Genus Lactuca (Asteraceae): A Comprehensive Review

Fatma M. Abdel Bar1,2*, Nouran H. Abdel Fatah2, Yhiya Amen2, Ahmed F. Halim2, Hassan-Elrady A. Saad2

1Department of Pharmacognosy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia
2Department of Pharmacognosy, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt

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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. © 2022 ACG Publications. All rights reserved.

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

*Corresponding author: E-Mail: f.abdelbar@psau.edu.sa; fatma_maar@yahoo.com; Phone:0966-54540-3617

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Genus *Lactuca* (Asteraceae)

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] |
|     |               | *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] |
|     |               | 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.

|   | Name                                           | Sources                                                                 |
|---|-----------------------------------------------|------------------------------------------------------------------------|
| 4 | 8-Deoxy lactucin                              | Roots of *L. sativa*                                                   |
|   |                                               | Aerial parts of *L. aculeata*                                           |
|   |                                               | Roots of *L. sibirica*                                                  |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Leaves and roots of *L. aculeata*                                      |
|   |                                               | Aerial parts of *L. aculeata*                                          |
|   |                                               | Aerial parts of *L. serriola*                                          |
|   |                                               | Roots of *L. sibirica*                                                  |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Roots of *L. virosa*                                                   |
| 5 | 8-Deoxy lactucin-15-oxalate                   | Latex of *L. sativa*                                                   |
| 6 | 8-Deoxy lactucin-15-sulfate                   | Latex of *L. sativa*                                                   |
| 7 | 15-Deoxy lactucin                             | Latex of *L. sativa*                                                   |
| 8 | 15-Deoxy lactucin-8-sulfate                   | Latex of *L. sativa*                                                   |
| 9 | 11β,13-Dihydrolactucin                        | Aerial parts of *L. sibirica*                                          |
|   |                                               | *L. indica* whole plant                                                |
|   |                                               | Roots of *L. altaica*                                                  |
|   |                                               | *L. tartarica* whole plant                                             |
|   |                                               | Roots of *L. tartarica*                                                |
|   |                                               | Leaves and roots of *L. aculeata*                                      |
|   |                                               | Aerial parts of *L. serriola*                                          |
|   |                                               | Roots of *L. sibirica*                                                  |
|   |                                               | Roots of *L. georgica*                                                 |
|   |                                               | Roots of *L. laciniata*                                                |
|   |                                               | Roots of *L. virosa*                                                   |
|   |                                               | Aerial parts of *L. saligna*                                           |
|   |                                               | Stem of *L. sativa* var. *angustana*                                   |
|   |                                               | Aerial parts and roots of *L. dregeana*                                 |
|   |                                               | Aerial parts of *L. sibirica*                                          |
| 10| 11β,13-Dihydrolactucin-8-O-acetate            | Roots of *L. georgica*                                                 |
| 11| 11β,13-Dihydrolactucin-8-O-methacrylate       | Roots of *L. georgica*                                                 |
| 12| 11β,13-Dihydrolactucopicin                   | Roots of *L. virosa*                                                   |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Roots of *L. sativa* var. *angustana*                                  |
|   |                                               | Roots of *L. altaica*                                                  |
|   |                                               | *L. tartarica* whole plant                                             |
|   |                                               | Roots of *L. tartarica*                                                |
|   |                                               | Roots of *L. georgica*                                                 |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Roots of *L. virosa*                                                   |
|   |                                               | Aerial parts and roots of *L. dregeana*                                 |
|   |                                               | Stem of *L. sativa* var. *angustana*                                   |
| 13| 11β,13-Dihydrolactucopicin glycoside          | Latex of *L. sativa*                                                   |
| 14| 11β-Hydroxycrepidinase B                      | Aerial parts of *L. aculeata*                                          |
| 15| 11β-Hydroxy-11,13-dihydrolactucin             | *L. tartarica* whole plant                                             |
| 16| 15-(4-Hydroxyphenylacetyl)-lactucin-8-sulfate | Latex of *L. sativa*                                                   |
| 17| Hypochoeroseside B                            | Roots of *L. georgica*                                                 |
| 18| Jacquinellin                                  | Latex of *L. sativa*                                                   |
|   |                                               | Roots of *L. aculeata*                                                 |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Aerial parts of *L. sibirica*                                          |
|   |                                               | Roots of *L. tartarica*                                                |
|   |                                               | Leaves and roots of *L. aculeata*                                      |
|   |                                               | Aerial parts of *L. aculeata*                                          |
|   |                                               | Aerial parts of *L. serriola*                                          |
|   |                                               | Roots of *L. sibirica*                                                 |
|   |                                               | Aerial parts of *L. sibirica*                                          |
|   |                                               | Roots of *L. virosa*                                                   |
|   |                                               | Roots of *L. saligna*                                                  |
|   |                                               | Roots of *L. virosa*                                                   |
Table 1. Continued..

|   | Genus | Species | Genotype | Plant Part | Reference |
|---|-------|---------|----------|------------|-----------|
| 19 | Lactucin | Lactuca sativa | | 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. dregena | [22] |
| 20 | Lactucin-8-O-acetate | Lactuca sativa | | Roots of L. georgica | [16] |
| 21 | Lactucin-8-O-methacrylate | Lactuca sativa | | Roots of L. georgica | [16] |
| 22 | Lactucopicrin | Lactuca sativa | | 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. dregena | [22] |
| 23 | Lactucopicriside | Lactuca sativa | | Roots of L. laciniata | [35] |
| 24 | Picriside A (Lactucin 15-glycoside) | Lactuca sativa | | Latex of L. sativa | [24] |
| 25 | Deacetoxymatricarin (leucodin, leucomisin) | Lactuca sativa | | Aerial parts of L. serriola | [13] |
|   |      |         |          | Roots of L. viminea | [33] |
|   |      |         |          | Roots of L. sativa var. angustana | [27] |
| 26 | Deacetylmatrixcarin (austricin) | Lactuca sativa | | L. tartarica whole plant | [16] |
| 27 | 8-Deacetylmatrixcarin-8-O-sulphate | Lactuca sativa | | Aerial parts and roots of L. dregena | [22] |
| 28 | 11β,13-Dehydro lactuside C | Lactuca sativa var. angustana | | Roots of L. canadensis | [38] |
| 29 | 11β-Hydroxy leucodin-11-O-β-glucoside | Lactuca sativa var. angustana | | Roots of L. sativa | [20] |
| 30 | Lactuside C | Lactuca sativa var. angustana | | Roots of L. aculeata | [27] |
|   |      |         |          | Aerial parts and roots of L. dregena | [22] |
|   |      |         |          | Aerial parts of L. serriola | [13] |
|   |      |         |          | Roots of L. albaica | [15] |
| 31 | Lactupicrin methyl ester | Lactuca sativa | | Roots of L. albaica | [15] |
| 32 | Lactucin methyl ester | Lactuca sativa | | Aerial parts of L. serriola | [13] |
| 33 | Hieracim I | Lactuca sativa | | Roots of L. aculeata | [25] |
| 34 | Hieracim II | Lactuca sativa | | Roots of L. aculeata | [25] |
| 35 | 1-Epichoralexin | Lactuca sativa | | Roots of L. viminea | [33] |
| 36 | Inybulide | Lactuca sativa | | Roots of L. altaica | [15] |
| 37 | 11β,13-Dihydro epizaluzianin C | Lactuca sativa var. angustana | | Roots of L. canadensis | [38] |
| 38 | 11β,13-Dihydrovernoflexuoside | Lactuca sativa var. angustana | | 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] |
| 39 | 11β,13,9α-Dihydroxy zaluzianin C | Lactuca sativa var. angustana | | 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.

| No. | Compound Description | Source Plant(s) | Reference(s) |
|-----|----------------------|-----------------|--------------|
| 40  | 11β,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  | 9α-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 (9α-hydroxy-11β,13-dihydrozaluzanin C-19-O-β-D-glucoside) | Roots of *L. saligna* | [26] |
| 47  | Scorzoside | Roots of *L. viminea* | [33] |
|     |                     | Roots of *L. sibirica* | [30] |
|     |                     | Roots of *L. perennis* | [32] |
| 48  | Vernoflexuoside (glucozaluzanin C) | Roots of *L. canadensis* | [38] |
|     |                     | Roots of *L. altaica* | [15] |
|     |                     | Roots of *L. aculeata* | [29] |
|     |                     | Roots of *L. sibirica* | [30] |
|     |                     | Roots of *L. laciniata* | [35] |
|     |                     | Roots of *L. saligna* | [26] |
|     |                     | Roots of *L. canadensis* | [38] |
|     |                     | Roots of *L. sativa var. angustana* | [27] |
|     |                     | Stem of *L. sativa var. angustana* | [21] |
| 49  | Zaluzanin C | Stems of *L. sativa var. angustana* | [21] |
| 50  | 4α-O-β-D-Glucopyranosyl-15-hydroxy-5α,6β-H-guaiane-10(14),11(13)-dien-12,6α-olide tetrahydrodihydrozaluzanin C | Stem of *L. sativa var. angustana* | [21] |
| 51  | 9α-Hydroxy-4β,15,11(13)-tetrahydrodihydrozaluzanin C | Roots of *L. aculeata* | [25] |
| 52  | 9α-Hydroxy-4β,11β,13,15 tetrahydrozaluzanin C | Stems of *L. sativa var. angustana* | [21] |
| 53  | 10β,14-Dihydroxyl-11β/H-guaiane-4(15)-ene-12,6α-olide | Stems of *L. sativa var. angustana* | [21] |
| 54  | 10β,14-Dihydroxy-10(14),11β(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] |
|     |                     | Stems of *L. sativa var. angustana* | [21] |
| 55  | Lettucenin A | *L. indica* whole plant | [24] |
| 56  | Lactucaain A | | [12] |
| 57  | Lactucaain B | | |
| 58  | Lactucaain C | | |
Genus *Lactuca* (Asteraceae)

1. $R_1=\text{Glc, } R_2=\text{OH, } X=H, \alpha\text{Me}$
2. $R_1=\text{Glc, } R_2=H, X=\text{CH}_2$
3. $R_1=\text{Glc, } R_2=H, X=H, \alpha\text{Me}$
4. $R_1=\text{OH, } R_2=H, X=\text{CH}_2$
5. $R_1=\text{OCOCH}_2\text{OH, } R_2=H, X=\text{CH}_2$
6. $R_1=\text{OSO}_3\text{H, } R_2=H, R_3=\text{CH}_2$
7. $R_1=\text{H, } R_2=\text{OH, } X=\text{CH}_2$
8. $R_1=\text{H, } R_2=\text{OSO}_3\text{H, } X=\text{CH}_2$
9. $R_1=R_2=\text{OH, } X=H, \alpha\text{Me}$
10. $R_1=\text{OH, } R_2=\text{OAc, } X=H, \alpha\text{Me}$
11. $R_1=\text{OH, } R_2=\text{OCOCH}_2\text{CH}_3, X=H, \alpha\text{Me}$
12. $R_1=\text{OH, } R_2=\text{OCOCH}_2\text{PhOH, } X=H, \alpha\text{Me}$
13. $R_1=\text{Glu, } R_2=\text{OCOCH}_2\text{PhOH, } X=H, \alpha\text{Me}$
14. $R_1=\text{Glc, } R_2=H, X=\text{OH, } \alpha\text{Me}$
15. $R_1=R_2=\text{OH, } X=\text{OH, } \alpha\text{Me}$
16. $R_1=\text{OCOCH}_2\text{PhOH, } R_2=\text{OSO}_3\text{H, } X=\text{CH}_2$
17. $R_1=\text{Glc, } R_2=\text{OCOCH}_2\text{CH}_3\text{CH}_3, X=H, \alpha\text{Me}$
18. $R_1=\text{OH, } R_2=\text{H, } X=\text{H, } \alpha\text{Me}$
19. $R_1=R_2=\text{OH, } X=\text{CH}_2$
20. $R_1=\text{OH, } R_2=\text{OAc, } X=\text{CH}_2$
21. $R_1=\text{OH, } R_2=\text{OCOCH}_2\text{CH}_3, X=\text{CH}_2$
22. $R_1=\text{OH, } R_2=\text{OCOCH}_2\text{PhOH, } X=\text{CH}_2$
23. $R_1=\text{Glc, } R_2=\text{OCOCH}_2\text{PhOH, } X=\text{CH}_2$
24. $R_1=\text{Glc, } R_2=\text{OH, } X=\text{CH}_2$

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

25. $R_1=R_2=\text{H, } X=H, \alpha\text{Me}$
26. $R_1=\text{H, } R_2=\text{OH, } X=H, \alpha\text{Me}$
27. $R_1=\text{H, } R_2=\text{OSO}_3\text{H, } X=H, \alpha\text{Me}$
28. $R_1=\text{Glc, } R_2=H, X=\text{CH}_2$
29. $R_1=R_2=\text{H, } X=\text{Glc, } \alpha\text{Me}$
30. $R_1=\text{Glc, } R_2=H, X=H, \alpha\text{Me}$
31. $R=\text{OCOCH}_2\text{PhOH}$
32. $R=\text{H}$
33. $X=\text{H, } \alpha\text{Me}$
34. $X=\text{CH}_2$
35. $R=\text{Glc}$
36. $R=\text{Glc}$

**Figure 1.2.** Guaiatolides (25-36) isolated from genus *Lactuca*
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 \( \gamma \)-lactone ring (5-membered lactone group) having a carbonyl group at the \( \alpha \)-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] |
| 60  | 3α-Hydroxyreynosin | Roots of *L. canadensis* | [38] |
| 61  | Armefolin      | Roots of *L. canadensis* | [38] |
| 62  | 1-Episodeerivanin | Roots of *L. canadensis* | [38] |
| 63  | Armexifolin    | Roots of *L. canadensis* | [38] |
| 64  | 1-Epidehydroisoerivanin | Roots of *L. canadensis* | [38] |
| 65  | 11β,13-Dihydrorsantamarin (1β-hydroxy-5α,6β/H-eudesman-3-ene-12,6α-olide) | Roots of *L. canadensis* | [38] |
|     | L. tartarica whole plant | | [16] |
|     | Roots of *L. viminea* | | [33] |
|     | Roots of *L. laciniata* | | [35] |
|     | Stems of *L. sativa* var. *angustana* | | [21] |
|     | Stems of *L. sativa* var. *angustana* | | [40] |
| 66  | Santamarin    | Roots of *L. canadensis* | [38] |
|     | Roots of *L. viminea* | | [33] |
| 67  | 1β-O-D-Glucopyranosyl-4α-hydroxy-5α,6β,11β/H-eudesma-3-en-12,6α-olide | Stems of *L. sativa* var. *angustana* | [40] |
| 68  | 1β-O-β-D-Glucopyranosyl-4α-hydroxy-5α,6β,11β/H-eudesma-3-en-12,6α-olide | Stems of *L. sativa* var. *angustana* | [40] |
| 69  | 1β-O-β-D-Glucopyranosyl-15-O-(p-methoxyphenylacetyl)-5α,6β/H-eudesma-3,11(13)-dien-12,6α-olide | *L. sativa* | [41] |
|     | *L. sativa* var. *angustata* whole plant | | |
| 70  | 2β-Hydroxy-11β,13 dihydrouglanin | *L. tartarica* whole plant | [16] |
| 71  | Methyl 3β-(β-D-glucopyranosyloxy)-6α-hydroxyeudesma-1,4(15),11(13)-trien-12-oate | Roots of *L. altaica* | [15] |
| 72  | 2-Oxo-11β,13-dihydrosantamarin | *L. tartarica* whole plant | [16] |
|     | Roots of *L. viminea* | | [33] |
| 73  | Tauremisin (vulgarin) | Roots of *L. viminea* | | [33] |

![Figure 2.1. Eudesmanolides (59-67) isolated from genus Lactuca](image-url)
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]       |
|     | (3β-Hydroxy-11β,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. sativa*                         | [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. viminalis*                      | [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]       |
Genus *Lactuca* (Asteraceae)

![Figure 3. Melampolides (74-77) isolated from genus *Lactuca*](image)

**Table 4. Germacrolides isolated from genus *Lactuca***

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

![Figure 4. Germacrolides (78-84) isolated from genus *Lactuca*](image)
3.2. Lignans

Lignans are polyphenolic compounds of 1,4-diarylbutane skeleton, derived from the shikimic acid biosynthetic pathway. Some lignans (as furfuran 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  | Dihydrodehydrodiconiferyl alcohol 9-O-β-D-glucoside | Roots of *L. viminea* | [33] |
| 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 | Aerial parts of *L. sibirica* | [31] |
| 91  | 4β-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  | 8α-Hydroxyepipinoresinol-4α-O-β-(6-p-methoxyphenylacetyl)-glucoside | Aerial parts of *L. sibirica* | [31] |
| 96  | 8α-Hydroxyepipinoresinol-4α-O-β-(6-p-hydroxyphenylacetyl)-glucoside | | |
| 97  | Lactucaside | *L. indica* whole plant | [12] |

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

![Image of compounds 92 and 93]

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

### 3.3. Coumarins

Among all *Lactuca* species, coumarins (2H-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] |

![Image of compounds 95 to 97]

**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 | OH | 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] |
| 110 | Japonicin A | *L. indica* whole plant | [12] |
| 111 | Lactucasativoside A (3,3′,4′,5,9,10-hexahydroxy-12-methylchroman | Seeds of *L. sativa* | [51] |
Genus *Lactuca* (Asteraceae)

**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.

**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 *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.
## Genus Lactuca (Asteraceae)

### 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]       |
| 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-cafeoylquinic acid          | Aerial parts of *L. indica*                  | [54]       |
| 134 | 3,5-Di-O-cafeoylquinic acid          | Aerial parts of *L. indica*                  | [54]       |
| 135 | 4,5-Di-O-cafeoyl quinic acid         | 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-cafeoyl-muco-quinic acid    |                                              |            |

![Figure 10](image_url). 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)       |
Genus *Lactuca* (Asteraceae)

**Table 12 continued**.

| No. | Compounds                                                                                                                                  | Sources                                                                 |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| 146 | Lactucenyl acetate                                                                                                                        | Roots of *L. indica*                                                   |
| 147 | Lupeol                                                                                                                                    | *L. indica* whole plant                                                |
|     |                                                                                                                                           | Aerial parts of *L. sativa*                                            |
|     |                                                                                                                                           | Aerial parts of *L. serriola*                                          |
| 148 | Lupenyl acetate                                                                                                                           | Roots of *L. indica*                                                   |
|     |                                                                                                                                           | Aerial parts of *L. serriola*                                          |
|     |                                                                                                                                           | *L. denticulata* whole plant                                           |
| 149 | Olean-18-ene                                                                                                                             | *L. indica* whole plant                                                |
| 150 | Pseudotaraxasterol                                                                                                                       | *L. indica* whole plant                                                |
| 151 | Taraxasterol                                                                                                                             | *L. indica* whole plant                                                |
| 152 | Taraxasteryl acetate                                                                                                                     | Roots of *L. indica*                                                   |
| 153 | Taraxast-20-ene-3β,30-diol                                                                                                                | Aerial parts of *L. serriola*                                          |
| 154 | Tarolupenyl acetate (lup-19(21)-en-3β-yl acetate)                                                                                         | Roots of *L. indica*                                                   |
| 155 | 3-O-[β-D-Galactopyranosyl-(1→3)-O-β-D-xylopyranosyl-(1→4)-O-α-L-rhamnopyranosyl]-oleanolic acid                                         | Seeds of *L. serriola*                                                 |
| 156 | 3β-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*                                                 |

![Figure 11](image-url)  
*Figure 11. Triterpenoids (139-156) isolate from genus *Lactuca* (the first part)*
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]       |
|     |                                 | Seeds of *L. serriola*           | [10, 23]   |
| 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]       |
Genus *Lactuca* (Asteraceae)

![Steroids (157-161)](image)

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*.

![Miscellaneous compounds (162-185)](image)

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-hydroxyphenylacetate   | Roots of *L. perennis*                                   | [15]       |
| 170 | Eugenyl-4-O-β-D-glucoside      | Roots of *L. altaica*                                     | [15]       |
| 171 | Glycerol monopalmitate         | Aerial parts of *L. serriola*                            | [23]       |
| 172 | (2S,3S,4R,2′R,14E)-2-(2′-hydroxytetrasanoylamino)-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]       |
| 175 | Methyl p-hydroxyphenylacetate  | 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 | Dihydroxyringin                | Root tubers of *L. tuberosa*                             | [45]       |
| 184 | Ethyl caffeate                 | Root tubers of *L. tuberosa*                             | [45]       |
| 185 | Methyl caffeate                | 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, spasmylytic, bronchodilator, and vasorelaxant activities depending on its dose. The spasmogenic activity may be related to some cholinergic constituents whereas the spasmylytic effect at higher concentrations may be attributed to Ca$^{2+}$ channel blocking constituents that may lead to relaxation of gastrointestinal, tracheal, and aorto smooth muscles. This may partially explain the traditional use of L. serriola in the management of conditions relating to spasm of the intestine, bronchiolo, and vasculature [61].

4.2.4. Anticancer Activity

Selected sesquiterpene lactones from L. sativa extract (1β-O-β-D-glucopyranosyl-4α-hydroxy-5α,6β,11βH-eudesma-12,6α-olide, 1β-hydroxy-15-O-(p-methoxyphenylacetyl)-5α,6β,11βH-eudesma-3-ene-12,6α-olide and 4α-O-β-D-glucopyranosyl-15-hydroxy-5α,6βH-guaiane-10(14),11(13)-dien-12,6α-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...
Genus *Lactuca* (Asteraceae)

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. Lactucopicrin 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 1000 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 1000 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 3-0-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-3-0-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 variation 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
Genus Lactuca (Asteraceae)

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 IC₅₀ values of 96.4 and 100.7 μM, respectively compared to the standard, acarbose (IC₅₀ 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 IC₅₀ value of 46.16±0.26 μg/mL. The EtOAc-soluble fraction showed remarkable inhibition among other tested fractions with an IC₅₀ value of 9.16±0.17 μg/mL compared to acarbose (IC₅₀, 6.11±0.22 μg/mL). A quite moderate α-glucosidase inhibitory activity was observed for the methylene chloride-soluble fraction with an IC₅₀ value of 16.88±0.28 μg/mL. As to petroleum ether fraction, it displayed low α-glucosidase inhibition with an IC₅₀ 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 IC₅₀ 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 subtilis, 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* spasmodenic (cholinergic) action on gastrointestinal, tracheal, and aortic smooth muscles | *L. serriola* Aerial parts Methanol extract [61] |
| *Ex vivo* spasmylytic 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 Methanol extract [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.

| Activity                              | Species                  | Methodology                                    | Reference |
|---------------------------------------|--------------------------|-----------------------------------------------|-----------|
| 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             | *L. runcinata*           | Aerial parts | Methanol extract | [74]      |
| Reduction of elevated SGOT, SGPT, ALP, and TB levels and improved histopathological properties in CCl4-induced hepatotoxicity | *L. sativa* | Seed and leaf | Aqueous and hydro-alcoholic extracts | [74]      |
| Antispermatogetic effect in male mice | *L. sativa*              | Seed | Aqueous extract | [74]      |
| In vivo increased testosterone level in mice | *L. sativa*              | Seed | Aqueous extract | [74]      |
| Antidiabetic activity                 | *L. indicus*             | Fresh herb | Lactucaside and latucain C | [12]      |
| α-Glucosidase inhibitory activity    | *L. indicus*             | 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.

ORCID

Fatma M. Abdel Bar: 0000-0003-0823-4015
Nouran H. Abdel Fatah: 0000-0002-0523-1807
Yhiya Amen: 0000-0003-2552-4567
Ahmed F. Halim: 0000-0002-6340-8949
Hassan-Eldrady A. Saad: 0000-0002-3030-7391

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