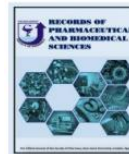




# RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES



## Chemical constituents and biological activities of genus *Lotus*: An updated review

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### Abstract

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Genus *Lotus* (Fabaceae) comprises several species, which are widely distributed in north temperate regions of the world, especially the Mediterranean region and West Asia. *Lotus* is represented in Egypt by 18 species: *L. edulis*, *L. polyphyllus*, *L. ornithopodioides*, *L. angustissimus*, *L. peregrinus*, *L. halophilus*, *L. creticus*, *L. cytisoides*, *L. palustris*, *L. corniculatus*, *L. pedunculatus*, *L. lanuginosus*, *L. nubicus*, *L. glinoides*, *L. lalambensis*, *L. arabicus*, *L. hebranicus* and *L. tetragonolobus*. Plants of this genus exhibited a significant role in traditional medicine. *Lotus* has a history of folkloric medicinal uses as contraceptives, prophylaxis and treatment of sexually transmitted diseases and peptic ulcers. Flavonoids, saponins, phenolic acids, coumarins and sterols were reported as the main bioactive constituents of this genus with a wide range of biological activities. Anti-inflammatory, anti-platelet aggregation, antibacterial, antifungal, estrogenic, hepatoprotective, anticancer and antioxidant activities were reported for *Lotus*. The present work is an overview of the reported biological activities together with the isolated compounds from genus *Lotus*.

**Keywords:** *Lotus*, Mediterranean region, flavonoidal constituents, biological activities.

### 1. Introduction:

Genus *Lotus* is belonging to family Fabaceae, subfamily Faboideae. It includes approximately about 100 species distributed in north temperate regions especially the Mediterranean region and West Asia (**Boulos 1999**; **El-Youssef et al. 2008**). *Lotus* is represented in Egypt by 18 species (**Täckholm 1974**; **Boulos 1999**): *L. edulis*, *L. polyphyllus* (*L. argenteus*), *L. ornithopodioides*, *L. angustissimus*, *L. peregrinus* (*L. carmeli*), *L. halophilus* (*L. villosus*, *L. pusillus*), *L. creticus* (*L. commutatus*, *L. salzmännii*), *L. cytisoides* (*L. prostratus*, *L. allionii*, *L. patens*), *L. palustris* (*L. lamprocarpus*, *L. palustris*), *L. corniculatus* (*L. glaber*, *L. tenuis*, *L. tenuifolius*), *L.*

*pedunculatus* (*L. uliginosus*, *L. decumbens*), *L. lanuginosus*, *L. nubicus*, *L. glinoides* (*L. schimperii*, *L. ehrenbergii*), *L. lalambensis*, *L. arabicus* (*L. roseus*, *L. mossamedensis*), *L. hebranicus* (*L. deserti*) and *L. tetragonolobus* (*L. palaestinus*).

*Lotus* has a history of folkloric medicinal uses as contraceptives, prophylaxis and treatment of sexually transmitted diseases and peptic ulcers (**El Mousallami et al. 2002**). Literature survey on *Lotus* revealed the presence of different types of flavonoids, saponins, phenolic acids, coumarins, sterols and miscellaneous compounds. Literature survey revealed that no updated review was published reporting the isolated compounds and biological activities of genus *lotus*. The present

work is an updated overview of the isolated compounds from *Lotus* together with the reported biological activities of that genus.

### Literature survey databases

All information on chemical constituents and biological activities of genus *Lotus* was compiled from electronic databases such as Medline, Google scholar, ScienceDirect, Springer Link, PubMed and SCOPUS.

### Results

Different types of flavonoids, saponins, phenolic acids, coumarins, sterols and miscellaneous compounds were previously isolated from genus *Lotus*. Table 1 highlights the flavonoidal constituents isolated from *Lotus* (Figures 1-4). Table 2 highlights the triterpenoidal saponins, coumarins and phenolic compounds isolated from *Lotus* (Figures 5-6). Table 3 highlights the sterols, alkylated sugars, cyanogenic glycosides and miscellaneous compounds isolated from *Lotus* (Figures 7-9).

### Biological activities of genus *Lotus*

#### Anti-inflammatory activity

The light petrol fraction of *L. lalambensis* showed an excellent anti-inflammatory effect against inflammation induced by carrageenan (**El-Youssef et al. 2008**). Studies investigated the anti-inflammatory effects of the ethanol extract of *Lotus corniculatus*, its derived hexane, ethyl acetate, *n*-butanol and aqueous fractions, in addition to, the isolated compounds kaempferitrin, oleanolic acid and  $\beta$ -sitosterol in a mouse model of pleurisy induced by carrageenan. Results revealed that The ethanol extract of *L. corniculatus*, its derived fractions and its isolated compounds, inhibited leukocytes, exudation, pro-inflammatory enzymes and mediators such as myeloperoxidase (MPO), adenosine-deaminase (ADA), interleukin-1 beta (IL-1b) mediator level and nitrite/nitrate concentration (**Fröde and Medeiros 2001; Koelzer et al. 2009**). The hexane and ethyl acetate fractions revealed a more pronounced anti-inflammatory response than the other fractions, since they were able to inhibit all the studied inflammatory parameters. On the contrary, the butanol fraction did not inhibit either MPO activity or nitrite/nitrate concentration. In conclusion, *L. corniculatus* showed an important anti-inflammatory property, and its constituent's kaempferitrin, oleanolic acid and  $\beta$ -sitosterol may well account for this anti-inflammatory activity (**Koelzer et al. 2009; Pereira et al. 2011**). These compounds have potential as novel lead compounds for the future development

of therapeutic intervention in the treatment of patients with inflammatory disorders.

#### Anti-platelet aggregation

The aqueous fraction of *L. lalambensis* showed a strong inhibition of platelet aggregation (**El-Youssef et al. 2008**). Platelet aggregation was induced by ADP (adenosine diphosphate) in blood samples of male wistar rats and the percentage inhibition of platelet aggregation induced by the ethanolic extract, the light petrol, chloroform, ethyl acetate, *n*-butanol and aqueous fractions were then calculated.

#### Antibacterial activity

The butanol extract of the aerial parts of *L. halophilus* exhibited a good antimicrobial activity against both Gram-positive and Gram-negative bacteria (**Mahasneh 2002**). However, the hexane fraction of *L. corniculatus* demonstrated effective inhibition against *Bacillus cereus*, *Enterococcus faecalis*, *Listeria monocytogenes*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Acinetobacter calcoaceticus* and *Providencia alcalifaciens*. Also, the ethyl acetate fraction showed an important antibacterial activity against *Bacillus cereus*, *Enterococcus faecalis* and *Cinetobacter calcoaceticus*. The oleanolic acid isolated from hexane fraction showed the same effect against methycillin-resistant *Staphylococcus aureus*, *Listeria monocytogenes* and *Bacillus cereus*. Furthermore, Kaempferitrin isolated from ethyl acetate fraction also shown antibacterial activity against *Shighella flexinerii*, *Salmonella typhimurium*, *Acinetobacter calcoaceticus*, *Enterococcus faecalis* and *Bacillus cereus*. These results confirmed that *L. corniculatus* have important antibacterial activity against Gram-positive and Gram-negative bacteria (**Dalmarco et al. 2010**). Another study showed that Kaempferitin which was isolated from the ethyl acetate extract of *L. corniculatus* aerial parts exhibited antibacterial effects against *Escherichia coli* (**El-Ghani et al. 2001**).

#### Antifungal activity

The butanol extract of the aerial parts of *L. halophilus* has a good antifungal activity against *Candida albicans* and *Aspergillus flavus* (**Mahasneh 2002**). Another study showed that the methanol extract of *L. tenuis* inhibited the mycelia growth of *Alternaria species* and *Fusarium graminearum* (**Girardi et al. 2014**). The greatest contents of coumarins, flavonoids and tannins in these plants are directly related to their antifungal activity. The antimicrobial action of the flavonoids may be related to the ability to bind to extracellular,

soluble proteins and cell wall structures (**Sandhar et al. 2011**; **Girardi et al. 2014**). Moreover, The ethanol, ethyl acetate, butanolic and aqueous extracts of *L. garcinii* were active against *Aspergillus niger*, *Alternaria solani*, *Penicillium funiculosium*, *Microsporium canis* and *Pleuroetous oustreatus* (**Azhar et al. 2004**).

#### *Estrogenic activity*

The chloroform fraction of *L. lalambensis* showed the highest estrogenic activity compared to the light petrol, the ethyl acetate and the aqueous fractions of the same plant (**El-Youssef et al. 2008**). Another study showed that mature legumes of *L. corniculatus* had significant anti-estrogenic and estrogenic activities after dissolving in physiological saline with or without 17- $\beta$ - estradiol, respectively. It was injected subcutaneously into immature rats. Six hours after injection, the animals were killed by ether inhalation and the uteri were removed and weighed. The estrogenic and the antiestrogenic activities were assessed by the increase or decrease of the uterine weight expressed as percent of body weight when compared with the appropriate controls (physiological saline with or without 17- $\beta$ - estradiol). The results revealed that the degree of anti-estrogenic activity was related to the date of harvest and stage of growth of the plant. An inverse relation between estrogenic and antiestrogenic activity was indicated (**Biely and Kitts 1964**).

#### *Hepatoprotective activity*

It was found that 70% ethanol extract and different fractions of *L. polyphyllus* aerial parts exhibited high hepatoprotective activity compared with standard silymarin at a dose of 300 mg/kg body weight using carbon tetrachloride (CCl<sub>4</sub>) intoxicated rats. This study depended on measuring the level of the biochemical parameters; aspartate aminotransferase (AST, serum glutamate oxaloacetate transaminase or SGOT), alanine aminotransferase (ALT, serum glutamate pyruvate or

SGPT) and alkaline phosphatase (ALP). The hepatoprotective activity was also supported by the histological examining of liver tissues (**Osman et al. 2013**).

#### *Anticancer activity*

An acetylated Kaempferol glycoside of *L. edulis* showed a significant inhibition of the growth of human cancer cell lines; MCF7 (breast cancer cells), HeLa (cervical cancer cells), and HepG2 (liver cancer cells). In addition, this compound was a strong catalytic inhibitor of topoisomerase enzymes. These enzymes are essential for all processes of DNA metabolism, and their inhibitors have been identified as potential anticancer agents (**Tselepi et al. 2011**). The antiproliferative activity of chloroform and butanol extracts of *L. corniculatus* aerial parts was evaluated using three continuous murine and human culture cell lines; J774A1 (murine monocyte/macrophage), HEK-293 (human epithelial kidney cells) and WEHI-164 (murine fibrosarcoma), the butanol extract showed a moderate cytotoxic activity (**Aissaoui et al. 2014**). Moreover, a lectin (tetrameric galactose) isolated from *L. corniculatus* seeds showed a strong antiproliferative activity towards human leukemic (THP-1), lung (HOP62) and colon (HCT116) cancer cells with IC<sub>50</sub> of 39  $\mu$ g/ml, 50  $\mu$ g/ml and 60  $\mu$ g/ml respectively (**Rafiq et al. 2013**).

#### *Antioxidant activity*

The antioxidant activity of the aqueous fraction of *L. corniculatus* was evaluated by the ESR (Electron Spin Resonance) spectroscopy method (**Yamaguchi et al. 2000**) in order to visualize the inhibition of the DPPH (1,1-diphenyl-2-picrylhydrazyl), superoxide and hydroxyl radicals. Also, it is evaluated by comparison with reference molecules, e.g. vitamin E and quercetin. It showed moderate antioxidant activity. Antioxidant effects were correlated with the total amount of phenolic compounds contained in the extract (**Trouillas et al. 2003**).

## 2. Chemical constituents reported from species of genus *Lotus*

**Table 1. Flavonoidal constituents:**

| Compound Name  | Occurrence   | Reference  |
|--|--|--|
| 1. Kaempferol  | <i>L. corniculatus</i> leaves and flowers<br><i>L. lalambensis</i> aerial parts<br><i>L. borbasii</i>                | (Harney and Grant 1964; Jay et al. 1978; Strittmatter et al. 1992; El-Ghani et al. 2001; Reynaud and Lussignol 2005)<br>(Reynaud and Lussignol 2005) (El-Youssef et al. 2008)<br>(Harney and Grant 1964) |
| 2. Kaempferol-3- <i>O</i> -glucoside (Astragalin)  | <i>L. corniculatus</i> leaves  | (Reynaud et al. 1982; Strittmatter et al. 1992; Reynaud and Lussignol 2005)  |
| 3. Kaempferol-3- <i>O</i> -glucoside-7-rhamnoside  | <i>L. corniculatus</i> seeds and aerial parts<br><i>L. lalambensis</i> aerial parts                                  | (Strittmatter et al. 1992; Reynaud and Lussignol 2005)<br>(El-Youssef et al. 2008)   |
| 4. Kaempferol-3,7 dirhamnoside (Kaempferitin)  | <i>L. corniculatus</i> seeds<br><br><i>Lotus lalambensis</i> aerial parts<br><i>L. ornithopodioides</i> aerial parts | (Reynaud et al. 1982; El-Ghani et al. 2001; Reynaud and Lussignol 2005; Dalmarco et al. 2010)<br><br>(El-Youssef et al. 2008)<br>(Abdel-Kader et al. 2007)   |
| 5. Kaempferol -7- <i>O</i> -rhamnoside   | <i>L. corniculatus</i> leaves<br><i>L. hebranicus</i>  | (Reynaud et al. 1982; Reynaud and Lussignol 2005)<br>(Kasem 2001)  |
| 6. Kaempferol -3- <i>O</i> -rhamnoside   | <i>L. corniculatus</i> leaves<br><i>L. lalambensis</i> aerial parts<br><i>L. hebranicus</i>                          | (Reynaud et al. 1982; Reynaud and Lussignol 2005)<br>(El-Youssef et al. 2008)<br>(Kasem 2001)  |
| 7. Kaempferol-3- <i>O</i> -rhamnoside-7- <i>O</i> -glucoside   | <i>L. corniculatus</i> leaves  | (Reynaud et al. 1982; Reynaud and Lussignol 2005)  |
| 8. Kaempferol-7- <i>O</i> - glucoside  | <i>L. corniculatus</i> seeds and leaves  | (Reynaud and Lussignol 2005)   |
| 9. Kaempferol -3,7-diglucoside   | <i>L. corniculatus</i> seeds and leaves<br><i>L. polyphyllus</i>   | (Reynaud and Lussignol 2005)<br>(El Mousallami et al. 2002)  |
| 10. Kaempferol-3- <i>O</i> - $\alpha$ -[ $\beta$ -D-glucopyranosyl -(1 <sup>'''</sup> →2 <sup>'''</sup> )-L-rhamnopyranoside]-7- <i>O</i> - $\alpha$ -L-rhamnopyranoside | <i>L. lalambensis</i> aerial parts   | (El-Youssef et al. 2008)   |
| 11. Kaempferol-3- <i>O</i> -[ $\beta$ -D-xylopyranosyl(1 <sup>'''</sup> -2 <sup>'''</sup> )- $\beta$ -D-galactopyranoside]-7- <i>O</i> - $\alpha$ -rhamnopyranoside      | <i>L. corniculatus</i> legumes   | (Kadry et al. 2007)  |
| 12. Kaempferol-3- <i>O</i> -[ $\beta$ -D-xylopyranosyl(1 <sup>'''</sup> -2 <sup>'''</sup> )- $\beta$ -D-galactopyranoside]   | <i>L. corniculatus</i> aerial parts  | (El-Gazzar 2016)   |
| 13. Kaempferol-3- <i>O</i> - $\beta$ -D-glucopyranoside-7- <i>O</i> - $\alpha$ -[ $\beta$ -D-glucopyranosyl -(1 <sup>'''</sup> →2 <sup>'''</sup> )-L-rhamnopyranoside]   | <i>L. lalambensis</i> aerial parts   | (El-Youssef et al. 2008)   |
| 14. Kaempferol -3- <i>O</i> - $\beta$ -(6 <sup>''</sup> - <i>O</i> -E- <i>p</i> -coumaroylglucoside)-7- <i>O</i> - $\beta$ -glucoside                                    | <i>L. polyphyllus</i>  | (El Mousallami et al. 2002)  |
| 15. Kaempferol 3- <i>O</i> - $\alpha$ -rhamnoside-7- <i>O</i> -sophoroside   | <i>L. hebranicus</i>   | (Kasem 2001; El Mousallami et al. 2002)  |
| 16. Kaempferol -3- <i>O</i> -sophoroside   | <i>L. hebranicus</i>   | (Kasem 2001; El Mousallami et al. 2002)  |
| 17. Kaempferol -3- <i>O</i> -(3 <sup>''</sup> - <i>O</i> - $\alpha$ -L-rhamnopyranosyl)- $\alpha$ -L-rhamnopyranosyl (Garcintin)   | <i>L. garcinii</i>   | (Ali et al. 2000)  |
| 18. Quercetin  | <i>L. corniculatus</i> leaves and flowers<br><i>L. polyphyllus</i> roots<br><i>L. japonicus</i>                      | (Harney and Grant 1964; Jay et al. 1978; El-Ghani et al. 2001; Reynaud and Lussignol 2005)<br>(Abdel-Kader et al. 2008)<br>(Morris and Lanot 2005)   |
| 19. Quercetin-3- <i>O</i> -rhamnoside (Quercitrin)   | <i>L. corniculatus</i> seeds and leaves  | (Reynaud et al. 1982; El-Ghani et al. 2001; Reynaud and Lussignol 2005)  |
| 20. Quercetin-3- <i>O</i> -rhamnoglucoside (Rutin)   | <i>L. corniculatus</i> leaves  | (Reynaud et al. 1982; Reynaud and Lussignol 2005)  |

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| 21. Quercetin -7-O-rhamnoside   | <i>L. corniculatus</i> seeds and leaves                     | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 22. Quercetin-3-O-galactoside   | <i>L. corniculatus</i> seeds and leaves                     | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 23. Quercetin-3,7-dirhamnoside  | <i>L. corniculatus</i> seeds and leaves                     | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 24. Quercetin-3-O-rhamnoside -7-O-glucoside   | <i>L. corniculatus</i> leaves                               | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 25. Quercetin-3-O-arabinoside   | <i>L. corniculatus</i> seeds                                | (Reynaud and Lussignol 2005)  |
| 26. Quercetin-3-O-glucoside-7-O-rhamnoside  | <i>L. corniculatus</i> seeds                                | (Reynaud and Lussignol 2005)  |
| 27. Quercetin 3-O-β-(6"-O-E-p-coumaroylglucoside)-7-O-β-glucoside                                   | <i>L. polyphyllus</i>                                       | (El Mousallami et al. 2002)   |
| 28. Quercetin 3,7-diglucoside   | <i>L. polyphyllus</i>                                       | (El Mousallami et al. 2002)   |
| 29. Quercetin 3-O-methyl-7-β-D-glucopyranoside (Transilin)  | <i>L. corniculatus</i> aerial parts                         | (Aissaoui et al. 2014)  |
| 30. Isorhamnetin  | <i>L. corniculatus</i> leaves and flowers                   | (Jay et al. 1978; Reynaud and Lussignol 2005)                       |
| 31. Isorhamnetin 3-O-β-(6"-O-E-p-coumaroyl glucoside)-7-O-β-glucoside                               | <i>L. polyphyllus</i>                                       | (El Mousallami et al. 2002)   |
| 32. Isorhamnetin 3,7-diglucoside  | <i>L. polyphyllus</i><br><i>L. hebranicus</i>               | (El Mousallami et al. 2002)<br>(Kasem 2001)                         |
| 33. Desoxy-5-kaempferol   | <i>L. corniculatus</i> leaves and flowers                   | (Jay et al. 1978; Reynaud and Lussignol 2005)                       |
| 34. Desoxy-5-quercetin (Fisetin)  | <i>L. corniculatus</i> leaves                               | (Jay et al. 1978; Reynaud and Lussignol 2005)                       |
| 35. Desoxy-5-isorhamnetin (Geraldol)  | <i>L. corniculatus</i> leaves and flowers                   | (Jay et al. 1978; Reynaud and Lussignol 2005)                       |
| 36. 6,7,4'-Trihydroxy-3,3'-dimethoxyflavonol  | <i>L. corniculatus</i> aerial parts                         | (El-Ghani et al. 2001)  |
| 37. 8-Methoxy kaempferol (Sexangularetin)   | <i>L. corniculatus</i> flowers                              | (Jay et al. 1978; Jay and Ibrahim 1986; Reynaud and Lussignol 2005) |
| 38. 8-Methoxy quercetin (Corniculatusin)  | <i>L. corniculatus</i> flowers                              | (Jay et al. 1978; Jay and Ibrahim 1986; Reynaud and Lussignol 2005) |
| 39. 8-Methoxy isorhamnetin (Limocitrin)   | <i>L. corniculatus</i> flowers                              | (Jay et al. 1978; Jay and Ibrahim 1986; Reynaud and Lussignol 2005) |
| 40. 8-Hydroxy quercetin (Gossypetin)  | <i>L. corniculatus</i> flowers                              | (Jay and Ibrahim 1986; Reynaud and Lussignol 2005)                  |
| 41. Gossypetin-3-O-galactoside  | <i>L. corniculatus</i> flowers                              | (Reynaud and Lussignol 2005)  |
| 42. 5,7, 3',4'-tetrahydroxy-8-methoxy-flavonol-3-O-β-D-galactoside (Corniculatusin-3-O-galactoside) | <i>L. corniculatus</i> flowers and leaves                   | (Nielsen 1970; Reynaud et al. 1982; Reynaud and Lussignol 2005)     |
| 43. Corniculatusin-3-O-glucoside  | <i>L. corniculatus</i> leaves                               | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 44. Sexangularetin-3-O-glucoside  | <i>L. corniculatus</i> leaves                               | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 45. Sexangularetin-3-O-rhamnoside-7-O-glucoside   | <i>L. corniculatus</i> leaves                               | (Reynaud et al. 1982; Reynaud and Lussignol 2005)                   |
| 46. Formononetin  | <i>L. corniculatus</i>                                      | (Sarelli et al. 2003; Reynaud and Lussignol 2005)                   |
| 47. Biochanin A   | <i>L. corniculatus</i>                                      | (Sarelli et al. 2003; Reynaud and Lussignol 2005)                   |
| 48. 4'-Methyl wighteone   | <i>L. creticus</i> roots                                    | (Yang et al. 1989)  |
| 49. Lupinalbin A  | <i>L. creticus</i> roots                                    | (Yang et al. 1989)  |
| 50. Lupinalbin B  | <i>L. creticus</i> roots<br><i>L. pusillus</i> aerial parts | (Yang et al. 1989)<br>(Golea et al. 2012)                           |
| 51. Lupinalbin C  | <i>L. creticus</i> roots                                    | (Yang et al. 1989)  |
| 52. Lupinalbin F  | <i>L. polyphyllus</i> roots                                 | (Abdel-Kader et al. 2006)   |
| 53. 4'-O-methylalpinum  | <i>L. polyphyllus</i> roots                                 | (Abdel-Kader et al. 2006)   |
| 54. 4'-O-methylerythrinin C   | <i>L. polyphyllus</i> roots                                 | (Abdel-Kader et al. 2006)   |
| 55. 4'-O-methyl-2"-hydroxydihydroalpinum  | <i>L. polyphyllus</i> roots                                 | (Abdel-Kader et al. 2006)   |
| 56. 4',7-Dimethoxy-5-hydroxyisoflavone  | <i>L. polyphyllus</i> roots                                 | (Abdel-Kader et al. 2006)   |
| 57. Euchrestaflavanone A  | <i>L. creticus</i> roots                                    | (Yang et al. 1989)  |

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| 58. (-)-7,2'-Dihydroxy-4'-methoxyisoflavan (Vestitol)                     | <i>L. lalambensis</i> roots<br><i>L. Corniculatus</i> leaves<br><br><i>L. hispidus</i> leaves<br><br><i>L. uliginosus</i><br><br><i>L. japonicas</i><br><i>L. edulis</i><br><br><i>L. angustissimus</i> leaves | (Alqasoumi et al. 2013)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Shimada et al. 2000; Morris and Lanot 2005)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)                    |
| 59. 5,7-Dimethoxy-2',4'-dihydroxyisoflavan (Lotisoflavan)                 | <i>L. lalambensis</i> roots<br><br><i>L. angustissimus</i><br><i>L. edulis</i>   | (Alqasoumi et al. 2013)<br><br>(Ingham and Dewick 1980)<br>(Ingham and Dewick 1980)  |
| 60. 7,2',4'-Trihydroxyisoflavan (Demethylvestitol)                        | <i>L. siliquosus</i><br><i>L. corniculatus</i><br><br><i>L. hipidus</i><br><br><i>L. edulis</i><br><br><i>L. angustissimus</i> leaves<br><br><i>L. uliginosus</i>  | (Ingham and Dewick 1979)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980) |
| 61. 5,4'-Dimethoxy-7,2'-dihydroxyisoflavan (5-Methoxyvestitol)            | <i>L. hispidus</i> leaves  | (Ingham and Dewick 1979, 1980)<br>(El-Youssef et al. 2008)   |
| 62. 7-Hydroxy-2',4'-dimethoxyisoflavan (Sativan)                          | <i>L. corniculatus</i> leaves<br><br><i>L. hispidus</i> leaves<br><i>L. japonicus</i><br><i>L. uliginosus</i><br><br><i>L. edulis</i><br><br><i>L. angustissimus</i> leaves                                    | (Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Ingham and Dewick 1979)<br>(Morris and Lanot 2005)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)<br>(Bonde et al. 1973; Ingham 1977; Ingham and Dewick 1979, 1980)  |
| 63. 7,4'-Dihydroxy-2'-methoxyisoflavan (Isovestitol)                      | <i>L. siliquosus</i>   | (Ingham and Dewick 1979)   |
| 64. Medicarpin-3-O- $\beta$ -D-glucopyranoside                            | <i>L. corniculatus</i> aerial parts  | (Aissaoui et al. 2014)   |
| 65. 5'-(Dimethyl-allyl)-5-Methoxycoumestrol                               | <i>L. creticus</i> roots   | (Mahmoud et al. 1990)  |
| 66. Catechin  | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 67. Epicatechin   | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 68. Gallocatechin   | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 69. Epigallocatechin  | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 70. Leucodelphinidin  | <i>L. corniculatus</i> leaves  | (Harney and Grant 1964)  |
| 71. Leucocyanidin   | <i>L. corniculatus</i> leaves  | (Harney and Grant 1964)  |
| 72. Catechin (4 $\alpha$ $\rightarrow$ 8) catechin                        | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |
| 73. Catechin(4 $\alpha$ $\rightarrow$ 8) epicatechin                      | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |
| 74. Gallocatechin(4 $\alpha$ $\rightarrow$ 8) epigallocatechin            | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |
| 75. Epicatechin (4 $\beta$ $\rightarrow$ 8)-catechin                      | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 76. Epicatechin (4 $\beta$ $\rightarrow$ 8) epicatechin                   | <i>L. pedunculatus</i><br><i>L. corniculatus</i>   | (Foo et al. 1997)<br>(Foo et al. 1996)   |
| 77. Epigallocatechin (4 $\beta$ $\rightarrow$ 8) catechin.                | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |
| 78. Epigallocatechin (4 $\beta$ $\rightarrow$ 8) Catechin peracetate      | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |
| 79. Epigallocatechin (4 $\beta$ $\rightarrow$ 8) gallocatechin peracetate | <i>L. pedunculatus</i>   | (Foo et al. 1997)  |

|   |  |  |
|---|--|--|
| 80. Epigallocatechin (4 $\beta$ $\rightarrow$ 8) epigallocatechin peracetate (Peracetate of the prodelphinidin) | <i>L. pedunculatus</i>                           | (Foo et al. 1997)                      |
| 81. Catechin (4 $\alpha$ $\rightarrow$ 2) phloroglucinol  | <i>L. pedunculatus</i><br><i>L. corniculatus</i> | (Foo et al. 1997)<br>(Foo et al. 1996) |
| 82. Gallo catechin (4 $\alpha$ $\rightarrow$ 2) phloroglucinol  | <i>L. pedunculatus</i>                           | (Foo et al. 1997)                      |
| 83. Epicatechin (4 $\beta$ $\rightarrow$ 2) phloroglucinol  | <i>L. pedunculatus</i><br><i>L. corniculatus</i> | (Foo et al. 1997)<br>(Foo et al. 1996) |
| 84. Epigallocatechin- (4 $\beta$ $\rightarrow$ 2) phloroglucinol  | <i>L. pedunculatus</i><br><i>L. corniculatus</i> | (Foo et al. 1997)<br>(Foo et al. 1996) |
| 85. Epicatechin- (4 $\beta$ $\rightarrow$ 8)- Epicatechin- (4 $\beta$ $\rightarrow$ 8)- catechin                | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 86. Epicatechin- (4 $\beta$ $\rightarrow$ 8)- epicatechin- (4 $\beta$ $\rightarrow$ 2)- phloroglucinol          | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 87. epicatechin- (4 $\beta$ $\rightarrow$ 8)- epicatechin- (4 $\beta$ $\rightarrow$ S)-benzylthioether          | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 88. Epigallocatechin- (4 $\beta$ $\rightarrow$ 8)- epicatechin (4 $\beta$ $\rightarrow$ 2)-phloroglucinol       | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 89. epigallocatechin- (4 $\beta$ $\rightarrow$ 8) epicatechin- (4 $\beta$ $\rightarrow$ S)-benzylthioether      | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 90. Epicatechin- (4 $\beta$ $\rightarrow$ 6)- epicatechin- (4 $\beta$ $\rightarrow$ 2)-phloroglucinol           | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 91. Epicatechin- (4 $\beta$ $\rightarrow$ 6) epicatechin- (4 $\beta$ $\rightarrow$ S)-benzylthioether           | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 92. epicatechin- (4 $\beta$ $\rightarrow$ S)-benzylthioether  | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |
| 93. epigallocatechin- (4 $\beta$ $\rightarrow$ S)-benzylthioether   | <i>L. corniculatus</i>                           | (Foo et al. 1996)                      |

**Table 2. Triterpenoidal saponins, coumarins and phenolic compounds:**

| Chemical class  | Compound Name  | Occurrence  | Reference   |
|---|--|---|---|
| Oleanane triterpenes  | 94. Soyasapogenol B  | <i>L. corniculatus</i>  | (Walter 1961)   |
|   | 95. Soyasaponin I  | <i>L. corniculatus</i> aerial parts   | (Aissaoui et al. 2014)  |
|   | 96. Astragaloside VIII   | <i>L. pusillus</i> aerial parts   | (Golea et al. 2012)   |
|   | 97. dehydrosoyasaponin I   | <i>L. corniculatus</i> aerial parts   | (Aissaoui et al. 2014)  |
|   | 98. Pharbitoside A   | <i>L. corniculatus</i> aerial parts   | (Aissaoui et al. 2014)  |
|   | 99. Oleanolic acid   | <i>L. lalambensis</i> aerial parts<br><i>L. corniculatus</i> aerial parts<br><i>L. ornithopodioides</i> aerial parts<br><i>L. garcinii</i><br><i>L. pusillus</i> aerial parts | (El-Youssef et al. 2008)<br>(Walter 1961; Dalmarco et al. 2010)<br>(Abdel-Kader et al. 2007)<br>(Ali et al. 2000; Ali et al. 2001)<br>(Golea et al. 2012) |
|   | 100. $\beta$ -amyrin   | <i>L. corniculatus</i> aerial parts   | (El-Ghani et al. 2001)  |
| Lupane triterpenes  | 101. Lupeol  | <i>L. lalambensis</i> aerial parts<br><i>L. garcinii</i>  | (El-Youssef et al. 2008)<br>(Ali et al. 2000; Ali et al. 2001)  |
| Lupane triterpenic acids  | 102. Betulinic acid  | <i>L. ornithopodioides</i> aerial parts<br><i>L. garcinii</i>   | (Abdel-Kader et al. 2007)<br>(Ali et al. 2000; Ali et al. 2001)   |
| Ursane triterpenic acids  | 103. Ursolic acid  | <i>L. corniculatus</i> aerial parts<br><i>L. criticus</i> roots   | (El-Ghani et al. 2001)<br>(Ingham 1977)   |
| Coumarins   | 104. 4',6'-Dihydroxy-7,2'-dimethoxy-3-aryl coumarin                    | <i>L. polyphyllus</i> roots   | (Abdel-Kader et al. 2008)   |
|   | 105. 2',7'-Dihydroxy-4',5'-dimethoxy-3-aryl coumarin                   | <i>L. lalambensis</i> roots<br><i>L. polyphyllus</i> roots  | (Alqasoumi et al. 2013)<br>(Abdel-Kader et al. 2008)  |
| Phenolics and phenolic acids  | 106. <i>n</i> -tetracosyl <i>p</i> -coumarate                          | <i>L. polyphyllus</i> roots   | (Abdel-Kader et al. 2006; Abdel-Kader et al. 2008)  |
|   | 107. Benzoic acid  | <i>L. corniculatus</i> aerial parts   | (Aissaoui et al. 2014)  |
|   | 108. <i>p</i> -coumaric acid   | <i>L. corniculatus</i> aerial parts<br><i>L. ornithopodioides</i>   | (Harney and Grant 1964; Aissaoui et al. 2014)<br>(Araniti et al. 2014)  |
|   | 109. Gallic acid   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 110. Salicyl alcohol   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 111. Caffeic acid  | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 112. Chlorogenic acid  | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 113. Vanillic acid   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 114. Syringic acid   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)   |
|   | 115. Sinapic acid  | <i>L. alpinus</i> , <i>L. japonicus</i> ,<br><i>L. krylovii</i> , <i>L. schoelleri</i><br><i>L. ornithopodioides</i>  | (Harney and Grant 1964)<br>(Araniti et al. 2014)  |
|   | 116. Ferulic acid  | <i>L. borbasii</i><br><i>L. ornithopodioides</i><br><i>L. corniculatus</i> leaves   | (Harney and Grant 1964)<br>(Araniti et al. 2014)<br>(Harney and Grant 1964)   |
| 117. 2-Hydroxybenzyl- $\beta$ -D-glucopyranoside (Isosalicin)               | <i>L. pusillus</i> aerial parts<br><i>L. corniculatus</i> aerial parts | (Golea et al. 2012)<br>(Golea et al. 2012)  |   |
| 118. Maltol 3- <i>O</i> -[6- <i>O</i> -benzoyl]- $\beta$ -D-glucopyranoside | <i>L. pusillus</i> aerial parts  | (Golea et al. 2012)   |   |



**Table 3. Sterols, alkylated sugars, cyanogenic glycosides and miscellaneous compounds:**

| Chemical class            | Compound Name  | Occurrence  | Reference  |
|---------------------------|--|---|--|
| Sterols                   | 119. $\beta$ -sitosterol   | <i>L. polyphyllus</i> roots<br><i>L. lalambensis</i> aerial parts<br><i>L. corniculatus</i> aerial parts<br><br><i>L. ornithopodioides</i> L. aerial parts<br><i>L. pusillus</i> aerial parts<br><i>L. creticus</i> roots | (Abdel-Kader et al. 2008)<br>(El-Youssef et al. 2008)<br>(El-Ghani et al. 2001; Dalmarco et al. 2010)<br>(Abdel-Kader et al. 2007)<br><br>(Golea et al. 2012)<br>(Ingham 1977) |
|                           | 120. $\beta$ -sitosterol-3-O- $\beta$ -D-glucopyranoside                       | <i>L. lalambensis</i> aerial parts<br><i>L. creticus</i> roots<br><i>L. pusillus</i> aerial parts   | (El-Youssef et al. 2008)<br>(Ingham 1977)<br>(Golea et al. 2012)   |
|                           | 121. $\beta$ -sitosterol-3-O-6'-palmitoyl- $\beta$ -D-glucopyranoside          | <i>L. pusillus</i> aerial parts   | (Golea et al. 2012)  |
|                           | 122. Stigmasterol glucoside  | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 123. Cholesterol   | <i>L. garcinii</i>  | (Ali et al. 2000; Ali et al. 2001)   |
|                           | 124. Taraxasterol  | <i>L. pusillus</i> aerial parts   | (Golea et al. 2012)  |
| Alkylated sugars          | 125. Butyl-O- $\alpha$ -L-rhamnoside   | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 126. Methyl-O- $\alpha$ -L-rhamnopyranoside                                    | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 127. Methyl-O- $\beta$ -L-rhamnopyranoside                                     | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 128. Ethyl-O- $\beta$ -D-glucopyranoside                                       | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 129. (+) D-pinitol   | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
| Cyanogenic glycosides     | 130. 2-( $\beta$ -D-glucopyranosyloxy)-2-methylpropionitrile (Linamarin)       | <i>L. ornithopodioides</i> aerial parts<br><i>L. creticus</i> roots<br><i>L. lalambensis</i> aerial parts   | (Abdel-Kader et al. 2007)<br>(Ingham 1977)<br>(El-Youssef et al. 2008)   |
|                           | 131. 2-( $\beta$ -D-glucopyranosyloxy)-2-methylbutyronitrile (Lotaustralin)    | <i>L. ornithopodioides</i> aerial parts<br><i>L. creticus</i> roots<br><i>L. lalambensis</i> aerial parts   | (Abdel-Kader et al. 2007)<br>(Ingham 1977)<br>(El-Youssef et al. 2008)   |
|                           | 132. 2-( $\beta$ -D-glucopyranosyloxy)-2-methylbutyronitrile (Epilotaustralin) | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
| Miscellaneous compounds   | 133. 1-Hexacosanol   | <i>L. polyphyllus</i> roots   | (Abdel-Kader et al. 2008)  |
|                           | 134. Heptadecanol  | <i>L. lalambensis</i> aerial parts  | (El-Youssef et al. 2008)   |
|                           | 135. Garceine  | <i>L. garcinii</i>  | (Ali et al. 2001)  |
|                           | 136. Garoside  | <i>L. garcinii</i>  | (Ali et al. 2001)  |
|                           | 137. Garthiol  | <i>L. garcinii</i>  | (Ali et al. 2001)  |
|                           | 138. Hexadecanoic acid   | <i>L. garcinii</i>  | (Ali et al. 2000; Ali et al. 2001)   |
|                           | 139. Isophytol   | <i>L. garcinii</i>  | (Ali et al. 2000; Ali et al. 2001)   |
|                           | 140. Phytone   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)  |
|                           | 141. Methyl hexadecanoate  | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)  |
|                           | 142. Ethyl hexadecanoate   | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)  |
|                           | 143. Methyl octadecanoate  | <i>L. ornithopodioides</i>  | (Araniti et al. 2014)  |
| 144. 4-Methyl-2-heptanone | <i>L. ornithopodioides</i>   | (Araniti et al. 2014)   |  |

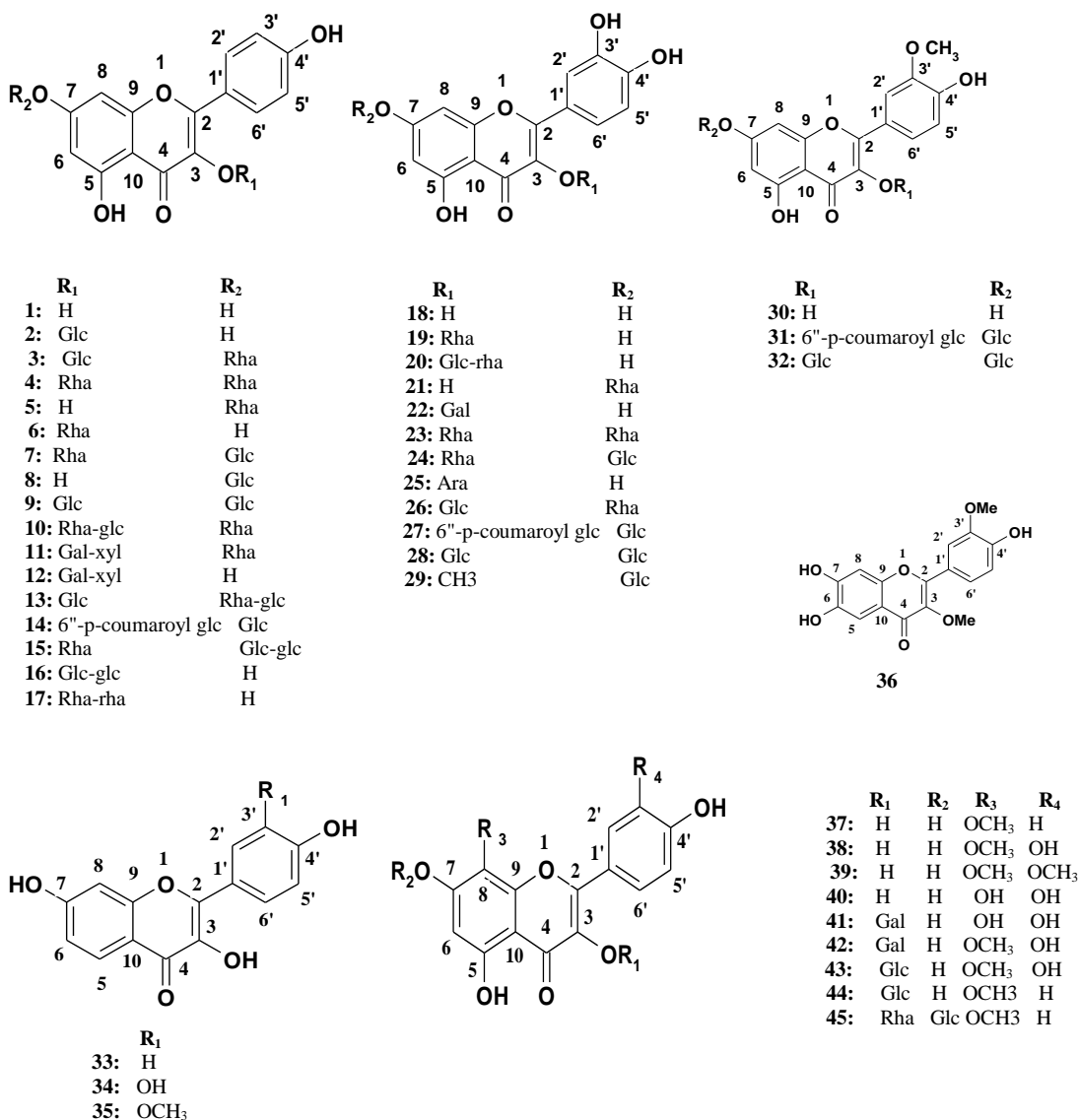


Figure 1. Chemical structures of flavonol derivatives isolated from genus *Lotus*.

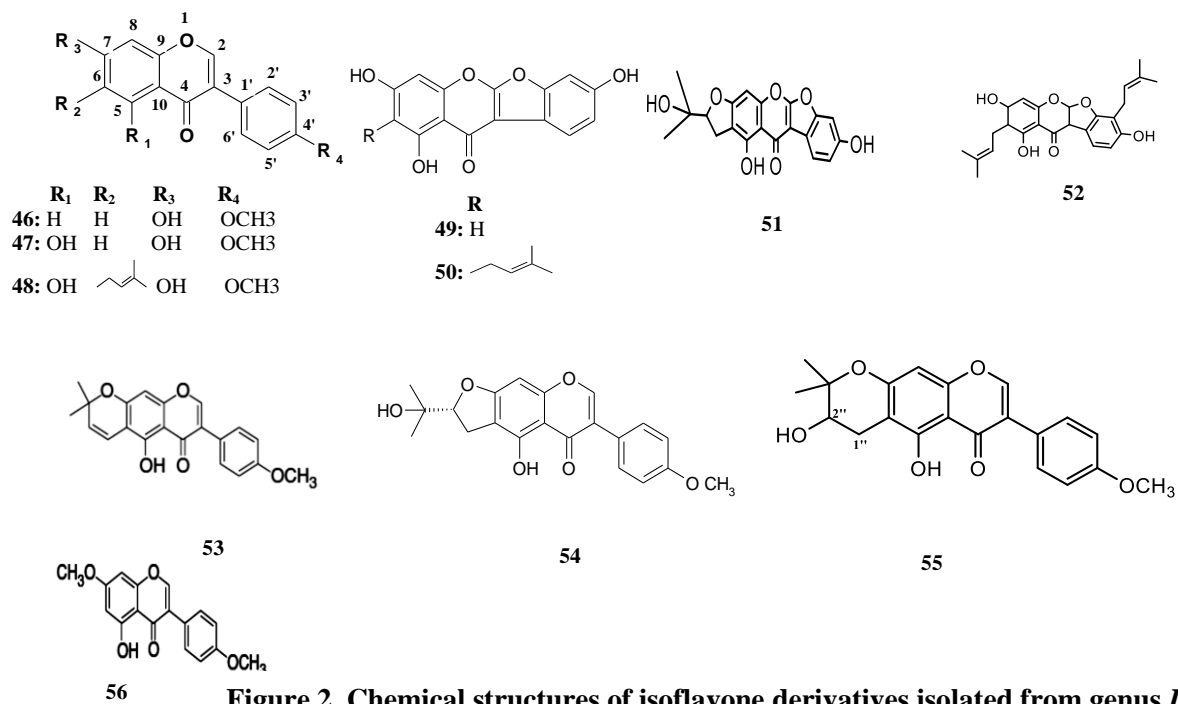


Figure 2. Chemical structures of isoflavone derivatives isolated from genus *Lotus*.

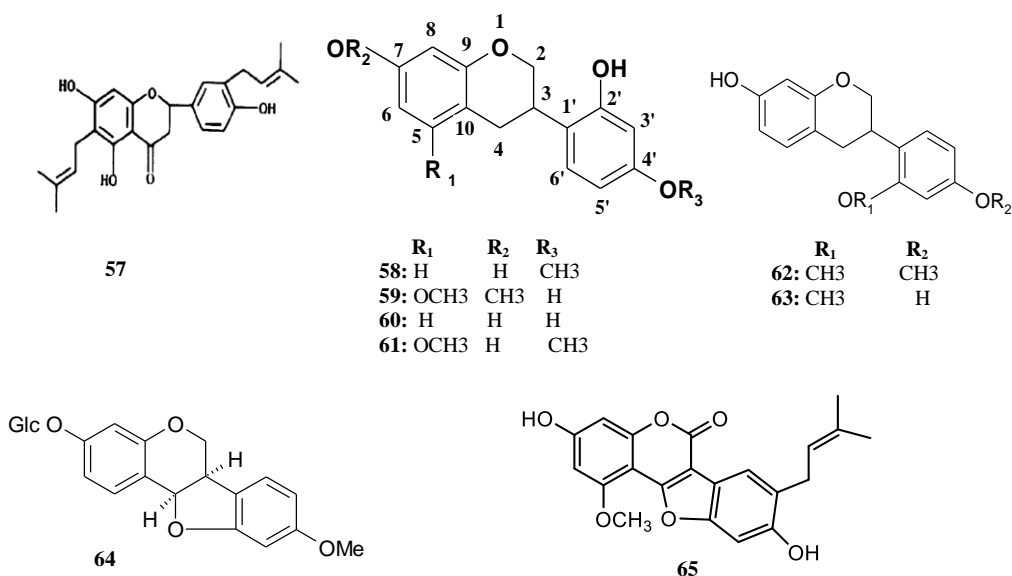


Figure 3. Chemical structures of flavanones, isoflavans, pterocarpan, coumestan isolated from genus *Lotus*.

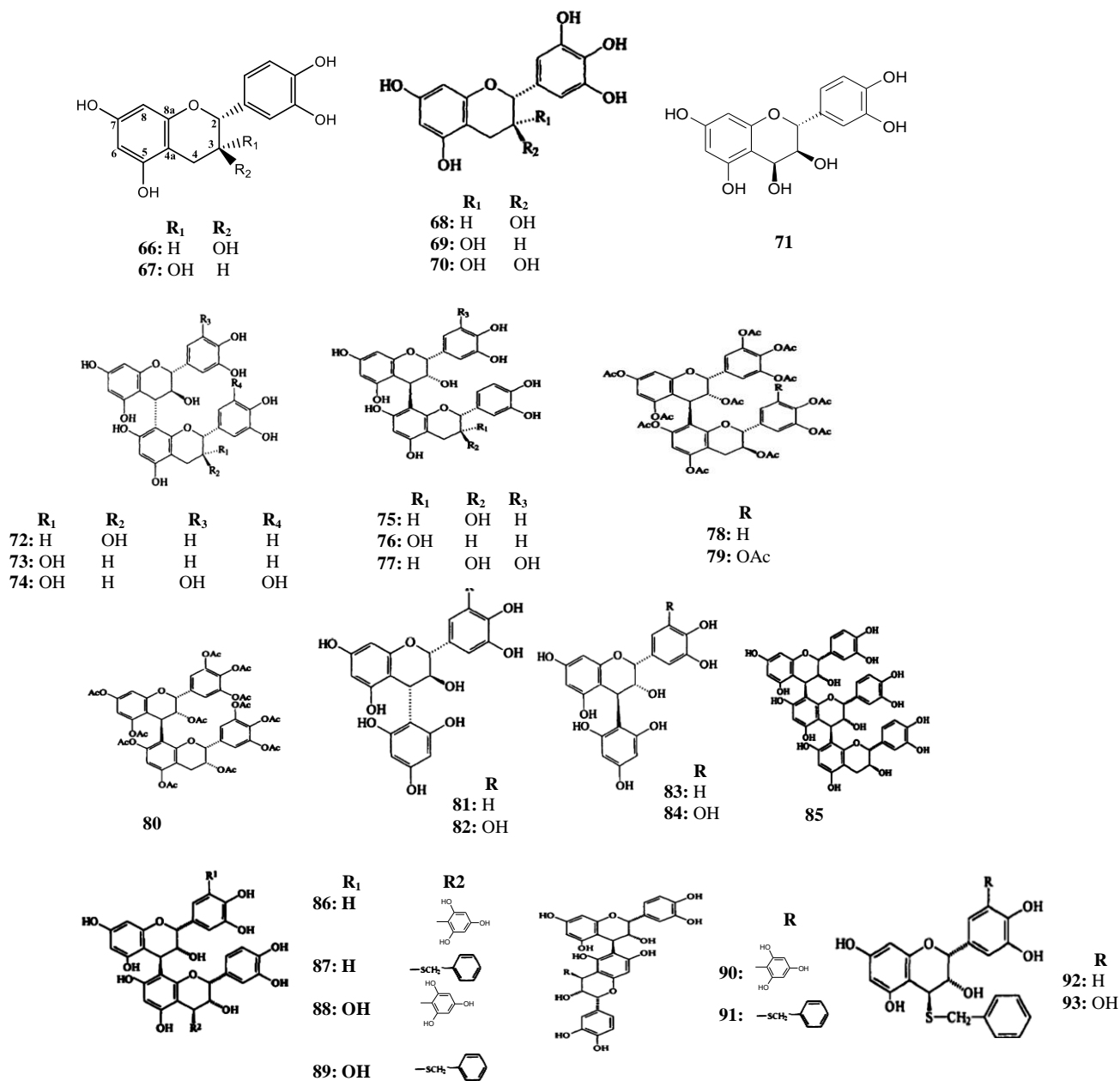


Figure 4. Chemical structures of flavans (Proanthocyanidins) isolated from genus *Lotus*.

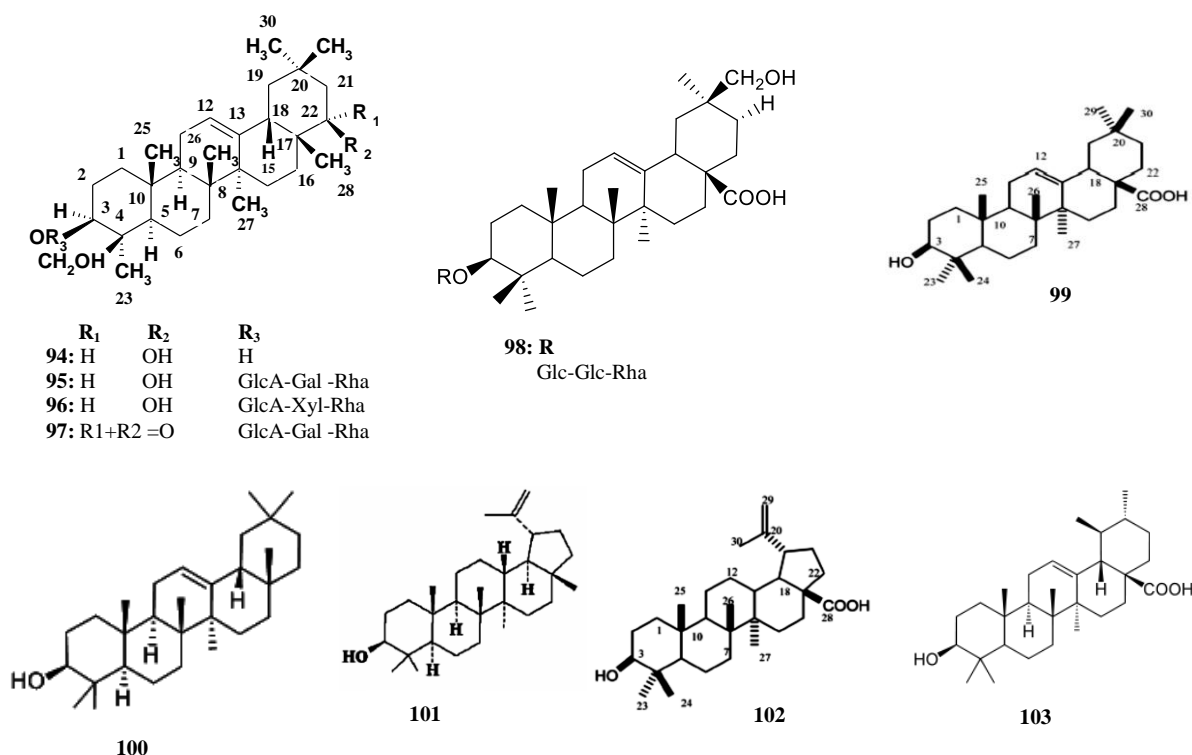


Figure 5. Chemical structures of triterpenoidal saponins isolated from genus *Lotus*.

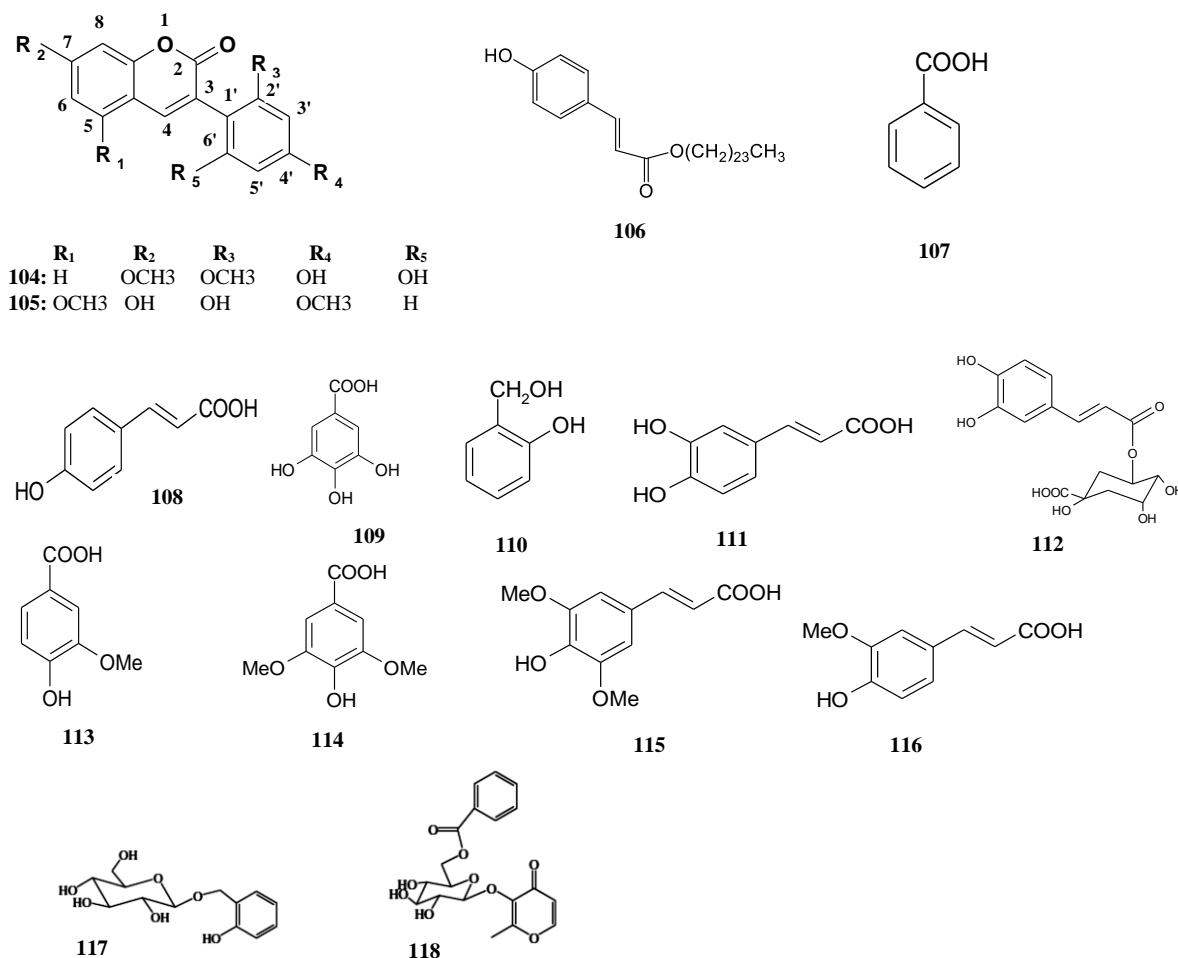


Figure 6. Chemical structures of coumarins and phenolic compounds isolated from genus *Lotus*.

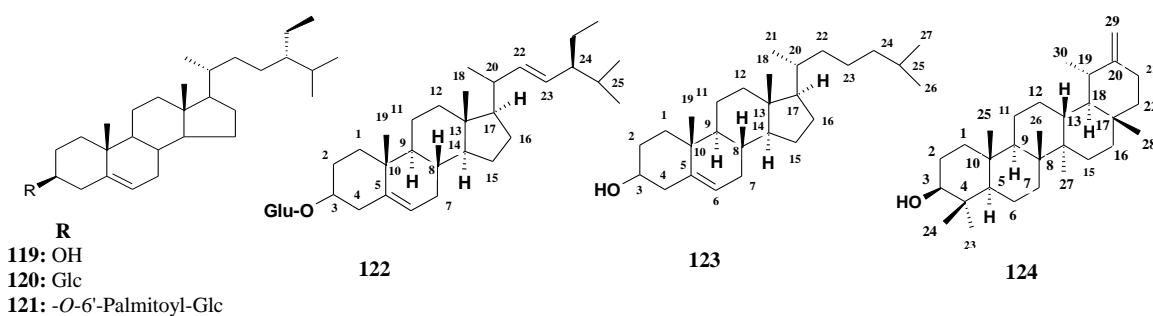


Figure 7. Chemical structures of sterols isolated from genus *Lotus*.

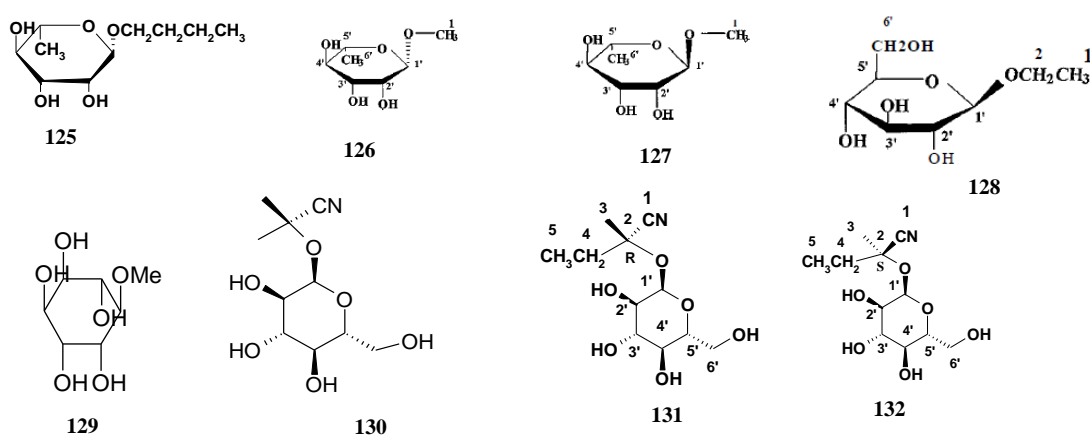


Figure 8. Chemical structures of alkyated sugars and cyanogenic glycosides isolated from genus *Lotus*.

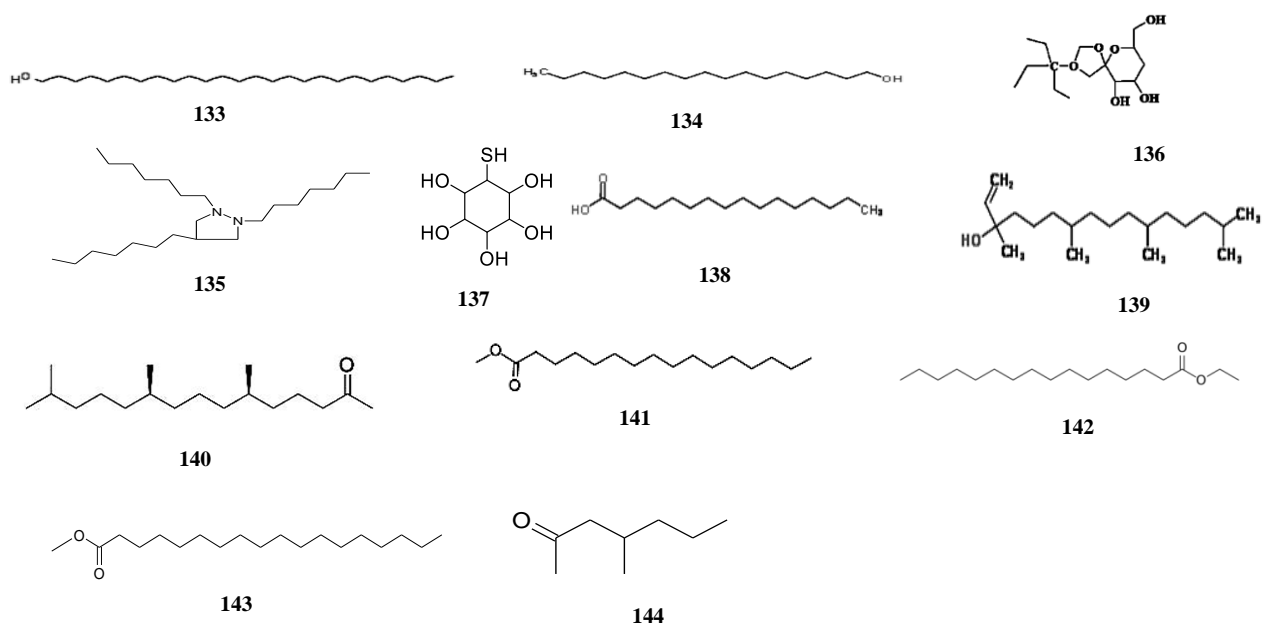


Figure 9. Chemical structures of miscellaneous compounds isolated from genus *Lotus*.

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