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A comprehensive review of phytoconstituents and biological activities of genus *Zinnia*

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Abstract

Zinnia genus contains annual and perennial plants belonging to the family Asteraceae and comprising about 20 species native to South America. *Zinnia* species are used in folk medicine for the treatment of malaria and stomach pain and are used as hepatoprotective, antiparasitic, antifungal and antibacterial agents. *Zinnia* plants are well known ornamental plants with large, beautiful and attractive flowers. Many studies reported that *Zinnia* contains numerous secondary metabolites of different classes including sterols, flavonoids, sesquiterpenes, diterpenes and hydrocarbons. *Zinnia* plants are also reported to possess a wide range of biological effects such as antioxidant, hepatoprotective, cytotoxic, antibacterial, antifungal and insecticidal activities. This review potentiates the researchers for carrying out further studies on this genus to isolate and develop new drugs from natural sources with wide margin of safety and understanding their effects and possible mechanism of actions.

Key words
Asteraceae, Zinnia, phytochemical components, biological activities

1. Introduction

Asteraceae (sunflower family) is considered the largest family of flowering plants that includes about 1600 genera and 24000 species of annual, biennial and perennial herbaceous plants, shrubs, and trees [1]. The plants of this family are widely distributed throughout the world and especially South Asia, South Africa and South America [2], comprising many economically important plants such as the food crops *Lactuca sativa* (lettuce), *Cynara scolymus* (globe artichoke) and *Helianthus nnuus* (sunflower), as well as many ornamentals including *Cosmos sulphureus* and *Zinnia elegans* [3]. *Zinnia* is a genus of 20 species of annual and perennial plants belonging to family Asteraceae and they are native to South America and Mexico. The genus members are popular attributed to their solitary colored flowers; therefore *Zinnia* plants considered the most important ornamental plants in the world because of its successively and rapidly growing rate and also their use as cut flower [4, 5]. *Zinnia* has attracted the interest of researchers due to its biological actions such as antibacterial, antifungal, antioxidant and hepatoprotective activities. Many species that have been investigated for their chemical constituents and biological properties are found to be medicinally useful such as *Z. tenuiflora, Z. citrea, Z. pauciflora, Z. elegans Z. linearis, Z. multiflora, Z. peruviana, Z. angustifolia, Z. verticillata, Z. haageana* and *Z. acerosa*.. This review assembling the published papers about biological actions and isolated phytochemical with regard to their constituents of this genus using different data bases i.e. ChemWeb, Google scholar, Science direct and PubMed. The literature data was collected from 1949 till 2018. All the reported data from pervious published researches are summarized and listed in two tables.

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2.1. Phytochemistry

Reviewing the available literature on genus *Zinnia* revealed the presence of a diversity of secondary metabolites of different classes including flavonoids, sesquiterpenes, sterols and diterpenes. The present review illustrated that 91 compounds were isolated from genus *Zinnia*, among them sesquiterpene lactones are the major constituents that have been isolated and they are assignable for various pharmacological properties of the genus.

2.1.1. Sterols

Phytosterols are naturally occurring compounds present in the plant cell, having a structure similar to the body's cholesterol. Consuming phytosterols is very important for reducing blood cholesterol level and decreasing the intestinal absorption of cholesterol leading to protection from coronary heart diseases.

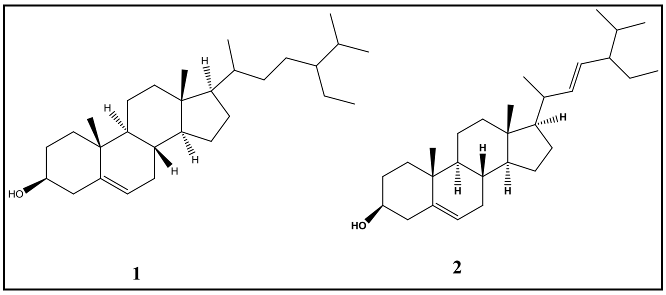


Figure 1: Chemical structures of sterols isolated from *Zinnia*.

Table 1: A list of isolated constituents from genus *Zinnia*

Classification	No	Compound Name	Source	Part used	Ref.
1) Sterols	**1**	*β*-Sitostrol	*Z. elegans*	Leaves	[6]
			Z. tenuiflora	Roots	[7]
	2	Stigmasterol	*Z. citrea*	Aerial parts	[8]
2) Flavonoids					
2.1) Flavonols	**3**	Kaempferol 3-*O*-β-glucoside	*Z. elegans*	Flowers	[9]
	4	Kaempferol 3-*O*-β- xyloside-7- *O*- β-glucoside	*Z. elegans*	Flowers	[9]
	5	Kaempferol 7-*O*- glucorhamnoside	*Z. pauciflora*	Aerial parts	[10]
	6	Quercetin 3-*O*-β- glucoside	*Z. elegans*	Flowers	[9]
2.2) Flavones	**7**	Genkwanin	*Z. citrea*	Aerial parts	[8]
	8	Apigenin 7-*O*-β- glucoside	*Z. elegans*	Flowers	[9]
	9	Apigenin 4'-*O*-β- glucoside	*Z. elegans*	Flowers	[9]
	10	Apigenin 7-*O*-β-(4"-*O*-acetyl)-xyloside	*Z. pauciflora*	Flowers	[10]
	11	Luteolin 7-*O*-β- glucoside	*Z. elegans*	Flowers	[9]
2.3) Aurones	**12**	Maritimein	*Z. linearis*	Flowers	[11]
	13	Sulphurein	*Z. linearis*	Flowers	[11]
2.4) Chalcones	**14**	Marein	*Z. linearis*	Flowers	[11]
2.5) Anthocyanins	**15**	Pelargonidin 3-*O*-β-(6"-acetylglucoside)-5-*O*-β-glucoside	*Z. elegans*	Flowers	[12]
	16	Cyanidin 3-*O*-β-(6"-acetylglucoside)-5-*O*-β-glucoside	*Z. elegans*	Flowers	[12]
	17	Cyanidin 3-*O*- (4"-malonyl)-arabinoside	*Z. pauciflora*	Flowers	[5]
	18	Cyanidin 3-*O*-glucopyranosyl-(6"→1"') (4"'-malonyl)-rhamoniside	*Z. pauciflora*	Flowers	[5]
3) Sesquiterpenes	**19**	Germacrene D	*Z. multiflora*	Aerial parts	[13]
			Z. peruviana	Aerial parts	[13]
			Z. elegans	Aerial parts	[13]
			Z. angustifolia	Aerial parts & roots	[7]
			Z. linearis	Aerial parts & roots	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
			Z. haageana	Aerial parts	[7]
	20	Isoalloalantolactone	*Z. linearis*	Roots	[7]
	21	3-β-Angeloyloxydesoxyinvangustin	*Z. angustifolia*	Roots	[7]
			Z. linearis	Roots	[7]
	22	3-β-Senecioyloxydesoxyivangustin	*Z. angustifolia*	Roots	[7]
			Z. linearis	Roots	[7]
	23	Alantolactone	*Z. angustifolia*	Roots	[7]
			Z. linearis	Roots	[7]
	24	4,5-Dimethyl-3-methylene-3,4,4a,5,6,7,9,9a-octahydronaphtho[2,3-b]furan-2(3H)-one	*Z. angustifolia*	Roots	[7]
			Z. linearis	Roots	[7]
	25	Ziniolide	*Z. multiflora*	Roots	[13]
			Z. angustifolia	Roots	[13]
			Z. elegans	Roots	[13]
			Z. haageana	Aerial parts & roots	[7]
			Z. linearis	Roots	[7]
			Z. tenuiflora	Aerial parts & roots	[7]
			Z. verticillata	Roots	[7]
	26	Eremanthine	*Z. acerosa*	Roots	[13]
	27	Zaluzanin C	*Z. acerosa*	-	[14]
	28	Zaluzanin D	*Z. acerosa*	-	[14]
	29	9α-Angeloyloxydehydrocostus lactone	*Z. acerosa*	Roots	[13]
			Z. linearis	Aerial parts	[7]
			Z. angustifolia	Aerial parts	[7]
	30	9α-Senecioyloxydehydrocostu lactone	*Z .acerosa*	Roots	[13]
			Z. linearis	Aerial parts	[7]
	31	9α- (2- Methylbutyryloxy)- dehydrocostus lactone	*Z. linearis*	Aerial parts	[7]
	32	9α- Isovaleryloxydehydrocostus lactone	*Z. linearis*	Aerial parts	[7]
	33	Angeloyl zaluzanin C	*Z. multiflora*	Roots	[13]
			Z. peruviana	Roots	[13]
			Z. linearis	Aerial parts	[7]
			Z. tenuiflora	Roots	[7]

Classification	No	Compound Name	Source	Part used	Ref.
	34	Senecioyl zaluzanin C	*Z. multiflora*	Roots	[13]
			Z. peruviana	Roots	[13]
			Z. acerosa	Roots	[13]
			Z. tenuiflora	Roots	[7]
	35	Isovaleryl zaluzanin C	*Z. tenuiflora*	Roots	[7]
	36	8α-Angeloyloxydehydrocostus Lactone	*Z. haageana*	Aerial parts	[7]
	37	11 β, 13-Dihydro zaluzanin C-angelate	*Z. verticillata*	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	
	38	14-Angeloyloxydehydrocostus lactone	*Z. linearis*	Aerial parts	[7]
	39	Haageanolide	*Z. haageana*	Leaves	[15]
				Aerial parts	[7]
	40	Haageanolide angelate	*Z. haageana*	Aerial parts & roots	[7]
	41	Zinangustolide	*Z. angustifolia*	Aerial parts & roots	[7]
	42	11 β,13-Dihydrozinangustolide	*Z. angustifolia*	Aerial parts	[7]
	43	9α-angeloyloxy-6-β-hydroxyzinamultiflorid	*Z. multiflora*	Aerial parts	[13]
			Z. peruviana	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	44	9α-[2-Methylacryloyloxy] -6-β-hydroxyzinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. peruviana	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	45	6β-Angeloyloxy 9-α-hydroxy zinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. peruviana	Aerial parts	[13]
			Z. elegans	Aerial parts	[13]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	46	6β-[2-Methylacryloyloxy] 9-α-hydroxy zinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. peruviana	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	47	6β- Angeloyloxy -9-α acetoxy -zinamultifloride	*Z. peruviana*	Aerial parts	[13]
	48	6β- Acetoxy-9-α- angeloyloxy-zinamultifloride	*Z. peruviana*	Aerial parts	[13]
	49	6β,9β-Diangeloyloxy-8-epizinamultifloride	*Z. tenuiflora*	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	50	6β -Angeloyloxy-9β - [2methylbutyryloxy]-8-Epizinamultifloride	*Z. tenuiflora*	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	51	6β -Angeloyloxy-9β -acetoxy-8-epizinamultifloride	*Z. tenuiflora*	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	52	6β-Angeloyloxy-9β-isobutyryloxy-8-epizinamultifloride	*Z. tenuiflora*	Aerial parts	[7]
	53	6β- Angeloyloxy-9β-methylacryloyloxy-8-epizinamultifloride	*Z. tenuiflora*	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	54	6β-Angeloyloxy -9α -hydroxy- epoxy-zinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	55	6β-[2-Methylacryloyloxy] -9α -hydroxy- epoxy-zinamultifloride (Zinaflorin III)	*Z. multiflora*	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[16]
			Z. peruviana	Aerial parts	[16]
	56	9α -Angeloyloxy- 6β-hydroxy- epoxy-zinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. elegans	Aerial parts	[7]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	57	9α-[2-Methylacryloyloxy] -6β-hydroxy- epoxy-zinamultifloride	*Z. multiflora*	Aerial parts	[13]
			Z. elegans	Aerial parts	[13]
			Z. tenuiflora	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]

Classification	No	Compound Name	Source	Part used	Ref.
	58	6β-[2-Methylbutyryloxy]-9α-hydroxy-epoxy zinamultifloride	*Z. acerosa*	Aerial parts	[13]
	59	6β -Isobutyryloxy-9α -hydroxy-epoxy zinamultifloride	*Z. acerosa*	Aerial parts	[13]
	60	9α -[2-Methylbutyryloxy]- 6β -hydroxy-epoxy zinamultifloride	*Z. acerosa*	Aerial parts	[13]
	61	9α-Isobutyryloxy-6β-hydroxy-epoxy zinamultifloride	*Z. acerosa*	Aerial parts	[13]
	62	Zinaflorine IV	*Z. peruviana*	Aerial parts	[17]
	63	Zinniadilactone	*Z. acerosa*	Aerial parts	[13]
	64	Elema-1, 3,11-trien-8α,12-olide (Igalan, 8α-H)	*Z. acerosa*	Roots	[13]
	65	Elema-1, 3,11-trien-8β,12-olide (Igalan, 8β-H)	*Z. acerosa*	Roots	[13]
	66	Juniperin	*Z. juniperifolia*	-	[18]
	67	Zinnacitrin	*Z. citrea*	Aerial parts	[8]
	68	Zinaflavin A	*Z. flavicoma*	Aerial parts	[20]
	69	Zinaflavin B	*Z. flavicoma*	Aerial parts	[20]
	70	Zinaflavin C	*Z. flavicoma*	Aerial parts	[20]
	71	Zinaflavin D	*Z. flavicoma*	Aerial parts	[20]
	72	Zinaflavin E	*Z. flavicoma*	Aerial parts	[20]
	73	Zinaflavin F	*Z. flavicoma*	Aerial parts	[20]
	74	Zinaflavin G	*Z. flavicoma*	Aerial parts	[20]
	75	Zinaflavin H	*Z. flavicoma*	Aerial parts	[20]
	76	Methacrylate elemanolides	*Z. peruviana*	Aerial parts	[16]
	77	Tiglate elemanolides	*Z. peruviana*	Aerial parts	[16]
	78	11,13-Dehydrozinarosin	*Z. acerosa*	Whole plant	[21]
	79	Zinaflorin V	*Z. peruviana*	Aerial parts	[22]
	80	Zinaflorin I	*Z. peruviana*	Aerial parts	[22]
	81	Zinaflorin II	*Z. peruviana*	Aerial parts	[22]
	82	Epoxizinnamultifloride	*Z. peruviana*	Aerial parts	[22]
	83	Zinagrandinolide A	*Z. grandiflora*	Aerial parts	[23]
	84	Zinagrandinolide B	*Z. grandiflora*	Aerial parts	[23]
	85	Zinagrandinolide C	*Z. grandiflora*	Aerial parts	[23]
	86	6*R*-(2"-Hydroxyisobutanoyloxy)-8*S*-acetoxy-15-oxo-1*S*,2-epoxy-3,11(13)-elemandien-12,9-olide	*Z. grandiflora*	Aerial parts	[19, 23]
	87	Zinarosin	*Z. acerosa*	-	[14]
	88	Dihydrozinarosin diaceate	*Z. acerosa*	-	[14]
4) Hydrocarbons	**89**	Pentaynene	*Z. multiflora*	Roots	[13]
			Z. acerosa	Roots	[13]
			Z. angustifolia	Roots	[7]
			Z. haageana	Roots& aerial parts	[7]
			Z. linearis	Roots	[7]
			Z. tenuiflora	Roots	[7]
			Z. *verticillata*	Roots	[7]
5) Diterpenes	**90**	12,18-Dihydroxy-6, 7 *Z*-geranylgeraniol	*Z. tenuiflora*	Aerial parts	[7]
			Z. verticillata	Aerial parts	[7]
	91	Phytol	*Z. verticillata*	Aerial parts	[7]

2.1.2. Flavonoids

Flavonoids are a class of polyphenolic natural substances widely distributed in the plants, having a various biological and pharmacological properties such as antioxidant, anti-inflammatory and cytotoxicity activities. They are divided in to subclasses including flavones, flavonols, flavanones, flavanonols, flavanols or catechins, anthocyanins and chalcones. Variable subclasses of flavonoids are found in *Zinnia* plants.

2.1.3. Sesquiterpenes

Sesquiterpenes are natural C15-terpenoids built from three isoprene units, occurring as hydrocarbons or in oxygenated form such as oxides, ketones, aldehydes, alcohols and lactones possessing several pharmacological actions including anti-inflammatory, antioxidant, antibacterial and cytotoxic activities.

2.1.4. Diterpenes and hydrocarbons

Diterpenes are C20-terpenoids consist of four isoprene units.

2.2. Biological activities

Several studies revealed that *Zinnia* plants exhibited a various pharmacological properties including antioxidant, hepatoprotective, insecticidal and antiviral activities [29-32]. Furthermore, the isolated sesquiterpene lactones from aerial parts *Z. flavicoma* and *Z. grandiflora* were reported to have cytotoxic properties [23, 28]. Also the different extracts have been shown to have antifungal and antibacterial activities [10, 24, 25, 26, 27].

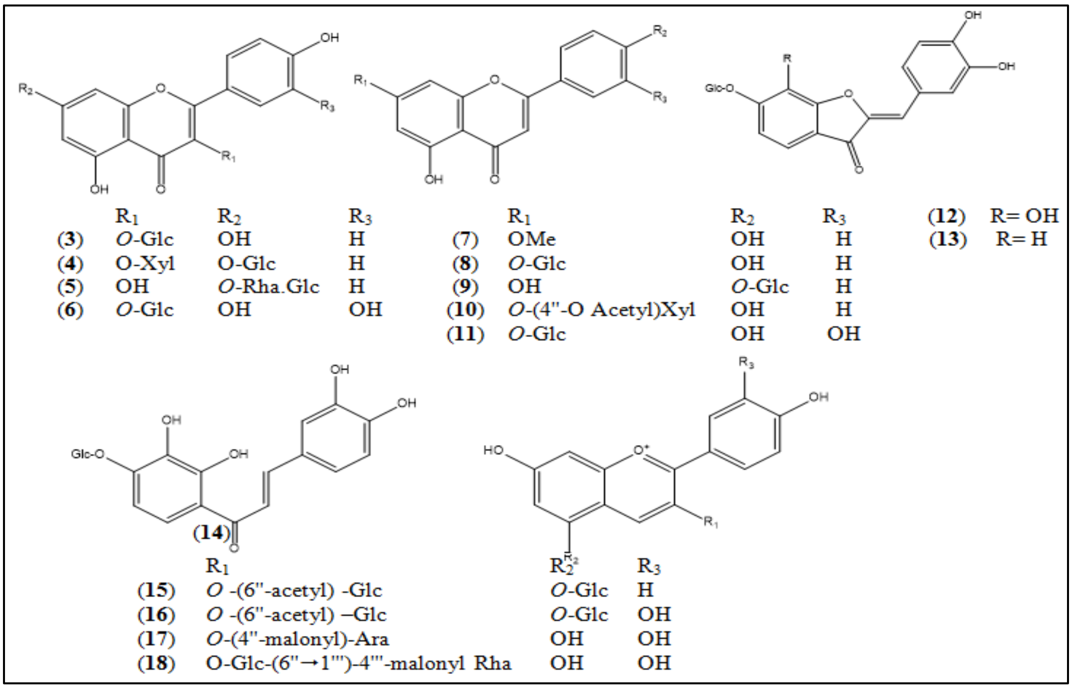
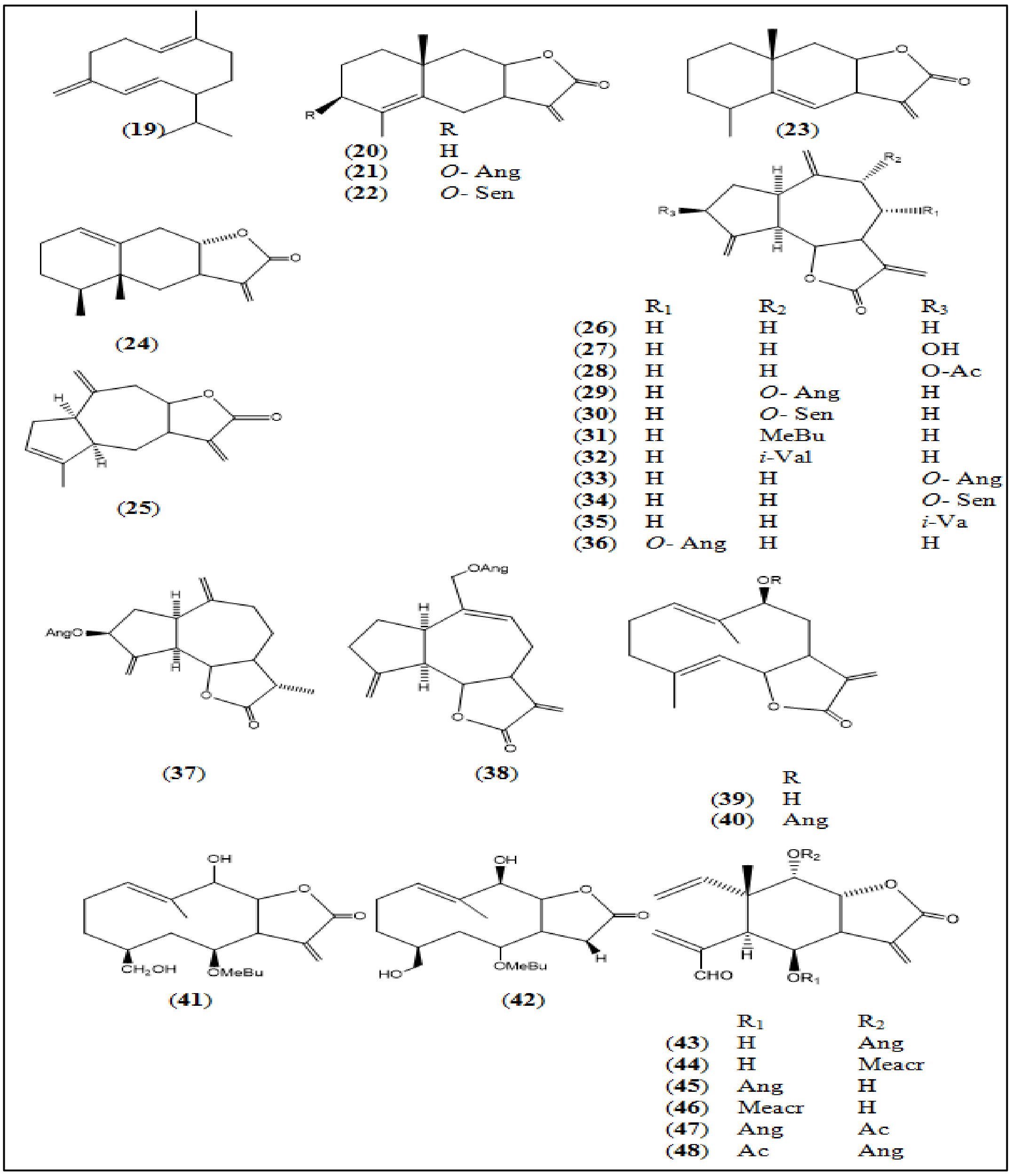


Figure 2: Chemical structures of flavonoids isolated from *Zinnia*.



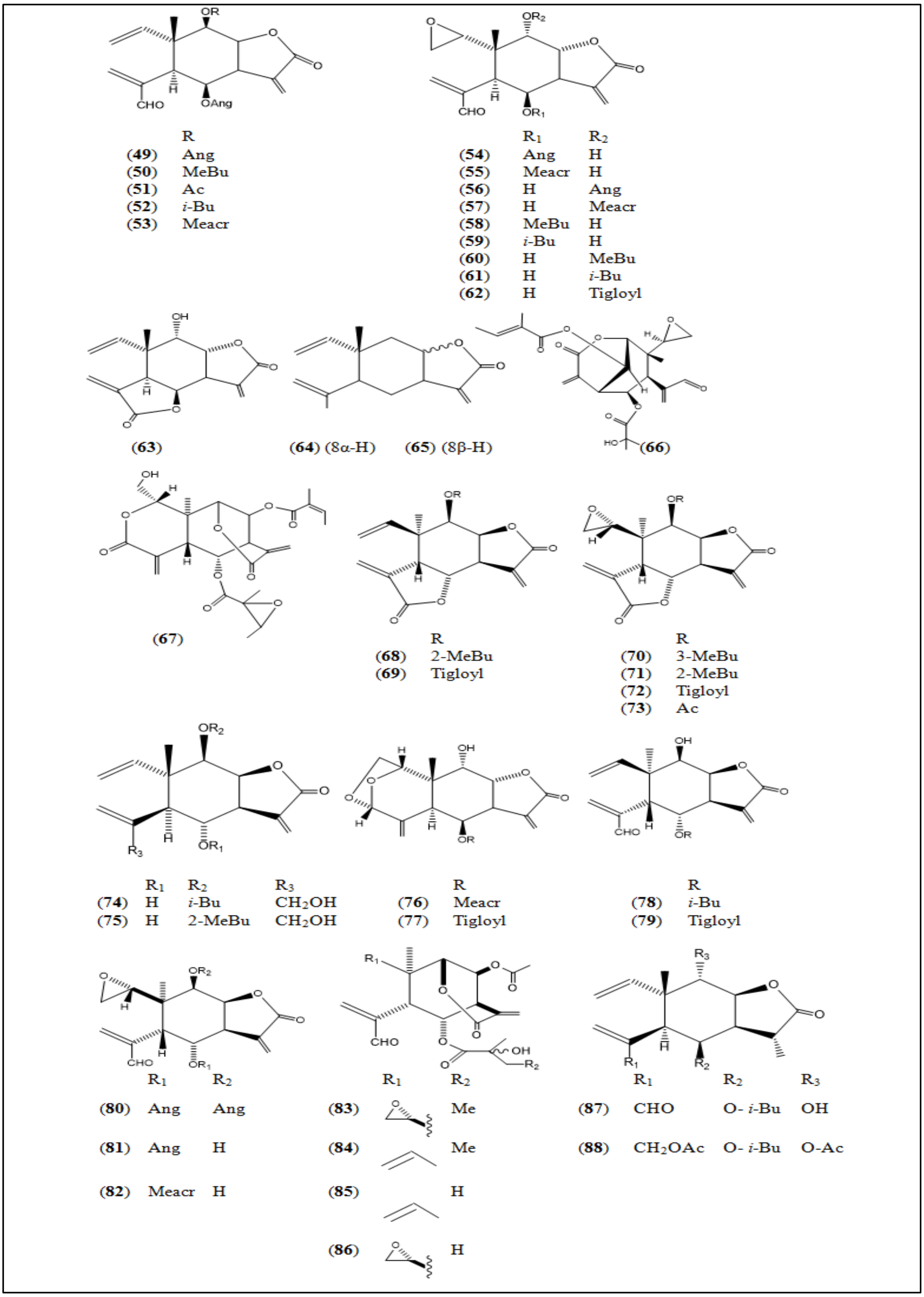


Figure 3: Chemical structures of sesquiterpenes isolated from *Zinnia.*

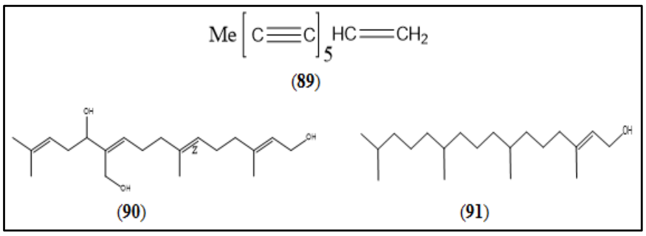


Figure 4: Chemical structures of diterpenes and hydrocarbons isolated from *Zinnia.*

Table 2: A list of different biological activities of genus *Zinnia*

Biological activity	Plant name (part used)	Extract, fraction or compounds	Method of induction	Ref.
1)Antifungal activity	*Zinnia elegans* (Whole plant)	Crude saponins	against *Fusarium oxysporum, F. moniliforme, Colletotrichum falcatum, Rhizoctonia solani, Macrophomina phaseolina*	[24]
	(Aerial parts)	Methanolic extract	against *F. oxysporum*	[25]
	Z. pauciflora (Herb & flowers)	Ethanolic extract	against *F. oxysporum, Aspergillus niger, Candida albicans*	[10]
2) Antibacterial activity	*Z. elegans* (Leaves, flowers & stems)	Hot aqueous, cold aqueous and ethanolic extracts	against *Mycobacterium tuberculosis*	[26]
	Z. peruviana (Aerial parts)	Ethyl acetate, 30% and 40% n-hexane/ethyl acetate extracts	against *Staphylococcus aureus, Pseudomonas aeruginosa, Listeria monocytogenes, Escherichia. coli* and *Bacillus cereus*	[27]
	Z. pauciflora (Herb & flowers)	Ethanolic extract	against *Bacillus subtilis* and *E. coli*	[10]
3) Cytotoxic activity	*Z. flavicoma* (Aerial parts)	Isolated sesquiterpene dilactones (Zinaflavin B, D and F)	against human laringeal carcinoma (HEp-2c) and normal murine connective tissue(L929 fibroblast)	[28]
	Z. grandiflora (Aerial parts)	Isolated sesquiterpene lactones (Zinagrandinolide A-C)	against human non-small-cell lung cancer (NCI-H460), human breast cancer (MCF-7), human CNS cancer (SF-268), human pancreatic carcinoma (MIA Pa Ca-2) and the normal human fibroblast cell type WI-38	[23]
4) Antioxidant activity	*Z. elegans* (Leaves)	Ethanolic extract	DPPH assay	[29]
5) Hepatoprotective activity	*Z. elegans* (Leaves)	Ethanolic extract	CCl_4 induced hepatotoxicity	[29]
6) Insecticidal activity	*Z. elegans* (Flowers)	Acetone-methanol extract	against milkweed bug (*Oncopeltus fasciatus* Dallas)	[30]
	Z. acerosa (Leaves& flowers)	Dried powder	against the maize weevil (*Sitophilus zeamais* Motsch)	[31]
	Z. juniperifolia (Leaves& flowers)	Dried powder	against the maize weevil (*Sitophilus zeamais* Motsch)	[31]
	Z. peruviana (Leaves & flowers)	Dried powder	against the maize weevil (*Sitophilus zeamais* Motsch)	[31]
7) Antiviral activity	*Z. acerosa* (Leaves & stems)	Acetone and methanolic extracts	against herpes simplex virus types 1 and 2 (HSV 1 and HSV 2)	[32]
6) Molluscicidal activity	*Z. elegans* (Leaves)	Water extract	against *Indoplanorbis exustus*	[33]

2.2.1. Antioxidant activity

Recently, exploration of antioxidants from natural source takes a great interest due to their known wide safety margin and lower side effects compared to other synthetic antioxidants. Plants with high content of flavonoids, phenolic acids, carotenoids and polyphenols can scavenge free radicals preventing various diseases such as atherosclerosis, arthritis and cancer [35, 36]. Determination of the total phenolic components of the total ethanolic extract of *Z. elegans* leaves was carried out by Mohamed *et al*., 2015 using Folin-Ciocalteu method, indicating the presence of high amount of phenolic compounds (2.6 mg/g d.w of plant) [29]. Furthermore, the antioxidant activity of the same plant was evaluated using the 2,2-diphenyl-1-picrylhydrazyl hydrate (DPPH) radical scavenging assay, the results demonstrated that the plant extract exhibited a dose dependent scavenging activity. It exhibited a potent scavenging effect (88%) at a concentration of 250 ppm and also showing a significant decrease in the MDA, H_2O_2, NO accumulation and increase of GSH content, indicating its suppression of the oxidative stress through its scavenging activity against the reactive oxygen species, which is directly related to its high phenolic content [29].

2.2.2. Hepatoprotective activity

The ethanolic extract of *Z. elegans* leaves was reported to have a potent hepatoprotective activity against CCl_4 induced liver damage [30]. In that study, the plant extract improved biomarkers levels of the liver (AST, ALT, GST, SOD, MDA and GSH) at different concentrations (50, 100 and 125 mg/100g b.w). In addition to recovering the activity of kidney function by reducing levels of creatinine and urea. Also, the extract improved the lipid profile of the experimental animals showing a significant increase in HDL level and a potent decrease in LDL level. The ethanolic extract of *Z. elegans* exhibited its hepatoprotective activity against CCl_4-induced liver damage due to the presence of antioxidant polyphenolic components in the plant [29].

2.2.3. Cytotoxic activity

Cancer is one of the most diseases causing mortality in the world. The administration of the medicinal plants along with other synthetic anticancer drugs are more effective in cancer prevention and treatment compared to the anticancer agent alone, that considered a potential step in the strategy of cancer prevention.

The isolated sesquiterpenes lactones (zinagrandinolides A-C (**83-85**) and 6*R*-(2''-Hydroxyisobutanoyloxy)-8*S*-acetoxy-15-oxo-1*S*, 2-epoxy-3,11(13)-elemandien-12,9-olide (**86**)) from the hexane extract of the aerial parts of *Z. grandiflora* were tested for their cytotoxic activity against four cancer cell lines . All the isolated compounds exhibited strong cytotoxicity against NCI-H460 (non-small cell lung), MCF-7 (breast), SF-268 (CNS glioma), MIA Pa Ca-2 (pancreatic carcinoma), and normal human fibroblast cells, WI-38 [23].

The isolated elemanolide dilactones including zinaflavins B, D, and F (**69, 71, 73**) from *Z. flavicoma* have been shown to be cytotoxic toward HEp-2c (human laryngeal carcinoma cell line) and L929 (fibroblast cells from normal murine connective tissue, NCTC clone 929) [28].

2.2.4. Antibacterial activity

It is important to search for new sources of antibacterial agents due to the continuous use of antibiotics for a long period of time leads to antibiotic resistance which is considered a serious global problem. The medicinal plants represent a rich source of antimicrobial agents as they produce certain active principles that react with microorganisms in the environment, inhibiting their growth [34].

Different extracts (ethyl acetate, 30% and 40% *n*-hexane/ethyl acetate) of the aerial parts of *Z. peruviana* were investigated against methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Listeria monocytogenes*, *Escherichia coli* and *Bacillus cereus* using microplate method. All extracts were found to have a potent antibacterial effects against the tested gram positive and gram negative bacteria. Furthermore, *S. aureus*, *B. cereus* and *L. monocytogenes* were strongly inhibited by 30% and 40% *n*-hexane/ethyl acetate extracts with MIC value of 0.2 mg/ml, while 100% ethyl acetate extract showed significant activities against all the tested strains at doses of 4 mg/ml [27].

The ethanolic extract of *Z. pauciflora* herb and flowers exhibited significant antibacterial properties against *B. subtilis*, and *E. coli*. The ethanolic extract of the flowers was more effective than herb. The flower extract showed a zone of inhibition of 20.75 and 19.25 mm against *E. coli* and *B. subtilis*, respectively, while the herb extract exhibited a zone of inhibition of 19.00 and 8.00 mm against *B. subtilis* and *E. coli*, respectively [10].

However, hot and cold aqueous and ethanolic extracts of *Z. elegans* of leaves, stems and flowers showed no activity against *Mycobacterium tuberculosis* [26].

2.2.5. Antifungal activity

Antifungal activity of crude saponins and their fractions (A-D) isolated from *Z. elegans* (whole plant) were determined against *Fusarium oxysporum*, *F. moniliforme*, *Colletotrichum falcatum*, *Rhizoctonia solani*, *Macrophomina phaseolina*. The crude saponins inhibited the growth of *F. moniliforme* up to the concentration of 207µg/ml. In addition to, the fraction B showed pronounced antifungal properties against *F. moniliforme* with MIC value of 34.5µg/ml [24].

However, the methanolic extract of aerial parts of *Z. elegans* exhibited no antifungal activity against *F. oxysporum* [25].

The ethanolic extract of *Z. pauciflora* herb and flowers were investigated for their antifungal activities against *F. oxysporum*, *Aspergillus niger* and *Candida albicans* using disc diffusion method. The results revealed the extract of flowers was potent against the tested strains than the extract of herb at all concentrations (100, 200, 300 ppm) [10].

2.2.6. Insecticidal activity

The dried powdered leaves and flowers of *Z. acerosa*, *Z. juniperifolia* and *Z. peruviana* were investigated for their insecticidal effects against maize weevil (*Sitophilus zeamais* Motsch). The results revealed that the powdered leaves of *Z. peruviana* showed the highest mortality percent (88.1%), followed by *Z. acerosa* powdered leaves with mortality percent value of 68.3%, while *Z. juniperifolia* didn't exhibit any activity [32]. However, no insecticidal properties were detected for the acetone- methanol extract of *Z. elegans* against milkweed bug (*Oncopeltus fasciatus* Dallas) [30].

2.2.7. Antiviral and Molluscicidal activities

Greer *et al.*, 2010 examined the acetone and methanolic extracts of thirty one different medicinal plants to evaluate antiviral activity against herpes simplex virus types 1 and 2. Among the tested plants *Z. acerosa* leaves and stems but unfortunately, none of the extracts showed any antiviral activity [32].

The crude water extract of leaves of *Z. elegans* showed no molluscicidal activity against *lndoplallorbis exustlls* [33].

2.2.8. Toxicological evaluation

The oral administration of the ethyl acetate extract of *Z. pauciflora* flowers at doses of 0.7, 1.4 and 2.8 g/kg body weight in male albino rats for two and four weeks showed that low dose of *Zinnia* extract did not give any deleterious effect, whereas the high dose (1.4 and 2.8 g/kg) for four weeks increased ALT, AST and ALP and reduced serum creatinine, blood urea and blood glucose levels [10].

Furthermore, administration of high dose (83.1 mg/100 g b. wt.) of ethanolic extract of *Z. elegans* flowers causing a significant elevation of AST and ALT levels which are indicative of hepatic dysfunction and my due to necrosis of the liver cells, and also the same dose significantly reduced creatinine [6].

Conclusion

The present review provides the data and information about pharmacological and phytochemical investigation of *Zinnia* species for the first time. It is reported that this genus contains several different classes of chemical constituents such as flavonoids, sterols, sesquiterpenes, and diterpenes. Many *Zinnia* plants are reported to possess a various biological properties including antioxidant, antibacterial, antifungal, hepatoprotective and insecticidal. Based on the present review, *Zinnia* plants need further studies for providing more information about their safety and their more pharmaceutical applications as genus *Zinnia* is considered a rich source for discovering and developing new drugs from natural source.

Conflict of interest

The authors declare that they have no conflict of interest.

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