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Chemical and Biological Studies on *Allium sativum* L. (1952-2020): A Comprehensive Review

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Abstract

Medicinal plants provide a variety of secondary metabolites with varied chemical structures and biological activities. Among them, *Allium sativum* L. (garlic) is one of the most common edible and traditional plant that is used for the prevention and treatment of several diseases. *A. sativum* belongs to the family Liliaceae and it demonstrated diverse groups of natural compounds (184 compounds), such as organosulfur compounds, amino acids, selenium derivatives, saponins, phenyl propanoids, flavonoids, alkaloids, fatty acids, sterols and others. Therefore, this review focuses on the different classes of secondary metabolites that have been isolated from *A. sativum*, along with their valued pharmacological and therapeutic effects, e.g., anti-infective (antiprotozoal, antibacterial, antifungal and antiviral activities), antidiabetic, antihyperlipidemic, antihypertensive, heart protective, neuroprotective, hepatoprotective, antioxidant, anticancer, antiobesity, wound and scar healing, antianxiety, antidepressant, immunostimulant and memory enhancing properties. The potential of garlic in the treatment of many diseases such as gastrointestinal disorders, nephropathic encephalopathy and osteoarthritis has been also reported.

1. Introduction

Liliaceae is a family of about 280 genera and 4000 species [1]. It has been divided into three subfamilies, Lilioideae, Calochortoideae and Streptopoideae [2]. Family Liliaceae members have six-segmented flowers and capsular fruits, that are three-chambered. The leaves always have veins, that are parallel to each other and are clustered at the plant base. Most species have bulb, that is considered as an underground storage structure [3]. *Veratrum* and *Fritillaria* are two main genera in the family Liliaceae. Native Americans utilized the *Veratrum* species to treat various diseases, including sore throats, inflamed tonsils, wounds, coughing, mania, epilepsy, snake bites and venereal illness. The alkaloids of *Veratrum* decreased high blood pressure and were prescribed until the nineteenth century, when emetic side effects restricted its use. For centuries in China, the rhizomes and roots of numerous *Veratrum* species known as "Li-lu" have been used to cure aphasia caused by apoplexy, chronic malaria, jaundice, scabies and dysentery [4].

Many species of *Fritillaria* have also been employed in traditional Japanese, Southeast Asian, Turkish and Pakistani herbal medicine. For more than 2000 years, the bulbs of various *Fritillaria* species have been used as anti-asthmatics, expectorants and antitussives under the Chinese name "Bei-mu" [4]. Plants of the family Liliaceae contain structurally complex and biologically active steroidal alkaloids [4].

One of the most important Liliaceae plants is garlic (*Allium sativum* L.) [5]. According to recent taxonomic classifications,

garlic is now in the plant family Amaryllidaceae [6]. Garlic has different biological activities, such as hypolipidemic, antitumor, antiarthritic, hypoglycemic, antithrombotic and anti-infective activities (antiprotozoal, antibacterial, antifungal and antiviral). Also, it shows potent antidiabetic, cardioprotective and antioxidant activities [5]. Such wide and interesting chemical and biological diversities of garlic have provoked us to prepare this work as a comprehensive overview on this valued plant species.

2. Methodology

We performed a systematic search on the previous literature (100 peer-reviewed articles) with *Allium sativum* as a key search word on different databases such as PubMed, Google Scholar, ACS Publications, SciFinder, DNP, which was also assembled using The Plant List, Global Biodiversity Information Facility and Scopus for bioactive compounds, chemistry, biological and pharmacological properties of *A. sativum*.

3. Phytochemical review

Garlic is one of the most common edible or medicinal plant species. It contains various classes of active secondary metabolites represented by about 184 compounds. A comprehensive list of the isolated compounds from *A. sativum* is presented in Table 1 and their structures are shown in Figure 1. Most of the characterized metabolites are organosulfur compounds (70 compounds, representing 38%) and saponins (29

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Table 1: A list of the previously reported compounds from *A. sativum* (1952-2020).

No.	Name	Molecular weight	Molecular formula	Organ	Ref.
A) Acyclic organosulfur compounds					
I) Acyclic monosulfides					
1	Diallyl sulfide	114.21	$C_6H_{10}S$	Bulb	[7-9]
2	2-Propenesulfenic acid	90.14	C_3H_6OS	Bulb	[10]
3	2-Propenesulfinic acid	106.14	$C_3H_6O_2S$	Bulb	[10]
4	Methiin [syn.: *S*-Methylcysteine sulfoxide]	151.19	$C_4H_9NO_3S$	Bulb	[11]
5	(+)-*S*-Methyl-L-cysteine sulfoxide	151.19	$C_4H_9NO_3S$	Leaf	[12]
6	*S*-1-Propenyl cysteine	161.22	$C_6H_{11}NO_2S$	Bulb	[13]
7	Ethiin [syn.: *S*-Ethylcysteine sulfoxide]	165.21	$C_5H_{11}NO_3S$	Bulb	[11]
8	Isoalliin [syn.: (*E*)-*S*-(1-propenyl) cysteine sulfoxide]	177.22	$C_6H_{11}NO_3S$	Bulb	[11]
9	(+)-*S*-(*E*-1-propenyl)-L-cysteine sulfoxide	177.22	$C_6H_{11}NO_3S$	Leaf	[12]
10	Alliin [syn.: *S*-allylcysteine sulfoxide]	177.22	$C_6H_{11}NO_3S$	Leaf	[5,12]
11	*N*-γ-L-Glutamyl-*S*-(*E*-1-propenyl)-L-cysteine	289.33	$C_{11}H_{17}N_2O_5S$	Bulb	[14]
12	γ-L-Glutamyl-*S*-allyl-L-cysteine	289.33	$C_{11}H_{17}N_2O_5S$	Bulb	[14]
13	Alliin-*N*-(1-deoxy-*β*-D-fructopyranosyl) [syn.: (-)-*N*-(1'-Deoxy-1'-*β*-D-fructopyranosyl)-*S*-allyl-L-cysteine sulfoxide]	339.36	$C_{12}H_{21}NO_8S$	Leaf	[12]
14	*S*-(2-Carboxypropyl) glutathione	393.42	$C_{14}H_{23}N_3O_8S$	Bulb	[15]
II) Acyclic disulfides					
15	Dimethyl disulfide	94.20	$C_2H_6S_2$	Bulb	[9]
16	2-Propeneperthiol	106.21	$C_3H_6S_2$	Bulb	[10]
17	Allyl methyl disulfide	120.24	$C_4H_8S_2$	Bulb	[9]
18	Methyl-(*Z*)-1-propenyl disulfide	120.24	$C_4H_8S_2$	Bulb	[9]
19	Methyl-(*E*)-1-propenyl disulfide	120.24	$C_4H_8S_2$	Bulb	[9]
20	Di-2-propenyl disulfide [syn.: Diallyl disulfide]	146.27	$C_6H_{10}S_2$	Bulb	[5,10]
21	(*E*)-1-Propenyl-2-propenyl disulfide [syn.: Allyl (*E*)-1-propenyl disulfide]	146.30	$C_6H_{10}S_2$	Bulb	[9]
22	(*Z*)-1-Propenyl-2-propenyl disulfide [syn.: Allyl-(*Z*)-1-propenyl disulfide]	146.30	$C_6H_{10}S_2$	Bulb	[16]
23	Methyl methanethiosulfinate	110.20	$C_2H_6OS_2$	Bulb	[10]
24	(*Z*)-Methyl-1-propenyl disulfide-5-Oxide	136.24	$C_4H_8OS_2$	Bulb	[10]
25	(*E*)-Methyl-1-propenyl disulfide-5-Oxide	136.24	$C_4H_8OS_2$	Bulb	[10]
26	Allyl methyl thiosulfinates	136.24	$C_4H_8OS_2$	Bulb	[10]
27	Isoallyl methyl thiosulfinates	136.24	$C_4H_8OS_2$	Bulb	[10]
28	Dihydroasparagusic acid	152.20	$C_4H_8O_2S_2$	Bulb	[17]
29	2-Propene-1-sulfinothioic acid-*S*-1-propenyl ester	162.27	$C_6H_{10}OS_2$	Bulb	[18]
30	Allicin [syn.: 2-Propene-1-sulfonic acid-*S*-2-propenyl ester]	162.27	$C_6H_{10}OS_2$	Bulb	[18,19]
31	2-Propenyl propyl disulfide-4-Oxide	164.29	$C_6H_{12}OS_2$	Bulb	[20]
32	2-Propenyl propyl disulfide-5-Oxide	164.29	$C_6H_{12}OS_2$	Bulb	[20]
33	*S,S*-Dioxide-di-2-propenyl disulfide [syn.: *S*-2-Propenyl-2-propene-1-sulfonothioate]	178.30	$C_6H_{10}O_2S_2$	Bulb	[21]
34	*S*-Allylmercapto-L-cysteine	193.30	$C_6H_{11}NO_2S_2$	Bulb	[22]
35	γ-L-Glutamyl-*S*-allylthio-L-cysteine	322.40	$C_{11}H_{18}N_2O_5S_2$	Bulb	[14]
36	Allithiamine	354.50	$C_{15}H_{22}N_4O_2S_2$	Bulb	[23]
III) Acyclic trisulfides					
37	Dimethyl trisulfide	126.30	$C_2H_6S_3$	Bulb	[9]
38	Methyl-2-propenyl trisulfide [syn.: Allyl methyl trisulfide]	152.30	$C_4H_8S_3$	Bulb	[18]
39	Diallyl trisulfide [syn.: Di-2-propenyl trisulfide]	178.30	$C_6H_{10}S_3$	Bulb	[24]
40	Allyl-1-propenyl trisulfide	178.30	$C_6H_{10}S_3$	Bulb	[24]
41	Allyl propyl trisulfide	180.40	$C_6H_{12}S_3$	Bulb	[9]
42	(*Z*)-Methyl-3-(methylthio)-1-propenyl disulfide-7-Oxide [syn.: (*Z*)-Methyl-3-(methylsulfinyl)-1- propenyl disulfide]	182.30	$C_5H_{10}OS_3$	Bulb	[25]
43	Diallyl trisulfane-*S*-oxide	194.30	$C_6H_{10}OS_3$	Bulb	[10]
44	Ajoene	234.40	$C_9H_{14}OS_3$	Bulb	[26]
45	Ajocysteine	281.40	$C_9H_{15}NO_3S_3$	Bulb	[26]

Table 1: Continued.

	IV) Acyclic tetrasulfides				
46	Methyl-2-propenyl tetrasulfide [syn.: Allyl methyl tetrasulfide]	184.40	$C_4H_8S_4$	Bulb	[27]
47	Di-2-propenyl tetrasulfide	210.40	$C_6H_{10}S_4$	Bulb	[9]
	V) Acyclic pentasulfides				
48	Methyl-2-propenyl pentasulfide [syn.: Allyl methyl pentasulfide]	216.40	$C_4H_8S_5$	Bulb	[28]
49	Di-2-propenyl pentasulfide	242.50	$C_6H_{10}S_5$	Bulb	[29]
	VI) Acyclic hexasulfides				
50	Di-2-propenyl hexasulfide	274.53	$C_6H_{10}S_6$	Bulb	[29]
	VII) Acyclic heptasulfides				
51	Di-2-propenyl heptasulfide	306.60	$C_6H_{10}S_7$	Bulb	[29]
	B) Cyclic organosulfur compounds				
52	Cyclic octaatomic sulfur	256.50	S_8	Bulb	[16]
53	1,2-Dithiolene	104.20	$C_3H_4S_2$	Bulb	[9]
54	1,2-Dithiolane	106.21	$C_3H_6S_2$	Bulb	[9]
55	3-Vinyl-[4*H*]-1,2-dithiin	144.30	$C_6H_8S_2$	Bulb	[24]
56	2-Vinyl-[4*H*]-1,3-dithiin	144.30	$C_6H_8S_2$	Bulb	[24]
57	2-Vinyl-1,3-dithiane	146.30	$C_6H_{10}S_2$	Bulb	[9]
58	3,5-Diethyl-1,2,4-trithiolane	180.40	$C_6H_{12}S_3$	Bulb	[24]
59	Garlicnin D [syn: 3,4-Dihydro-1-mercapto-1-methyl-3-vinyl-1,2-dithiin-*S*"-Oxide]	208.40	$C_7H_{12}OS_3$	Bulb	[30]
60	Garlicnin B	220.35	$C_9H_{16}O_2S_2$	Bulb	[30]
61	5-Hexyl-2-thiopheneoctanoic acid	310.49	$C_{18}H_{30}O_2S$	Bulb	[31]
62	2,3,4,5-Tetrahydro-5-hexyl-2-thiopheneoctanoic acid	314.53	$C_{18}H_{34}O_2S$	Bulb	[31]
63	8-[(6-Pentyl-tetrahydro-2*H*-thiopyran-2-yl) octanoic acid]	314.53	$C_{18}H_{34}O_2S$	Bulb	[31]
64	Foliogarlic disulfanes A1	320.38	$C_{12}H_{16}O_6S_2$	Leaf	[32]
65	Foliogarlic disulfanes A2	320.38	$C_{12}H_{16}O_6S_2$	Leaf	[32]
66	Foliogarlic disulfanes A3	320.38	$C_{12}H_{16}O_6S_2$	Leaf	[32]
67	Garlicnin A	324.55	$C_{12}H_{20}O_2S_4$	Bulb	[30]
68	Garlicnin C1 [syn.: (2*S*,3*S*,4*S*,5*R*)-3,4-Dimethyl-2-(prop-2-enyldisulfanyl)-5-[(*E*)-prop-1-enyl] sulfinylthiolane 1-oxide]	324.55	$C_{12}H_{20}O_2S_4$	Bulb	[30]
69	Foliogarlic trisulfane A1	352.45	$C_{12}H_{16}O_6S_3$	Leaf	[32]
70	Foliogarlic trisulfane A2	352.45	$C_{12}H_{16}O_6S_3$	Leaf	[32]
	C) Aminoacids				
71	$α$-Aminobutyric acid	103.12	$C_4H_9NO_2$	Bulb	[8]
72	Choline	104.17	$C_5H_{14}NO^+$	Bulb	[33]
73	Proline	115.13	$C_5H_9NO_2$	Bulb	[33]
74	Valine	117.15	$C_5H_{11}NO_2$	Bulb	[33]
75	5-Oxoproline	129.11	$C_5H_7NO_3$	Bulb	[33]
76	Leucine	131.17	$C_6H_{13}NO_2$	Bulb	[33]
77	Aspartic acid	133.10	$C_4H_7NO_4$	Bulb	[33]
78	Lysine	146.19	$C_6H_{14}N_2O_2$	Bulb	[33]
79	Glutamic acid	147.13	$C_5H_9NO_4$	Bulb	[33]
80	Hydroxylysine	162.19	$C_6H_{14}N_2O_3$	Bulb	[33]
81	Arginine	174.20	$C_6H_{14}N_4O_2$	Bulb	[33]
82	L-L-*N*-$γ$-Glutamylphenylalanine	294.38	$C_{14}H_{18}N_2O_5$	Bulb	[14]
	D) Selenium derivatives				
83	Se-Methylselenocysteine	182.09	$C_4H_9NO_2Se$	Bulb	[34]
84	$γ$-Glutamyl-Se-methylselenocysteine	310.20	$C_9H_{15}N_2O_5Se^-$	Bulb	[34]
	D) Saponins				
85	Diosgenin	414.60	$C_{27}H_{42}O_3$	Clove	[35]
86	Laxogenin	430.60	$C_{27}H_{42}O_4$	Bulb	[36]
87	Gitogenin	432.60	$C_{27}H_{44}O_4$	Clove	[35]
88	$β$-Chlorogenin	432.64	$C_{27}H_{44}O_4$	Bulb	[35,36]
89	Agigenin	448.60	$C_{27}H_{44}O_5$	Bulb	[36]
90	Agapanthagenin	448.60	$C_{27}H_{44}O_5$	Clove	[35]

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Table 1: Continued.

91	Ampeloside Bs1	935.10	$C_{45}H_{74}O_{20}$	Bulb	[36]
92	Degalactotigonin	1035.20	$C_{50}H_{82}O_{22}$	Root	[35,37]
93	Chinenoside I	1037.10	$C_{49}H_{80}O_{23}$	Bulb	[36]
94	F-Gitonin	1051.20	$C_{50}H_{82}O_{23}$	Root	[37]
95	Eruboside B	1081.20	$C_{51}H_{84}O_{24}$	Bulb	[18]
96	Isoeruboside B	1081.20	$C_{51}H_{84}O_{24}$	Bulb	[18]
97	Ampeloside Bf1	1115.20	$C_{51}H_{86}O_{26}$	Bulb	[36]
98	Sativoside R2	1197.31	$C_{56}H_{92}O_{27}$	Root	[37,38]
99	Proto-desgalactotigonin	1215.30	$C_{56}H_{94}O_{28}$	Clove	[35,38]
100	Proto-eruboside B	1261.35	$C_{57}H_{96}O_{30}$	Bulb	[38]
101	Proto-isoeruboside B	1261.35	$C_{57}H_{96}O_{30}$	Bulb	[38]
102	Sativoside R1	1377.50	$C_{62}H_{104}O_{33}$	Root	[37,38]
103	Sativoside B1	1423.50	$C_{63}H_{106}O_{35}$	Bulb	[37]
104	Voghieroside E1 [syn: Furosta-2α,3β,22α,26-tetrol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-α-L-rhamnopyranoside]	1245.35	$C_{57}H_{96}O_{29}$	Bulb	[39]
105	Voghieroside E2 [syn: Furosta-2α,3β,22β,26-tetrol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-α-L-rhamnopyranoside]	1245.35	$C_{57}H_{96}O_{29}$	Bulb	[39]
106	Voghieroside B1 [syn: Furosta-2α,3β,5α,22α,26-pentol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1277.35	$C_{57}H_{96}O_{31}$	Bulb	[39]
107	Voghieroside B2 [syn: Furosta-2α,3β,5α,22β,26-pentol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1277.35	$C_{57}H_{96}O_{31}$	Bulb	[39]
108	Voghieroside C1 [syn: Furosta-2α,3β,6β,22α,26-pentol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1277.35	$C_{57}H_{96}O_{31}$	Bulb	[39]
109	Voghieroside C2 [syn: Furosta-2α,3β,6β,22β,26-pentol-3-*O*-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1277.35	$C_{57}H_{96}O_{31}$	Bulb	[39]
110	Voghieroside D1 [syn: Furosta-2α,3β,22α,26-tetrol-3-*O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-α-L-rhamnopyranoside]	1407.50	$C_{63}H_{106}O_{34}$	Bulb	[39]
111	Voghieroside D2 [syn: Furosta-2α,3β,22β,26-tetrol-3-*O*-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl (1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-α-L-rhamnopyranoside]	1407.50	$C_{63}H_{106}O_{34}$	Bulb	[39]
112	Voghieroside A1 [syn: Furosta-2α,3β,5α,22α,26-pentol-3-*O*-β-D-glucopyranosyl-(1→3)-[β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl (1→3)]-β-D-glucopyranosyl-(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1438.49	$C_{63}H_{106}O_{36}$	Bulb	[39]
113	Voghieroside A2 [syn: Furosta-2α,3β,5α,22β,26-pentol-3-*O*-β-D-glucopyranosyl-(1→3)-[β-D-glucopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl(1→4)-β-D-galactopyranosyl-26-*O*-β-D-glucopyranoside]	1438.64	$C_{63}H_{106}O_{36}$	Bulb	[39]

E) Phenyl propanoids

114	*p*-Coumaric acid	164.16	$C_9H_8O_3$	Garlic husk waste	[40]
115	Caffeic acid	180.16	$C_9H_8O_4$	Garlic husk waste	[40]
116	Ferulic acid	194.18	$C_{10}H_{10}O_4$	Garlic husk waste	[40]

Table 1: Continued.

117	Eugenyl-*O*-α-L-rhamnopyranosyl-(1→6)-*β*-D-glucopyranoside	470.51	$C_{23}H_{34}O_{10}$	Bulb	[41]
118	Eugenol-1-*O*-rutinoside	472.48	$C_{22}H_{32}O_{11}$	Bulb	[39]
119	Eugenyl-*O*-*β*-D-glucopyranosyl-(1→6)-*β*-D-glucopyranoside	486.51	$C_{23}H_{34}O_{11}$	Bulb	[41]
120	Eugenol-1-*O*-diglucoside	488.48	$C_{22}H_{32}O_{12}$	Bulb	[39]
121	4-*O*-*β*-D-Gucopyranosyl-(1→6)-*β*-D-glucopyranosyl-5-methoxy eugenol	516.54	$C_{24}H_{36}O_{12}$	Bulb	[41]
122	*N*-Feruloyltyramine	313.30	$C_{18}H_{19}NO_4$	Root	[38]
123	*N*-Feruloyltyrosine	357.40	$C_{19}H_{19}NO_6$	Root	[38]
F) Flavonoids					
F-1) Flavane and its derivatives					
124	Naringenin	272.25	$C_{15}H_{12}O_5$	Bulb	[42]
125	Catechin	290.27	$C_{15}H_{14}O_6$	Bulb	[33]
126	Gallocatechol	306.27	$C_{15}H_{14}O_7$	Bulb	[33]
127	Naringin	580.50	$C_{27}H_{32}O_{14}$	Bulb	[42]
F-2) Flavone and its derivatives					
128	Apigenin	270.24	$C_{15}H_{10}O_5$	Bulb	[18]
129	Quercetin	302.23	$C_{15}H_{10}O_7$	Bulb	[18]
130	Myricetin	318.23	$C_{15}H_{10}O_8$	Bulb	[38]
131	3,5,6,7-Tetramethoxyflavone	342.30	$C_{19}H_{18}O_6$	Bulb	[33]
132	5,6,7,8,4'-Pentamethoxyflavone	372.40	$C_{20}H_{20}O_7$	Bulb	[33[
133	Tangeretin	372.40	$C_{20}H_{20}O_7$	Bulb	[42]
134	Nobiletin	402.40	$C_{21}H_{22}O_8$	Bulb	[42]
135	Rutin	610.50	$C_{27}H_{30}O_{16}$	Bulb	[18]
F-3) Anthocyanins					
136	Anthocyanin	207.25	$C_{15}H_{11}O$	Bulb	[33]
137	Pelargonidin	271.24	$C_{15}H_{11}O_5$	Bulb	[33]
138	Cyanidin	287.24	$C_{15}H_{11}O_6$	Bulb	[33]
139	Delphinidin	338.69	$C_{15}H_{11}ClO_7$	Bulb	[33]
G) Alkaloids					
140	Theophylline	180.16	$C_7H_8N_4O_2$	Bulb	[33]
141	Nicotine	162.23	$C_{10}H_{14}N_2$	Bulb	[33]
142	(3*S*)-1,2,3,4-Tetrahydro-*β*-carboline-3-carboxylic acid	216.24	$C_{12}H_{12}N_2O_2$	Bulb	[41]
143	(1*S*,3*S*)-1-Methyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic acid	230.26	$C_{13}H_{14}N_2O_2$	Bulb	[41]
144	(1*R*,3*S*)-1-Methyl-1,2,3,4-tetrahydro-*β*-carboline-3-carboxylic acid	230.26	$C_{13}H_{14}N_2O_2$	Bulb	[41]
145	(1*R*,3*S*)-1-Methyl-1,2,3,4-tetrahydro-*β*-carboline-1,3-dicarboxylic acid	274.27	$C_{14}H_{14}N_2O_4$	Bulb	[43]
146	(1*S*,3*S*)-1-Methyl-1,2,3,4-tetrahydro-*β*-carboline-1,3-dicarboxylic acid	274.27	$C_{14}H_{14}N_2O_4$	Bulb	[43]
H) Fatty acids					
147	Myristic acid [syn.: *n*-Tetradecanoic acid]	228.37	$C_{14}H_{28}O_2$	Bulb	[33]
148	Palmitic acid [syn.: *n*-Hexadecanoic acid]	256.42	$C_{16}H_{32}O_2$	Bulb	[33,44]
149	Oleic acid [syn.: (9*Z*)-Octadecenoic acid]	282.50	$C_{18}H_{34}O_2$	Bulb	[33]
I) Sterol					
150	Campesterol	400.70	$C_{28}H_{48}O$	Bulb	[18]
J) Miscellaneous compounds					
151	2-Propen-1-ol	58.08	C_3H_6O	Bulb	[10]
152	Aminoacrylic acid	87.08	$C_3H_5NO_2$	Bulb	[10]
153	2-Hydroxy propanamide	89.09	$C_3H_7NO_2$	Bulb	[44]
154	Lactic acid	90.08	$C_3H_6O_3$	Bulb	[33]
155	2-Methylene-4-pentenal	96.13	C_6H_8O	Bulb	[9]
156	Ammonium pyruvate	105.09	$C_3H_7NO_3$	Bulb	[10]
157	Succinic acid	118.09	$C_4H_6O_4$	Bulb	[33]
158	Malic acid	134.09	$C_4H_6O_5$	Bulb	[33]
159	1-Oxaspiro(2,5)oct-5-ene, 8,8-dimethyl-4-methylene	150.22	$C_{10}H_{14}O$	Bulb	[44]
160	Carvacrol	150.22	$C_{10}H_{14}O$	Bulb	[33]
161	Carvone	150.22	$C_{10}H_{14}O$	Bulb	[16]
162	*p*-Tert-butylphenol	150.22	$C_{10}H_{14}O$	Bulb	[44]
163	Mandelic acid	152.15	$C_8H_8O_3$	Bulb	[33]
164	Geraniol	154.25	$C_{10}H_{18}O$	Bulb	[18]
165	Linalool	154.25	$C_{10}H_{18}O$	Bulb	[33]
166	4-(1,1-Dimethylpropyl) phenol	164.24	$C_{11}H_{16}O$	Bulb	[44]

Table 1: Continued.

167	Arabinoic acids	166.13	$C_5H_{10}O_6$	Bulb	[33]
168	(*S*)-2-(3,4-Dimethyl-1*H*-pyrrol-1-yl) propanoic acid	167.21	$C_9H_{13}NO_2$	Bulb	[45]
169	D-Galactosamine	179.17	$C_6H_{13}NO_5$	Bulb	[33]
170	Aldohexose	180.16	$C_6H_{12}O_6$	Bulb	[33]
171	(*S*)-2-(3,4-Dimethyl-1*H*-pyrrol-1-yl)-3-methyl butanoic acid	195.26	$C_{11}H_{17}NO_2$	Bulb	[45]
172	4-(1-Phenylethyl) phenol	198.26	$C_{14}H_{14}O$	Bulb	[44]
173	3-Hydroxy-2,2-dimethyl, 3-hydroxy-2,2-dimethylpropyl propanoic acid	204.26	$C_{10}H_{20}O_4$	Bulb	[44]
174	Proflavine	209.25	$C_{13}H_{11}N_3$	Bulb	[33]
175	Allixin	226.27	$C_{12}H_{18}O_4$	Bulb	[46]
176	Pyridoxamine phosphate	248.17	$C_8H_{13}N_2O_5P$	Bulb	[33]
177	Thiamine	265.36	$C_{12}H_{17}N_4OS^+$	Bulb	[33]
178	Hexestrol	270.40	$C_{18}H_{22}O_2$	Bulb	[44]
179	[1,4-Dimethyl-7-(1-methylethyl)-2-azulenyl] phenyl methanone	302.40	$C_{22}H_{22}O$	Bulb	[44]
180	2,4-Bis(1-phenylethyl) phenol	302.40	$C_{22}H_{22}O$	Bulb	[44]
181	(*Z*)-14-Tricosenyl formate	366.60	$C_{24}H_{46}O_2$	Bulb	[44]
182	4,5-2*H*-Oxazole-5-one, 4-[3,5-Di-t-butyl-4-methoxyphenyl]-methylene-2-phenyl	391.50	$C_{25}H_{29}NO_3$	Bulb	[44]
183	Retinoyl-*β*-glucuronic acid	476.60	$C_{26}H_{36}O_8$	Bulb	[33]
184	*β*-Carotene	536.90	$C_{40}H_{56}$	Bulb	[18]

compounds, representing 16%), while other classes, such as flavonoids (16 compounds, representing 9%), amino acids (12 compounds, representing 6%), phenyl propanoids (10 compounds, representing 5%), alkaloids (7 compounds, representing 4%), fatty acids (3 compounds, representing 2%), selenium derivatives (2 compounds, representing 1%) and sterol (one compound, representing less than 1%). Bulbs and cloves were the most phytochemically investigated parts (166 compounds, representing 90% of the identified compounds), followed by the leaves (9 compounds, representing 5%), roots (6 compounds, representing 3%) and husk wastes (3 compounds, representing 2%). These results are displayed in Figures 2-3.

4. Biological review

4.1. Anti-infective
Active constituents from garlic exhibited anti-infective activity such as antiprotozoal, antibacterial, antiviral and antifungal activities.

4.1.1. Antiprotozoal
The extract was found to be effective against protozoa hosts such as *Opalina ranarum*, *Opalina dimidicita*, *Balantidium entozoon*, *Entamoeba histolytica*, *Crithidia, Leptomonas*, *Leishmania* and *Trypanosomes* in several studies. Often, it was used in giardiasis therapy, alleviating symptoms throughout 24 h and suggesting, that giardiasis is fully eliminated from the stool throughout 72 h (1 mg/L twice daily from the aqueous extract) or (0.6 mg/mL garlic capsule, that was prepared). The crude extract of garlic showed inhibitory activity against *E. histolytica* (25 μg/mL) and the lethal dosage was 50 μg/mL [5,47].

Allicin, which degrades to give diallyl trisulfide (DATS), that is more stable than allicin and is highly volatile. It is prescribed for *Trichomonas vaginalis* and *E. histolytica* infections [5, 48].

4.1.2. Antibacterial
Garlic has broad spectrum antibiotic properties towards Gram-negative, acid-fast and Gram-positive bacteria such as, *Staphylococcus aureus*, *Escherichia coli, Bacillus subtulis, Mycobacterium, Pseudomonas, Klebsiella, Salmonella. Micrococcus, Proteus* and *Clostridium.* Growth inhibition seen in *E. coli* was 10 times or greater than, that observed in *Lactobacillus casei* for the same dose of garlic. This may be due to the difference in compositions of bacterial membranes and their permeability for antibacterial constituent allicin. On vancomycin-resistant *enterococci*, allicin and garlic extract have bacteriostatic properties, when they were coupled with vancomycin, an inhibitory synergistic effect was seen [5,48,49].

4.1.3. Antifungal
Garlic has antifungal properties against many fungal genera including *Candida, Aspergillus*, *Trichophyton*, *Cryptococcus, Torulopsis*, *Trichosporon* and *Rhodotorula*. Garlic extracts decrease the oxygen uptake, resulting in decreasing the organism growth through inhibition of the synthesis of lipids, nucleic acids and proteins and hence membranes damages were occurred. Pure allicin was seen to have antifungal effect. DATS demonstrated also antifungal activity against *Cryptococcal meningitis* and *Aspergillus*. Furthermore, *Candida* adhesion is considerably reduced in the presence of garlic extract [5,50-53]. Garlic was also effective in treating oral candidiasis and recurrent aphthous ulcers without the side effects associated with standard medication. Researchers should investigate the usage of garlic *in vivo* to see if it could be used to treat oral illness [54].
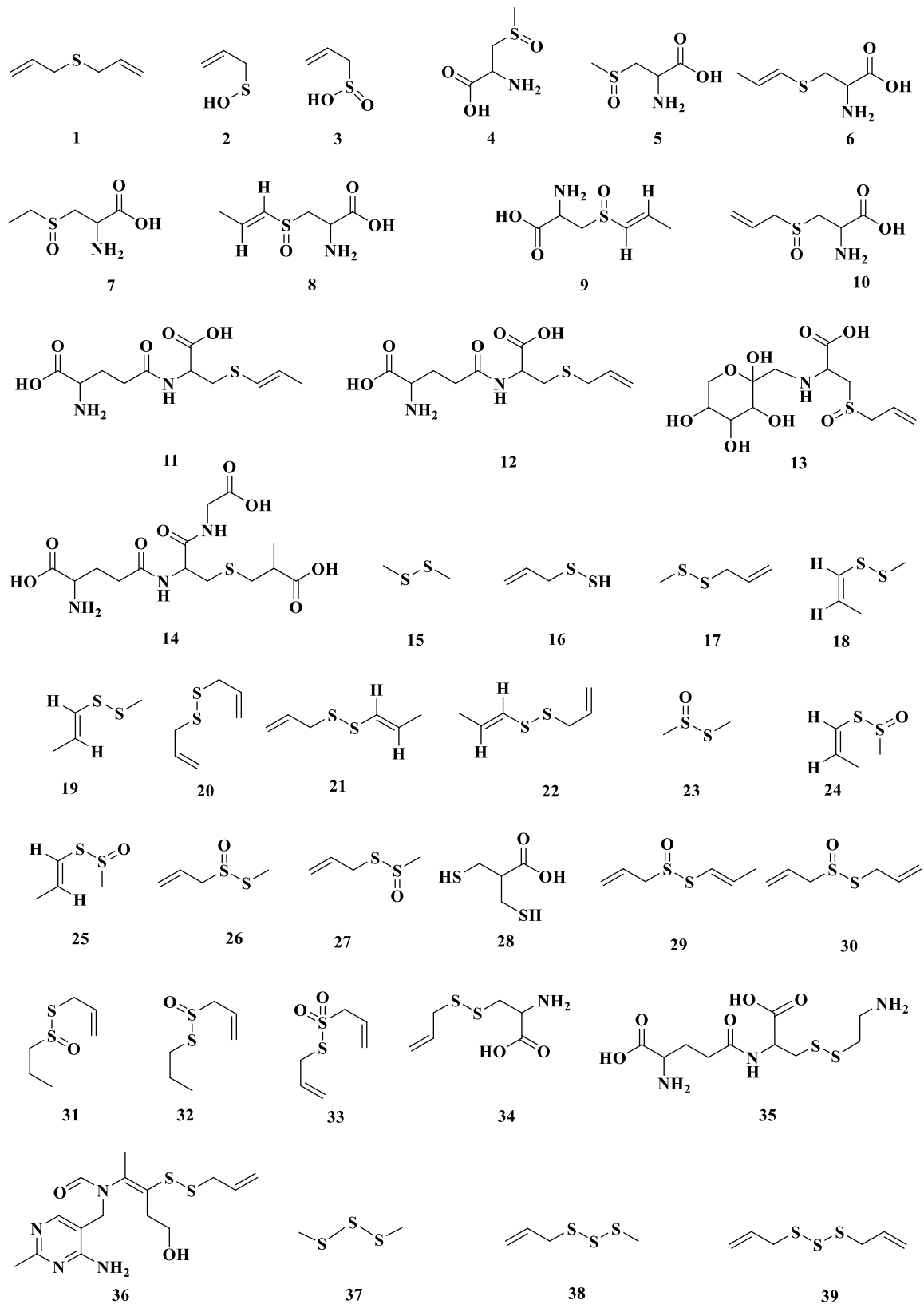
Figure1: Chemical structures of the previously reported compounds from *A. sativum* (**1-14** Acyclic monosulfides, **15-36** Acyclic disulfides and **37-39** Acyclic trisulfides).
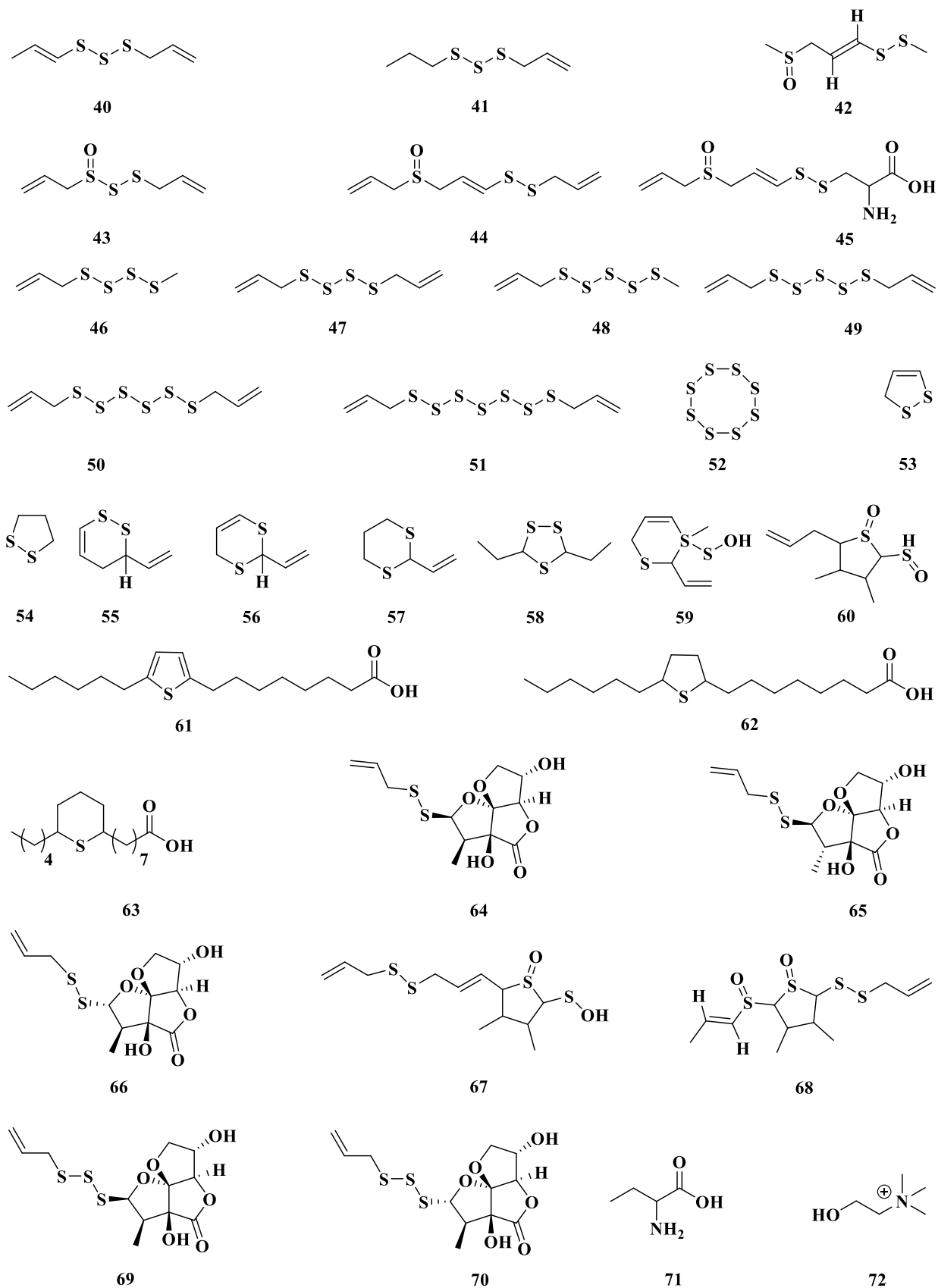
Figure 1: Continued (**40-45** Acyclic trisulfides, **46-47** Acyclic tetrasulfides, **48-49** Acyclic pentasulfides, **50** Acyclic hexasulfides, **51** Acyclic heptasulfides, **52-70** Cyclic organosulfur compounds and **71-72** Aminoacids).

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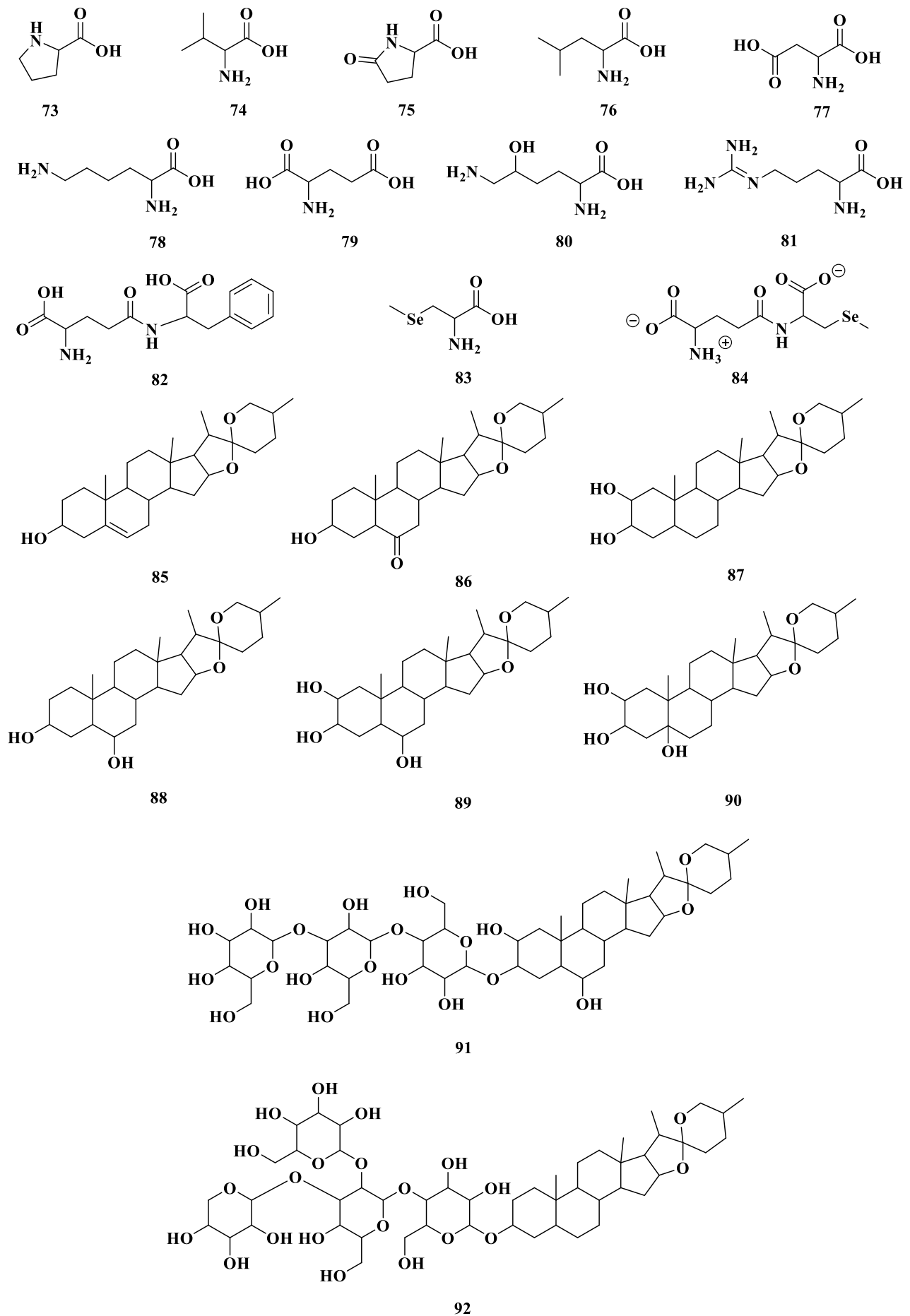
Figure 1: Continued (**73-82** Aminoacids, **83-84** Selenium derivatives and **85-92** Saponins).

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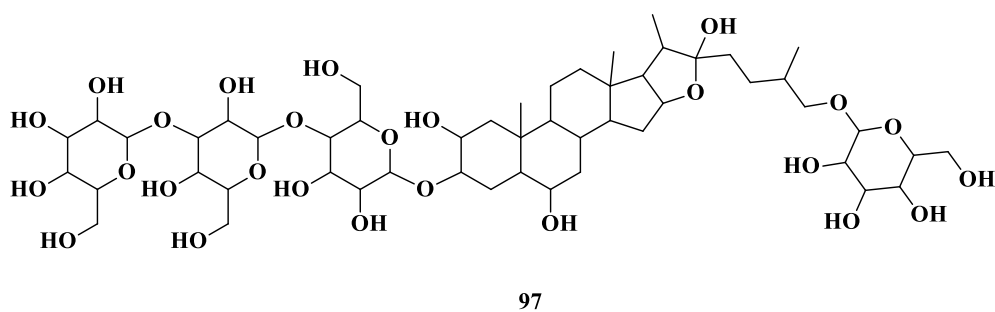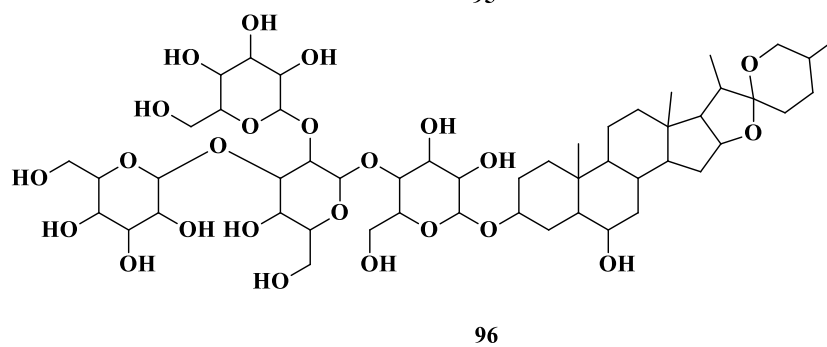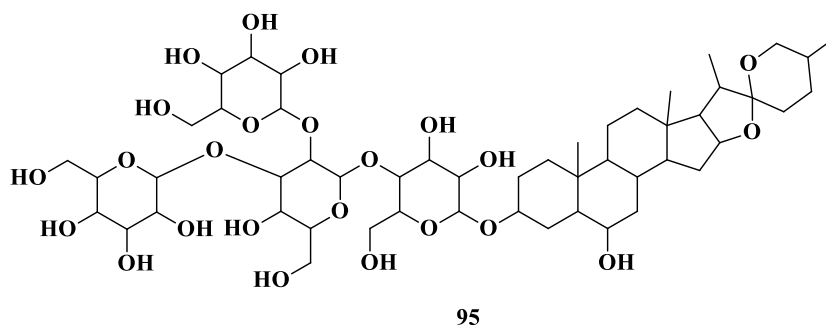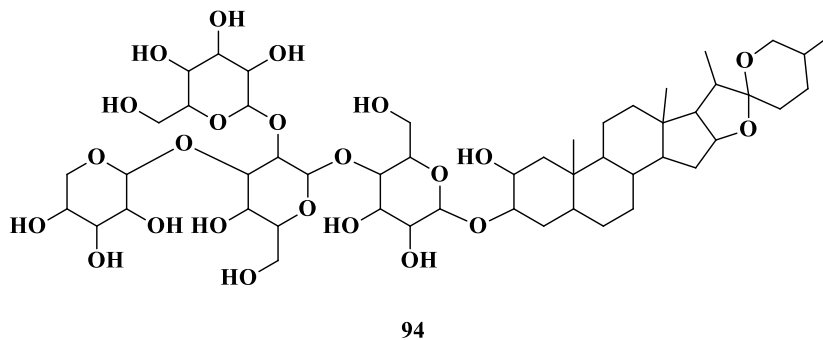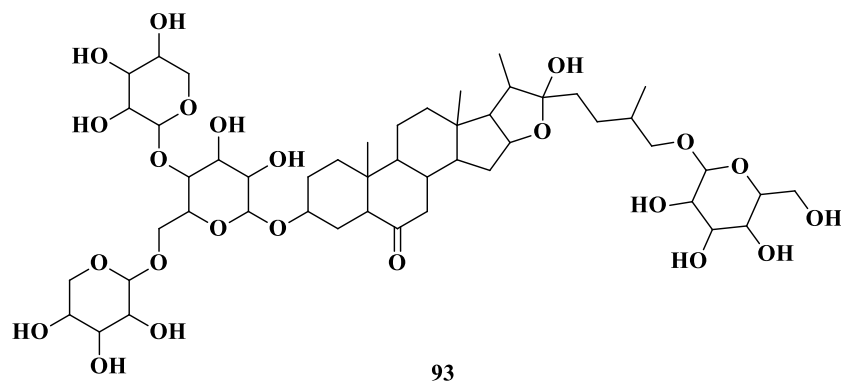
Figure 1: Continued (**93-97** Saponins).

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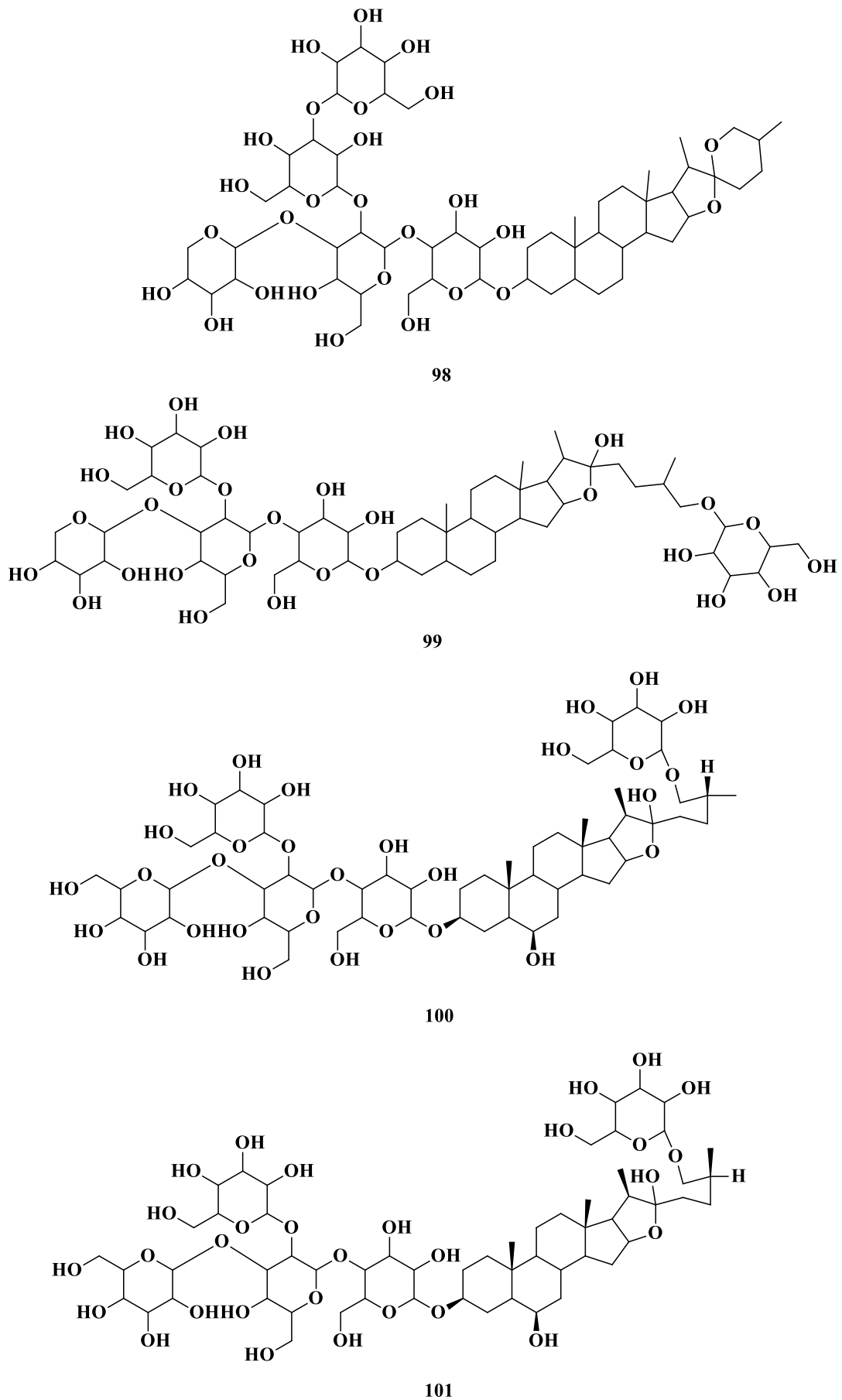
Figure 1: Continued (**98-101** Saponins).

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		R_1	R_2	R_3	R_4
104	(22α)	H	H	H	CH$_3$
105	(22β)	H	H	H	CH$_3$
106	(22α)	OH	H	H	CH$_2$OH
107	(22β)	OH	H	H	CH$_2$OH
108	(22α)	H	OH	H	CH$_2$OH
109	(22β)	H	OH	H	CH$_2$OH
110	(22α)	H	H		CH$_3$
111	(22β)	H	H		CH$_3$
112	(22α)	OH	H		CH$_2$OH
113	(22β)	OH	H		CH$_2$OH

Figure 1: Continued (**102-113** Saponins).

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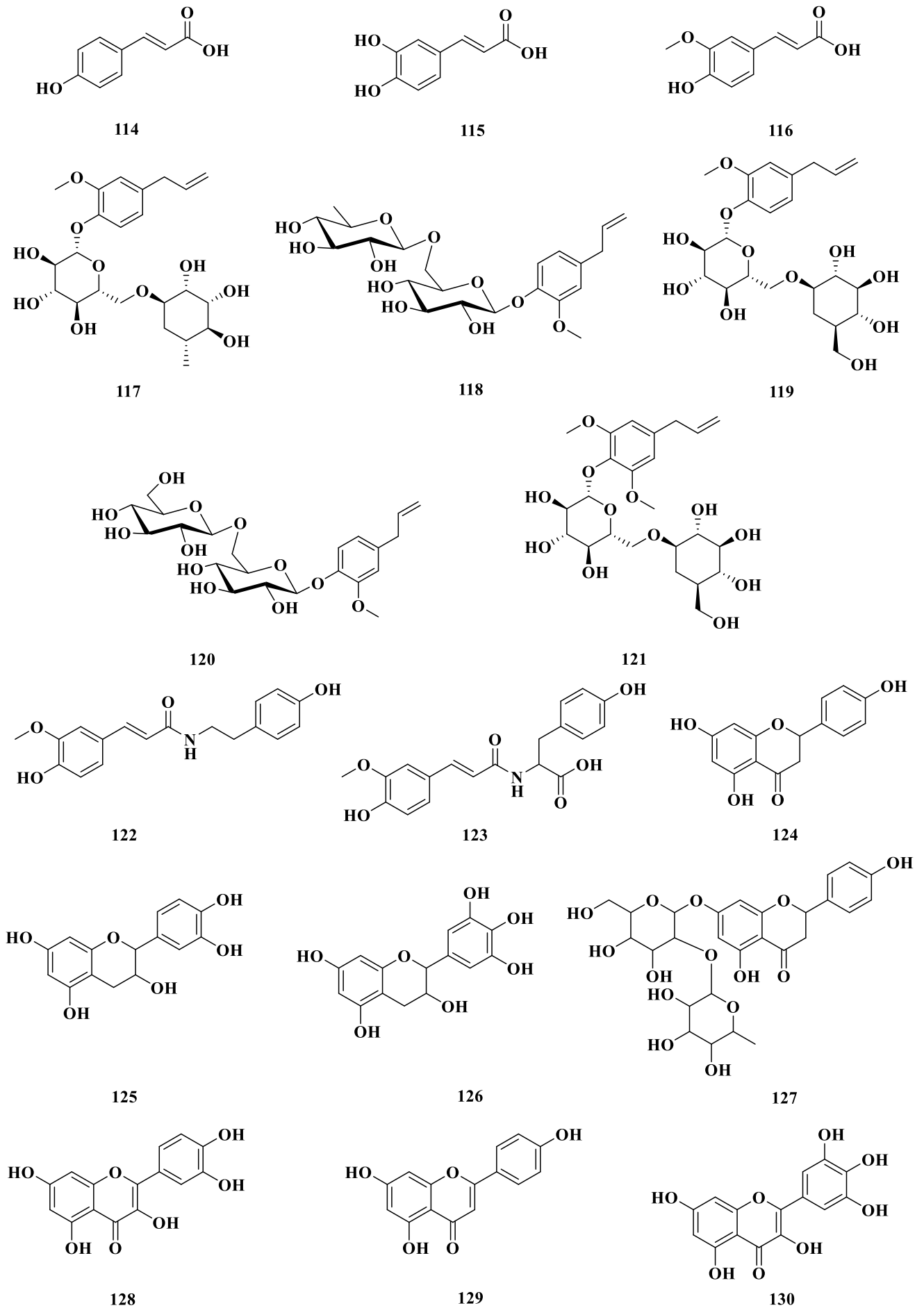
Figure 1: Continued (**114-123** Phenyl propanoids and **124-130** Flavonoids).
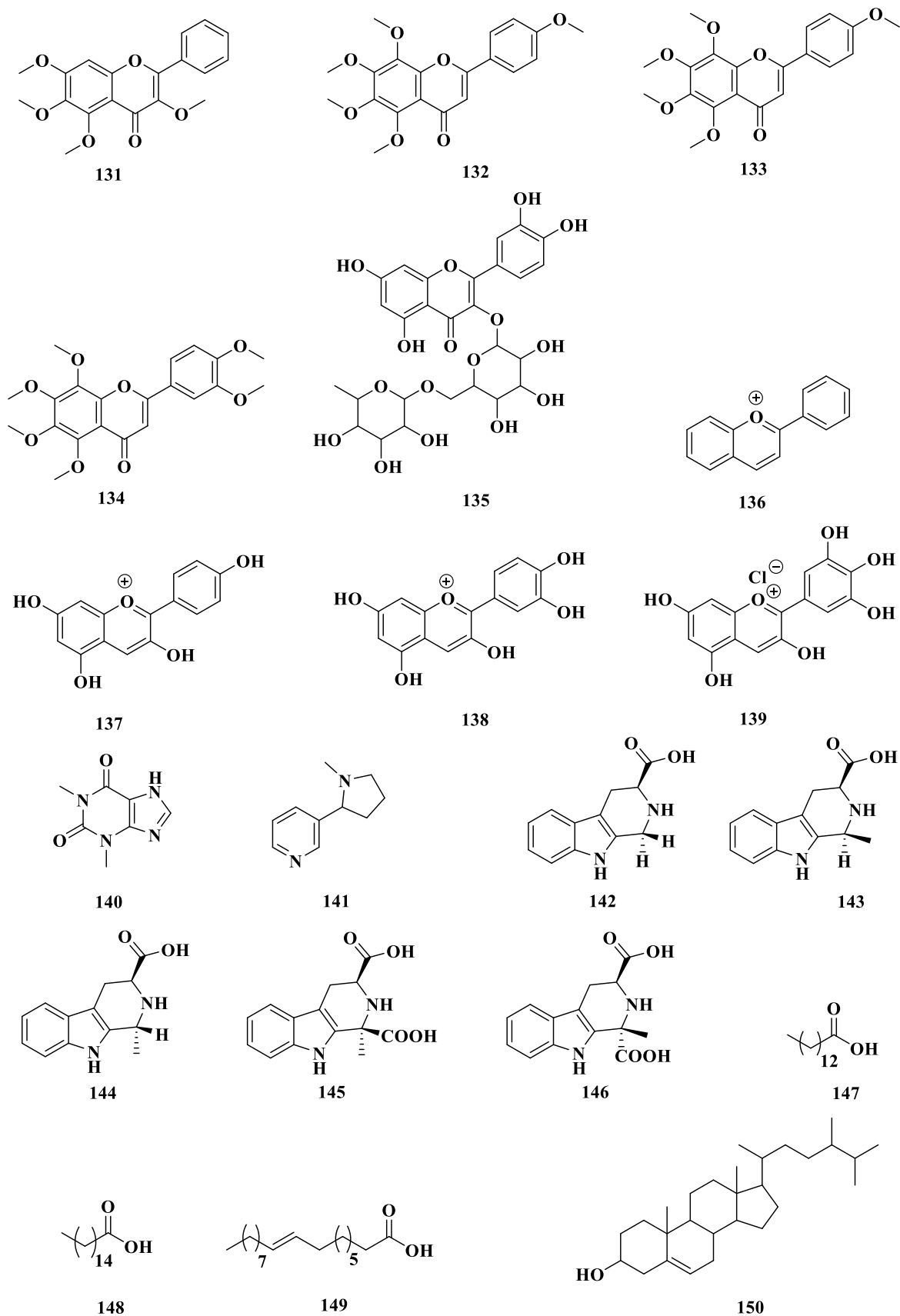
Figure 1: Continued (**131-139** Flavonoids, **140-146** Alkaloids, **147-149** Fatty acids and **150** Sterol).

151 **152** **153** **154** **155**

156 **157** **158** **159** **160**

161 **162** **163** **164**

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177 **178** **179** **180**

181 **182** **183**

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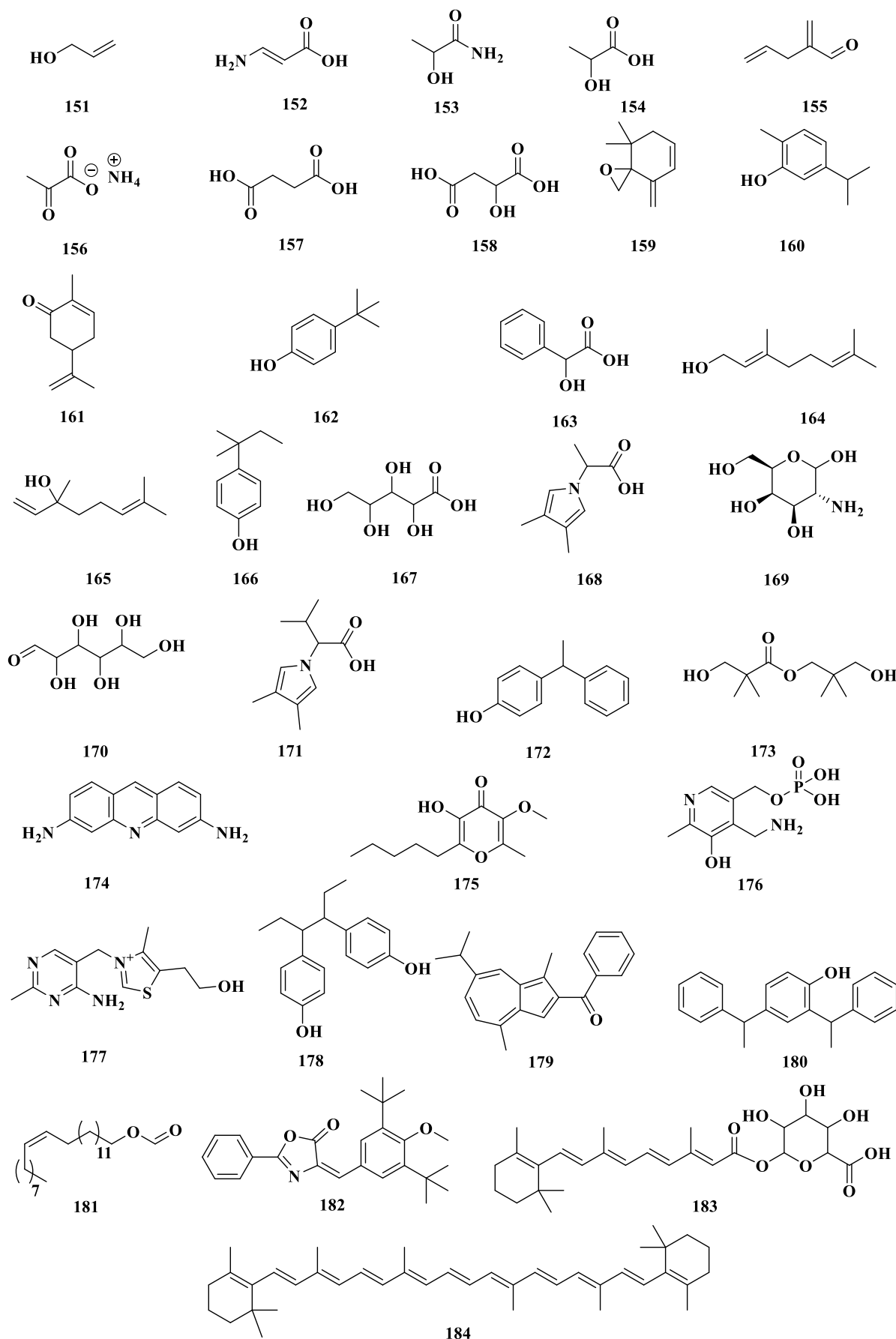
Figure 1: Continued (**151-184** Miscellaneous compounds).
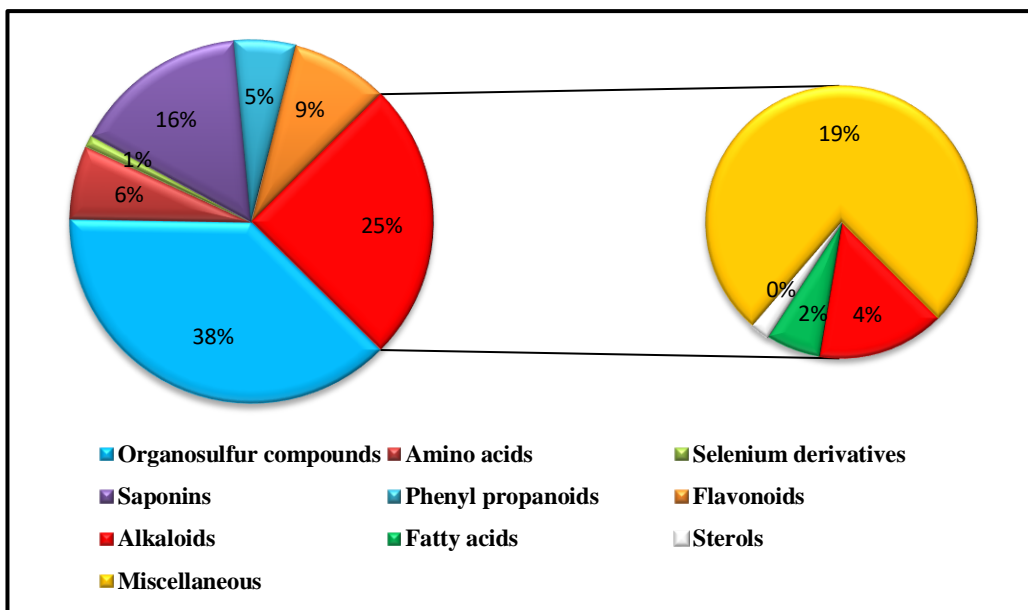
Figure 2: Different classes of secondary metabolites reported from *A. sativum.*
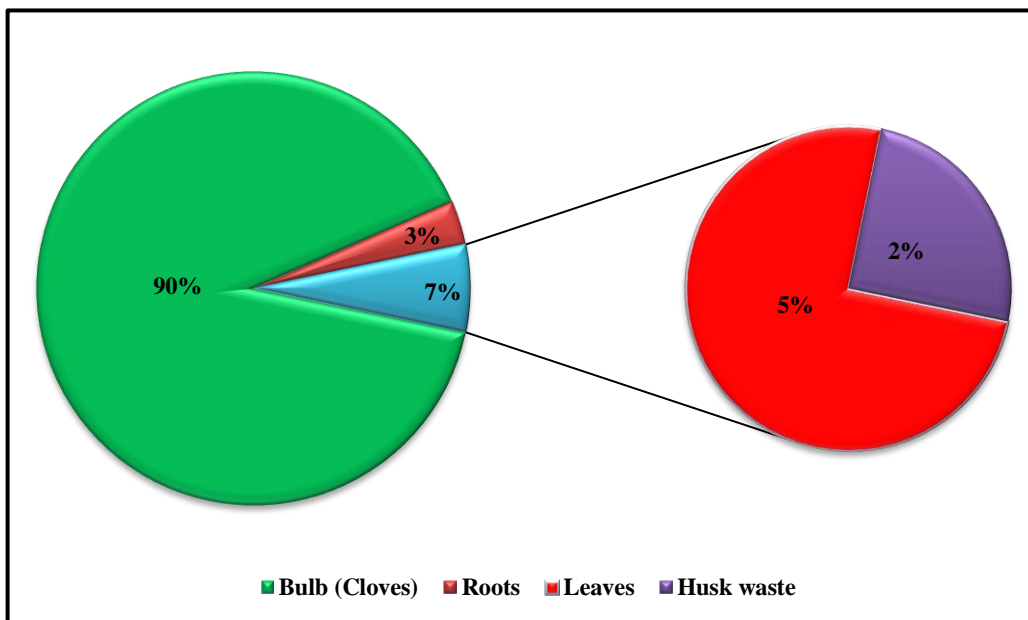
Figure 3: Distribution of the reported secondary metabolites in the different parts *A. sativum.*

4.1.4. Antiviral

Allicin, ajoene and DATS had *in vitro* antiviral activity against influenza A and B, HIV, cytomegalovirus, herpes simplex virus, viral pneumonia, rhinovirus and rotavirus. *S*-allylcysteine sulfoxide (alliin) or *S*-allylcysteine (SAC) has no activity [5,51,55]. Garlic is a powerful natural antimicobial that can fight many viruses and bacteria. Organosulfur (e.g. allicin and alliin) and flavonoid (e.g. quercetin) components are responsible for the immunomodulatory properties of garlic. According to the World Health Organization, Coronavirus illness (COVID-19), caused by the novel coronavirus (SARS-CoV-2), has spread rapidly over the globe, affecting 213 countries or territories and resulting in more than six million confirmed cases and 0.37 million deaths. Fever, cough and shortness of breath are common symptoms of the infection and severe cases reveal acute respiratory infection and multiple organ failure. The likelihood of these serious indications increases with age, as well as underlying comorbidities including diabetic, cardiovascular, or thoracic problems, as well as an immunocompromised state [56]. Reduced immune system cells, such as reduced regulatory T cells, cytotoxic and helper T cells, natural killer cells, monocytes/macrophages and enhanced pro-inflammatory cytokines, are common characteristics [57]. Garlic provides therapeutic benefits for acute respiratory tract infections like pulmonary fibrosis, diffuse alveolar damage, pneumonia, acute respiratory distress syndrome, as well as septic shock, lung and kidney injury, all of which are signs of COVID-19 infection [56]. Compounds derived from garlic have the potential to lower pro-inflammatory cytokine expression and revert immunological abnormalities to more acceptable levels. Before becoming infected with the SARS CoV2 virus, garlic is indicated as a useful prophylactic intervention. Finally, garlic may be used as a COVID-19 infection prevention strategy by boosting immune system cells and suppressing the generation and secretion of pro-inflammatory cytokines, as well as the pro-inflammatory hormone leptin produced from adipose tissue [57].

4.2. Antidiabetic

The effect of aqueous extract of garlic was tested against normal and alloxan-induced diabetic rabbits. The aqueous extract of garlic has great hypoglycemia effect [58]. Also, many studies of garlic oil (GO) on diabetic animals were done, in order to confirm the hypoglycemic properties of garlic, alliin, allyl sulfide, had the same hypoglycemic action as that of glibenclamide. In streptozotocin-induced diabetic rats, the hypoglycemic effect of GO (10 mg/kg i.p.) and organosulfur constituents of garlic as DATS, displayed higher secretion and sensitivity of insulin (60 mg/kg, i.p.) [34,59,60].

4.3. Cardiovascular activity
4.3.1. Antihyperlipidemic

When compared to placebo, garlic preparations may result in minor reductions in total cholesterol levels after 1 month [0.03-0.45 mmol/L (1.2-17.3 mg/dL)] and 3 months [0.32-0.66 mmol/L (12.4-25.4 mg/dL)], but not after 6 months. Low-density lipoprotein (LDL) and triglyceride (TG) levels changed in perfect agreement with total cholesterol levels, but there were no statistically significant changes in high-density lipoprotein levels. In trials, significant reductions in platelet aggregation and mixed effects on blood pressure were also documented. On glycemic-related outcomes, there were no findings. Breath and body odour that is offensive has been proved to be dangerous. Other side effects included flatulence, esophageal & stomach pain, allergic responses and bleeding [61].

4.3.2. Antihypertensive

Garlic can also lower blood pressure *via* reducing oxidative stress, increasing nitric oxide (NO) and hydrogen sulphide (H_2S) production and inhibiting angiotensin converting enzyme [62]. In the separated rat aortic rings, aged garlic extract (AGE) appears to enhance NO production, leading to endothelial-dependent vasodilation. Furthermore, l-arginine in AGE was critical for NO synthase-mediated NO production [63]. Within 3 h of treatment with S-1-propenylcysteine (6.5 mg/kg), the systolic blood pressure of a suddenly hypertensive rat was reduced by around 10% and the systolic blood pressure returned to the normal level within 24 h. S-1-Propenylcysteine had a dose-dependent effect, with the maximum effect occurring within 3 h at a dosage of 6.5 mg/kg. Other AGE agents such as SAC and S-allylmercaptocysteine (SAMC) were ineffective in any case. S-1-Propenylcysteine had no effect on the systolic blood pressure of control Wistar Kyoto rats after expansion. Furthermore, at a dose of 6.5 mg/kg, S-1-propenylcysteine enhanced blood flow within 3 h of administration [13]. According to a meta-analysis of 12 research with 553 hypertensive participants, garlic supplements drop systolic blood pressure (SBP) by an average of 1.9-8.3 mmHg and diastolic blood pressure (DBP, n=8 trials, n=374 patients) by 1.9-5.5 mmHg, which is comparable to standard antihypertensive drugs. Blood pressure lowering was connected to a 16-40% reduction in the risk of cardiovascular events. Blood pressure response to garlic is influenced by vitamin B12 levels in the body. Furthermore, AGE significantly reduced central blood pressure, pulse pressure, pulse wave velocity and arterial stiffness [64].

4.3.3. Heart protection

In streptomycin-induced diabetic rats (250 mg/kg/day), AGE activated the sirtuin 3-manganese superoxide dismutase (SOD) pathway by deacetylating manganese SOD, ensuring heart function [65]. Another study found that dietary mediations containing (10% fenugreek seed powder), (2% freeze-dried garlic powder) and (10% fenugreek seed powder with 2% garlic powder) promoted obsessive cardiac tissue alterations in rats. Myocardial infarction was induced with isoproterenol (80 mg/kg, i.p.) twice at 12-hour intervals after the diet regimen was completed [66].

4.4. Antioxidant

AGE owns more antioxidant effects than fresh garlic and other garlic supplements on the market. Organosulfur compounds, that are water soluble as SAC and SAMC have higher antioxidant activity. SAC and SAMC are the main organosulphur components, that are present in AGE. There are some other components, which have an antioxidant potential as fat-soluble allylsulphides as diallyl disulfide (DADS), DATS and diallyl sulfide (DAS) [34,43].

4.5. Anticancer

Both water and fat-soluble organosulphur compounds present in garlic have anticarcinogenic properties as DAS, DADS, DATS, SAC and diallyl sulphoxide. SAMC, DADS, DATS, ajoene and methiin can stimulate apoptosis in many cells in human as human leukemic cells. Steroidal saponin as eruboside B extracted from bulb of garlic also has anticancer activity. The pure selenium compounds have great anticancer potential than S-analogues as diallyl selenide, that has activity of about 300 times greater than DAS in the mammal cancer treatment [67,68]. Selenium-methyl selenocysteine and γ-glutamyl-Se-methyl selenocysteine are the

main two selenium compounds, that have anticancer potential [34].

4.5.1. Regulation of metabolism of carcinogenic substances
Garlic and its sulfur components have been shown to reduce the activation of carcinogens, lowering cancer risk. Furthermore, garlic allyl sulfides can prevent DNA alkylation, which is a key step in nitrosamine carcinogenesis [69]. Garlic and its natural allyl sulfides can also reduce the production of nitrosamines, a type of carcinogen produced during cooking [70,71].

4.5.2. Induction of apoptosis
Admissions of crude and crushed garlic were found to upregulate apoptotic-associated genes such as receptor of aryl hydrocarbon, hypoxia-inducible factor 1 and proto-oncogene c-Jun, which influenced the expression of genes connected to immunity and cancer in human blood [72]. DATS induced tumor apoptosis in SGC-7901 gastric cancer cells in a mouse model [73]. SAC may induce apoptosis in A2780 human epithelial ovarian cancer cells, decrease pro-caspase-3, poly (ADP-ribose) polymerase-1 (PARP-1) and Bcl-2 expression and increase dynamic caspase-3 and Bax protein production [74]. In SW620 cells of human colorectal cancer, SAMC induced apoptosis *via* the Jun N-terminal kinase (JNK) and p38 mitogen activated protein kinase (p38 MAPK) pathways [75].

4.5.3. Inhibition of invasion and migration
Tumor cells engage in malignant behaviors such as invasion and migration. Garlic extract inhibited the invasion and migration of bladder cancer EJ cells by suppressing MMP-9 expression, decreasing the binding activity of the translation factor activator protein 1 (AP-1) (specificity the protein-1 and NF-κB themes) and increasing the expression of A6 (heat shock protein) [76]. By inhibiting cell motility and proliferation, AGE reduced the capacity of colorectal cancer cells SW480 and SW620 to invade [77]. SAC also inhibited the migration of A2780 epithelial ovarian tumor cells by lowering the expression of the wingless-type MMTV integration location family member 5A (Wnt5a), phosphor-protein kinase B and c-Jun proteins [74].

4.6. Neuroprotective
Neuroprotective effects of AGE and SAC against neuroinflammation and neurodegeneration are possible. Despite the fact that little is known about the metabolic function of *N-α*-(1-deoxy-D-fructos-1-yl)-L-arginine (FruArg), it is another bioactive component in AGE. Both AGE and FruArg are involved in gene transcription and protein expression regulation. In a cell-based neuroinflammation worldview fortified by lipopolysaccharide (LPS) in murine BV-2 microglial cells, AGE has been shown to turn around 67% of the transcriptome change triggered by endotoxins LPS, while FruArg has been shown to account for the defensive effects by turning around 55% of qualities changed. AGE and FruArg can reduce neuroinflammatory reactions *via* a variety of signaling pathways, including Toll-like receptor and interleukin (IL-6) signaling, as well as upregulation of the nuclear factor erythroid 2-related calculate 2 (Nrf2)-mediated oxidative stretch pathways, which have been shown to improve microglial resistance to neuroinflammation and neurodegeneration. FruArg's capacity to cross the blood-brain barrier (BBB) suggests that it could be used as a medicinal drug [78]. DADS and DATS were found to have neuroprotective properties. However, the potential of these organosulfur compounds in the treatment of neuropathic pain has yet to be examined. A study examined the pain-relieving abilities

of DADS and DATS in rats with chronic constriction injury (CCI)-induced neuropathic pain. The pain-attenuating mechanisms of H_2S, brain-derived neurotrophic factor (BDNF) and nuclear factor erythroid 2-related factor 2 (Nrf2) were studied using their modulation. CCI rats were administered DADS (25 and 50 mg/kg) and DATS (20 and 40 mg/kg) for 14 days and showed a significant reduction in discomfort. After treatment with these organosulfur compounds, the levels of H_2S, BDNF and Nrf2 in the sciatic nerve and dorsal root ganglia were likewise recovered. Without affecting H_2S levels, administration of ANA-12 (a BDNF blocker) abolished pain-relieving effects in addition to BDNF and the Nrf2 restorative actions of DADS and DATS [79].

4.7. Obesity
Garlic or sulfur-containing compounds derived from garlic, can help people lose weight. Garlic-derived compounds have an anti-adipogenic action *in vitro*, reducing 3T3-L1 adipocyte development *via* adenosine monophosphate-activated protein kinase (AMPK) activation, acetyl-CoA carboxylase (ACC-1) suppression and carnitine palmitoyltransferase upregulation (CPT-1) [80]. Allicin was found to improve the expression of brown adipocyte-specific genes, including UCP-1, *via* the kruppel like factor 15 (KLF15) flag cascade, which may help to avoid obesity and related metabolic disorders [81]. In diet-induced obese mice, oral administration of fermented garlic extract (250 and 500 mg/kg) for 8 weeks showed to have anti-obesity effects by lowering body weight, adiposity, triglyceride and cholesterol levels, as well as suppressing adipogenesis [82]. The administration of GO (80 mg/kg, p.o.) reduced body weight gain and white adipose tissue (WAT) mass, which had been raised by eating a high-fat diet based on AIN76 (vitamin mixture, 60% kcal fat). However, carbohydrate oxidation was unaltered by the GO treatment, which increased O_2 consumption during the dark period (at night) and increased energy expenditure during the light period (during the day) [83].

4.8. Anti-inflammatory
Garlic supplementation significantly lowered circulating C-reactive protein (CRP) ($p < 0.05$), but had little effect on IL-6 levels ($p > 0.05$). A sub-group study revealed that AGE significantly reduced CRP and tumor necrosis factor-$α$ (TNF-$α$) ($p < 0.05$) [84]. The effects of garlic supplementation on blood levels of several inflammatory biomarkers, clinical symptoms and exhaustion in women with active rheumatoid arthritis were investigated in a study, based on the anti-inflammatory characteristics of garlic. Seventy women with rheumatoid arthritis were divided into 2 groups at random: For 8 weeks, the intervention group received 1000 mg of garlic and the control group received a placebo. Clinical complaints, fatigue, CRP, TNF-$α$ and erythrocyte sedimentation rate (ESR) were measured at the start and end of the trial. When compared to the placebo group, CRP ($p=0.018$) and TNF-$α$ ($p < 0.001$) levels in the garlic group declined sharply after treatment. Furthermore, pain intensity, painful joint count, disease activity score and tiredness were all significantly lower in the intervention group than in the control group ($p < 0.001$ for all). The garlic group had a significantly reduced number of swollen joints ($p < 0.001$) than the placebo group ($p= 0.123$). Garlic supplementation, which reduced inflammatory mediators and improved clinical symptoms in rheumatoid arthritis patients, could be utilized as an adjuvant treatment [85]. DADS is the major organosulfur constituent in garlic. Through its powerful anti-inflammatory and antioxidant effects, DADS could be employed as an alternate

therapy for alleviating the pathophysiological alterations associated with the genesis of paw edema [86].

BPH (benign prostatic hyperplasia) is a benign prostate enlargement that affects a high number of older men. To produce BPH in rats, daily subcutaneous injections of testosterone propionate (TP) (3 mg/kg, s.c.) were given for 4 weeks. Finasteride (Fin) (5 mg/kg, p.o.) or DAS (50 mg/kg, p.o.) were given orally throughout BPH induction. On the other hand, DAS or Fin treatment, reversed all testosterone-induced abnormalities. Fin and DAS treatment significantly lowered prostate weight, with Fin reducing it by 53% and DAS reducing it by 60%. Furthermore, in line with decreased protein expression of androgen receptor (AR) and prostate-specific antigen (PSA), blood testosterone and dihydrotestosterone (DHT) levels were reduced by 55% and 52%, respectively, with Fin and by 68% and 75%, respectively, with DAS (PSA). Finally, DAS can be used as a dietary preventative agent for BPH due to its anti-inflammatory and immunomodulatory properties [87].

4.9. Wound healing and scarring

According to patients and the onsite physician, the garlic site healed better in 59% of the wounds and 65% of the wounds, respectively at 2 weeks. After 4 weeks, patients and the onsite physician agreed that the garlic site healed better in 76% of wounds and 88% of wounds, respectively. Surgical wounds treated with 30% garlic ointment healed with more visually appealing scars than those treated with vaseline [88].

4.10. Anxiety and depression

Raw garlic extract improved anxiety and depression-related behaviors in diabetic rats, possibly by lowering oxidative stress and increasing antioxidant defenses against diabetes. For 10 days, garlic extract (0.1, 0.25 and 0.5 g/kg) was fed to the animals. At the end of the treatments, the elevated plus maze (EPM) and forced swimming test (FST) were employed to assess anxiety and depressive-related behaviors. In the brain, the activities of SOD and glutathione peroxidase (GPx) were investigated, as well as malondialdehyde (MDA) levels. When compared to diabetic rats, the diabetic + garlic (0.5 g/kg) group exhibited less anxiety and depressive-like behaviors. Garlic therapy (0.5 g/kg) also reduced MDA levels, while increased SOD and GPx activity in the brain [89].

Depression is a psychiatric condition in which oxidative stress is a key cause of damage. An increase in oxidative stress indicators and a decrease in endogenous antioxidants, or antioxidant enzymes, characterize this condition. Antioxidants may therefore have antidepressant effects. SAC is a free radical scavenger as well as an antioxidant. Male BALB/c mice were given SAC (30, 70, 120, 250 mg/kg, i.p.) daily for 17 days, followed by the Porsolt forced swim test (FST) on day 18. Oxidative stress markers were examined in the midbrain, prefrontal cortex and hippocampus (reactive oxygen species, superoxide generation, lipid peroxidation and antioxidant enzyme activity). The immobility scores in the FST were reduced by 44% when SAC (120 mg/kg) was used. Changes in locomotor activity had no effect on protection. Reduced oxidative stress, as demonstrated by lipid peroxidation and manganese-superoxide dismutase (Mn-SOD) activity in the hippocampus, was connected to this antidepressant-like effect. SAC has been linked to the prevention of oxidative damage in the hippocampus and had an antidepressant-like effect [90].

4.11. Hepatoprotective

Sixty male Wistar albino rats were separated into 4 groups: control, AGE (250 mg/kg), ethephon (200 mg/kg orally) and (AGE with ethephon), which received ethephon for 4 weeks before receiving AGE at the same dosage for another 4 weeks. AGE administration attenuated the histological deformations and biochemical alteration caused by ethephon. Through its antioxidant activity, AGE supplementation could be employed to reverse hepatic damage caused by ethephon exposure [91]. Garlic and its bioactive components may help to prevent hepatic steatosis by modulating hepatic lipid metabolism, according to new research. Adult patients with ultrasound-diagnosed non-alcoholic fatty liver disease (NAFLD) were enrolled in a clinical research. Eligible participants were randomly assigned to receive 800 mg garlic or placebo for 15 weeks using the stratified blocked technique. The primary outcome was an improvement in hepatic steatosis as evaluated by ultrasonography after 15 weeks of treatments. Garlic intake resulted in significant weight loss and reductions in blood ALT, AST, FBS, Hb A1C, total cholesterol, LDL-cholesterol and TG concentrations when compared to placebo ($p < 0.05$). After controlling for weight loss, energy intake and physical activity, the results were still significant. Garlic consumption did not cause any major side effects [92].

4.12. Gastrointestinal disorders

Inflammatory bowel disease (IBD) is a health problem. The most important explanations for the pathophysiology of this disease are the weakening of immune responses and the loss of tolerance to bacteria in the intestinal flora. A study was conducted to see how GO affected an experimental colitis model. Group 1 (sham), group 2 (negative control), group 3 (topical treatment) and group 4 (topical and systemic treatment) were chosen at random from a total of 28 rats. Normal saline, topical GO, topical and systemic GO were delivered to groups 2, 3 and 4, respectively, in an acetic acid-induced colitis model. GO decreased intestinal damage and inflammation, with effects on both local and systemic treatment, but with a stronger effect on local treatment [93]. The gut microbiota improved after 3 months of treatment, as seen by increased microbial richness and diversity, as well as a significant increase in the number of *Lactobacillus* and *Clostridia* species found [64].

4.13. Nephropathic encephalopathy

DAS is a garlic-derived organosulfur compound. Rats were given DAS (100 mg/kg) orally for 4 days, then injected with cyclophosphamide (CP) (150 mg/kg) 60 min later. When compared to CP-treated rats, DAS therapy reduced serum urea, creatinine, sodium, potassium, calcium, blood urea nitrogen (BUN), CRP, IL-6, interleukin-1ß and TNF-α. In the renal tissues, when compared to CP-treated rats, DAS treatment reduced malondialdehyde (MDA), increased SOD and reduced glutathione (GSH) levels, as well as significantly lowering elevated neurotransmitters N-methyl-D-aspartate/adenosine triphosphate (NMDA), γ-aminobutyric acid (GABA) and restoring neuronal NO level and NO synthase activity in the brain. DAS for 4 days before CP resulted in moderate positive immunohistochemical expression of glial fibrillary acidic protein (GFAP) in the brain and renal tissues, similar to CP-treated rats. Due to its ability to improve the aforementioned biochemical markers, DAS provided renal and neuroprotection against CP-induced nephropathic encephalopathy, which was validated by histological and immunohistochemical testing [94]. By stimulating the Nrf2/ARE signaling pathway, DATS, a garlic

polysulfide, protects rats from oxidative nephrotoxicity, apoptosis and inflammation caused by arsenic [95].

4.14. Osteoarthritis

X-ray, staining, ELISA and immunoblotting were used to investigate the effect of SAMC in a surgically induced osteoarthritis (OA) model. The role of Nrf2 in IL-1 stimulated chondrocytes *in vitro* was next examined using a gene knockdown approach. SAMC targeted Nrf2 to defend against OA *in vivo* and *in vitro*, which could lead to a new pharmaceutical approach to OA treatment [96].

4.15. Uterine activity

DAS (10^{-8}-10^{-6} M) reduced spontaneous peristaltic activity in uterine strips and caused KCl (60 mM)-induced contractions to relax in a concentration-dependent manner ($p < 0.05$). Any of the following antagonists ($p > 0.05$) had no effect on the inhibitory effect of DAS on both KCl-precontracted uterine strips and spontaneous peristaltic activity of the uterus: NO synthase inhibitor N(ω)-nitro-L-arginine methyl ester (L-NAME, 10^{-4} M), aminooxyacetic acid (10^{-4} M), H$_2$S-producing enzymes cystation β synthase and cystation γ-lyase inhibitors, propargylglycine (10^{-3} M) and nonselective cyclooxygenase inhibitor indomethacin (10^{-4} M). DAS, in a calcium-free Krebs solution containing high KCl (30 mM), on the other hand, considerably reduced CaCl$_2$ (10^{-5}-10^{-2} M)-induced uterine contractions in a concentration-dependent manner ($p < 0.05$) [97].

4.16. Lead toxicity

Lead is a common heavy metal that has toxicological effects on a wide range of animal and human tissues. Lead has been shown to have a number of toxic effects the renal system, the central nervous system, on reproductive organs, the liver, blood parameters and the lungs [98]. Several studies showed that garlic causes reduction in lead absorption in both bones and soft tissues. Vitamins (C and E) together improved the biological recovery caused by lead and help to mobilize heavy metals like lead from intracellular sites [98].

4.17. Immunostimulant

The effect of aqueous garlic extract on immunological parameters in *Poecilia reticulata* skin mucus was examined. In 12 experimental glass tanks, 240 *P. reticulata* juveniles weighing 1-13 mg were randomly stocked at a density of 30 fish each tank. The fish were fed garlic extract diets comprising concentrations of 0, 0.10, 0.15 and 0.20 mL/kg of feed three times a day at a ratio of 2.5 percent of their body weight for 80 days. The researchers discovered that lysozyme activity increased sharply ($p < 0.05$) in the skin mucus of garlic-treated Guppys. ACH50 values in fish were significantly increased ($p < 0.05$) by increasing the concentration of garlic extract in the meal from 0 to 0.15 mL/kg. Air changes per hour at 50 pascals (Pa) pressure differential (ACH50) decreased significantly ($p < 0.05$) when the concentration of garlic extract was increased from 0.15 to 0.20 mL/kg. Total immunoglobulin (Ig) content was also significantly increased in the 0.15 and 0.20 mL/kg treatments. In comparison to the control, garlic-fed treatments had considerably higher alkaline phosphatase (ALP) activity. The effects of garlic extract in the diet on final body weight and weight gain were determined to be insignificant. According to the findings, 0.15 mL of extract of garlic/kg diet should be given to *P. reticulata* to achieve optimal skin mucus immunity [99].

4.18. Memory improvement

A study examined the effect of garlic treated with subcritical water on memory impairment in ovariectomized (OVX) rats. Garlic powder was given to OVX rats for 84 days. The Morris water maze test was used to examine hippocampus-dependent spatial memory. When compared to sham-operated rats, the OVX animals' escape latency increased. Following the injection of garlic powder, the OVX rats' delayed escape latency was reduced to that of sham-operated rats (0.5% in feed). Garlic powder administration had no effect on the weights of the body, uterus, or brain. These findings imply that garlic powder mixed with subcritical water helps OVX rats remember things [100].

5. Conclusion

This review afforded a comprehensive overview on the phytochemical and biological profiles of *A. sativum* as one of the most important food and medicinal plant species. The reviewed data indicated the availability of a cornucopia of organosulfur compounds, which have been extensively reported from garlic, while further phytochemical attention should be paid to the other classes of metabolites, including flavonoids, phenylpropanoids, sterols, and non-polar metabolites, among others. Moreover, most of the reported phytoconstituents in garlic have been primarily identified from the bulbs and cloves, and to a much less extent from the leaves, roots, and husks; highlighting the necessity for a detailed chemical exploration of these plant parts of *A. sativum* in the future.

Conflict of Interests

The authors declare that there is no conflict of interests regarding this review.

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