.* **2002**, *8*, 439–444.
96. Kurkin, V.A. Antioxidant Activity of Silybin and 2,3-Dehydrosilybin from *Silybum marianum* (L). Gaertn. Fruits. *J. Pharmacogn. Phytochem.* **2016**, *5*, 256–259.
97. Filippopoulou, K.; Papaevgeniou, N.; Lefaki, M.; Paraskevopoulou, A.; Biedermann, D.; Křen, V.; Chondrogianni, N. 2,3-Dehydrosilybin A/B as a pro-Longevity and Anti-Aggregation Compound. *Free Radic. Biol. Med.* **2017**, *103*, 256–267. [CrossRef]
98. Ung, L.; Le, Q.-U.; Lay, H.-L.; Wu, M.-C.; Kumar Joshi, R.; Ming-Chang Wu, C. Phytoconstituents and Pharmacological Activities of *Silybum marianum* (Milk Thistle): A Critical Review. *Am. J. Essent. Oils Nat. Prod.* **2018**, *6*, 41–47.
99. Tahmasbi, Z.; Boroughani, M.; Heidari, M.M.; Namvar, E.; Hashempur, M.H.; Faraji, S.N.; Nazarpour-Servak, M.; Heydari, M. Potential Therapeutic Effects of Milk Thistle (*Silybum marianum*) in Eye Diseases, a Scoping Review. *Discov. Appl. Sci.* **2025**, *7*, 17. [CrossRef]
100. Ahmed, A.; Matlint, S.A.; Ohb, U.K. Awed of the Flowers. *Phytochemistry* **1989**, *28*, 1751–1753. [CrossRef]
101. van de Venter, M.; Roux, S.; Bungu, L.C.; Louw, J.; Crouch, N.R.; Grace, O.M.; Maharaj, V.; Pillay, P.; Sewnarian, P.; Bhagwandin, N.; et al. Antidiabetic Screening and Scoring of 11 Plants Traditionally Used in South Africa. *J. Ethnopharmacol.* **2008**, *119*, 81–86. [CrossRef] [PubMed]
102. Venter, F.; Venter, J. *Making the Most of Indigenous Trees*; Briza Publications: Pretoria, South Africa, 1996.
103. Maroyi, A. Brachylaena Elliptica and B. Ilicifolia (Asteraceae): A Comparative Analysis of Their Ethnomedicinal Uses, Phytochemistry and Biological Activities. *J. Pharm. Nutr. Sci.* **2020**, *10*, 223–229. [CrossRef]
104. Beentje, H.J. The Genus Brachylaena (Compositae: Mutisieae). *Kew Bull.* **2000**, *55*, 1. [CrossRef]
105. Manning, J.; Goldblatt, P. Hyacinthaceae. In *Plants of Southern Africa: An Annotated Checklist [4th Approach to the List of Species of Southern African Plants]*; Germishuizen, G., Meyer, N.L., Eds.; National Botanical Institute: Lucknow, India, 2003; Volume 14, pp. 1054–1071.
106. Van Wyk, B. *Field Guide to Trees of Southern Africa*; Penguin Random House South Africa: Johannesburg, South Africa, 2013.
107. Maroyi, A. Traditional Use of Medicinal Plants in South-Central Zimbabwe: Review and Perspectives. *J. Ethnobiol. Ethnomed.* **2013**, *9*, 31. [CrossRef] [PubMed]

108. Schmidt, E.; Lötter, M.C.; McCleland, W. *Trees and Shrubs of Mpumalanga and Kruger National Park*; Jacana Media: Johannesburg, South Africa, 2002.
109. Williams, V.L.; Balkwill, K.; Witkowski, E.T.F. A Lexicon of Plants Traded in the Witwatersrand Umuthi Shops, South Africa. *Bothalia* **2001**, *31*, 71–98. [CrossRef]
110. Sabiu, S.; Madende, M.; Ayokun-nun Ajao, A.; Adepemi Ogundeji, O.; Lekena, N.; Adekunle Alayande, K. The Scope of Phytotherapy in Southern African Antidiabetic Healthcare. *Trans. R. Soc. S. Afr.* **2019**, *74*, 1–18. [CrossRef]
111. Strothmann, A.L.; Berne, M.E.A.; Capella, G.d.A.; de Moura, M.Q.; da Silva Terto, W.D.; da Costa, C.M.; Pinheiro, N.B. Antiparasitic Treatment Using Herbs and Spices: A Review of the Literature of the Phytotherapy. *Braz. J. Vet. Med.* **2022**, *44*, e004722. [CrossRef]
112. Odeyemi, S.; Bradley, G. Medicinal Plants Used for the Traditional Management of Diabetes in the Eastern Cape, South Africa: Pharmacology and Toxicology. *Molecules* **2018**, *23*, 2759. [CrossRef] [PubMed]
113. Mellem, J.J.; Baijnath, H.; Odhav, B. Effect of the Methanolic Extract of Brachylaena Discolor in a Streptozotocin-Induced Diabetic Rat Model. *Afr. J. Pharm. Pharmacol.* **2013**, *7*, 636–642. [CrossRef]
114. Monjane, J.A.; Capusiri, D.; Giménez, A.; Sterner, O. Leishmanicidal Activity of Onopordopicrin Isolated from the Leaves of Brachylaena Discolor. *Trop. J. Nat. Prod. Res.* **2018**, *2*, 328–331. [CrossRef]
115. De Wet, H.; Nciki, S.; van Vuuren, S.F. Medicinal Plants Used for the Treatment of Various Skin Disorders by a Rural Community in Northern Maputaland, South Africa. *J. Ethnobiol. Ethnomed.* **2013**, *9*, 51. [CrossRef] [PubMed]
116. Bohlmann, F.; Zdero, C. Sesquiterpene Lactones from Brachylaena Species. *Phytochemistry* **1982**, *21*, 647–651. [CrossRef]
117. Adam, S.A.E. Isolation and Identification of Antidiabetic Compounds from *Brachylaena Discolor* DC. Ph.D. Thesis, University of KwaZulu-Natal, Pietermaritzburg, South Africa, 2017.
118. Semenya, S.; Maroyi, A.; Potgieter, M.; Erasmus, L. Herbal Medicines Used by Bapedi Traditional Healers to Treat Reproductive Ailments in the Limpopo Province, South Africa. *Afr. J. Tradit. Complement. Altern. Med.* **2013**, *10*, 331–339. [CrossRef]
119. Nair, S.A.; Sabulal, B.; Radhika, J.; Arunkumar, R.; Subramoniam, A. Promising Anti-Diabetes Mellitus Activity in Rats of β-Amyrin Palmitate Isolated from Hemidesmus Indicus Roots. *Eur. J. Pharmacol.* **2014**, *734*, 77–82. [CrossRef]
120. Santos, F.A.; Frota, J.T.; Arruda, B.R.; De Melo, T.S.; Da Silva, A.A.D.C.A.; Brito, G.A.D.C.; Chaves, M.H.; Rao, V.S. Antihyperglycemic and Hypolipidemic Effects of α,β-Amyrin, a Triterpenoid Mixture from Protium Heptaphyllum in Mice. *Lipids Health Dis.* **2012**, *11*, 98. [CrossRef]
121. Xu, W.; Zhang, H.; Zhang, Q.; Xu, J. β-Amyrin Ameliorates Diabetic Nephropathy in Mice and Regulates the MiR-181b-5p/HMGB2 Axis in High Glucose-Stimulated HK-2 Cells. *Environ. Toxicol.* **2022**, *37*, 637–649. [CrossRef] [PubMed]
122. Duc Viet, T.; Hoang Anh, L.; Dang Xuan, T.; Duy Dong, N. The Pharmaceutical Potential of α- and β-Amyrins. *Nutraceuticals* **2025**, *5*, 21. [CrossRef]
123. Ngenge Tamfu, A.; Mfifen Munvera, A.; Veronica Dediu Botezatu, A.; Talla, E.; Ceylan, O.; Tagatsing Fotsing, M.; Tanyi Mbafor, J.; Shaheen, F.; Mihaela Dinica, R. Synthesis of Benzoyl Esters of β-Amyrin and Lupeol and Evaluation of Their Antibiofilm and Antidiabetic Activities. *Results Chem.* **2022**, *4*, 100322. [CrossRef]
124. Thirupathi, A.; Silveira, P.C.; Nesi, R.T.; Pinho, R.A. β-Amyrin, a Pentacyclic Triterpene, Exhibits Anti-Fibrotic, Anti-Inflammatory, and Anti-Apoptotic Effects on Dimethyl Nitrosamine-Induced Hepatic Fibrosis in Male Rats. *Hum. Exp. Toxicol.* **2017**, *36*, 113–122. [CrossRef] [PubMed]
125. Maroyi, A. Medicinal Uses of the Asteraceae Family in Zimbabwe: A Historical and Ecological Perspective. *Ethnobot. Res. Appl.* **2023**, *25*, 1–30. [CrossRef]
126. Mellem, J.; Baijnath, H.; Odhav, B. Antidiabetic Potential of Brachzylaena Discolor. *Afr. J. Tradit. Complement. Altern. Med.* **2015**, *12*, 38–44. [CrossRef]
127. Mtshali, S.N. Identification of Triterpenoids in Brachylaena Discolor DC, a Plant with Antidiabetic Activity. Ph.D. Thesis, University of KwaZulu-Natal, Pietermaritzburg, South Africa, 2019.
128. Dikhoba, P.M.; Mongalo, N.I.; Elgorashi, E.E.; Makhafola, T.J. Antifungal and Anti-Mycotoxigenic Activity of Selected South African Medicinal Plants Species. *Heliyon* **2019**, *5*, e02668. [CrossRef]
129. Khoza, N.; Dukhan, S.; Ramalepe, P.; Risenga, I. Medicinal Plants Used to Treat Maternal and Paediatric Health Related Ailments in the Nkomazi Local Municipality, Mpumalanga Province, South Africa. *Ethnobot. Res. Appl.* **2023**, *26*, 1–16. [CrossRef]
130. Holanda Pinto, S.A.; Pinto, L.M.S.; Cunha, G.M.A.; Chaves, M.H.; Santos, F.A.; Rao, V.S. Anti-Inflammatory Effect of α, β-Amyrin, a Pentacyclic Triterpene from Protium Heptaphyllum in Rat Model of Acute Periodontitis. *Inflammopharmacology* **2008**, *16*, 48–52. [CrossRef]
131. Han, G.; Lee, D.G. Antibacterial Mode of Action of β-Amyrin Promotes Apoptosis-Like Death in Escherichia Coli by Producing Reactive Oxygen Species. *J. Microbiol. Biotechnol.* **2022**, *32*, 1547–1552. [CrossRef]
132. Wu, J.; Sun, J.; Liu, M.; Zhang, X.; Kong, L.; Ma, L.; Jiang, S.; Liu, X.; Ma, W. Botany, Traditional Use, Phytochemistry, Pharmacology and Quality Control of Taraxaci Herba: Comprehensive Review. *Pharmaceuticals* **2024**, *17*, 1113. [CrossRef] [PubMed]

133. Jiao, F.; Tan, Z.; Yu, Z.; Zhou, B.; Meng, L.; Shi, X. The Phytochemical and Pharmacological Profile of Taraxasterol. *Front. Pharmacol.* **2022**, *13*, 927365. [CrossRef]
134. Gupta, R.; Sharma, A.K.; Sharma, M.C.; Dobhal, M.P.; Gupta, R.S. Evaluation of Antidiabetic and Antioxidant Potential of Lupeol in Experimental Hyperglycaemia. *Nat. Prod. Res.* **2012**, *26*, 1125–1129. [CrossRef] [PubMed]
135. Kahksha; Alam, O.; Al-Keridis, L.A.; Khan, J.; Naaz, S.; Alam, A.; Ashraf, S.A.; Alshammari, N.; Adnan, M.; Beg, M.A. Evaluation of Antidiabetic Effect of Luteolin in STZ Induced Diabetic Rats: Molecular Docking, Molecular Dynamics, In Vitro and In Vivo Studies. *J. Funct. Biomater.* **2023**, *14*, 126. [CrossRef]
136. Monjane, J.A. *Secondary Metabolites from Mozambican Plants Isolation and Characterization*; Lund University: Lund, Sweden, 2017; ISBN 9789174225549.
137. De Pablos, R.M.; Espinosa-oliva, A.M.; Hornedo-ortega, R.; Cano, M.; Arguelles, S. Hydroxytyrosol Protects from Aging Process via AMPK and Autophagy; a Review of Its Effects on Cancer, Metabolic Syndrome, Osteoporosis, Immune-Mediated and Neurodegenerative Diseases. *Pharmacol. Res.* **2019**, *143*, 58–72. [CrossRef]
138. Espíndola, K.M.M.; Ferreira, R.G.; Narvaez, L.E.M.; Silva Rosario, A.C.R.; da Silva, A.H.M.; Silva, A.G.B.; Vieira, A.P.O.; Monteiro, M.C. Chemical and Pharmacological Aspects of Caffeic Acid and Its Activity in Hepatocarcinoma. *Front. Oncol.* **2019**, *9*, 541. [CrossRef]
139. Bertelli, M.; Kiani, A.K.; Paolacci, S.; Manara, E.; Kurti, D.; Dhuli, K.; Bushati, V.; Miertus, J.; Pangallo, D.; Baglivo, M.; et al. Hydroxytyrosol: A Natural Compound with Promising Pharmacological Activities. *J. Biotechnol.* **2020**, *309*, 29–33. [CrossRef] [PubMed]
140. Wu, S.; Ai, W.; Nie, L.; Lu, X. Antidiabetic Activity of Eupafolin through Peroxisome Proliferator-Activated Receptor-Gamma and PI3K/Akt Signaling in Type 2 Diabetic Rats. *J. Biochem. Mol. Toxicol.* **2023**, *37*, e23463. [CrossRef]
141. El Menyiy, N.; Aboulaghras, S.; Bakrim, S.; Moubachir, R.; Taha, D.; Khalid, A.; Abdalla, A.N.; Algarni, A.S.; Hermansyah, A.; Ming, L.C.; et al. Genkwanin: An Emerging Natural Compound with Multifaceted Pharmacological Effects. *Biomed. Pharmacother.* **2023**, *165*, 115159. [CrossRef] [PubMed]
142. Al-Ishaq, R.K.; Abotaleb, M.; Kubatka, P.; Kajo, K.; Büsselberg, D. Flavonoids and Their Anti-Diabetic Effects: Cellular Mechanisms and Effects to Improve Blood Sugar Levels. *Biomolecules* **2019**, *9*, 430. [CrossRef] [PubMed]
143. Yang, D.; Wang, T.; Long, M.; Li, P. Quercetin: Its Main Pharmacological Activity and Potential Application in Clinical Medicine. *Oxidative Med. Cell. Longev.* **2020**, *2020*, 8825387. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.