REVIEW ARTICLE

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Genus *Lactuca* (Asteraceae): A Comprehensive Review

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Abstract: Genus *Lactuca* L. belongs to one of the major families of flowering plants, Asteraceae. It includes about 150 species, distributed in warm and temperate areas, commonly in the Northern Hemisphere. Since ancient times, numerous *Lactuca* L. species have been cultivated for their economic and medicinal significance. Cultivated lettuce (*Lactuca sativa*), a representative member of the genus, is the most important leafy salad vegetable. The current review aims to provide comprehensive information on the taxonomy, phytochemistry, traditional uses, and biological activities of plants of the genus *Lactuca*.

Keywords: Lactuca; Asteraceae; Lettuce; phytochemistry; sesquiterpene lactones; biological activities.

1. Introduction

Family Asteraceae is the largest family of flowering plants (Angiosperms), comprising about 1,600 genera and 24,000 species of herbs, shrubs, and trees [1]. Plants belonging to this family are cosmopolitan in distribution and exist in almost all habitats. They are abundant in the temperate and tropical lands but are also found in the alpine and arctic regions. In addition to mesophytes, some are xerophytes, aquatic or marsh plants, and epiphytes. Most of the plants are herbs either annual or perennial, rarely trees, some are shrubs, and a few are woody climbers [2,3].

2. Taxonomy

The generic name "*Lactuca*" and the common name "lettuce" are derived from the Greek word "*Lac*" or the Latin word "*lactus*" which means milk, which describes the milky sap of the plant. The common (vernacular) name of the species belonging to the genus *Lactuca* was "lettuce" [2,4–6]. Lettuce was first cultivated in ancient Egypt to produce oil from its seeds [7]. Genus *Lactuca* includes about 150 species, distributed in warm and temperate areas, commonly in the Northern Hemisphere (Europe, Asia, Indonesia, North and Central America and Africa). The majority of the species are xerophytes, well modified to suit dry climatic conditions, except for some endemic species of the central African rain forests [8,9]. Ecologically, *Lactuca* species are diverse and occur in different habitats. Some more

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common European species (e.g., *L. serriola*, *L. virosa*, *L. saligna*) are commonly ruderal, preferring disturbed habitats [2]. The species *Lactuca sativa* L. is the most common garden variety and is known as "salad lettuce". *Lactuca serriola* L., commonly known as “Prickly Lettuce” or “Wild Lettuce”, is possibly the closest relative of *L. sativa*. Whereas *L. virosa* is a variety closely related to *L. serriola* [7].

3. Chemistry of Genus *Lactuca*

Previous phytochemical studies of *Lactuca* plants showed the presence of a diversity of secondary plant metabolites including sesquiterpene lactones, triterpenoids, phenolics, saponins, coumarins, lignans, phytosterols, and numerous miscellaneous metabolites. The combination of these phytochemicals is directly responsible for the plants’ great medicinal value in the treatment of various disorders [10].

3.1. Sesquiterpene Lactones

Species of the genus *Lactuca* produce a wide variety of sesquiterpene lactones, most often in a glycosidic form, as their distinctive constituents. Lactucin-type guaianolides (lactucin, lactucopicrin), eudesmanolides, germacranolides and the melampolide-type germacranolide lactuside A are among the most representative secondary metabolites of *Lactuca* species [11–14].

3.1.1. Guaianolides

Guaianolide sesquiterpene lactones are characterized by having a 7-membered ring, a 5-membered one with a methyl group at C-4, and a fused γ-lactone ring (5-membered lactone) having a carbonyl group at the α-position [11] as listed in Table 1 and Figures 1.1.-1.3.

Table 1. Guaianolides isolated from genus *Lactuca*.

No.	Compound name	Species	References
1	Cichorioside B	*L. indica* whole plant	[12]
		Roots of *L. altaica*	[15]
		L. tartarica whole plant	[16]
		Roots of *L. tartarica*	[17]
		Roots of *L. georgica*	[18]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa*	[20]
		Stem of *L. sativa* var. *angustata*	[21]
		Aerial parts and roots of *L. dregeana*	[22]
		Aerial parts of *L. serriola*	[23]
2	Crepidiaside A (8-deoxylactucin-15-glycoside)	Latex of *L. sativa*	[24]
3	Crepidiaside B (11,13 dihydro-8-deoxylactucin-15-glycoside (jacquinellin glycoside)	Roots of *L. aculeata*	[25]
		Roots of *L. saligna*	[26]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. altaica*	[15]
		Roots of *L. tartarica*	[17]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. sibirica*	[30]
		Aerial parts of *L. sibirica*	[31]
		Roots of *L. georgica*	[18]
		Roots of *L. saligna*	[26]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa*	[20]
		Roots of *L. perennis*	[32]
		Aerial parts and roots of *L. dregeana*	[22]
		Latex of *L. sativa*	[24]

Table 1. Continued..

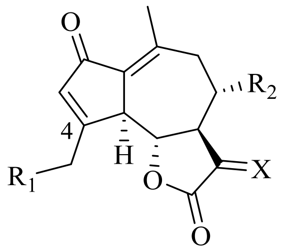
4	8-Deoxylactucin	Latex of *L. sativa*	[24]
		Roots of *L. aculeata*	[25]
		Aerial parts of *L. sibirica*	[31]
		Roots of *L. saligna*	[26]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. aculeata*	[29]
		Aerial parts of *L. serriola*	[13]
		Roots of *L. sibirica*	[30]
		Aerial parts of *L. sibirica*	[31]
		Roots of *L. viminea*	[33]
		Roots of *L. saligna*	[26]
		Roots of *L. virosa*	[19]
5	8-Deoxylactucin-15-oxalate	Latex of *L. sativa*	[24]
6	8-Deoxylactucin-15-sulfate	Latex of *L. sativa*	[24]
7	15-Deoxylactucin	Latex of *L. sativa*	[24]
8	15-Deoxylactucin-8-sulfate	Latex of *L. sativa*	[24]
9	11*β*,13-Dihydrolactucin	Aerial parts of *L. sibirica*	[31]
		L. indica whole plant	[12]
		Roots of *L. altaica*	[15]
		L. tartarica whole plant	[16]
		Roots of *L. tartarica*	[17]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. serriola*	[13,23,34]
		Roots of *L. sibirica*	[30]
		Roots of *L. georgica*	[18]
		Roots of *L. laciniata*	[35]
		Roots of *L. virosa*	[19]
		Aerial parts of *L. sativa*	[36]
		Stem of *L. sativa* var. *angustata*	[21]
		Aerial parts and roots of *L. dregeana*	[22]
		Aerial parts of *L. sibirica*	[31]
10	11*β*,13-Dihydrolactucin-8-*O*-acetate	Roots of *L. georgica*	[18]
11	11*β*,13-Dihydrolactucin-8-*O*-methacrylate	Roots of *L. georgica*	[18]
		Roots of *L. virosa*	[19]
12	11*β*,13-Dihydrolactucopicrin	Roots of *L. saligna*	[26]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. altaica*	[15]
		L. tartarica whole plant	[16]
		Roots of *L. tartarica*	[17]
		Roots of *L. georgica*	[18]
		Aerial parts of *L. saligna*	[37]
		Roots of *L. saligna*	[26]
		Roots of *L. virosa*	[19]
		Aerial parts and roots of *L. dregeana*	[22]
		Stem of *L. sativa* var. *angustana*	[21]
13	11*β*,13-Dihydrolactucopicrin glycoside	Latex of *L. sativa*	[24]
14	11*β*-Hydroxycrepidiaside B	Aerial parts of *L. aculeata*	[29]
15	11*β*-Hydroxy-11,13-dihydrolactucin	*L. tartarica* whole plant	[16]
16	15-(4-Hydroxyphenylacetyl)-lactucin-8-sulfate	Latex of *L. sativa*	[24]
17	Hypochoeroside B	Roots of *L. georgica*	[18]
18	Jacquinellin	Latex of *L. sativa*	[24]
		Roots of *L. aculeata*	[25]
		Roots of *L. saligna*	[26]
		Aerial parts of *L. sibirica*	[31]
		Roots of *L. tartarica*	[17]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. aculeata*	[29]
		Aerial parts of *L. serriola*	[13]
		Roots of *L. sibirica*	[30]
		Aerial parts of *L. sibirica*	[31]
		Roots of *L. viminea*	[33]
		Roots of *L. saligna*	[26]
		Roots of *L. virosa*	[19]

Table 1. Continued..

19	Lactucin	Latex of *L. sativa*	[24]
		Roots of *L. sativa* var. *angustana*	[27]
		Aerial parts of *L. sativa*	[36]
		Roots of *L. altaica*	[15]
		L. tartarica whole plant	[16]
		Roots of *L. tartarica*	[17]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. serriola*	[13]
		Aerial parts of *L. saligna*	[26]
		Roots of *L. saligna*	[26]
		Aerial parts and roots of *L. dregeana*	[22]
20	Lactucin-8-*O*-acetate	Roots of *L. georgica*	[16]
21	Lactucin-8-*O*-methacrylate	Roots of *L. georgica*	[16]
22	Lactucopicrin	Latex of *L. sativa*	[22]
		Roots of *L. sativa* var. *angustana*	[25]
		Aerial parts of *L. sativa*	[36]
		Roots of *L. altaica*	[15]
		L. tartarica whole plant	[16]
		Roots of *L. tartarica*	[17]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. serriola*	[13,23]
		Roots of *L. georgica*	[18]
		Aerial parts of *L. saligna*	[37]
		Roots of *L. saligna*	[26]
		Aerial parts and roots of *L. dregeana*	[22]
23	Lactucopicriside	Roots of *L. laciniata*	[35]
24	Picriside A (Lactucin 15-glycoside)	Latex of *L. sativa*	[24]
25	Deacetoxymatricarin (leucodin, leucomisin)	Aerial parts of *L. serriola*	[13]
		Roots of *L. viminea*	[33]
		Roots of *L. sativa* var. *angustana*	[27]
26	Deacetylmatricarin (austricin)	*L. tartarica* whole plant	[16]
27	8-Deacetylmatricarin-8-*O*-sulphate	Roots of *L. sativa* var. *angustana*	[27]
		Aerial parts and roots of *L. dregeana*	[22]
28	11,13-Dehydrolactuside C	Roots of *L. canadensis*	[38]
29	11*β*-Hydroxyleucodin-11-*O*-*β*-glucoside	Roots of *L. sativa* var. *angustana*	[27]
30	Lactuside C	Roots of *L. sativa*	[20]
		Roots of *L. sativa* var. *angustana*	[27]
		Aerial parts and roots of *L. dregeana*	[22]
31	Lactupicrin methyl ester	Roots of *L. altaica*	[15]
32	Lactucin methyl ester	Aerial parts of *L. serriola*	[13]
33	Hieracin I	Roots of *L. aculeata*	[25]
34	Hieracin II	Roots of *L. aculeata*	[25]
35	1-Epicichoralexin	Roots of *L. viminea*	[33]
36	Intybulide	Roots of *L. altaica*	[15]
37	11*β*,13-Dihydro epizaluzanin C	Roots of *L. canadensis*	[38]
38	11*β*,13-Dihydrovernoflexuoside	Roots of *L. aculeata*	[25]
		Roots of *L. canadensis*	[38]
		Roots of *L. altaica*	[15]
		Roots of *L. tartarica*	[17]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. sibirica*	[30]
		Roots of *L. viminea*	[33]
		Roots and aerial parts of *L. inermis*	[39]
		Roots of *L. georgica*	[18]
		Roots of *L. laciniata*	[35]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. perennis*	[32]
39	11*β*,13,9*α*-Dihydrohydroxyzaluzanin C	Roots of *L. aculeata*	[25]
		Roots of *L. altaica*	[15]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. viminea*	[33]
		Roots and aerial parts of *L. inermis*	[39]
		Roots of *L. laciniata*	[35]
		Roots of *L. virosa*	[19]

Table 1. Continued..

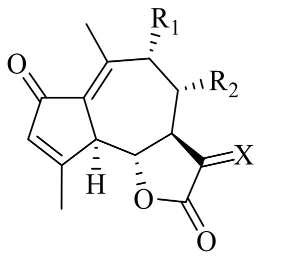
40	11*β*,13-Dihydrozaluzanin C	Roots of *L. canadensis*	[38]
41	3-Epizaluzanin C	Roots of *L. canadensis*	[38]
42	3-Epizaluzanin C-3-*O*-*β*-D-glucoside	Roots of *L. canadensis*	[38]
43	9*α*-Hydroxyzaluzanin C	Roots of *L. aculeata*	[25]
		Roots of *L. altaica*	[15]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. viminea*	[33]
		Roots and aerial parts of *L. inermis*	[39]
		Roots of *L. laciniata*	[35]
		Roots of *L. virosa*	[19]
44	Ixerin F	Roots of *L. aculeata*	[25]
		Roots of *L. canadensis*	[38]
		Roots of *L. saligna*	[26]
		Roots of *L. altaica*	[15]
		Roots of *L. tartarica*	[17]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. sibirica*	[30]
		Roots of *L. viminea*	[33]
		Roots and aerial parts of *L. inermis*	[39]
		Roots of *L. virosa*	[19]
		Roots of L. sativa var. angustana	[27]
45	Macrocliniside A	Roots of *L. aculeata*	[25]
		Roots of *L. canadensis*	[38]
		Roots of *L. saligna*	[26]
		Roots of *L. altaica*	[15]
		Roots of *L. tartarica*	[17]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. sibirica*	[30]
		Roots of *L. georgica*	[18]
		Roots of *L. laciniata*	[35]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa*	[20]
		Roots of *L. sativa* var. *angustana*	[27]
		Stem of *L. sativa* var. *angustana*	[21]
46	Salignoside (9*α*-hydroxy-11*β*,13-dihydrozaluzanin C-9-*O*-*β*-D-glucoside)	Roots of *L. saligna*	[26]
		Roots of *L. viminea*	[33]
47	Scorzoside	Roots of *L. viminea*	[33]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. perennis*	[32]
48	Vernoflexuoside (glucozaluzanin C)	Roots of *L. canadensis*	[38]
		Roots of *L. altaica*	[15]
		Aerial parts of *L. aculeata*	[29]
		Roots of *L. sibirica*	[30]
		Roots of *L. laciniata*	[35]
		Roots of *L. saligna*	[26]
49	Zaluzanin C	Roots of *L. canadensis*	[38]
50	4*α*-*O*-*β*-D-Glucopyranosyl-15-hydroxyl-5*α*,6*β*H-guaiane-10(14),11(13)-dien-12,6*α*-olide	Stem of *L. sativa* var. *angustana*	[21]
51	9*α*-Hydroxy-4*β*,15,11*β*,13 tetrahydrodehydrozaluzanin C	Roots of *L. aculeata*	[25]
51	9*α*-Hydroxy-4*β*,11*β*,13,15 tetrahydrozaluzanin C	Stem of *L. sativa* var. *angustana*	[21]
53	10*β*,14-Dihydroxyl-11*β*H-guaiane-4(15)-ene-12,6*α*-olide	Stem of *L. sativa* var. *angustana*	[21]
54	10*β*,14-Dihydroxy-10(14),11*β*(13)-tetrahydro-8,9-didehydro-3-deoxyzaluzanin C-10-*O*-*β*-D-glucoside	Roots of *L. altaica*	[15]
		Roots of *L. viminea*	[33]
		Roots of *L. sativa* var. *angustana*	[27]
		Stem of *L. sativa* var. *angustana*	[21]
55	Lettucenin A	*L. sativa*	[24]
56	Lactucain A		[12]
57	Lactucain B	*L. indica* whole plant	
58	Lactucain C		

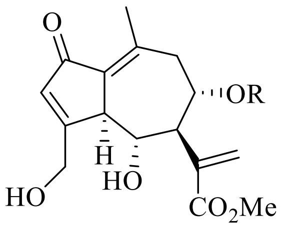


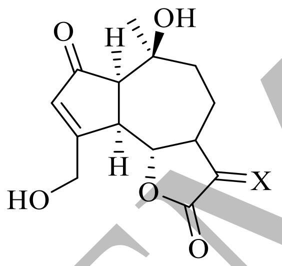
1 R_1=OGlc, R_2=OH, X=H, αMe
2 R_1=OGlc, R_2=H, X=CH_2
3 R_1=OGlc, R_2=H, X=H, αMe
4 R_1=OH, R_2=H, X=CH_2
5 R_1=OCOCOOH, R_2=H, X=CH_2
6 R_1=OSO_3H, R_2=H, R_3=CH_2
7 R_1=H, R_2=OH, X=CH_2
8 R_1=H, R_2=OSO_3H, X=CH_2
9 R_1=R_2=OH, X=H, αMe
10 R_1=OH, R_2=OAc, X=H, αMe
11 R_1=OH, R_2=OCOCH(CH_2)CH_3, X=H, αMe
12 R_1=OH, R_2=OCOCH$_2$(Ph)OH, X=H, αMe
13 R_1=OGlu, R_2=OCOCH$_2$(Ph)OH, X=H, αMe
14 R_1=OGlc, R_2=H, X=OH, αMe
15 R_1=R_2=OH, X=OH, αMe
16 R_1=OCOCH$_2$(Ph)OH, R_2=OSO_3H, X=CH_2
17 R_1=OGlc, R_2=OCOCH(CH_2)CH_3,X=H, αMe
18 R_1=OH, R_2=H, X=H, αMe
19 R_1=R_2=OH, X=CH_2
20 R_1=OH, R_2=OAc, X=CH_2
21 R_1=OH, R_2=OCOCH(CH_2)CH_3, X=CH_2
22 R_1=OH, R_2=OCOCH$_2$(Ph)OH, X=CH_2
23 R_1=OGlc, R_2= OCOCH$_2$(Ph)OH, X=CH_2
24 R_1=OGlc, R_2=OH, X=CH_2

Figure 1.1. Guaianolides (**1-24**) isolated from genus *Lactuca*

25 R_1=R_2=H, X=H, αMe
26 R_1=H, R_2=OH, X=H, αMe
27 R_1=H, R_2=OSO_3H, X=H, αMe
28 R_1=OGlc, R_2=H, X=CH_2
29 R_1=R_2=H, X=OGlc, αMe
30 R_1=OGlc, R_2=H, X=H, αMe

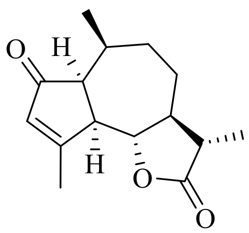






31 R=OCOCH$_2$(Ph)OH
32 R=H

33 X=H, αMe
34 X=CH_2



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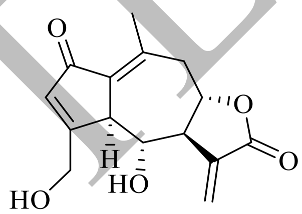

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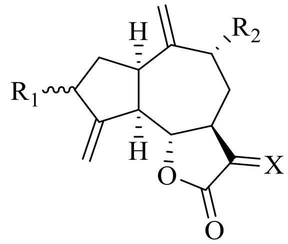
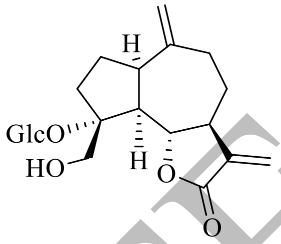
Figure 1.2. Guaianolides (**25-36**) isolated from genus *Lactuca*

37 R_1=*α*OH, R_2=H, X=H, *α*Me
38 R_1=*β*-OGlc, R_2=H, X=H, *α*Me
39 R_1=*β*OH, R_2=OH, X=H, *α*Me
40 R_1=*β*OH, R_2=H, X=H, *α*Me
41 R_1=*α*OH, R_2=H, X=CH_2
42 R_1=*α*-OGlc, R_2=H, X=CH_2
43 R_1=*β*OH, R_2=OH, X=CH_2
44 R_1=*β*-OGlc, R_2=OH, X=H, *α*Me
45 R_1=*β*-OGlc, R_2=OH, X=CH_2
46 R_1= OH, R_2=OGlc, X=H, *α*Me
47 R_1=H, R_2=OGlc, X=H, *α*Me



48 R_1=*β*-OGlc, R_2=H, X=CH_2
49 R_1=*β*OH, R_2=H, X=CH_2



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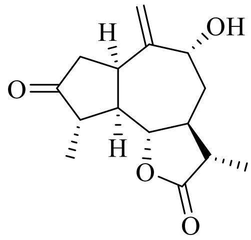

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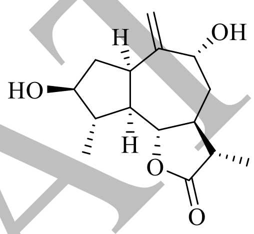

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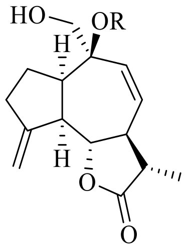
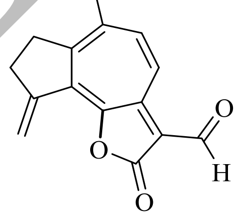


53 R=H
54 R=Glc



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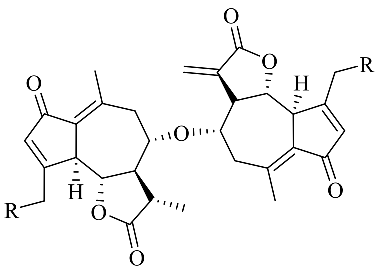


56 R=H
57 R=OH
58 $OCOCH_2(Ph)OH$

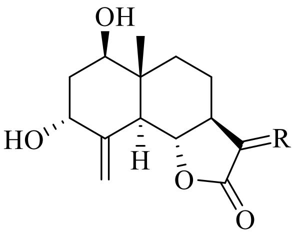
Figure 1.3. Guaianolides (**37-58**) isolated from genus *Lactuca*

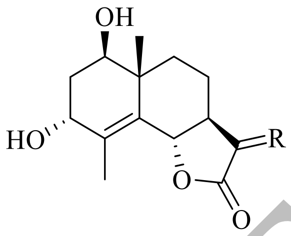
3.1.2. Eudesmanolides

Eudesmanolide sesquiterpene lactones are characterized by having two fused 6-membered rings and a fused γ-lactone ring (5-membered lactone group) having a carbonyl group at the α-position [11] as summarized in Table 2 and Figures 2.1., 2.2. As seen in Table 2, there are many representative examples, isolated from the roots of several members of *Lactuca*, rather than other plant parts. The roots of *L. canadensis* and *L. viminea* are considered rich sources for the isolation of this particular class of compounds.

Table 2. Eudesmanolides isolated from genus *Lactuca*

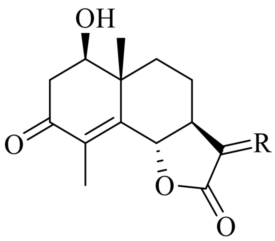
No.	Compound name	Species	References
59	1-Epierivanin	Roots of *L. canadensis*	[38]
		Roots of *L. viminea*	[33]
60	3*α*-Hydroxyreynosin	Roots of *L. canadensis*	[38]
61	Armefolin	Roots of *L. canadensis*	[38]
62	1-Epiisoerivanin	Roots of *L. canadensis*	[38]
		Roots of *L. viminea*	[33]
63	Armexifolin	Roots of *L. canadensis*	[38]
64	1-Epidehydroisoerivanin	Roots of *L. canadensis*	[38]
		Roots of *L. viminea*	[33]
65	11*β*,13-Dihydrosantamarin (1*β*-hydroxyl-5*α*,6*β*H-eudesman-3-ene-12,6*α*-olide)	Roots of *L. canadensis*	[38]
		L. tartarica whole plant	[16]
		Roots of *L. viminea*	[33]
		Roots of *L. laciniata*	[35]
		Stem of *L. sativa* var. *angustana*	[21]
66	1*β*-Hydroxy-15-*O*-(*p*-methoxyphenylacetyl)-5*α*,6*β*,11*β*H-eudesma-3-en-12,6*α*-olide	Stem of *L. sativa* var. *angustana*	[40]
67	Santamarin	Roots of *L. canadensis*	[38]
		Roots of *L. viminea*	[33]
68	1*β*-*O*-*β*-D-Glucopyranosyl-4*α*-hydroxy-5*α*,6*β*,11*β*H-eudesma-12,6*α*-olide	Stems of *L. sativa* var. *angustana*	[40]
69	1*β*-*O*-*β*-D-Glucopyranosyl-15-*O*-(*p*-methoxyphenylacetyl)-5*α*,6*β*H-eudesma-3, 11(13)-dien-12, 6*α*-olide	*L. sativa* L. *var. angustata* whole plant	[41]
70	2*β*-Hydroxy-11*β*,13 dihydrouglanin	*L. tartarica* whole plant	[16]
71	Methyl 3*β*-(*β*-D-glucopyranosyloxy)-6*α*-hydroxyeudesma-1,4(15),11(13)-trien-12-oate	Roots of *L. altaica*	[15]
72	2-Oxo-11*β*,13-dihydrosantamarin	*L. tartarica* whole plant	[16]
		Roots of *L. viminea*	[33]
73	Tauremisin (vulgarin)	Roots of *L. viminea*	[33]

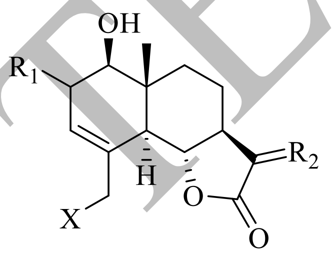




59 R=H, *α*Me
60 R=CH_2

61 R=CH_2
62 R=H, *α*Me

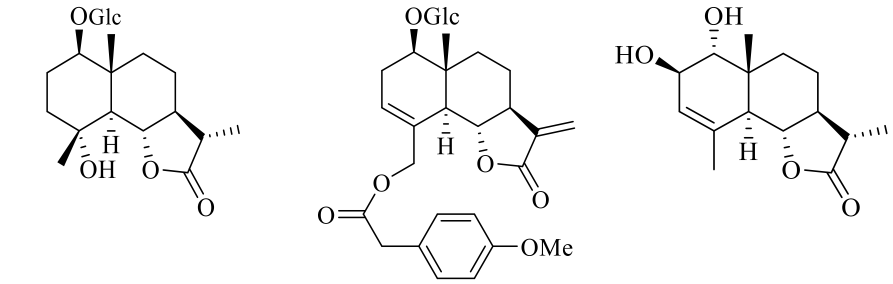




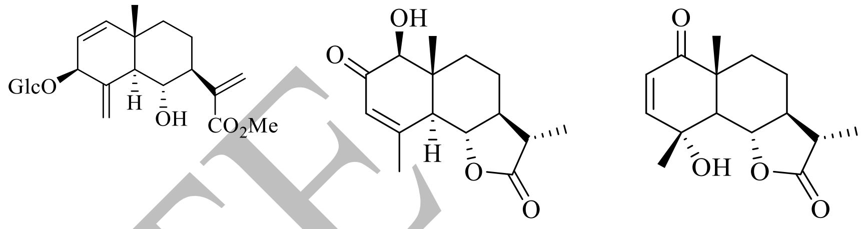
63 R=CH_2
64 R=H, *α*Me

65 R_1=X=H, R_2=H, *α*Me
66 R_1=H, R_2=H, *α*Me, X= $OCOCH_2(Ph)OH$
67 R_1=X=H, R_2=CH_2

Figure 2.1. Eudesmanolides (**59-67**) isolated from genus *Lactuca*



68 **69** **70**



71 **72** **73**

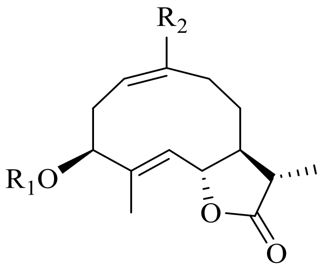
Figure 2.2. Eudesmanolides (**68-73**) isolated from genus *Lactuca*

3.1.3. Germacranolides

Germacranolide sesquiterpene lactones are characterized by having a 10 membered ring with a fused γ-lactone (5-membered lactone group) having a carbonyl group at the α-position [11] and include melampolide and germacrolide sesquiterpene lactones as listed respectively in Tables 3, 4 and Figures 3, 4.

Table 3. Melampolides isolated from genus *Lactuca*

No.	Compound name	Species	References
74	Lactulide A	Roots of *L. aculeata*	[25]
	(3*β*-Hydroxy-11*β*,13-	Roots of *L. laciniata*	[35]
	dihydroacanthospermolide)	Aerial parts of *L. sativa*	[36]
75	Lactulide B	Roots of *L. sativa* var. *angustana*	[27]
76	Lactuside A	Roots of *L. aculeata*	[25]
		Roots of *L. saligna*	[26]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. altaica*	[15]
		Leaves and roots of *L. aculeata*	[28]
		Aerial parts of *L. aculeata*	[29]
		Aerial parts of *L. serriola*	[13,23]
		Roots of *L. viminea*	[33]
		Roots of *L. georgica*	[18]
		Roots of *L. laciniata*	[35]
		Roots of *L. saligna*	[26]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa*	[20]
		Roots of *L. perennis*	[32]
		Aerial parts and roots of *L. dregeana*	[22]
		Roots of *L. virosa*	[19]
		Roots of *L. sativa*	[20]
		Roots of *L. perennis*	[32]
		Aerial parts and roots of *L. dregeana*	[22]
77	Lactuside B	Roots of *L. laciniata*	[35]
		Aerial parts of *L. serriola*	[23]

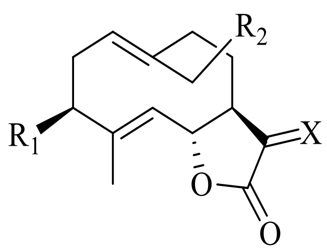


74 R_1=H, R_2=CHO
75 R_1=H, R_2=CH_2OH
76 R_1=Glc, R_2=CHO
77 R_1=Glc, R_2=CH_2OH

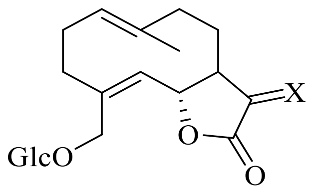
Figure 3. Melampolides (**74-77**) isolated from genus *Lactuca*

Table 4. Germacrolides isolated from genus *Lactuca*

No.	Compound name	Species	References
78	3*β*,14-Dihydroxy-11*β*,13-dihydrocostunolide	Aerial parts of *L. sativa*	[36]
79	3*β*,14-Dihydroxy-11*β*,13-dihydrocostunolide-3-*O*-*β*-D-glucoside	Roots of *L. aculeata*	[25]
		Roots of *L. altaica*	[15]
		Roots of *L. sibirica*	[30]
		Roots of *L. georgica*	[18]
		Roots of *L. virosa*	[19]
80	Picriside C	Roots of *L. tartarica*	[17]
81	Sonchuside A	Roots of *L. tartarica*	[17]
		Roots of *L. virosa*	[19]
		Roots of *L. viminea*	[33]
		Roots of *L. georgica*	[18]
		Roots of *L. sativa* var. *angustana*	[27]
82	Tartaroside (3*β*,11*β*,14-trihydroxy-11*β*,13-dihydrocostunolide-3-*O*-*β*-D-glucoside)	Roots of *L. tartarica*	[42]
83	Ixerin H	Roots of *L. viminea*	[33]
		Roots of *L. sativa* var. *angustana*	[27]
84	Picriside B	Roots of *L. aculeata*	[25]
		Roots of *L. canadensis*	[38]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. tartarica*	[17]
		Roots of *L. viminea*	[33]
		Roots of *L. virosa*	[19]



78 R_1= R_2=OH, X=H, *α*Me
79 R_1=OGlc, R_2=OH, X=H, *α*Me
80 R_1=OGlc, R_2=H, X=CH_2
81 R_1=OGlc, R_2=H, X=H, *α*Me
82 R_1=OGlc, R_2=OH, X=OH, *α*Me



83 X=H, *α*Me
84 X=CH_2

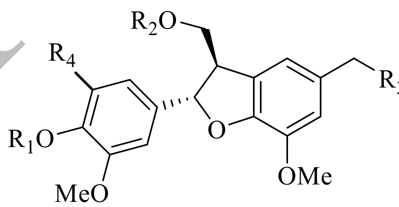
Figure 4. Germacrolides (**78-84**) isolated from genus *Lactuca*

3.2. Lignans

Lignans are polyphenolic compounds of 1,4-diarylbutane skeleton, derived from the shikimic acid biosynthetic pathway. Some lignans (as furofuran lignans and neolignans) have been reported from several *Lactuca* species mainly dihydrodehydrodiconiferyl alcohol 9-*O*-β-D-glucoside. Lignans isolated from the genus *Lactuca* are summarized in Table 5 and Figure 5. Furfuran-type lignans are considered to be the predominant class of lignans, distributed among *Lactuca* species. Interestingly, compounds **95-96** represent furfuran lignans containing acylated sugar moieties which are rare in plants.

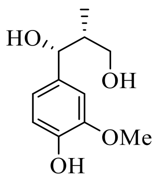
Table 5. Lignans isolated from genus *Lactuca*

No.	Compound name	Species	References
85	(+)-Balanophonin-9-*O*-*β*-D-glucoside	Callus culture of *L. aculeata*	[43]
86	(+)-Buddlenol A	Callus culture of *L. aculeata*	[43]
87	Dihydrodehydro diconiferyl alcohol 9-*O*-*β*-D-glucoside	Roots of *L. viminea* Aerial parts and roots of *L. tenerrima* Aerial parts and roots of *L. dregeana* Roots of *L. altaica*	[33] [44] [22] [15]
88	(+)-5-Methoxybalanophonin	Callus culture of *L. aculeata*	[43]
89	(-)-Dihydrodehydrodiconiferyl alcohol 4-*O*-*β*-D-glucoside	Callus culture of *L. aculeata*	[43]
90	(-)-Dihydrodehydrodiconiferyl alcohol 9-*O*-*β*-D-glucoside		
91	4*β*-Hydroxy-epipinoresinol 4-*O*-*β*-D-glucoside	Root tubers of *L. tuberosa*	[45]
92	Syringaresinol	Callus culture of *L. aculeata*	[43]
93	Lactuberin A	Root tubers of *L. tuberosa*	[45]
94	Lactuberin B		
95	8*α*-Hydroxypinoresinol-4*α*-*O*-*β*-(6-*p*-hydroxyphenylacetyl)-glucoside	Aerial parts of *L. sibirica*	[31]
96	8*α*-Hydroxypinoresinol-4*α*-*O*-*β*-(6-*p*-methoxyphenylacetyl)-glucoside		
97	Lactucaside	*L. indica* whole plant Aerial parts of *L. sibirica*	[12] [31]



85 R_1=R_4=H, R_2=Glc, R_3= CH═CHCHO

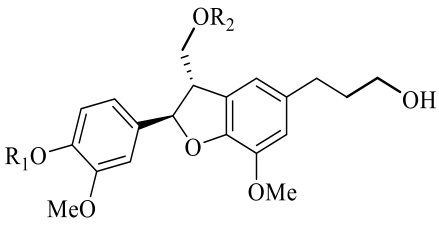
86 R_1=



R_2=H, R_3= CH═CHCHO, R_4=OMe

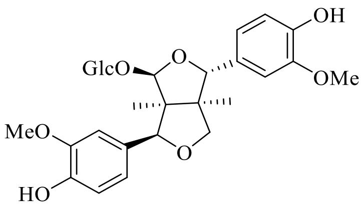
87 R_1= R_4=H, R_2=Glc, R_3=*n*-propylalcohol

88 R_1=R_2=H, R_3= CH═CHCHO, R_4=OMe



89 R_1=Glc, R_2=H

90 R_1=H, R_2=Glc



91

Figure 5. Lignans (**85-97**) isolated from genus *Lactuca* (The first part)

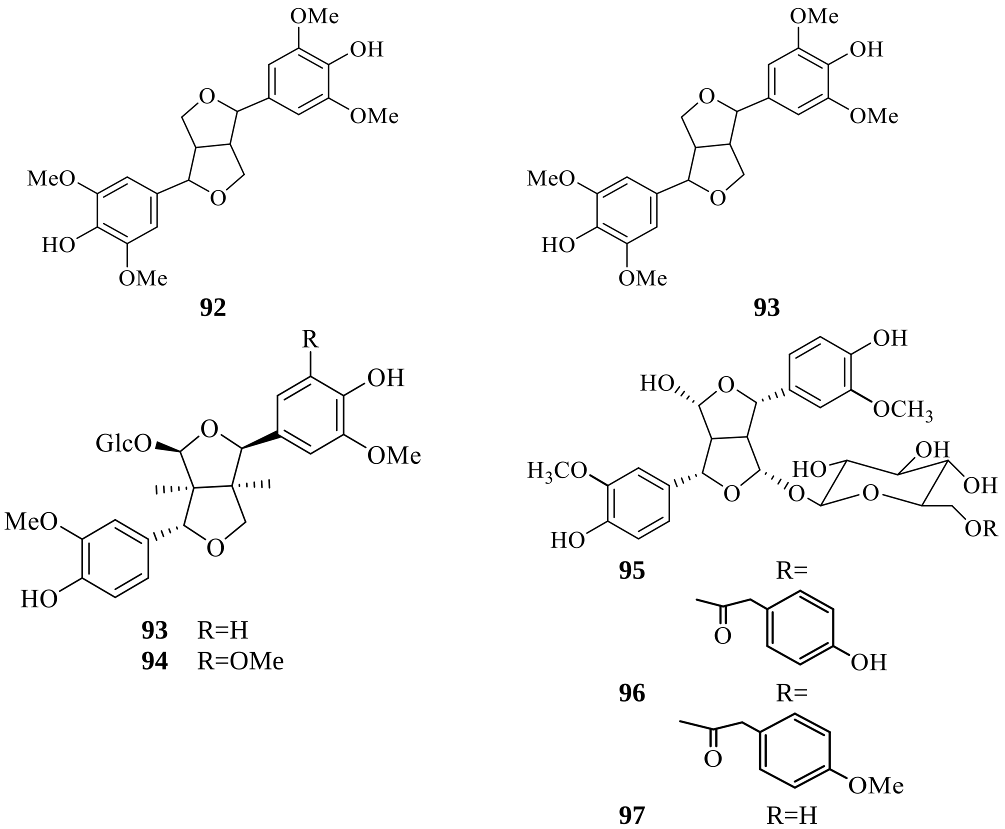


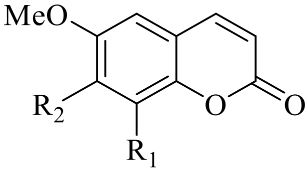
Figure 5. Lignans (**85-97**) isolated from genus *Lactuca* (The second part)

3.3. Coumarins

Among all *Lactuca* species, coumarins (2*H*-1-benzopyran-2-one), mainly scopolin, have only been reported from roots and aerial parts of both *L. tenerrima* and *L. inermis* as their major characteristic secondary metabolites [41,46]. Coumarins isolated from the genus *Lactuca* are summarized in Table 6 and Figure 6.

Table 6. Coumarins isolated from genus *Lactuca*

No.	Compound name	Species	References
98	Isofraxoside	Roots and aerial parts of *L. inermis*	[39]
99	Scopoletin	Aerial parts and roots of *L. tenerrima*	[44]
100	Scopolin	Roots and aerial parts of *L. inermis*	[39]
		Aerial parts and roots of *L. tenerrima*	[44]



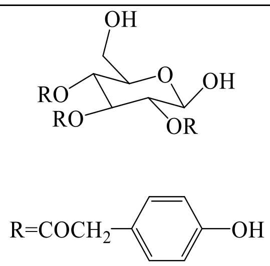
98 R_1=OH, R_2=OGlc
99 R_1=R_2=H
100 R_1=H, R_2=OGlc

Figure 6. Coumarins (**98-100**) isolated from genus *Lactuca*

3.4. Tannins

Uncommon tannins have been reported from the latex of *L. sativa* in the form of 4-hydroxyphenylacetyl conjugates of β-D-glucose [24] as in Table 7.

Table 7. Tannins isolated from genus *Lactuca*

No.	Compound name	Structure	Species	References
101	2,3,4-Tri-(4-hydroxyphenylacetyl)-*β*-D-glucopyranose		Latex of *Lactuca sativa*	[24]

3.5. Flavonoids

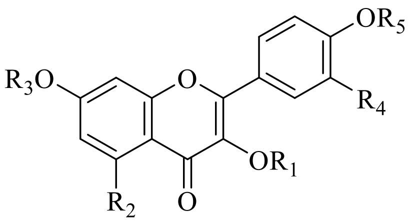
Several flavonoids as flavonols, flavones and flavanols have been reported from most of *Lactuca* L. species mainly quercetin, quercetin-3-*O*-*β*-D-glucoside (isoquercitrin), luteolin-7-*O*-*β*-D-glucopyranoside, luteolin and apigenin. Flavonoids isolated from the genus *Lactuca* are summarized in Tables 8, 9, and Figures 7 and 8.

3.5.1. Flavonols

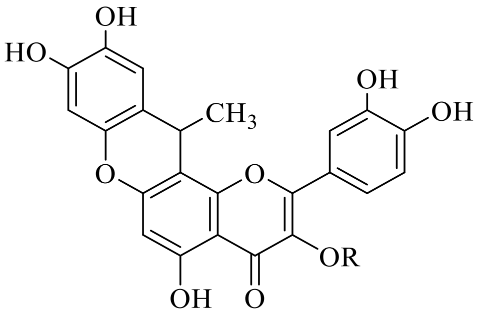
Flavonols are a class of flavonoids that have the 3-hydroxyflavone backbone. Kampfeol, quercetins, and their glycosylated derivatives were reported in several *Lactuca* species, mostly from the aerial parts. From the seeds of *L. sativa*, two complex structures of flavonol-based skeleton, named Japonicin A and Lactucasativoside A were reported.

Table 8. Flavonols and flavonol glycosides isolated from genus *Lactuca*

No.	**Compound name**	**Species**	**References**
102	Kaempferol	Aerial parts of *L. serriola*	[23,34]
103	Kaempferol-3-*O*-*β*-D-glucoside	Aerial parts of *L. tartarica*	[46]
		Aerial parts and roots of *L. tenerrima*	[44]
104	Kaempferide-3-*O*-*β*-D-glucuronide	*L. sativa* leaves	[47]
105	Quercetin	The aerial parts of *L. viminea*	[48]
		L. indica whole plant	[12]
		Aerial parts of *L. serriola*	[23,34]
106	Quercetin-3-*O*-*β*-D-glucoside (Isoquercitrin)	Aerial parts of *L. indica*	[34,49]
		Aerial parts of *L. serriola*	[34]
		L. indica whole plant	[12]
		The aerial parts of *L. viminea*	[48]
		Aerial parts of *L. quercina* and *L. tartarica*	[46]
		Aerial parts and roots of *L. tenerrima*	[44]
		Aerial parts of *L. tenerrima*	[50]
		Aerial parts and roots of *L. dregeana*	[22]
		Seeds of *L. sativa*	[51,52]
107	Quercetin-3-*O*-*α*-L-rhamnoside	*L. sativa* leaves	[53]
108	Quercetin-5-*O*-*β*-D-glucoside	Aerial parts of *L. indica*	[54]
109	Quercetin-3-*O*-*α*-L-rhamnopyranosyl-(1→6)-*β*-D-glucoside (rutin)	Aerial parts of *L. indica*	[54]
		L. indica whole plant	[12]
110	Japonicin A	Seeds of *L. sativa*	[51]
111	Lactucasativoside A (3,3',4',5,9,10-hexahydroxy-12-methylchroman [2,3-h] flavone 3-*O*-*β*-D-glucopyranoside		



102 $R_1=R_3=R_4=R_5=H$, $R_2=OH$
103 $R_1=Glc$, $R_2=OH$, $R_3=R_4=R_5=H$
104 $R_1=$glucuronic acid, $R_2=OH$, $R_3=R_4=H$, $R_5=CH_3$
105 $R_1=R_3=R_5=H$, $R_2=R_4=OH$
106 $R_1=Glc$, $R_2=R_4=OH$, $R_3= R_5=H$
107 $R_1=Rha$, $R_2=R_4=OH$, $R_3=R_5=H$
108 $R_1=R_3=R_5=H$, $R_2=OGlu$, $R_4=OH$
109 $R_1=Rut$, $R_2=R_4=OH$, $R_3=R_5=H$

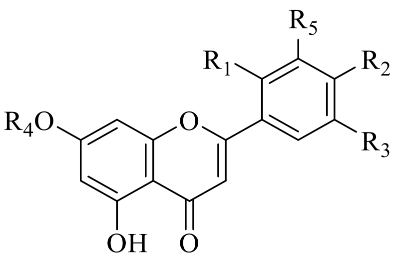


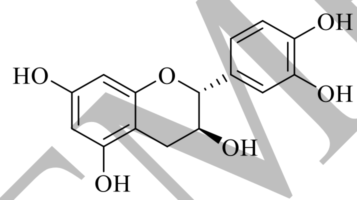
110 R=H
111 R=Glc

Figure 7. Flavonols and flavonol glycosides (**102-111**) isolated from genus *Lactuca*

3.5.2. Flavones

Flavones are a class of flavonoids based on the backbone of 2-phenylchromen-4-one (2-phenyl-1-benzopyran-4-one). Apigenin, luteolin, and their glycosylated derivatives were the predominant flavones in several *Lactuca* species, mostly identified from the aerial parts of the investigated plants.





120

112 $R_1=R_3=R_4=R_5=H$, $R_2=OH$
113 $R_1=R_3=R_5=H$, $R_2=OH$, $R_4=Glc$
114 $R_1=R_3=R_5=H$, $R_2=OH$, $R_4=Glc\text{-}Api$
115 $R_1=OH$, $R_2=R_3=R_5=H$, $R_4=$glucuronic acid
116 $R_1=R_3=R_4=H$, $R_2=R_5=OH$
117 $R_1=R_5=H$, $R_2=R_3=OH$, $R_4=$glucuronic acid
118 $R_1=R_5=H$, $R_2=R_3=OH$, $R_4=$glucuronate methyl ester
119 $R_1=R_5=H$, $R_2=R_3=OH$, $R_4=Glc$

Figure 8. Flavones and flavone glycosides (**112-119**) isolated from genus *Lactuca*

Table 9. Flavones, flavone glycosides and flavonols isolated from genus *Lactuca*

No.	Compound name	Species	References
112	Apigenin	Aerial parts of *L. perennis*	[32]
		Aerial parts of *L. viminea*	[48]
		L. indica whole plant	[12]
		Aerial parts of *L. quercina* and *tartarica*	[46]
		Aerial parts of *L. tenerrima*	[50]
		The aerial parts of *L. indica*	[49]
113	Apigenin-7-*O*-*β*-D-glucoside	Aerial parts of *L. tartarica.*	[46]
		Aerial parts of *L. tenerrima*	[50]
		Roots of *L. perennis*	[32]
114	Apigenin-7-*O*-apiofuranosyl (1-2) *β*-D-glucoside	Seeds of *L. sativa*	[52]
115	5,2'-Dihydroxy-7-*O*-*β*-D-glucuronylflavone	Aerial parts of *L. indica*	[54]
116	Luteolin	Aerial parts of *L. perennis*	[32]
		Aerial parts of *L. serriola*	[34]
		The aerial parts of *L. viminea*	[48]
		L. indica whole plant	[12]
		Aerial parts of *L. quercina* and *L. tartarica*	[46]
		Aerial parts of *L. tenerrima*	[50]
		The aerial parts of *L. indica*	[49]
117	Luteolin-7-*O*-*β*-D-glucuronide	*L. indica* whole plant	[12]
118	Luteolin-7-*O*-*β*-D-glucuronide-6''-methyl ester	Aerial parts of *L. viminea*	[48]
		Aerial parts of *L. tenerrima*	[50]
119	Luteolin-7-*O*-*β*-D-glucoside	*L. dentata* Makino	[55]
		Aerial parts of *L. viminea*	[48]
		Aerial parts of *L. quercina*	[46]
		Aerial parts of *L. serriola*	[23,34]
		Aerial parts and roots of *L. tenerrima*	[44]
		Aerial parts of *L. tenerrima*	[50]
		Aerial parts and roots of *L. dregeana*	[22]
		Seeds of *L. sativa*	[52]
120	Epicatechin	*L. sativa* leaves	[53]

3.6. Phenolic acids

Phenolic compounds found in lettuce are considered natural antioxidants. They can protect against harmful free radicals thus reducing the risk of incidence of several types of chronic degenerative diseases, such as cancer and diabetes, and they can decelerate aging. Several common phenolic acids have been reported from different species of *Lactuca*, either with hydroxybenzoic acid or hydroxycinnamic acid-based skeletons. Phenolic acids isolated from the genus *Lactuca* are summarized in Table 10, Figure 9.

Table 10. Phenolic acids isolated from genus *Lactuca*

No.	Compound name	Species	References
121	*Trans*-Caffeic acid	Aerial parts of *L. viminea*	[48]
		Seeds of *L. sativa*	[51]
		Root tubers of *L. tuberosa*	[45]
122	Chlorogenic acid (5-*O*-Caffeoylquinic acid)	Aerial parts of *L. indica*	[49,54]
		L. indica whole plant	[12]
		Callus culture of *L. aculeata*	[43]
		The aerial parts of *L. viminea*	[48]
123	*Trans*-Cinnamic acid	Aerial parts of *L. indica*	[49]
124	*Trans*-*p*-Coumaric acid	Aerial parts of *L. indica*	[49]
		Aerial parts of *L. serriola*	[23]
125	*Trans*-Ferulic acid	The aerial parts of *L. viminea*	[48]
126	*p*-Hydroxybenzoic acid	Aerial parts of *L. serriola*	[23]
127	*p*-Hydroxymethyl benzoic acid	The aerial parts of *L. indica*	[49]
128	4-Hydroxyphenylacetic Acid	Roots and aerial parts of *L. inermis*	[39]
129	Protocatechuic acid	Root tubers of *L. tuberosa*	[45]
		Aerial parts of *L. indica*	[49]
		Aerial parts of *L. serriola*	[23]
130	Sinapic acid	*L. sativa* leaves	[53]
131	Syringic acid	Roots and aerial parts of *L. inermis*	[39]

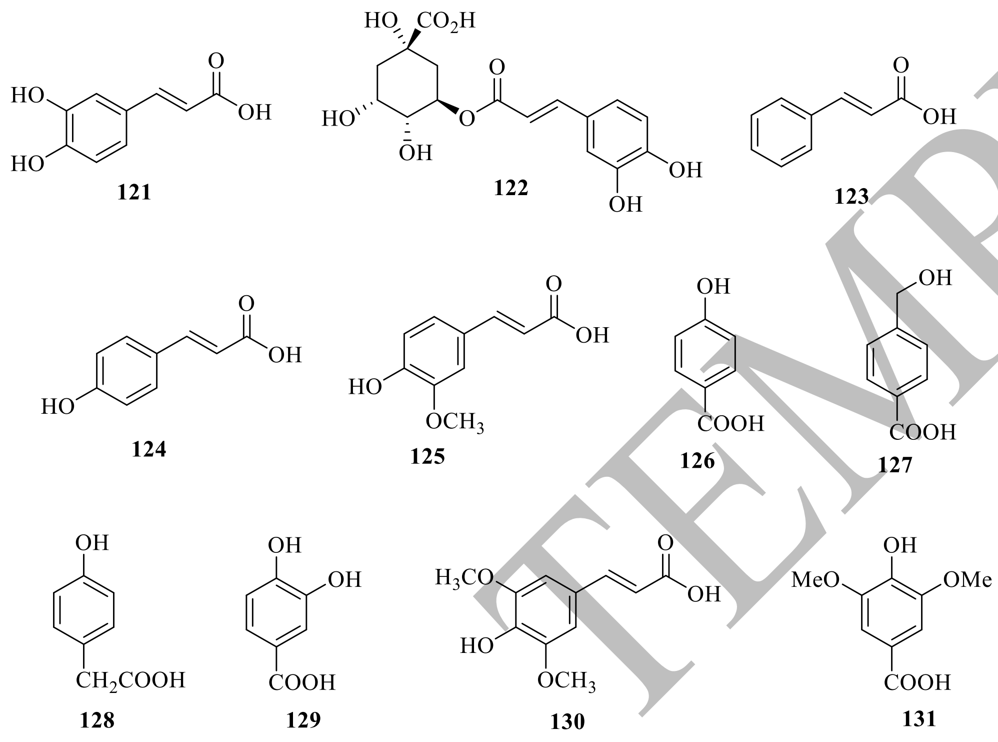


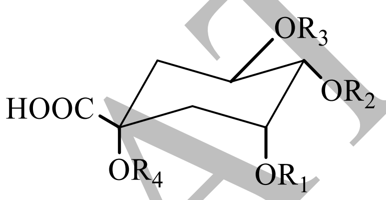
Figure 9. Phenolic acids (**121-131**) isolated from genus *Lactuca*

3.7. Cyclic polyols

Polyols are organic compounds containing multiple hydroxyl groups. From two species of *Lactuca*, several cyclic polyols were reported with a quinic acid backbone, as shown in Table 11 and Figure 10.

Table 11. Cyclic polyols isolated from genus *Lactuca*

No.	Compound name	Species	References
132	1,5-Dicaffeoylquinic acid	Callus culture of *L. aculeata*	[43]
133	3,4-Di-*O*-caffeoylquinic acid	Aerial parts of *L. indica*	[54]
134	3,5-Di-*O*-caffeoylquinic acid		
135	4,5-Di-*O*-caffeoyl quinic acid	Aerial parts of *L. indica*	[54]
		Callus culture of *L. aculeata*	[43]
136	3-*O*-Caffeoylquinic acid	Aerial parts of *L. indica*	[54]
137	5-*O*-(*E*)-*p*-Coumaroylquinic acid		
138	3,5-Di-*O*-caffeoyl-*muco*-quinic acid		



132	R_1=R_2=H, R_3=R_4=caffeoyl
133	R_1=R_2=caffeoyl, R_3=R_4=H
134	R_1=R_3=caffeoyl, R_2=R_4=H
135	R_1=R_4=H, R_2=R_3=caffeoyl
136	R_1=caffeoyl, R_2=R_3=R_4=H
137	R_1=R_2=R_4=H, R_3=(*E*)-*p*-coumaroyl
138	R_1=R_3=caffeoyl, R_2=R_4=H

Figure 10. Cyclic polyols (**132-138**) isolated from genus *Lactuca*

3.8. Triterpenoids

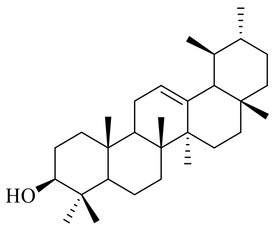
Plants belonging to the family Asteraceae of the subfamily, Cichorioideae are rich in milky latex from which several triterpenoids are reported. Previous phytochemical investigation showed that these plants are rich sources of triterpenoids with wide structural diversity mainly α-amyrin, β-amyrin, germanicol, lupeol, and taraxasterol [56]. Triterpenes isolated from the genus *Lactuca* are summarized in Table 12 and Figure 11.

Table 12. Triterpenoids isolated from genus *Lactuca*

No.	Compound name	Species	References
139	*α*-Amyrin	*L. indica* whole plant	[12]
		Roots of *L. tartarica*	[17]
		Aerial parts of *L. serriola*	[10]
		Seeds of *L. sativa*	[52]
140	*α*-Amyrin acetate	Roots of *L. indica*	[56]
		L. denticulata whole plant	[57]
141	*β*-Amyrin	*L. indica* whole plant	[12,57]
		Aerial parts of *L. serriola*	[10]
142	*β*-Amyrin acetate	Roots of *L. indica*	[56]
		L. denticulata and *L. indica* whole plant	[57]
143	Bauerenyl acetate	Roots of *L. indica*	[56]
144	Germanicol	*L. indica* whole plant	[12]
		Aerial parts of *L. serriola*	[10]
145	Germanicyl acetate	Roots of *L. indica*	[56]

Table 12 continued..

146	Lactucenyl acetate	Roots of *L. indica*	[56]
147	Lupeol	*L. indica* whole plant	[12]
		Aerial parts of *L. sativa*	[36]
		Aerial parts of *L. serriola*	[10,23]
148	Lupenyl acetate	Roots of *L. indica*	[56]
		Aerial parts of *L. serriola*	[10]
		L. denticulata whole plant	[57]
149	Olean-18-ene	Aerial parts of *L. serriola*	[10]
150	Pseudotaraxasterol	*L. indica* whole plant	[12]
151	Taraxasterol	*L. indica* whole plant	[12,57]
152	Taraxasteryl acetate	Roots of *L. indica*	[56]
153	Taraxast-20-ene-3*β*,30-diol	Aerial parts of *L. serriola*	[23]
154	Tarolupenyl acetate (lup-19(21)-en-3*β*-yl acetate)	Roots of *L. indica*	[56]
155	3-*O*-[*β*-D-Galactopyranosyl-(1→3)-*O*-*β*-D-xylopyranosyl-(1→4)-*O*-*α*-L-rhamnopyranosyl]-oleanolic acid	Seeds of *L. serriola*	[58]
156	3*β*-*O*-[*α*-L-rhamnopyranosyl]-30-norolean-12,19-diene-28-oic acid 28-*O*-[*β*-D-glucopyranosyl-(1→4)-*O*-*β*-D-galactopyranosyl]-ester	Stems of *L. serriola*	[59]



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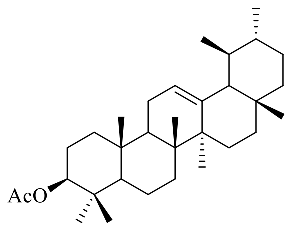

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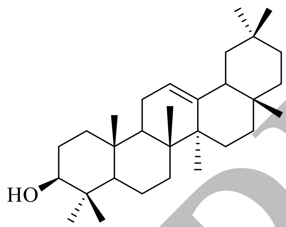

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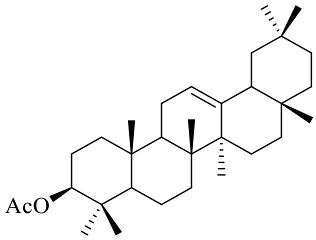

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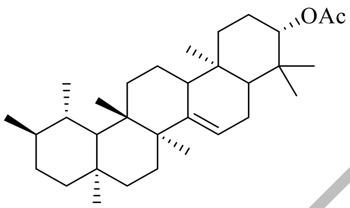

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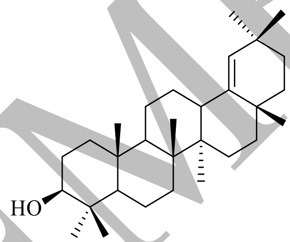

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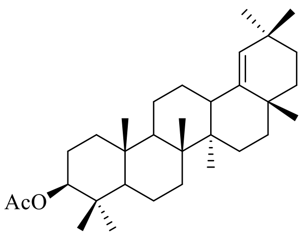

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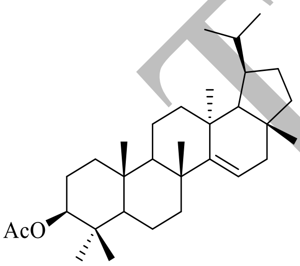

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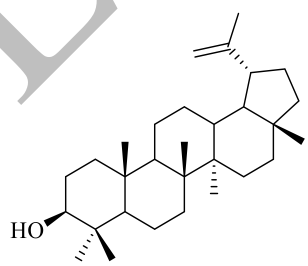
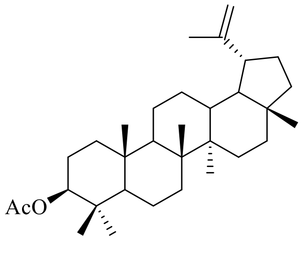


147

Figure 11. Triterpenoids (**139-156**) isolate from genus *Lactuca* (the first part)



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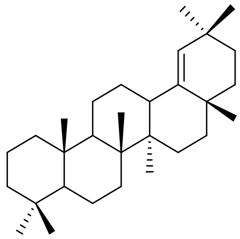

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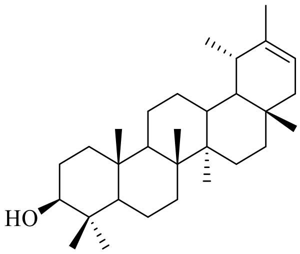

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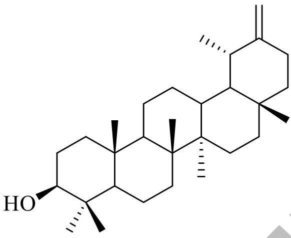

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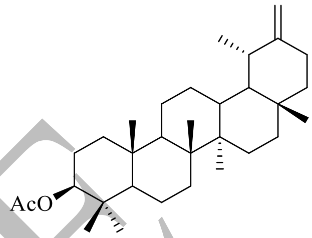

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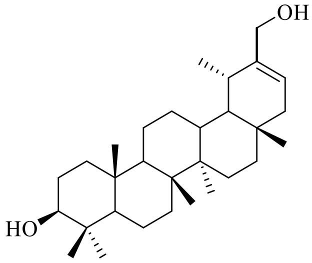

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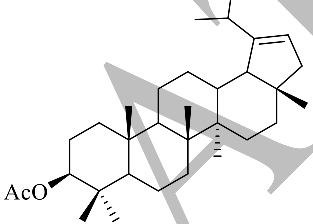

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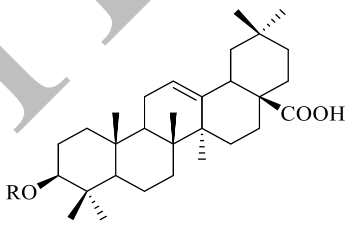
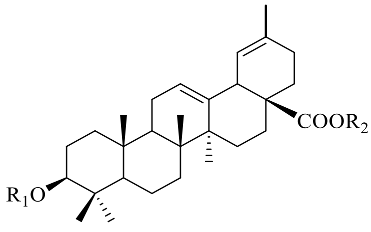


155 R=Gal-(1→3)-Xyl-(1→4)-Rha



156 R_1=Rha, R_2=Glc-(1→4)-Gal

Figure 11. Triterpenoids (**139-156**) isolated from genus *Lactuca* (the second part)

3.9. Steroids

Plant steroids are key hormones throughout the plant kingdom. They regulate many aspects of growth and development. From *Lactuca*, several common steroids were reported, including campesterol, *β*-sitosterol, and stigmasterol (Table 13). The glycosylated forms of some of these common steroids were also reported.

Table 13. Steroids isolated from genus *Lactuca*

No.	Compound name	Species	References
157	Campesterol	Aerial parts of *L. serriola*	[10]
158	*β*-Sitosterol	*L. denticulata* and *L. indica*	[57]
		Aerial parts of *L. sativa*	[36]
		Aerial parts of *L. serriola*	[10,23]
		Seeds of *L. sativa*	[52]
159	*β*-Sitosterol-3-*O*-*β*-D-glucoside (Daucosterol)	Aerial parts of *L. sativa*	[36]
		Seeds of *L. sativa*	[52]
		Aerial parts of *L. serriola*	[23]
160	Stigmasterol	*L. denticulata* and *L. indica*	[57]
161	Stigmasterol acetate	Aerial parts of *L. serriola*	[10]

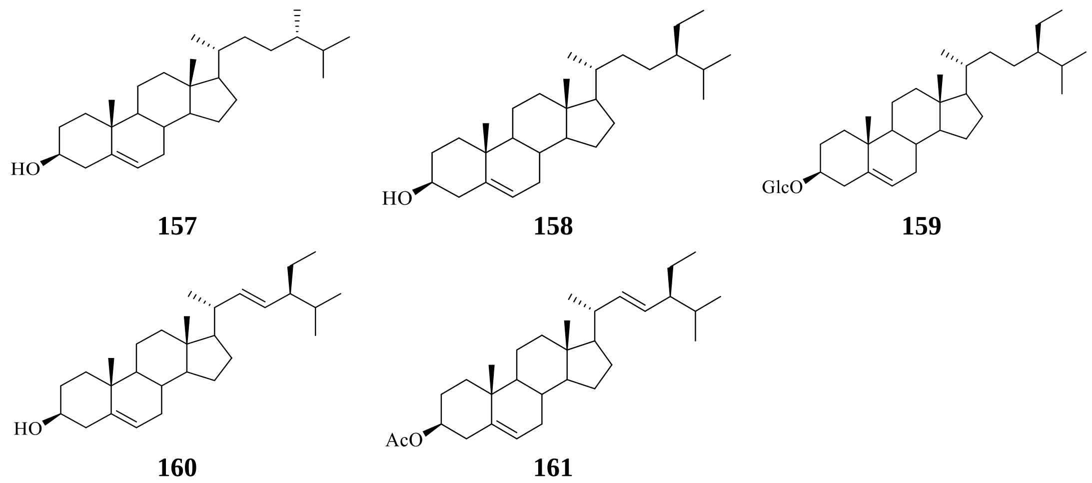


Figure 12. Steroids (**157-161**) isolated from genus *Lactuca*

3.10. Miscellaneous compounds

Apart from the distinct classes explained, some other miscellaneous compounds were reported (Table 14). Interestingly, from the aerial parts of *L. serriola* [23], a ceramide was isolated by our research group, and this was the first report of isolation of such class of compounds from *Lactuca*.

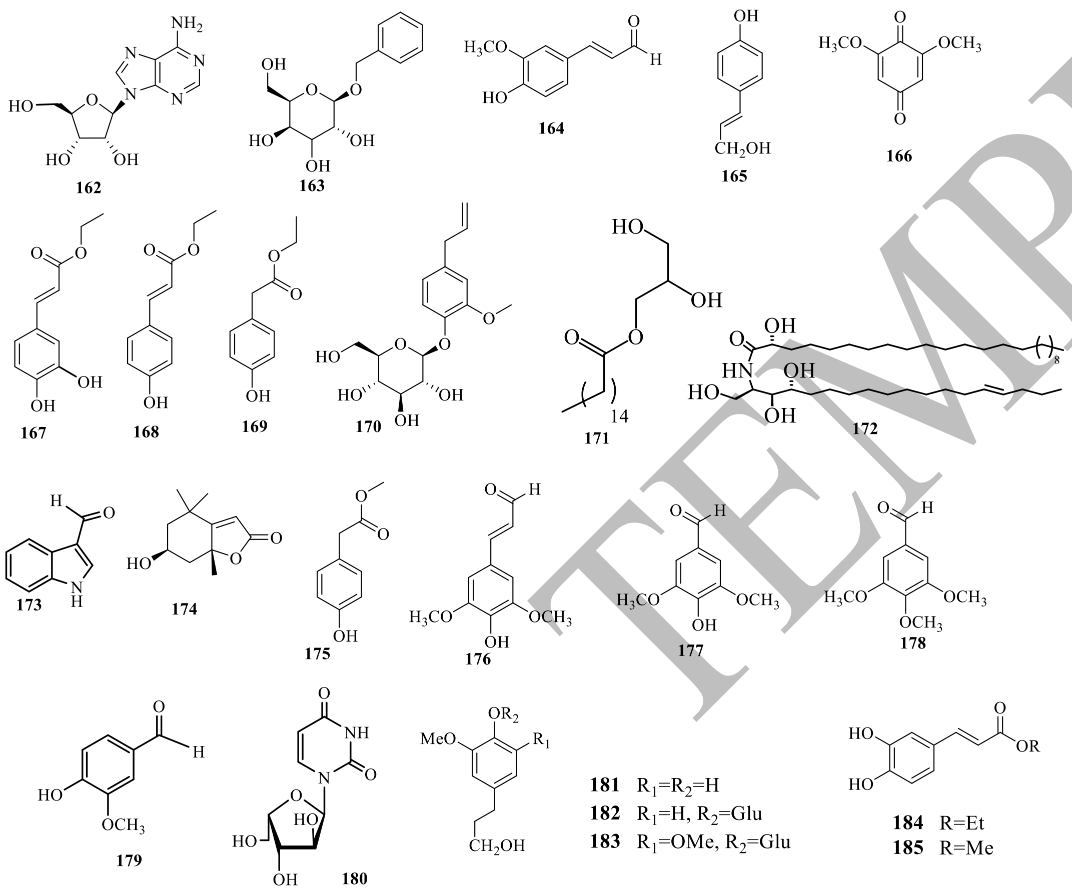


Figure 13. Miscellaneous compounds (**162-185**) isolated from genus *Lactuca*

Table 14. Miscellaneous compounds isolated from genus *Lactuca*

No.	Compound name	Species	References
162	Adenosine	Aerial parts and roots of *L. tenerrima*	[44]
163	Benzyl-β-D-glucoside	Roots of *L. tartarica*	[17]
164	Coniferyl aldehyde	Roots of *L. altaica*	[15]
		Roots of *L. sativa* var. *angustana*	[27]
		Roots of *L. sativa* var. *angustana*	[27]
		Callus culture of *L. aculeata*	[43]
165	*p*-Coumaryl alcohol	Root tubers of *L. tuberosa*	[45]
166	2,6-Dimethoxy benzoquinone	Roots of *L. altaica*	[15]
167	Ethyl 3',4'-dihydroxy-*trans*-cinnamate	Roots of *L. perennis*	[32]
168	Ethyl 4'-hydroxy-*trans*-cinnamate	Roots of *L. perennis*	[32]
169	Ethyl *p*-hyrdoxyphenylacetate	Roots of *L. perennis*	[32]
170	Eugenyl-4-*O*-β-D-glucoside	Roots of *L. altaica*	[15]
171	Glycerol monopalmitate	Aerial parts of *L. serriola*	[23]
172	(2*S*,3*S*,4*R*,2'*R*,14*E*)-2-(2`-hydroxytetracosanoylamino)-14-octadecene-1,3,4-triol	Aerial parts of *L. serriola*	[23]
173	3-Indolecarbaldehyde	Roots of *L. altaica*	[15]
		Roots of *L. aculeata*	[25]
174	Loliolide	Aerial parts of *L. serriola*	[13]
		Roots of *L. aculeata*	[25]
175	Methyl *p*-hyrdoxyphenylacetate	Root tubers of *L. tuberosa*	[45]
		Roots of *L. altaica*	[15]
176	Sinapyl aldehyde	Roots of *L. sativa* var. *angustana*	[27]
177	Syringaldehyde	Roots of *L. altaica*	[15]
178	3,4,5-Trimethoxybenzaldehyde	Roots of *L. sativa* var. *angustana*	[27]
179	Vanillaldehyde	Roots of *L. altaica*	[15]
180	β-Xylofuranosyluracil	Roots and aerial parts of *L. inermis*	[39]
		Aerial parts and roots of *L. dregeana*	[22]
181	Dihydroconiferylalcohol	Roots of *L. aculeata*	[25]
182	Dihydroconiferin	Aerial parts and roots of *L. tenerrima*	[44]
183	Dihydrosyringin		
184	Ethyl caffeate	Root tubers of *L. tuberosa*	[45]
185	Methyl caffeate	Root tubers of *L. tuberosa*	[45]
		Callus culture of *L. aculeata*	[43]

4. Biological Activities of Genus *Lactuca*

4.1. Ethnomedical Uses

All species of *Lactuca* produce a milky latex, called lactucarium, when a stem is cut. This latex was found to be a mixture, including lactucin and lactucopicrin, and was used in the 19th century as an adulterant for opium (*Papaver Somniferum*) [6,7]. In traditional medicine (Unani medicine), *Lactuca sativa* was used as a sedative, hypnotic, anesthetic, blood purifier, anti-convulsive, diuretic, and as a lactogauge [7]. One of the considerable uses of lettuce (*Lactuca sativa*) seeds, in traditional medicine, was to reduce semen, sperm, and sexuality [60]. *Lactuca indica* was used in folk medicine for the management of intestinal disorders [49]. *Lactuca scariola* is a vital drug in traditional medicine. Its seeds were used for ages for the management of nervousness, insomnia, headache, fever, hypertension, palpitation, acute cold/coryza, asthma, chronic bronchitis, scorpion sting, ... etc. [6,61].

4.2. Pharmacological Screening of Genus Lactuca

The reported pharmacological activities of different plants of the genus *Lactuca* are summarized in Table 15 and are described below.

4.2.1. Anti-inflammatory Action

Lactuca sativa extract decreased reactive oxygen species (ROS), inducible nitric oxide synthase (iNOS), nitric oxide (NO) release, and cyclooxygenase-2 (COX-2) expression resulting in an overall decrease in the inflammation process. This activity could be due to the presence of high amounts of hydroxycinnamic acid derivatives, coumarins, and flavon-3-ols suggesting its value in both nutritional and nutraceutical fields [47]. In another study, the extract of *L. sativa* established a significant regulation of the inflammatory process induced by carrageenan in the hind paw edema test in a rat model. The results revealed that the oral dose of *L. sativa* suppressed the edema from the first hour till the end of the inflammation stages which may be due to the inactivation of certain inflammatory mediators. It seems that the anti-inflammatory potential of *L. sativa* might be attributed to its triterpenoids and saponins content [62]. The anti-inflammatory effect of the aqueous leaf extract of *L. sativa* was assessed also using a human red blood cell (HRBC) membrane stabilization assay and albumin denaturation assay using diclofenac as a standard drug where the lysosomal membrane stabilization inhibits the release of the inflammatory mediators and consequently inhibits the process of oxidative stress and inflammation. Also, protein denaturation is one of the causes of inflammation. The extract showed a significant effect on membrane stabilization and inhibit protein denaturation at a concentration range of 100-500 µg/mL. This action could be due to triterpenoids, saponins, and phenols in *L. sativa* leaf [63].

On the other hand, the methanolic extract of *L. serriola* failed to show any inhibitory effect on the "mean increase in paw volume" induced by injection of carrageenan in the sub-plantar region of paw rat so failed to exhibit anti-inflammatory effects [6].

4.2.2. Antimicrobial Activity

Both the methanolic and *n*-butanol extracts of *L. sativa* exhibited an antibacterial activity while the methanolic extract showed the most remarkable activity with the lowest MIC against all tested Gram-negative (*Escherichia coli, Klebsilla pneumonia, Enterobacter cloacae, Serratia marcescens and Acinetobacter baumannii*) and Gram-positive bacteria (*Staphylococcus aureus, Bacillus subtilus, Enterococcus faecium,* and *Corynebacterium spp.*). Both extracts of *L. sativa* also exhibited anticytomegalovirus (anti-HCMV) and anti-coxsackie B3 activity. The activity may be due to the high phenolic content of the species especially flavonoids and tannins which are known to possess good antimicrobial activity [64].

Antibacterial activity of the crude terpenoid, phenolic, and alkaloid compounds' extracts of *L. serriola* against some pathogenic bacteria, was examined at 50 and 100 mg/mL. Among nine tested pathogenic bacteria, only the Gram-positive bacteria *Staphylococcus saprophyticus* and *Staphylococcus aureus* were susceptible for the terpenoid, alkaloid and phenolic content of the plant while *Staphylococcus epidermidis* was resistant to active compounds. The results also showed that all the examined Gram-negative bacteria were resistant to active compounds including Klebsilla, *Escherichia coli*, and Pseudomonas [65]. In another study, the effect of *L. indica* on uroepithelial infection by *Escherichia coli* was investigated. Despite the lack of bactericidal effect against *Escherichia coli*, *L. indica* remarkably decreased bacterial colonization of epithelial cells in the bladder. This was followed by decreased activation of focal adhesion kinase (FAK) in *L. indica*-exposed cells. These results showed that, in addition to its diuretic action, *L. indica* exerts other actions directly on epithelial cells to protect against

E. coli infection which is the main cause of urinary tract infections (UTI). This might be an alternative valuable strategy for the treatment of UTIs [66].

4.2.3. *Pharmacological Effects of Lactuca serriola in Experimental Models of Gastrointestinal, Respiratory, and Vascular Ailments*

The methanol extract of *L. serriola* was found to exhibit spasmogenic, spasmolytic, bronchodilator, and vasorelaxant activities depending on its dose. The spasmogenic activity may be related to some cholinergic constituents whereas the spasmolytic effect at higher concentrations may be attributed to Ca^{+2} channel blocking constituents that may lead to relaxation of gastrointestinal, tracheal, and aortic smooth muscles. This may partially explain the traditional use of *L. serriola* in the management of conditions relating to spasm of the intestine, bronchioles, and vasculature [61].

4.2.4. *Anticancer Activity*

Selected sesquiterpene lactones from *L. sativa* extract (1*β*-*O*-*β*-D-glucopyranosyl-4*α*-hydroxy-5*α*,6*β*,11*βH*-eudesma-12,6*α*-olide, 1*β*-hydroxy-15-*O*-(p-methoxyphenylacetyl-5*α*,6*β*,11*βH*-eudesma-3-en-12,6*α*-olide and 4*α*-*O*-*β*-D-glucopyranosyl-15-hydroxyl-5*α*,6*βH*-guaiane-10(14),11(13)-dien-12,6*α*-olide) have been tested for their *in vitro* cytotoxicity using MTT assay against human epithelial carcinoma (HeLa) and human colon carcinoma (HCT116) cell lines. None of the tested compounds exhibited cytotoxic activity against both cell lines. The lack of activity may be related to what has been reported that sesquiterpene lactones with an α,β-unsaturated-γ-lactone system generally show adequate cytotoxic activity [21,67]. The cytotoxic activity of crude *n*-hexane and methanol extracts of *L. serriola* was evaluated *in vitro* against MCF7, A549, HepG2 and HCT116 cell lines using MTT assay. The crude methanolic extract exhibited potent activity against MCF7 at concentrations of 100, 50, and 25 µg/mL and showed good cytotoxicity against HepG2 at a concentration of 100 µg/mL. Whereas the *n*-hexane extract exhibited reasonable activity against HepG2 and A549 with no activity against HCT116 and MCF7 [10]. In addition, *L. serriola* extract showed antitumor activity against EAC (Ehrlich ascites carcinoma). Intraperitoneal administration of the methanol extract of *L. serriola* in Swiss albino mice decreased viable EAC cells, augmented the survival time, and restored altered hematological parameters. Obvious efficacy was also observed from its fruit extract at a high concentration (400 mg/kg dose) [68].

4.2.5. *Protective Effect on Doxorubicin-Induced Toxicity*

Doxorubicin (DOX) is broadly used as an antineoplastic agent in the management of various solid malignancies, but its use results in cardiotoxicity. Pretreatment with *L. serriola* showed a protective effect against DOX-induced oxidative stress in cardiomyocytes from rat heart embryonic tissue (H9C2 cell line). This effect is mediated by reducing oxidative stress due to the high total phenolic contents like quercetin and by inhibiting apoptotic pathways. Latest studies showed that *L. serriola* also had Ca^{2+} channel blocking activity so it can be used in cardiovascular disorders. Therefore, *L. serriola* has the potential to be used as a cardioprotective drug for patients having cardiovascular diseases [69].

4.2.6. *Analgesic and Sedative Activity*

Lactuca sativa leaf and seed extracts produced a significant analgesic effect in the hot plate assay in rats, using aspirin as a positive control, where the leaf extract was more effective in analgesic activity than the seed extract. Also, aqueous extracts were more active than the MC (methanol and chloroform; 1:1) extracts. Flavonoids isolated from *Lactuca* species have been reported to inhibit prostaglandin synthase. It is well-known that prostaglandins are incriminated in the perception of pain. Hence, it could be suggested that limited accessibility of prostaglandin synthase by flavonoids might be responsible for its analgesic activity [62]. Lactucin and its derivatives: 11β,13-dihydrolactucin and lactucopicrin from *L. virosa* have been evaluated for its potential analgesic and sedative activity in mice. The compounds exhibited analgesic effects at doses of 15 and 30 mg/kg in the hot plate test, comparable to that of the standard ibuprofen at a dose of 30 mg/kg. The analgesic effect of the compounds at a dose of 30 mg/kg in the tail-flick test was similar to that of ibuprofen at a dose of 60 mg/kg. Lactucopicin proved to be the most potent analgesic of the three tested compounds. Lactucin and lactucopicrin, but not 11β,13-dihydrolactucin, also exhibited sedative effects in the spontaneous locomotor activity test [70]. Also, *Lactuca serriola* extract showed a potent analgesic activity at the dose levels of 300, 500, and l000 mg/kg. The analgesic activity shown by 300 mg/kg extract was nearly similar to that shown by aspirin. Whereas at the dose levels of 500 mg/kg, *L. serriola* exerted better analgesic activity than the standard drug and at the dose level of l000 mg/kg, the duration and intensity of analgesia was also higher than aspirin. Hence, the methanolic extract of *L. serriola* can produce a significant analgesic activity providing evidence for its use in folk medicine [71].

4.2.7. Anxiolytic Effect

The anxiolytic properties of hydro-alcoholic extract of *L. sativa*, locomotor activity, and exploratory behavior of mice have been studied using hyponeophagia and elevated T maze models. *L. sativa* extract showed an increase in the number of entrances into the open arms and the time consumed in the open arm compared to the untreated group. The dose at 400 mg/kg body weight was nearly equivalent to that of diazepam drug-administered group. The polyphenols including *p*-coumaric acid, quercetin, quercetin-3-*O*-*α*-L-rhamnoside, chlorogenic acid, caffeic acid, vanillin, epicatechin, rutin, and sinapic acid in the extract may be responsible for such activity [53].

4.2.8. Antioxidant Activity

Treatment with the aqueous leaf extract of *L. sativa* exhibited dose-dependent radical scavenging activity against superoxide, nitric oxide, hydroxyl, hydrogen peroxide, and DPPH (1,1-diphenyl-2-picrylhydrazyl) radicals, using ascorbic acid as a standard drug. The antioxidant activity of *L. sativa* might be due to the triterpenoids, saponins, and phenols in its leaf extract [63]. In another study, the high antiradical scavenging activity of *L. sativa* extract shown by DPPH assay, was attributed to 3-*O*-glucosidic flavonols, such as quercetin-3-*O*-β-D-glucoside and kaempferide-3-*O*-β-D-glucuronide in addition to other phenolics [47]. The hydroethanolic extract of *L. sativa* was able to dose-dependently guard against the oxidation of important biomolecules like DNA, lipids, and proteins. The extract also inhibited the damage of DNA in the COMET assay by reducing the tail length of DNA [72]. In addition, luteolin, isoquercitrin, chlorogenic acid and *p*-hydroxymethyl benzoic acid isolated from the methanolic extract of the aerial parts of *L. indica* showed significant antioxidant activities when compared to ascorbic acid using the *in vitro* DPPH radical scavenging assay [49]. The methanolic extract of the aerial parts of *L. serriola* exhibited a strong radical scavenging effect on DPPH radical using ascorbic acid as a positive control and the EtOAc-soluble fraction showed higher activity than the other fractions. Luteolin, quercetin, kaempferol, quercetin-3-*O*-β-D-glucopyranoside, luteolin-7-*O*-β-D-glucopyranoside, and 11β,13-dihydrolactucin isolated from the EtOAc-soluble fraction were the active constituents [34]. In another study, the volatile oils extracted from the aerial parts of *L. serriola* showed remarkable antioxidant activity. This activity may be attributed to the high content of oxygenated sesquiterpenes and diterpenes in the oil that is reported to have a significant role as antioxidant agents [73]. In our study [38], the antioxidant capacity of *L. serriola* L. was assessed using three different techniques: ABTS radical scavenging assay, DPPH radical scavenging assay, and ferric reducing antioxidant power (FRAP) assay. In the ABTS radical scavenging assay, the EtOAc-soluble fraction showed the strongest radical scavenging activity compared to other tested fractions with an IC_{50} value of

34.88±0.22 μg/mL, followed by the methylene chloride-soluble fraction with an IC_{50} value of 37.11±0.28 μg/mL. The *n*-butanol-soluble fraction exhibited moderate antioxidant activity with an IC_{50} value of 46.06±0.27 μg/mL. The petroleum ether-soluble fraction showed a poor radical scavenging activity compared to standard ascorbic acid. Concerning the major compounds isolated from the EtOAc-soluble fraction, quercetin showed the highest radical scavenging activity with an IC_{50} value of 33.53±0.21 μM, followed by kaempferol with an IC_{50} value of 35.16±0.24 μM. The varaiation in activity between both compounds may be due to the presence of a catechol group in ring B of quercetin which appeared to be crucial for high antioxidant activity. Both protocatechuic acid and luteolin-7-*O*-β-D-glucoside showed noticeable antioxidant activity with IC_{50} values of 36.56±0.23 and 37.64±0.25 μM, respectively. The sesquiterpenoid structure, lactuside A exhibited moderate antioxidant action compared to ascorbic acid. However, 4-hydroxybenzoic acid showed weak radical scavenging activity. In the DPPH radical scavenging assay, the highest scavenging activity against the stable DPPH radical was recorded for EtOAc-soluble fraction (26.80±2.43 μg/mL). Quercetin showed remarkable antioxidant activity with an IC_{50} value of 19.15±0.89 μM followed by luteolin-7-*O*-β-D-glucoside and kaempferol with an IC_{50} value of 41.47±0.71 and 41.60±2.2 μM, respectively compared to that recorded for the standard, trolox (56.82±0.87 μM). Protocatechuic acid showed moderate radical scavenging activity. In the FRAP assay, the EtOAc-soluble fraction exhibited the highest ferric reduction potential among the tested fractions with 1288.6±43.8 μM TEAC/mg. The highest reducing power among the isolated compounds was recorded for quercetin as 2333.5±88.77 μM TEAC/mM followed by luteolin-7-*O*-β-D-glucoside and kaempferol with reducing powers of 1304.5±82.3 and 883.18±65.26 μM TEAC/mM, respectively. Moderate reduction potential was observed with protocatechuic acid.

4.2.9. Anti-Coagulant Activity

A strong anti-coagulant effect has been suggested for the methanol and chloroform, (1:1) leaf extract of *L. sativa* (clotting time 110 s) which is comparable to that of aspirin (positive control) in the capillary tube method. While the coagulation time in seed extracts was lower than the negative control indicating their potential coagulation nature which can be used for the treatment of diseases like hemophilia [62].

4.2.10. Antidepressant Activity

The methanol and chloroform, (1:1) and aqueous extracts of *L. sativa* seed showed the least immobility time compared with the negative control in the forced swimming model in rats using fluoxetine HCl as a positive control. The report concluded that the extract could act as an anti-depressant on the central nervous system. The leaf extracts also exhibited moderate anti-depressant activities. In addition, no abnormal behavior or lethality was observed in any of the tested animals [62].

4.2.11. Hepatoprotective activity

Lactuca runcinata methanolic extract showed hepatoprotective action and proved to be useful in herbal medicine for the treatment of liver diseases specifically for hepatotoxicity induced by CCl_4. The extract given to rats in a dose-dependent manner significantly reduced the elevated levels of SGOT, SGPT, ALP, and TB induced by CCl_4. Consequently, it reduced the hepatic injury caused by CCl_4, and the histopathological results supported this activity. The activity may be attributed to presence of flavonoids and other phenols in *L. runcinata* extract [74].

4.2.12. Antispermatogenic Effect

The aqueous and hydro-alcoholic extracts of *L. sativa* seeds (50 mg/kg) exhibited *in vivo* antispermatogenic effects in male mice. Also, the aqueous extract (50 mg/kg) *in vivo* increased the testosterone level in mice. Therefore, *L. sativa* seed could be a potential contraceptive drug [60].

4.2.13. Antidiabetic Activity

Lactucaside and latucain C, isolated from the aqueous acetone extract of fresh *L. indica*, were found to have a significant antidiabetic activity [12]. In another study, luteolin and apigenin isolated from *L. indica* exhibited significant α-glucosidase inhibitory activity with IC_{50} values of 96.4 and 100.7 µM, respectively compared to the standard, acarbose (IC_{50} 310.2 µM) [49]. Aqueous extract of *L. serriola* leaves as supplementation in alloxan-induced male diabetic rats, showed a greater glucose tolerance and hypoglycemic regulation of blood sugar [75]. In our study [38], the α-glucosidase inhibitory activity of *L. serriola* was investigated and the total methanol extract exhibited a good inhibition with an IC_{50} value of 46.16±0.26 µg/mL. The EtOAc-soluble fraction showed remarkable inhibition among other tested fractions with an IC_{50} value of 9.16±0.17 µg/mL compared to acarbose (IC_{50}, 6.11±0.22 µg/mL). A quite moderate α-glucosidase inhibitory activity was observed for the methylene chloride-soluble fraction with an IC_{50} value of 16.88±0.28 µg/mL. As to petroleum ether fraction, it displayed low α-glucosidase inhibition with an IC_{50} value of 24.88±0.12 µg/mL. It is worth mentioning that the lowest α-glucosidase inhibitory activity among the tested fractions was recorded for the *n*-butanol fraction. The compounds isolated from EtOAc-soluble fraction were further investigated for their α-glucosidase inhibitory activity. Kaempferol and quercetin showed the highest inhibitory action against α-glucosidase with IC_{50} values of 39.72±0.43 and 39.82±1.12 µM, respectively.

Table 15. Reported pharmacological activities of *Lactuca* species

Pharmacological activities	Species/part used	Extract /or component used	References
Anti-inflammatory action			
Decreased ROS, iNOS, NO release, and COX-2 expression	*L. sativa*/ Fresh leaf	Total extract	[47]
Inhibition of carrageenan-induced hind paw edema in rats	*Lactuca sativa*/ Leaf and seed	Methanol and chloroform, (1:1) and aqueous extracts	[62]
Stabilization of human red blood cell (HRBC) membrane and albumin denaturation	*L. sativa*/ Leaf	Aqueous leaf extract	[63]
Antimicrobial activity			
Inhibition of Gram-negative (*Escherichia coli, Klebsilla pneumonia, Enterobacter cloacae, Serratia marcescens,* and *Acinetobacter baumannii*) and Gram-positive bacteria (*Staphylococcus aureus, Bacillus subtilus, Enterococcus faecium,* and *Corynebacterium spp.*)	*L. sativa*/ Aerial parts	Methanol extract	[64]
Anticytomegalovirus (anti-HCMV) activity	*L. sativa*/ Aerial parts	Methanol and *n*-butanol extracts	[64]
Anti-coxsackie B3 activity	*L. sativa*/ Aerial parts	Methanol and *n*-butanol extracts	[64]
Inhibition of Gram-positive bacteria (*Staphylococcus saprophyticus* and *Staphylococcus aureus*)	*L. serriola*/ Aerial parts	Crude terpenoid, phenolic, and alkaloid extracts	[65]
Inhibition of urinary tract infection with *Escherichia coli*	*L. indica*/ Aerial parts	Total extract	[66]

Table 15 continued..

Gastrointestinal, respiratory, and vascular ailments			
Ex vivo spasmogenic (cholinergic) action on gastrointestinal, tracheal, and aortic smooth muscles	*L. serriola*/ Aerial parts	Methanol extract	[61]
Ex vivo spasmolytic action on gastrointestinal, tracheal, and aortic smooth muscles	*L. serriola*/ Aerial parts	Methanol extract	[61]
Anticancer activity			
In vitro cytotoxicity using MTT assay against MCF7 and HepG2 cell lines	*L. serriola*/ Whole plant	Methanol extract	[10]
In vitro cytotoxicity using MTT assay against HepG2 and A549	*L. serriola*/ Whole plant	*n*-Hexane and	[10]
In vivo reduction of EAC (Ehrlich ascites carcinoma) in Swiss albino mice	*L. serriola*/ Aerial parts/fruits	Methanol extract	[68]
Protective effect on doxorubicin (DOX)-induced toxicity			
In vitro protective activity against DOX-induced oxidative stress in cardiomyocytes (H9C2 cell line)	*L. serriola*/ Aerial parts	Methanol extract and its phenolic content	[69]
Analgesic and sedative activity			
Analgesic effect using the hot plate assay in rats	*Lactuca sativa*/ Leaf and seed	Methanol and chloroform, (1:1) and aqueous extracts	[62]
Analgesic effect using the hot plate and the tail-flick assays in rats	*L. virosa*/ Leaf and root	Lactucin and its derivatives: 11β,13-dihydrolactucin and lactucopicrin	[70]
Analgesic activity using tail flick latency in the tail-immersion assay in mice	*L. serriola*/ Seed and stem	Methanolic extract	[71]
Sedative effects by decreasing the spontaneous locomotor activity in mice	*L. virosa*/ Leaf and root	Lactucin and lactucopicrin	[70]
Anxiolytic effect			
Anxiolytic properties on locomotor activity, and exploratory behavior of mice using hyponeophagia and elevated T maze models	*L. sativa*/ Whole plant	Hydro-alcoholic extract/Polyphenols	[53]
Antioxidant activity			
Radical scavenging activity against superoxide, nitric oxide, hydroxyl, hydrogen peroxide, and DPPH	*L. sativa*/ Leaf	Aqueous leaf extract	[63]
Radical scavenging activity using DPPH	*L. sativa*/ Fresh leaf	Phenolics, such as quercetin-3-*O*-β-D-glucoside and kaempferide-3-*O*-β-D-glucuronide	[47]
Inhibition of DNA damage in the COMET assay	*L. sativa* Whole plant	Hydroethanolic extract	[72]
Radical scavenging activity using DPPH	*L. indica*/ Aerial parts	Luteolin, isoquercitrin, chlorogenic acid and *p*-hydroxymethyl benzoic acid from the methanolic extract	[49]
Radical scavenging activity using DPPH	*L. serriola*/ Aerial parts	Methanolic extract, EtOAc-soluble fraction, luteolin, quercetin, kaempferol, quercetin-3-*O*-β-D-glucopyranoside, luteolin-7-*O*-β-D-glucopyranoside, and 11β,13-dihydrolactucin	[34]
Radical scavenging activity using DPPH	*L. serriola*/ Aerial parts	Volatile oils	[73]
Antioxidant activities using ABTS, DPPH, and ferric reducing antioxidant power (FRAP) assays	*L. serriola*/ Aerial parts	EtOAc-soluble fraction, the methylene chloride, *n*-butanol-soluble fraction, quercetin, kaempferol, protocatechuic acid, luteolin-7-*O*-β-D-glucoside, lactuside A	[38]
Anti-coagulant/coagulant activity			
Anti-coagulant effect using the capillary tube method	*L. sativa*/ Leaf	Methanol and chloroform, (1:1) and aqueous extracts	[62]
Coagulation effect using the capillary tube method	*L. sativa*/ Seed	Methanol and chloroform, (1:1) and aqueous extracts	[62]

Table 15 continued..

Antidepressant activity			
Antidepressant effect in the forced swimming model in rats	*L. sativa*/ Seed and leaf	Methanol and chloroform, (1:1) and aqueous extracts	[62]
Hepatoprotective activity			
Reduction of elevated SGOT, SGPT, ALP, and TB levels and improved histopathological properties in CCl_4-induced hepatotoxicity	*L. runcinate*/ Aerial parts	Methanol extract	[74]
Antispermatogenic effect			
In vivo antispermatogenic effects in male mice	*L. sativa*/ Seed	Aqueous and hydro-alcoholic extracts	[74]
In vivo increased testosterone level in mice	*L. sativa*/ Seed	Aqueous extract	[74]
Antidiabetic activity			
Antihyperglycemic effect in diabetic rats	*L. indica*/ Fresh herb	Lactucaside and latucain C	[12]
α-Glucosidase inhibitory activity	*L. indica*/ Aerial parts	Luteolin and apigenin	[49]
α-Glucosidase inhibitory activity	*L. serriola*/ Aerial parts	Methanol extract and EtOAc-soluble fraction, methylene chloride-soluble fraction, kaempferol, and quercetin	[38]
Increased glucose tolerance and antihyperglycemic effect in diabetic rats	*L. serriola*/ Leaf	Aqueous extract of	[75]

5. Conclusions

In conclusion, the present review summarizes the phytochemistry and biological activities of the genus *Lactuca*. A wide diversity of compounds was reported. Several species were found to have a good medicinal value that could be used as a natural remedy, providing that most of them are consumed as vegetables. The review highlighted the fact that some members of the genus were poorly chemically investigated. In this regard, it would be useful for other researchers to identify the specific compounds in these species. Moreover, several isolated compounds have not been fully investigated in terms of their bioactivity, it would be interesting to deeply understand their bioactivity potential and detailed mechanism of action.

Competing Interests

The authors declare that there are no competing interests exist.

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References

[1] M. S. Al-Ahmadi (2017). Proteins patterns of eight genera of the Asteraceae family, *Afr. J. Biotechnol.* **16**, 536–546.

[2] A. Lebeda, I. Dolezalová, V. Feráková and D. Astley (2004). Geographical distribution of wild *Lactuca* species (Asteraceae, Lactuceae), *Bot. Rev.* **70**, 328-356.

[3] P. Shukla and S. P. Misra (1979). Introduction to taxonomy of Angiosperms, Vikas Publishing House. New Delhi, India.

[4] L. Boulos and N. El-Hadidi (1989). The weed flora of Egypt. In the American University in Cairo, Cairo, Egypt., p. 37.

[5] F. T. Frietema (1994). The systematic relationship of *Lactuca sativa* and *Lactuca serriola*, in relation to the distribution of prickly lettuce, *Acta. Bot. Neerl* **43**, 79.

[6] A. Mohammad (2013). Traditional use of kahu (*Lactuca scariola* L.)-a review, *Glob.J. Res. Med. Plants Indig. Med.* **2**, 465.

[7] W. Ali, A. A. Hamiduddin, M. Aslam and A. Nasir (2016). Tukh-e-karhu (*Lactuca sativa* Linn.): pharmacological and phytochemical profile and uses in unani medicine. *J. Pharm. Sci. Innov.* **5**, 1–4.

[8] V. Feráková (1976). The genus *Lactuca* L. in Europe. Univerzita Komenského, Slovakia.

[9] K. L. Meena (2014). *Lactuca serriola* L. (Asteraceae): an extended distribution to the states of Rajasthan, *J. Ind. Bot. Soc.* **93**, 132–134.

[10] E. Elsharkawy and M. Alshathly (2013). Anticancer activity of *Lactuca steriolla* growing under dry desert condition of Northern Region in Saudi Arabia, *J. Nat. Sci.* **3**, 5–18.

[11] M. Chadwick, H. Trewin, F. Gawthrop and C. Wagstaff (2013). Sesquiterpenoids lactones: benefits to plants and people, *Int. J. Mol. Sci.* **14**, 12780–12805.

[12] C. C. Hou, S. J. Lin, J. T. Cheng and F. L. Hsu (2003). Antidiabetic Dimeric Guianolides and a Lignan Glycoside from *Lactuca indica*, *J. Nat. Prod.* **66**, 625–629.

[13] J. A. Marco, J. F. Sanz and R. Albiach (1992). A sesquiterpene ester from *Lactuca serriola*, *Phytochemistry* **31**, 2539–2540.

[14] K. Michalska, A. Stojakowska, J. Malarz, I. Doležalová, A. Lebeda and W. Kisiel (2009). Systematic implications of sesquiterpene lactones in *Lactuca* species, *Biochem. Syst. Ecol.* **37**, 174–179.

[15] K. Michalska, E. Szneler and W. Kisiel (2010). *Lactuca altaica* as a rich source of sesquiterpene lactones, *Biochem. Syst. Ecol.* **38**, 1246–1249.

[16] X. X. Wang, X. Gao and Z. J. Jia (2010). Sesquiterpenoids from *Lactuca tatarica*, *Fitoterapia* **81**, 42–44.

[17] W. Kisiel, B. Barszcz and E. Szneler (1997). Sesquiterpene lactones from *Lactuca tatarica*, *Phytochemistry* **45**, 365–368.

[18] K. Michalska K, A. Beharav and W. Kisiel (2014). Sesquiterpene lactones from roots of *Lactuca georgica*, *Phytochem. Lett.* **10**, 10–12.

[19] W. Kisiel and B. Barszcz (1997). Minor sesquiterpene lactones from *Lactuca virosa*, *Phytochemistry* **46**, 1241–1243.

[20] N. Ishihara, T. Miyase and A. Ueno (1987). Sesquiterpene glycosides from *Lactuca sativa* L, *Chem. Pharm. Bull.* **35**, 3905–3908.

[21] Y. F. Han, G. X. Cao, X. J. Gao and M. Xia (2010). Isolation and characterisation of the sesquiterpene lactones from *Lactuca sativa* L *var. anagustata*, *Food Chem.* **120**, 1083–1088.

[22] K. Michalska, W. Kisiel and A. Stojakowska (2015). Chemical constituents of *Lactuca dregeana*, *Biochem. Syst. Ecol.* **59,** 302–304.

[23] N. H. Abdel Fatah, Y. Amen, F. M. Abdel Bar, A. F. Halim and H-E. A. Saad (2020). Antioxidants and α-glucosidase inhibitors from *Lactuca serriola* L., *Rec. Nat. Prod.* **14**, 410–415.

[24] R. A. Sessa, M. H. Bennett, M. J. Lewis, J. W. Mansfield and M. H. Beale (2000). Metabolite profiling of sesquiterpene lactones from *Lactuca* species major latex components are novel oxalate and sulfate conjugates of lactucin and its derivatives, *J. Biol. Chem.* **275**, 26877–26884.

[25] K. Michalska and W. Kisiel (2010). Sesquiterpene lactones from roots of *Lactuca aculeata*, *Biochem. Syst. Ecol.* **38**, 830–832.

[26] W. Kisiel and D. Gromek (1993). Sesquiterpene lactones from *Lactuca saligna*, *Phytochemistry* **34**, 1644–1646.

[27] K. Michalska, O. Michalski and A. Stojakowska (2017). Sesquiterpenoids from roots of *Lactuca sativa* var. *angustana* cv."Grüner Stern.", *Phytochem. Lett.* **20**, 425–428.

[28] A. Beharav, R. Ben-David, J. Malarz, A. Stojakowska, K. Michalska, I. Doležalová, A. Lebeda and W. Kisiel (2010). Variation of sesquiterpene lactones in *Lactuca aculeata* natural populations from Israel, Jordan and Turkey, *Biochem. Syst. Ecol.* **38**, 602–611.

[29] K. Michalska and W. Kisiel (2012). A new guaianolide glucoside from aerial parts of *Lactuca aculeata*, *Phytochem. Lett.* **5**, 301–303.

[30] K. Michalska and W. Kisiel (2009). Root constituents of *Lactuca sibirica* and a comparison of metabolite profiles of *L. sibirica* and *L. tatarica*, *Acta Soc. Bot. Pol.* **78**, 25–27.
[31] W. Kisiel and K. Michalska (2008). Lignans and sesquiterpenoids from *Lactuca sibirica*, *Fitoterapia* **79**, 241–244.
[32] W. Kisiel and K. Zielińska (2000). Sesquiterpenoids and phenolics from *Lactuca perennis*, *Fitoterapia* **71**, 86–87.
[33] K. Michalska and W. Kisiel (2013). Structural diversity of sesquiterpene lactones in roots of *Lactuca viminea*, *Biochem. Syst. Ecol.* **51**, 16–18.
[34] D. K. Kim (2001). Antioxidative components from the aerial Parts of *Lactuca scariola* L, *Arch. Pharm. Res*. **24**, 427–430.
[35] K. Nishimura, T. Miyase, A. Ueno, T. Noro, M. Kuroyanagi and S. Fukushima (1986). Sesquiterpene lactones from *Lactuca laciniata*, *Phytochemistry* **25**, 2375–2379.
[36] Z. F. Mahmoud, F. F. Kassem, N. A. Abdel-Salam and C. Zdero (1986). Sesquiterpene lactones from *Lactuca sativa*, *Phytochemistry* **25**, 747–748.
[37] A. T. Khalil, H. A. El-fattah and E. S. Mansour (1991). Guaianolides from *Lactuca saligna*, *Planta Med*. **57**, 190–191.
[38] K. Michalska, E. Szneler and W. Kisiel (2013). Sesquiterpene lactones from *Lactuca canadensis* and their chemotaxonomic significance, *Phytochemistry* **90**, 90–94.
[39] K. Michalska and W. Kisiel (2014). Chemical constituents from *Lactuca inermis*, a wild African species, *Biochem. Syst. Ecol.* **55**, 104–106.
[40] Y. F. Han, G. X. Cao and M. Xia (2009). Two new eudesmane sesquiterpenes from *Lactuca sativa var. anagustata* L, *Chin. Chem. Lett.* **20**, 1211–1214.
[41] H. Huang, B. C. Zhou, J. S. Wang, J. J. Du, P. P. Yu and Y. F. Han (2012). A New Eudesmane Sesquiterpenoid Glycoside from *Lactuca Sativa* L *var. anagustata*, *Adv. Mat. Res.* **441**, 462–465.
[42] W. Kisiel and B. Barszcz (1998). A germacrolide glucoside from *Lactuca tatarica*, *Phytochemistry* **48**, 205–206.
[43] A. Stojakowska and J. Malarz (2017). Bioactive phenolics from *in vitro* cultures of *Lactuca aculeata* Boiss. et Kotschy, *Phytochem. Lett.* **19**, 7–11.
[44] K. Michalska, A. Stojakowska and W. Kisiel (2012). Phenolic constituents of *Lactuca tenerrima*, *Biochem. Syst. Ecol.* **42,** 32–34.
[45] A. Stojakowska, K. Michalska, J. Malarz, A. Beharav and W. Kisiel (2013). Root tubers of *Lactuca tuberosa* as a source of antioxidant phenolic compounds and new furofuran lignans, *Food Chem.* **138**, 1250–1255.
[46] W. Kisiel (1998). Flavonoids from *Lactuca quercina* and *L. tatarica*, *Acta Soc. Bot. Pol. Pol.* **67**, 247.
[47] G. Pepe, E. Sommella, M. Manfra, M. de Nisco, G. C. Tenore, A. Scopa, A. Sofo, S. Marzocco, S. Adesso and T. Novellino (2015). Evaluation of anti-inflammatory activity and fast UHPLC–DAD–IT-TOF profiling of polyphenolic compounds extracted from green lettuce (*Lactuca sativa L.; var. Maravilla de Verano*), *Food Chem.* **167**, 153–161.
[48] M. C. Terencio, M. J. Sanz, M. L. Fonseca, S. Máñez and J. L. Ríos (1992). Phenolic compounds from *Lactuca viminea* L., *Z Naturforsch C.* **47**, 17–20.
[49] C. I. Choi, H. J. Eom and K. H. Kim (2016). Antioxidant and α-glucosidase inhibitory phenolic constituents of *Lactuca indica* L., *Russ. J. Bioorg. Chem.* **42**, 310–315.
[50] V. Sareedenchai and C. Zidorn (2010). Flavonoids as chemosystematic markers in the tribe Cichorieae of the Asteraceae, *Biochem. Syst. Ecol.* **38**, 935–957.
[51] F. Xu, G. A. Zou, Y. Q. Liu and H. A. Aisa (2012). chemical constituents from seeds of *Lactuca sativa*, *Chem. Nat. Compd.* **48**, 574–576.
[52] M. Hamed, M. H. Assaf, A. S. Ahmed and M. S. Ahmed (2003). Phytochemical and biological study of *Lactuca sativa* L. seeds growing in Egypt, *Bull. Fac. Pharm. Cairo Univ.* **41**, 239–252.
[53] S. N. Harsha and K. R. Anilakumar (2013). Anxiolytic property of *Lactuca sativa*, effect on anxiety behaviour induced by novel food and height, *Asian Pac. J. Trop. Med.* **6**, 532–536.
[54] K. H. Kim, Y. H. Kim and K. R. Lee (2007). Isolation of quinic acid derivatives and flavonoids from the aerial parts of *Lactuca indica* L. and their hepatoprotective activity *in vitro*, *Bioorg. Med. Chem. Lett.* **17**, 6739–6743.
[55] K. H. Chung, K. R. Yoon and J. P. Kim (1994). Flavonoidal constituent in Korean *Lactuca dentata* Makino, *J. Korean Soc. Food Cult.* **9**, 131–136.

[56] J. Shinozaki, T. Nakane, N. Onodera, A. Takano and K. Masuda (2011). Composite constituent: lactucenyl acetate, a novel migrated lupane triterpenoid from *Lactuca indica* revision of structure of tarolupenyl acetate, *Chem. Pharm. Bull.* **59**, 767–769.

[57] W. H. Hui and W. K. Lee (1971). Triterpenoid and steroid constituents of some *Lactuca* and *Ageratum* species of Hong Kong, *Phytochemistry* **10**, 899–901.

[58] R. N. Yadava and J. Jharbade (2007). A new bioactive triterpenoid saponin from the seeds of *Lactuca scariola* Linn, *Nat. Prod. Res.* **21**, 500–506.

[59] R. N. Yadava and J. Jharbade (2008). New antibacterial triterpenoid saponin from *Lactuca scariola*, *Fitoterapia* **79**, 245–249.

[60] A. Ahangarpour, A. A. Oroojan and M. Radan (2014). Effect of aqueous and hydro-alcoholic extracts of lettuce (*Lactuca sativa*) seed on testosterone level and spermatogenesis in NMRI mice, *Iran J. Reprod. Med.* **12**, 65.

[61] K. H. Janbaz, M. F. Latif, F. Saqib, I. Imran, M. Zia-Ul-Haq and V. de Feo (2013). Pharmacological effects of *Lactuca serriola* L. in experimental model of gastrointestinal, respiratory, and vascular ailments, *Evid. Based Complement. Altern. Med.* **2013**, ID 304394.

[62] H. Ismail and B. Mirza (2015). Evaluation of analgesic, anti-inflammatory, anti-depressant and anti-coagulant properties of *Lactuca sativa* (CV. Grand Rapids) plant tissues and cell suspension in rats, *BMC Complement. Altern. Med.* **15**, 199.

[63] B. R. Nallamilli, K. Nataraj and R. K. Jat (2018). Antioxidant and anti-inflammatory activities of *Lactuca sativa*: An *In Vitro* Study, *Int. J. Pharm. Pharm. Sci.* **11**, 1.

[64] H. áL. Edziri, M. A. Smach, S. Ammar, M. A. Mahjoub, Z. Mighri, M. Aouni and M. Mastouri (2011). Antioxidant, antibacterial, and antiviral effects of *Lactuca sativa* extracts, *Ind. Crops Prod.* **34**, 1182–1185.

[65] A. H. Al-Marzoqi, H. J. Hussein and N. M. S. Al-Khafaji (2015). Antibacterial activity of the crude phenolic, alkaloid and terpenoid compounds extracts of *Lactuca serriola* L. on human pathogenic bacteria, *Chem. Mat. Res.* **7**, 8–10.

[66] P. Lüthje, D. N. Dzung and A. Brauner (2011). *Lactuca indica* extract interferes with uroepithelial infection by *Escherichia coli*, *J. Ethnopharmacol.* **135**, 672–677.

[67] B. Nosse, R. B. Chhor, W. B. Jeong, C. Böhm and O. Reiser (2003). Facile asymmetric synthesis of the core nuclei of xanthanolides, guaianolides, and eudesmanolides, *Org. Lett*. **5**, 941–944.

[68] M. Alshathly and E. Elsharkawy (2014). Inhibition of Ehrlich ascites carcinoma by *Lactuca serriola* in Swiss albino mice, *J. Chem. Chem. Eng.* **8**, 66.

[69] A. Hosseini and D. Mahdian (2016). Protective effect of *Lactuca serriola* on doxorubicin-induced toxicity in H9c2 cells, *Acta. Pol. Pharm*. **73**, 659–666.

[70] A. Wesołowska, A. Nikiforuk, K. Michalska, W. Kisiel and E. Chojnacka-Wójcik (2006). Analgesic and sedative activities of lactucin and some lactucin-like guaianolides in mice, *J Ethnopharmacol.* **107**, 254–258.

[71] F. Ahmad, R. A. Khan and S. Rasheed (1992). Study of analgesic and anti-inflammatory activity from plant extracts of *Lactuca scariola* and *Artemisia absinthium*, *J. Islamic World Acad. Sci.* **5**, 111–114.

[72] S. N. Harsha, K. R. Anilakumar and M. Mithila (2013). Antioxidant properties of *Lactuca sativa* leaf extract involved in the protection of biomolecules, *Biomed. Prev. Nutr.* **3**, 367–373.

[73] A. M. Abd-ElGawad, A. I. Elshamy, A. El-Nasser El Gendy, S. L. Al-Rowaily and A. M. Assaeed (2019). Preponderance of oxygenated sesquiterpenes and diterpenes in the volatile oil constituents of *Lactuca serriola* L. revealed antioxidant and allelopathic activity, *Chem. Biodivers.* **16**, e1900278.

[74] L. K. Kanthal, K. Satyavathi, P. Bhojaraju and M. P. Kumar (2017). Hepatoprotective activity of methanolic extracts of *Lactuca runcinata* DC and Gyrocarpus asiaticus Willd, *Beni Suef Univ. J. Basic. Appl. Sci.* **6**, 321–325.

[75] K. S. Chadchan, J. G. Jargar and S. N. Das (2016). Anti-diabetic effects of aqueous prickly lettuce (*Lactuca scariola* Linn.) leaves extract in alloxan-induced male diabetic rats treated with nickel (II), *J. Basic. Clin. Physiol. Pharmacol.* **27**, 49–56.

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