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Review Article

Phytochemical Profile, Ethnobotanical and Biological Impacts of Various *Zamia* Species: A Mini-Review

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ABSTRACT

Genus *Zamia* is a diverse group of cycads belonging to the family Zamiaceae which includes most cycads. It is ranked as the second-largest genus of extant cycads in the new world. In contrast to other cycad species, *Zamia* species are trunkless, deciduous shrubs. The genus *Zamia* is by far the most ecologically varied, widely dispersed, and species-rich genus in the Americas. They are dioecious plants with male and female reproductive cones. *Zamia* plants are considered rich sources of numerous different natural metabolites, which may contribute to various biological activities such as cytotoxic, antimicrobial, antioxidant, and anti-inflammatory activities. These metabolites include flavonoids, biflavonoids, phenolic acids, volatile oils, and lignans that are considered the significant components of the phytochemical profile of *Zamia*. *Zamia* is a popular ornamental plant. It is also acknowledged as a therapeutic herb in both conventional and Western medicine. Various *Zamia* species have traditionally been used to treat a range of ailments by elderly locals in various locations. These ethnobotanical uses have led researchers to discover some valuable pharmacological properties of some *Zamia* species like cytotoxic, antiprotozoal, antioxidant, antimicrobial, and anti-Alzheimer activities. In this review, we have given an overview of different phytochemicals types present in *Zamia* species and their reported bioactivities in addition, the pharmacological, and ethnobotanical properties of certain *Zamia* species.

Keywords: Antileishmanial, Biflavonoids, Cytotoxicity, Phenolic acids, Toxoplasmocidal.

1. INTRODUCTION

Genus *Zamia* is regarded as the second largest cycad genus after *Cycas* [1], which belongs to the family Zamiaceae that is considered the largest family of order cycadales [2]. Nine genera with 263 species are included in the family Zamiaceae based on the recent world cycads list [1]. *Zamia* has 83 species which are primarily found in South, Central, and North America[1].
The word *Zamia*, which means "loss or damage," is borrowed from Latin. It was originally used to designate barren pinecones [3]. *Zamia* is frequently found from sea level to a height of around 100 metres in hammocks, dunes, dry pinelands, and dry oak forests [3]. *Zamia* species are widely distributed from Florida USA south to Bolivia [4].

They are small evergreen shrubs with partially or entirely underground woody stems that sustain the leaves. Their leaves are arranged on the central rachis in pinnately manner with symmetric glossy and smooth lanceolate leaflets (Figure 1). Their petioles and rachis have no spines [3,5]. *Zamia* plants can reproduce by cones, just like other cycads. Female cones are relatively larger than male cones with various colors and both are pedunculated below the leaf crown (Figure 1) [3,5].

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Numerous natural metabolites, including biflavonoids, flavonoids, phenolics, lignans, and volatile oils, are abundant in *Zamia* and may contribute to significant bioactivities such as cytotoxic, antioxidant, antimicrobial, anti-inflammatory, and antiprotozoal effects. This variable phytochemical profile enabled *Zamia* plants to possess valuable traditional and pharmacological potentials either in the treatment of various human health issues or utilized in daily human needs. [6]

Due to the high starch content of their underground stems, *Zamia* species were first used by ancient Indians as a source of flour for making bread so they are known as coontie [3]. Many locals in diverse places have traditionally utilized different *Zamia* species to treat a variety of illnesses like muscle aches and snakebites [7,8].

However, a few numbers of *Zamia* species have been evaluated for their biological activities, it has been discovered that *Zamia* possesses a wide range of significant bioactivities including antioxidant, antibacterial, and cytotoxic properties [9–12].

Thus, in this review, we summarize data about the content, distribution, and bioactivity of various phytochemicals in diverse *Zamia* species as well as the traditional uses and biological activities of different *Zamia* species.

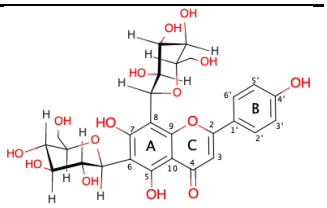
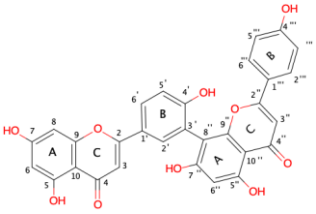
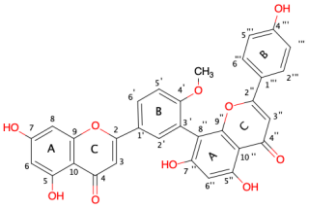
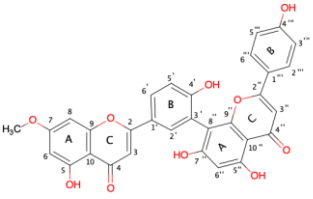
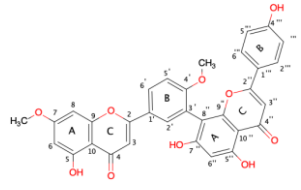
2. METHODS OF COLLECTING DATA

Common research engines like ScienceDirect, Web of Science, PubMed, SciFinder-n, and Scopus were used for collecting the data used in this study. These engines used the keywords "phytochemicals", "*Zamia*", "traditional uses", "pharmacological", and "biological activity". A Total of 123 research articles from the earliest investigation on *Zamia* to the present were examined out of which 54 research articles include information concerning reported phytochemicals of *Zamia* species and their traditional and biological effects.

3. PHYTOCHEMICAL CONTENT OF VARIOUS ZAMIA SPECIES AND THEIR BIOACTIVITIES

Various active constituents are present in *Zamia* species like biflavonoids, flavonoids, phenolic acids, lignans, and volatile oils **(Figure 2-4, Table 1-3)**. Like other cycad species, *Zamia* species are abundant in biflavonoids, which make up most of the phytochemical content. Only the 3'-8'' and 4'-O-6'' series of biflavonoids and their derivatives were found in several *Zamia* species out of these various biflavonoids [6] **(Figure 2, Table 1)**. Examples of these diverse phytochemicals, their distribution in Zamia species (Table 1-3), as well as their bioactivities are listed in **(Table 4)**.

Table 1. Distribution of different flavonoids and biflavonoids in *Zamia* species

Compound name	Class / Plant sources	Chemical structure
Apigenin 6,8-C-β-D-glucoside (Vicenin-2) [12]	Flavonoid glycoside *Zamia floridana*	
Amentoflavone [12]	Biflavonoid (3′-8′′ Series) *Z. angustifolia* *Z. chigua* *Z. debilis* *Z. kickxii* *Z. loddigesi* *Z. muricata* *Z. pumila* *Z. skinneri* *Z. umbrosa* *Z. latifoliata* *Z. pseudoparasitica* *Z. portoricensis* *Z. fischeri* *Z. furfuracea* *Z. inermis* *Z. paucijuga* *Z. splendens* *Z. floridana* Biflavonoid (3′-8′′ Series)	
Bilobetin [12]	*Z. angustifolia* *Z. chigua* *Z. debilis* *Z. skinneri* *Z. umbrosa* *Z. pseudoparasitica* *Z. portoricensis* *Z. inermis* *Z. loddigesi* *Z. floridana* Biflavonoid (3′-8′′ Series)	
Sequoiaflavone [13–15]	*Z. angustifolia* *Z. chigua* *Z. debilis* *Z. floridana* *Z. kickxii* *Z. loddigesi* *Z. muricata* *Z. pumila* *Z. skinneri* *Z. umbrosa* *Z. latifoliata* *Z. pseudoparasitica* *Z. portoricensis* Biflavonoid (3′-8′′ Series)	
Ginkgetin [13–15]	/ *Z. angustifolia* *Z. chigua* *Z. debilis* *Z. floridana* *Z. kickxii* *Z. loddigesi* *Z. muricata*	

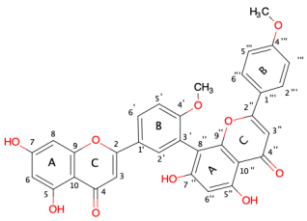
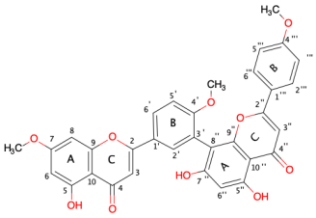
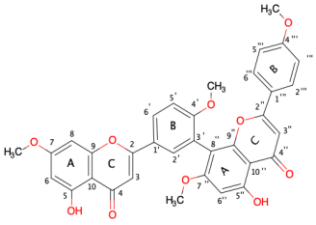
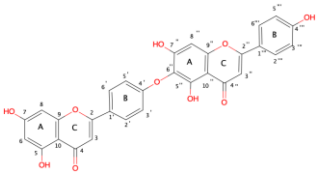
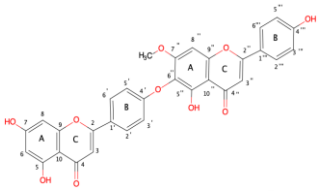
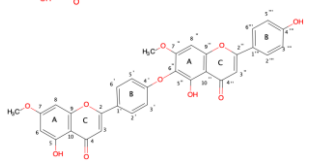
	Z. pumila *Z. skinneri* *Z. umbrosa* *Z. latifoliata* *Z. pseudoparasitica* *Z. portoricensis*	
Isogink-getin [12]	Biflavonoid (3′-8″ Series) *Z. inermis* *Z. loddigesi* *Z. skinneri* *Z. floridana*	
Sciadopi-tysin [14,15]	Biflavonoid (3′-8″ Series) *Z. angustifolia* *Z. chigua* *Z. debilis* *Z. floridana* *Z. kickxii* *Z. loddigesi* *Z. muricata* *Z. pumila* *Z. skinneri* *Z. umbrosa* *Z. latifoliata* *Z. pseudoparasitica* *Z. portoricensis* *Z. fischeri* *Z. furfuracea* *Z. inermis* *Z. paucijuga* *Z. splendens*	
Amentof-lavone tetra methyl ether [14,15]	Biflavonoid (3′-8″ Series) *Z. angustifolia* *Z. chigua* *Z. debilis* *Z. floridana* *Z. kickxii* *Z. loddigesi* *Z. muricata* *Z. pumila* *Z. skinneri* *Z. umbrosa* *Z. latifoliata* *Z. pseudoparasitica* *Z. portoricensis* *Z. fischeri* *Z. furfuracea* *Z. inermis* *Z. paucijuga* *Z. splendens*	
Hinokifl-avone [13,16]	Biflavonoid (4′-O-6″ Series) *Z. fischeri* *Z. furfuracea* *Z. inermis* *Z. floridana* *Z. loddigesi* *Z. paucijuga* *Z. splendens* *Z. skinneri*	
Isocrypt-omerin [16]	Biflavonoid (4′-O-6″ Series) *Z. furfuracea*	
Chamae-cyparin [16]	Biflavonoid (4′-O-6″ Series) *Z. furfuracea*	

Table 2. Distribution of different phenolics in *Zamia* species

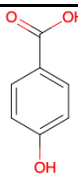
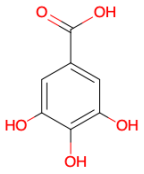
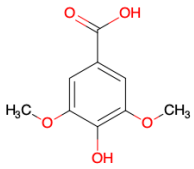
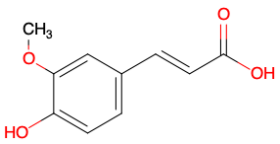
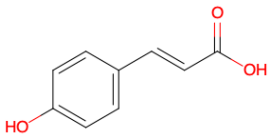
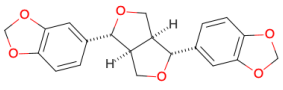
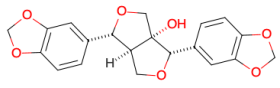
Compound name	Class / Plant sources	Chemical structure
p-Hydroxy benzoic acid [17]	Phenolic acid *Z. floridana*	
Gallic acid [12]	Phenolic acid *Z. floridana*	
Syringic acid [12]	Phenolic acid *Z. floridana*	
Ferulic acid [17]	Phenolic acid *Z. floridana*	
p-Coumaric acid [17]	Phenolic acid *Z. floridana*	
Sesamin [11]	Lignans *Z. furfuracea*	
Paulownin [11]	Lignans *Z. furfuracea*	

Table 3. Distribution of different volatile oils in *Zamia* species

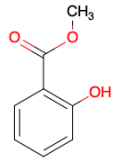
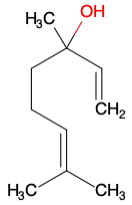
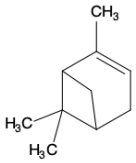
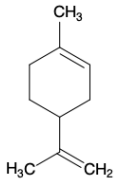
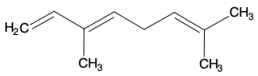
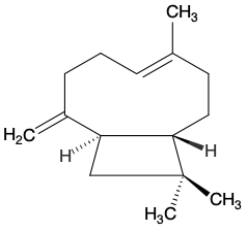
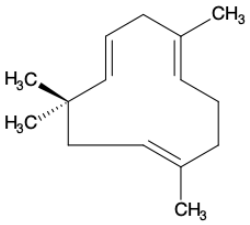
Compound name	Class / Plant source	Chemical structure
Methyl salicylate [18]	Volatile oil *Z. pumila*	
Linalool [18]	Volatile oil *Z. furfuracea*	
α-Pinene [18]	Volatile oil *Z. furfuracea*	
Limonene [18]	Volatile oil *Z. furfuracea*	
Trans-β-ocimene [18]	Volatile oil *Z. furfuracea*	
Trans-β-Caryophyllene [18]	Volatile oil *Z. pumila*	
α-Humulene [18]	Volatile oil *Z. pumila*	

Table 4. Some reported biological activities of various phytochemicals isolated from *Zamia* species

Phytochemical name	Biological activity
Apigenin 6,8-C-β-D-glucoside (Vicenin-2)	In silico docking study indicated that vicenin-2 has a significant inhibitory effect against the toxoplasma gondii parasite due to its high affinity toward thymidylate synthase reductase dihydrofolate reductase (TSDHFR) with high docking score of -8.74 kcal/mol. [12]
	Vicenin-2 has a significant affinity to a cyclin-dependent kinase target protein (CDK-2) using a docking study with high docking score of -8.38 kcal/mol which suggest that vicenin-2 may be used as a cytotoxic drug in cancer disease. [12]
Amentoflavone	Amentoflavone has a high docking score of -7.63 kcal/mol against (TSDHFR) using in silico experiment which proposed that amentoflavone can afford toxoplasmocidal activity. [12]
	In addition, the high docking score (-7.60 kcal/mol) of amentoflavone against (CDK-2) suggested that amentoflavone can be a potent anticancer compound. [12]
	Amentoflavone exerted potent cytotoxic effects against both MCF-7 with IC_{50} of 25 μM using MTT assay method. [19]
	In a dose-dependent manner, amentoflavone exhibited potent antioxidant ability (19.21-75.52%) in scavenging DPPH, ABTS, superoxide, and hydroxyl radicals. [20]
	Amentoflavone exhibited a significant antibacterial inhibitory spectrum against both target foodborne pathogens, *Staphylococcus aureus*, and *Escherichia. coli* with MIC values of 62.5 and 125 µg/mL, respectively. [20]
	It was found that the human neuroblastoma SH-SY5Y cells pretreated with 5 or 10 μM of amentoflavone 6 h before Aβ1-42 treatment significantly reduced Aβ1-42-induced cell death of SH-SY5Y cells. [21]
Bilobetin	Bilobetin has a high binding affinity to (TSDHFR) with a docking score of -8.95 kcal/mol that explain the potent expected Toxoplasmocidal activity of this compound. [12]
	Bilobetin was found to exhibit significant anti-proliferative activities against MCF-7 in a dose-dependent manner with IC_{50} of 57.62 µg/mL [22]. In addition, the high docking score (-7.58 kcal/mol) of bilobetin against (CDK-2). [12]
Sequoiaflavone	Sequoiaflavone was the most potent inhibitor of cytochrome p-450 catalyzed ethoxycumarin O-desalkylation (ECOD) with a percent inhibition of 75.2%. therefore, Sequoiaflavone can be considered a potential anticancer and chemopreventive agent. [23]

	Sequoiaflavone had stronger inhibition toward *Alternaria alternata* at concentrations of 100 μmol/L. [24]
Ginkgetin	Ginkgetin reduced cell viability of human breast cancer cell lines (MCF-7) with IC_{50} of 10 μM in addition to an increased indication of apoptosis, including apoptotic bodies and cell shrinkage, as observed under an inverted microscope. [25]
	In the study conducted by Choi *et al.* ginkgetin was tested to inhibit amyloid-beta fibrillation and to disaggregate amyloid-beta fibrils. The results showed that the IC_{50} value of ginkgetin was 4.92 μM in the inhibition of Aβ fibrils assay. In addition, ginkgetin exhibited a disaggregation effect on Aβ fibrils with the IC_{50} value of 6.81 μM. [26]
	Ginkgetin had stronger antifungal activity toward *Alternaria alternata* at concentrations of 100 μmol/L. [24]
Isoginkgetin	Isoginkgetin was found to exhibit significant anti-proliferative activities against different cell lines including cervical (HeLa), lymphoma (Daudi), and myelogenous leukemia cell lines (K562) in a dose-dependent manner with IC_{50} of 8.38, 20.07, and 18.76 μg/mL, respectively [22]. In addition, the high binding affinity to (CDK-2) with a docking score of -7.62 kcal/mol. [12]
	Isoginkgetin was predicted as a promising Toxoplasmocidal agent due to its high affinity to (TSDHFR) with a high binding energy of -8.54 kcal/mol. [12]
Sciadopitysin	Sciadopitysin showed to prevent myocardial necrosis via reducing the levels of creatine kinase-MB and lactate dehydrogenase activities. The level of cardiac-specific troponin-T (Tn-T), tumor necrosis factor-α, and interleukin-6 were shown to be declined in SDN-treated group as determined by ELISA analysis. [27]
	Osteoblastic MC3T3-E1 cells pretreated with sciadopitysin prior to antimycin A exposure significantly reduced antimycin A-induced cell damage by preventing mitochondrial membrane potential dissipation, adenosine triphosphate (ATP) loss, and reactive oxygen species (ROS) release, suggesting that sciadopitysin has an antioxidant ability that may be useful for protecting mitochondria against a burst of oxidative stress. [28]
	Sciadopitysin exhibited a strong inhibitory effect on *Cladosporium* oxysporum at ED_{50} value of 9 μmol/L. [24]
Hinokiflavone	Hinokiflavone showed significant cytotoxic activity against the colorectal carcinoma cell line (HCT-116) with IC_{50} of 13 μM with an indication of induced apoptosis due to shrinkage and morphology changes of cells after hinokiflavone treatment. In addition, the results indicated that hinokiflavone could reduce the migration and invasion of colorectal tumor cells in a dose-dependent manner. [29]
	Isocryptomerin had powerful antifungal activity against *Candida albicans*, which might be due to its membrane-disruption mechanism. [30]
Isocryptomerin	Isocryptomerin showed remarkable antibacterial activity against *Bacillus subtilis*, MRSA *S. aureus*, and *E.coli* with MIC of 20, 10, and 20 μg/mL, respectively. [31]
	Isocryptomerin at a concentration of 10 μM improved the viability of pheocromocytomas cells of rat's adrenal medulla (PC-12) pretreated with 0.1 μM of Aβ42 fibrils, resulting in a cell viability percentage of 65.7%. [16]
Chamaecyparin	Chamaecyparin a concentration of 10 μM improved the viability of pheocromocytomas cells of rat's adrenal medulla (PC-12) pretreated with 0.1 μM of Aβ42 fibrils, resulting in a cell viability percentage of 55.5%. [16]
p-Hydroxy benzoic acid	*p*-Hydroxy benzoic acid is reported to exhibit antimicrobial activity against *E. coli*, *Bacillus aureus*, *S. aureus*, , *Pseudomonas aeruginosa, C. albicans, Salmonella typhi and Proteus vulgaris.* [32]
Gallic acid	An in vitro study reported that gallic acid suppressed *E. coli* and *Shigella flexneri* biofilm formation. [33]
	Gallic acid had induced toxic effects and morphological changes in breast cancer cells (MCF-7) with IC_{50} 18 μg/mL. [34]
Syringic acid	Using MTT assay method, syringic acid was found to significantly inhibit the proliferation of the colorectal cell line (SW-480) in a dose-dependent manner with IC_{50} value of 1200 μM. In addition, syringic acid showed a significant tumor volume and incidence reduction when compared to the control using in vivo model. [35]
Ferulic acid	Treatment of breast cancer cells (MCF-7) and liver cancer cells (HepG2) with ferulic acid resulted in significant suppression of cell growth with (IC_{50}) of 75.4 and 81.38 μg/mL, respectively. In addition, the elevation of caspase-8 and 9 levels indicated induction of apoptosis in the tested cancer cell lines. [36]
	It was found that ferulic acid had a significant antioxidant effect using ABTS assay method compared to Trolox standard. [37]
p-Coumaric acid	Significant improvement of tissue superoxide dismutase, glutathione peroxidase, and catalase with a reduction in tissue MDA was observed by *p*-Coumaric acid treatment of bilateral renal ischemic rats. [38]
Sesamin	Sesamin exhibited antioxidant activity with percent 68% as well as 96% inhibition of linoleic acid peroxidation. [39]

	At 2 mg/mL (MIC) sesamin inhibited the growth of *Bacillus cereus, S. aureus* , and *P. aeruginosa with percent* 69, 69, and 59 %, respectively. [39]
Paulownin	Paulownin showed antifungal activity against *Trametes versicolor* with MIC of 20 µg. [40]
Methyl salicylate	The oil effectively inhibited the biofilm formation of oral *Streptococcus mutans* and *C. albicans* as well with MIC 25.00 and 12.50 mg/ml, respectively [41]. In addition, oil exhibited a dose-dependent DPPH-radical-scavenging activity with IC_{50} value of 30.61 mg/ml. [41]
Linalool	Linalool had strong antibacterial activity against *Pseudomonas fluorescens with MIC of 1.25* µL with a suggested antibacterial mechanism of membrane damage, bacterial metabolic, and oxidative respiratory perturbations, interfering in the cellular functions of susceptible bacteria. [42]
α-Pinene	*α*-Pinene was found to be highly toxic to *Cryptococcus neoformans with MIC of 117* µg/mL. [43]
Limonene	Limonene inhibited the growth of *Salmonella senftenberg, E. coli, S. aureus.* [44]
	Limonene has significant anti-inflammatory activity by inhibiting 5-lipoxygenase using in vitro model. However, in vivo study revealed that inhalation of limonene by sensitized rats significantly prevented bronchial obstruction by reducing peribronchial inflammatory cell infiltration. [44]
Trans-*β*-ocimene	Using agar diffusion disc method, trans-*β*-ocimene which constitutes more than 40% of the essential oil composition of *Chaerophyllum macropodum* leaf showed potent antibacterial activity against *S. typhi* and *E. coli* with a zone of inhibition of (10, 12 mm), respectively. [45]
Caryophyllene	It displayed selective antibacterial activity against *S. aureus* with MIC of 3 µM. [46]
	In addition, caryophyllene demonstrated specific anti-proliferative effects against colorectal cancer cells with IC_{50} value of 19 µM. [46]
Humulene	It has anti-inflammatory ability by inhibiting both tumor necrosis factor-α (TNFα) and interleukin-1β (IL-1β) generation in carrageenan-injected rats. [47]
	Additionally, it reduced the carrageenan-induced expression of nitric oxide synthase (iNOS) and cyclooxygenase (COX-2) as well as the production of prostaglandin E_2 (PGE_2). [47]

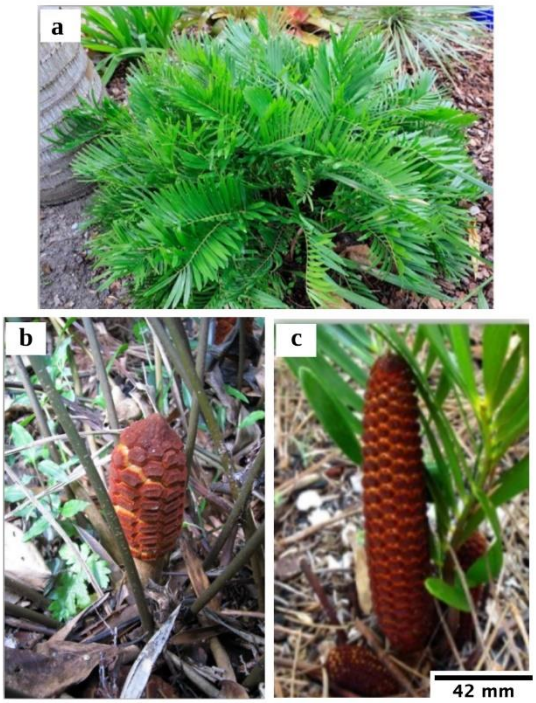


Figure 1. A photograph of *Zamia floridana* shrubs with lanceolate leaflets (a), male cone (b), and female cone (c)*

4. ETHNOBOTABICAL USES OF *ZAMIA* SPECIES

Several ethnobotanical uses have explored the economic and medical importance that *Zamia* likely had for the ancient people. The roots of *Z. pumila* and *Z. floridana* are widely consumed as food by Florida Indians, who prepare flour known as "Sago" from the roots after washing or boiling them to remove cycasin toxins [48]. The Panamian people utilize the decoction of *Z. pseudoparasitica* root tubers as an emetic. Additionally, the stems paste is applied topically to relieve muscle pain [7].

Z. neurophyllidia is used by locals in Costa Rica to cure snakebites [8]. *Z. skinneri* rhizome decoction is used by local herbalists in Panama to enhance and hasten wound healing [49]. Since *Z. furfuraceae* contains deadly azoxy glycosides, people in Honduras and Costa Rica utilize it as a poison for criminals [50]. The Chayahuitas ethnic group, which lives in North Eastern Peru, is extremely vulnerable to leishmaniasis [51]. They utilized crushed *Z. amazonum* roots that had been mixed with some cold water and let to soak overnight. After drinking the mixture, the solid portion is used as a poultice on the injured area. Moreover, the ancient Peruvians applied the juice of crushed *Z. lindenii* stems directly to the leishmanial ulcer [52].

5. BIOLOGICAL ACTIVITIES OF SOME *ZAMIA* SPECIES

5.1. Antioxidant activity

Using the DPPH free radical scavenging and Ferric Reducing Ability (FRAP) assay methods, the aqueous extract of *Z. furfuraceae* leaves has a powerful antioxidant capability that inhibits free radicals with a percent inhibition of 84.51% at the concentration of 0.50% of plant powder, which suggests that *Z. furfuraceae* can be a valuable source in the chemotherapy protective therapy [9]. The antioxidant potential of *Z. furfuraceae* may be attributed to its content of amentoflavone, sciadopitysin, and sesamin, which have significant antioxidant effects as mentioned in Table 4.

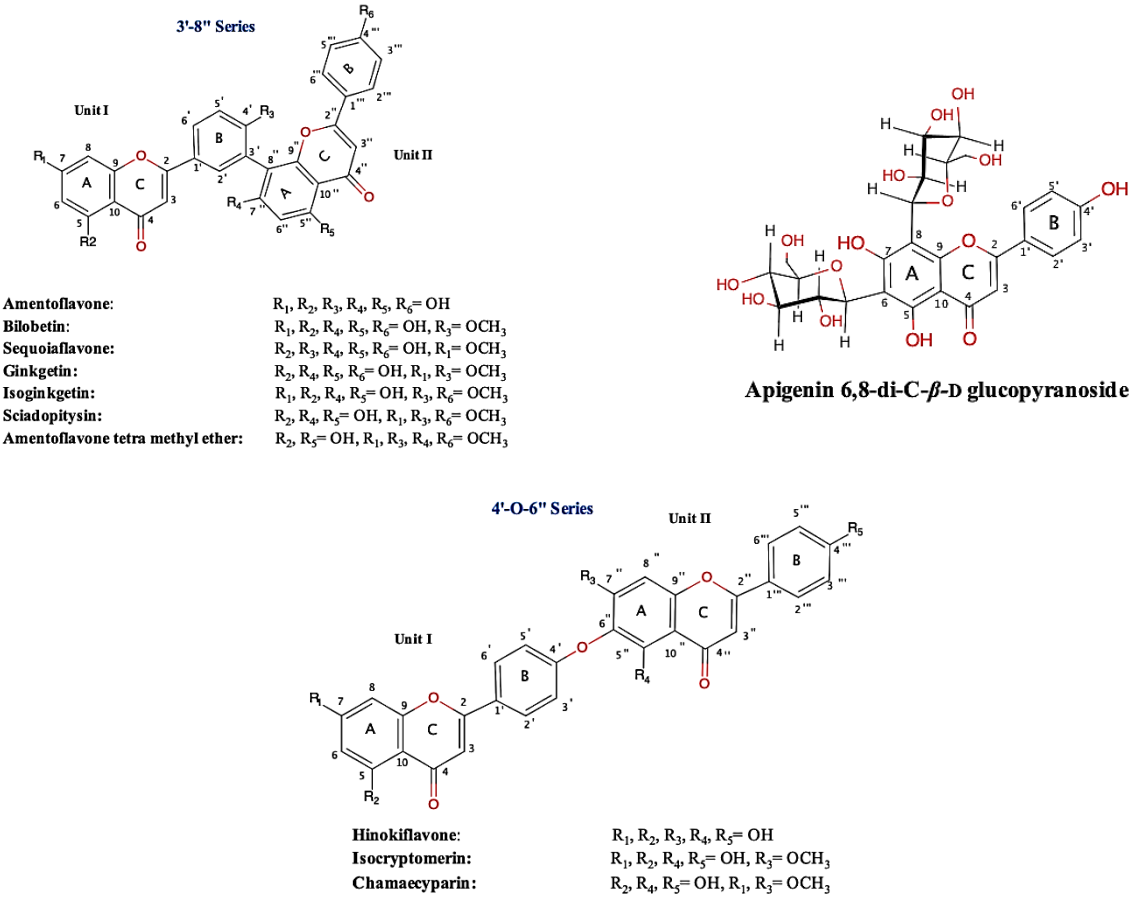


Figure 2: Various biflavonoids and flavonoids structures isolated from *Zamia* species

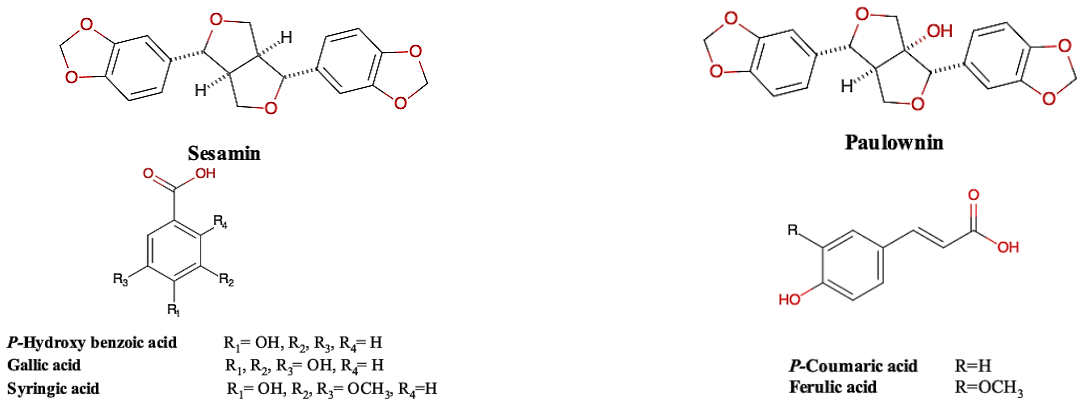


Figure 3. Various phenolic structures isolated from *Zamia* species

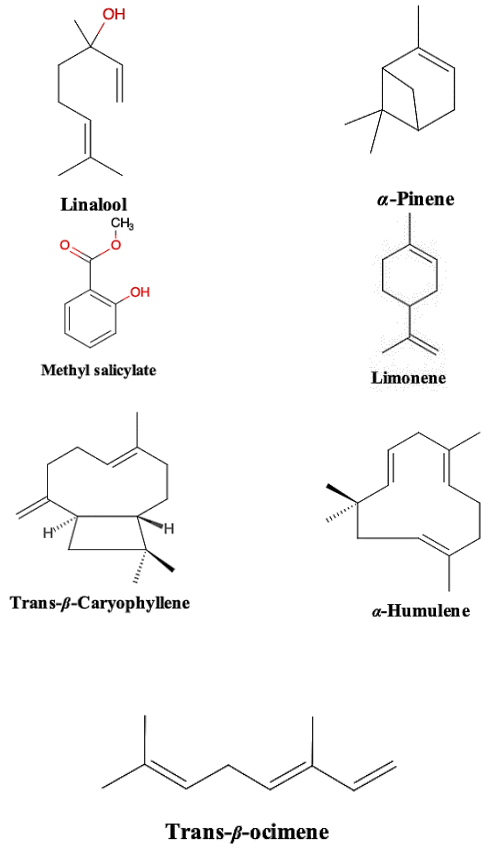


Figure 4. Various volatile oils structures isolated from *Zamia* species

5.2. Antimicrobial activity

Using the well diffusion method, *Z. furfuraceae* methanol extract showed a substantial antibacterial impact against Gram +ve (*Bacillus coagulans*) and Gram -ve (*Escherichia*. coli) [10] due to its antimicrobial components like amentoflavone, isocryptomerin, sesamin, and limonene.

5.3. Cytotoxic activity

Using the MTT assay technique, the crude extract of *Z. furfuraceae* demonstrated a substantial cytotoxic activity against the human gastric cancer cell line (AGS) with an IC_{50} of 18.9 µg/mL [11]. The cytotoxic effect of hinokiflavone against HCT-116 cell line suggests that hinokiflavone can be responsible for *Z. furfuraceae* cytotoxic effect.

In another study, the methanol extract of *Z. floridana* has a cytotoxic potential against MCF-7 and HCT-116 cell lines with IC_{50} of 20.57 and 27.33 µg/mL, respectively compared to that of doxorubicin as a positive control drug (IC_{50} of 4.17 and 5.23 µg/mL, respectively). Interestingly, the methanol extract from *Z. floridana* had a low cytotoxicity effect on the normal cell line (WISH), with an IC_{50} of 40.29 µg/mL. Moreover, The *Z. floridana* fractions were also tested against the preexisting cell lines, and the results revealed that ethyl acetate (EtOAc) and *n*-butanol (*n*-BuOH) fractions had the highest cytotoxic potential against MCF-7 and HCT-116 cell lines, with IC_{50} values of 12.33 and 17.88 µg/mL, respectively for the latter and 22.89 and 9.04 µg/mL, respectively for the former [12]. *Z. floridana* has many cytotoxic components which had been reported for their cytotoxic efficacy against breast and colorectal cancer cells lines such as amentoflavone, vicenin-2, gallic acid, bilobetin, and syringic acid **(Table 1, 2 and 4)**.

5.4. Anti-Alzheimer activity

Z. furfuraceae contains biflavonoids that have cytoprotective properties against the cytotoxicity of amyloid-*β*-peptide 42 (A*β*42) in PC-12 cells due to its high content of isocryptomerin and chamaecyparin which had significant inhibitory effects against (A*β*42) protein with cell viability improvement of 65.7 and 55.5%, respectively. Consequently, it can be used to stop the development of Alzheimer's disease [16].

5.5. Antiprotozoal activity

In our prior investigation, we used the trypan blue exclusion assay method to assess the toxoplasmocidal activity of a methanol extract of *Z. floridana* against *Toxoplasma gondii* RH strain tachyzoites. According to the findings, *Z. floridana* had strong toxoplasmocidal activity, with an EC_{50} of 8.19 µg/mL compared to the standard medicine cotrimoxazole's EC_{50} of 4.18 µg/mL. Additionally, the EC_{50} values for the *n*-BuOH, EtOAc, $CHCl_3$, and pet-ether fractions were 7.16, 9.74, 16.71, and 31.95 µg/mL, respectively. These values were indicated that the *n*-BuOH fraction had the highest toxoplasmocidal activity due to its isolated components that had proved to possess high binding affinity toward (TSDHFR) target proteins such as vicenin-2, isoginkgetin, bilobetin, and amentoflavone [12].

Z. lindenii stems and *Z. amazonum* roots were reported to exhibit considerable antileishmanial activity against *Leishmania amazonensis*, with IC_{50} values of 33 and 81 µg/mL, respectively when compared to amphotericin B as the reference medication [52]. Moreover, a poor antileishmanial activity against *Leishmania infantum* is another property of the ethanol extract of *Z. ulei* [53].

Additionally, the $CHCl_3$ extract of *Z. ulei* stem showed dose-dependent inhibition of *T. cruzi* epimastigotes at concentrations of 100, 400, and 800 µg/mL with growth inhibition percent of 62.9, 88.2 and 92.5%, respectively [54].

6. CONCLUSION

This research reviewed the content and distribution of different phytochemicals in various *Zamia* species and their previously reported biological activities. Additionally, this study emphasized the wide range of ethnobotanical, conventional uses, and biological activities of several *Zamia* species that can be associated with their different chemical components. Although, few numbers of research studies concerning the phytochemical investigation of *Zamia* species; this study found that *Zamia* is a rich source with a wide variety of valuable chemicals with significant biological values. However, few biological activities of little numbers of *Zamia* species were assessed, and it was found that *Zamia* has an important medicinal role in treating and improving many health problems. There are other unstudied species of *Zamia* that require additional phytochemical and pharmacological research. These species may hold the key to finding novel, less harmful treatments for a variety of serious ailments.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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