Review Article

Euonymus alatus: A Review on Its Phytochemistry and Antidiabetic Activity

Xifeng Zhai,1,2 George Binh Lenon,1 Charlie C. L. Xue,1 and Chun-Guang Li1,3

1Traditional & Complementary Medicine Program, School of Health Sciences, RMIT University, Bundoora, VIC 3083, Australia
2School of Pharmaceutical Sciences, Xi’an Medical University, Xi’an 710021, China
3National Institute of Complementary Medicine, Western Sydney University, Penrith, NSW 2751, Australia

Correspondence should be addressed to Chun-Guang Li; c.li@westernsydney.edu.au

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Euonymus alatus (E. alatus) is a medicinal plant used in some Asian countries for treating various conditions including cancer, hyperglycemia, and diabetic complications. This review outlines the phytochemistry and bioactivities of E. alatus related to antidiabetic actions. More than 100 chemical constituents have been isolated and identified from E. alatus, including flavonoids, terpenoids, steroids, lignans, cardenolides, phenolic acids, and alkaloids. Studies in vitro and in vivo have demonstrated the hypoglycemic activity of E. alatus extracts and its certain constituents. The hypoglycemic activity of E. alatus may be related to regulation of insulin signaling and insulin sensitivity, involving PPARγ and aldose reductase pathways. Further studies on E. alatus and its bioactive compounds may help to develop new agents for treating diabetes and diabetic complications.

1. Introduction

Euonymus alatus (E. alatus) is a medicinal plant used traditionally in many Asian countries, including China and Korea, for treating various conditions. It has long been used in China as a Chinese Materia Medica for pain and menstrual disorders. The first record of its clinical use in China was documented in Shen Nong Ben Cao Jing (The Classic of Herbal Medicine) written between 300 BC and 200 AD. Ben Cao Gang Mu (Compendium of Materia Medica, AD1578, written by Li Shizhen) later recorded its applications for vaginal bleeding, abdominal distention, and detoxification, and Ben Cao Jing Ji Zhu (Collective Notes to Canon of Materia Medica) recorded its use for abdominal pain, killing worms, and eliminating skin swelling caused by various reasons [1]. The interest in E. alatus has been increased recently largely due to the research on its bioactivities against cancer and diabetes. Recent studies have demonstrated a wide range of bioactivities of E. alatus, including hypoglycemic, antihypertensive [2], antitumor [3, 4], sedative [2], and regulation of blood lipid [5, 6] and immune functions [7]. There is also clinical evidence for its efficacy against hyperglycemia [8], chronic nephropathy [9], rheumatoid arthritis [10], cor pulmonale [11], bronchial asthma [12], anaphylactic disease [13, 14], urinary tract infection, and prostate diseases [15]. This short review outlines the phytochemistry of E. alatus and its pharmacology related to antidiabetic actions.

2. Phytochemistry

More than 128 chemical constituents have been isolated and identified from E. alatus. The main chemical classes include flavonoids, terpenoids, steroids, lignans, cardenolides, phe-noolic acids, and alkaloids.

2.1. Flavonoids. A total of 26 flavonoids have been isolated and identified from E. alatus. The main structure types include flavonoid, flavanone, and flavonol. The aglycones of flavonoid glycosides isolated from E. alatus include quercetin, kaempferol, naringenin, aromadendrene, and dihydroquercetin. The flavonoids are mainly distributed in the leaves and wings of E. alatus [16]. The structures of main flavonoids identified in E. alatus are listed in Tables 1–4.
Table 1: Quercetin and glycosides in E. alatus.

| Skeleton Number | Name                      | R₁    | R₂    | Reference       |
|-----------------|---------------------------|-------|-------|-----------------|
| 1               | Quercetin                 | H     | H     | [24, 39, 48–50] |
| 2               | Quercitrin                | 𝛼-L-Rhamnose | H     | [17, 49]       |
| 3               | Quercetin-7-O-𝛼-L-rhamnose| H     | 𝛼-L-Rhamnose | [50]           |
| 4               | Quercetin-3,7-O-𝛼-L-dirhamnose| H    | 𝛼-L-Rhamnose | [17, 50]      |
| 5               | Quercetin 3-D-galactoside  | 3-D-Galactose | H     | [17, 20]       |
| 6               | Rutin                     | 𝛼-L-Rhamnopyranosyl-(1 → 6)-𝛽-D-glucopyranose | H | [39] |

Table 2: Kaempferol and the glycosides in E. alatus.

| Skeleton Number | Name                      | R₁    | R₂    | Reference       |
|-----------------|---------------------------|-------|-------|-----------------|
| 7               | Kaempferol                | H     | H     | [18, 21, 48, 49]|
| 8               | Kaempferol-7-O-𝛼-L-rhamnose| H    | 𝛼-L-Rhamnose | [50]           |
| 9               | Kaempferol-3,7-O-𝛼-L-rhamnose (kaempferitrin) | H    | 𝛼-L-Rhamnose | [17, 50]      |
| 10              | Kaempferol-7-O-𝛽-D-glucoside| H    | 𝛼-L-Glucose | [50]            |
| 11              | Apigenin-3-O-L-rhamnopyranoside | 𝛼-L-Rhamnose | H | [49] |

Other flavonoids include catechin (19) [17–21], symplcoside (20) [17], quercetin-3-galactosyl-xyloside (21) [20], catechin lactone A (22) [17], dehydrodicatechin A (23) [17–21], 3-hydroxycomarinflavanol (24), 7,4'-dihydroxy-8-C-glucosylisoflavone (25) [22], and 5-hydroxy-6,7-dimethoxyflavone (26) [23].

2.2. Steroids. Eight steroids including sterols and sterones have been isolated and identified from E. alatus. The main structures of the steroids are shown in Table 5. Other steroids include 24R-methylphenol (34) and 𝛼-spinasterol (35) [22].

2.3. Terpenoids. The main terpenoids isolated from E. alatus include triterpenes and sesquiterpenes.

2.3.1. Triterpenes. Multiple types of triterpenes were found in E. alatus. Most of the triterpenes in E. alatus belong to lupane type and oleane type. Other types include hopane, ursane, and friedelane. Table 6 shows the lupane type and friedelane type triterpenes isolated from E. alatus.

Other triterpenes include oleanic acid (45), wilforlide A (46) [24], hop-(22)-29-en-3β-ol (47) [25], 3β-hydroxy-21αH-hop-22(29)-en-30-ol (48), 2α,3β-dihydroxyurs-12,19-dien-23,28-oic acid (49) [21], arborinone (50), taraxerol (51) and germanicol (52) [22], 11-keto-β-boswellic acid (53), acetyl 11-keto-β-boswellic acid (54), camaldulenic acid (55) [23], 3β,28,30-lup-20(29)-ene triol (56), 28,30-dihydroxy-3-oxolup-20(29)-ene (57), glut-5-en-3β-ol (58), maslinic acid (59), hederagenin (60), 3-oxo-1αlpha-methoxyolean-12-ene (61), 3β-hydroxy-1-oxo-olean-12-en-28-oic acid (62), ursolic acid (63), and 2α-hydroxy-ursolic acid (64) [26]. The structures of compounds 45–64 are shown in Figure 1.

2.3.2. Sesquiterpenes. Two new sesquiterpenes (65, 66) and two known ones were isolated from 95% ethanol extract of the stems of E. alatus. The known ones were identified as 6α,12-diacetoxy-2β,9α-di((b-furancarbonyloxy)-4α-hydroxy-1β-(2-methylbutanoyloxy)-β-dihydroagarofuran (67), 1α,2α,6β-triacetoxy-4β-hydroxy-9β-(β- furancarboxy-15-[(amethyl butyroyloxy)-β-dihydroagarofuran (68) [27]. The structures of sesquiterpenes isolated from E. alatus are shown in Figure 2.

2.4. Alkaloids. Five alkaloids have been isolated from E. alatus and identified as alatamine (69), alatusamine (70) and alatusinine (71) [28], 1β,2β,3α,8β,11-pentaacetoxy-4α-hydroxy-3α-(2-methylbutanoyl)-15-nicotinoyl-7-oxo-dihydroagarofuran (72), evonine (73), and neoevonine (74) [27]. The structures of alkaloids isolated from E. alatus are shown in Figure 3.
Table 3: Apigenin and glycoside in *E. alatus*.

| Skeleton | Number | Name                          | R<sub>1</sub> | R<sub>2</sub> | Reference |
|----------|--------|-------------------------------|---------------|---------------|-----------|
| ![Apigenin](image) | 12     | Apigenin                      | H             | H             | [48]      |
|          | 13     | Acacetin-7-O-rutinoside (Linarin) | Rutinose     | H             | [18]      |

Table 4: Flavanone and the glycoside in *E. alatus*.

| Skeleton | Number | Name                          | R<sub>1</sub> | R<sub>2</sub> | R<sub>3</sub> | R<sub>4</sub> | Reference |
|----------|--------|-------------------------------|---------------|---------------|---------------|---------------|-----------|
| ![Flavanone](image) | 14     | Dihydroquercetin              | OH            | H             | OH            | H             | [49, 50]         |
|          | 15     | Aromadendrene                 | OH            | H             | H             | H             | [19, 39, 49, 50] |
|          | 16     | Naringenin                    | H             | H             | H             | H             | [48–50]           |
|          | 17     | Naringin                      | H             | Neohesperidose | H             | H             | [18]       |
|          | 18     | Hesperidin                    | H             | Rutinose      | OH             | CH<sub>3</sub> | [50]      |

Table 5: Steroids in *E. alatus*.

| Skeleton | Number | Name                          | R  | References |
|----------|--------|-------------------------------|----|------------|
| ![Steroids](image) | 28     | β-Sitosterol                  | OH | [18, 20, 24, 39, 51, 52] |
|          | 29     | β-Sitosterone                 | =O | [51]       |
|          | 30     | Daucosterol                   | Glucose | [21, 48]   |
|          | 31     | Stigmaster-4-en-3-one (sitostenone) | H | [51, 52] |
|          | 32     | 6β-Hydroxy-stigmaster-4-en-3-one | OH | [51, 52] |
|          | 33     | Stigmast-4-en-3,6-dione       | =O | [51]       |

Table 6: Lupane type and friedelane type triterpenes in *E. alatus*.

**Lupane type**

| Lupane type | Number | Name                          | R<sub>1</sub> | R<sub>2</sub> | R<sub>3</sub> | R<sub>4</sub> | R<sub>5</sub> | References |
|-------------|--------|-------------------------------|---------------|---------------|---------------|---------------|---------------|------------|
| ![Lupane type](image) | 36     | Lupeol                        | OH            | H             | H             | CH<sub>3</sub> | CH<sub>2</sub> | [21, 48]   |
|          | 37     | Lupenone                      | =O            | H             | H             | CH<sub>3</sub> | CH<sub>2</sub> | [24]       |
|          | 38     | Betulin                       | OH            | H             | H             | CH<sub>2</sub>O | CH<sub>2</sub> | [24]       |
|          | 39     | Betulone                      | =O            | H             | H             | CH<sub>2</sub>O | CH<sub>2</sub> | [26]       |
|          | 40     | Betulinic acid                | OH            | H             | H             | COOH          | CH<sub>2</sub> | [23]       |
|          | 41     | Messagenin                    | OH            | OH            | H             | CH<sub>2</sub>O | O            | [26]       |
|          | 42     | (−)-Nepetidone                | OH            | OH            | OH            | CH<sub>3</sub> | O            | [48]       |

**Friedelane type**

| Friedelane type | Number | Name                          | R<sub>1</sub> | R<sub>2</sub> | Reference |
|-----------------|--------|-------------------------------|---------------|---------------|-----------|
| ![Friedelane type](image) | 43     | Epifriedelanol                | OH            | CH<sub>3</sub> | [18, 24, 39, 52] |
|                 | 44     | Friedelin                     | =O            | CH<sub>3</sub> | [20, 24]  |
2.5. Cardenolides. Kitanaka et al. [3] isolated three cytotoxic cardenolides from the woods of *E. alatus* and identified them as acovenosigenin A 3-O-α-L-rhamnopyranoside (75), euonymoside A (76), and euonymusoside A (77).

2.6. Lignans. Jeong et al. [29] identified three new lignans from 80% methanolic extract of *E. alatus* leaves and twigs, including ($\pm$)-threo-4,9,4′,9′-tetrahydroxy-3,7,3′,5′-tetramethoxy-8-O-8′-neolignan (78), ($\pm$)-threo-4,9,4′,9′-tetrahydroxy-3,5,7,3′-tetramethoxy-8-O-8′-neolignan (79), and (7R,8R,7′R)-(−)-lyoniresinol (80). The other known compounds identified include (+)-simulanol (81), (+)-dehydrodiconiferyl alcohol (82), (−)-simulanol (83), (−)-dehydrodiconiferyl alcohol (84), (+)-dihydrodehydrodiconiferyl alcohol (85), 7R,8S-guaiacylglycerol-8-O-4′-(coniferyl alcohol) ether (86), 7S,8R-guaiacylglycerol-8-O-4′-(coniferyl alcohol) ether (87), 7S,8R-syringylglycerol-8-O-4′-(sinapyl alcohol) ether (88), 7S,8S-guaiacylglycerol-8-O-4′-(sinapyl alcohol) ether (89), 7S,8S,4,9,9′-tri hydroxy-3,3′-dimethoxy-8-O-4′-neolignan (90), 7R,8R,4,9,9′-tri hydroxy-3,3′-dimethoxy-8-O-4′-neolignan (91), (+)-syringaresinol (92), de-4′-methylangabin (93), hedyotol C (94), threo-buddlenol B (95), hedyotisol C (96),...
Figure 2: Structures of sesquiterpenes (compounds 65–68) isolated from *E. alatus*.

Figure 3: Structures of alkaloids (compounds 69 and 71–74) isolated from *E. alatus*. 
and hedyotisol B (97). The structures of compounds 78–97 are shown in Figure 4.

2.7. Other Constituents. E. alatus also contains organic acids, esters, and aldehydes, as illustrated examples in Table 7.

In addition, 3,4-dihydroxybenzoic acid (114), p-propoxybenzoic acid (115), p-coumaric acid (116), ferulic acid (117), 1-feruloyl-β-D-glucoside (118), tetradecyl (E)-ferulate (119) [22], ethyl 2,4-dihydroxy-6-methylbenzoate (120), 4,4'-dimethoxy-1,1'-biphenyl (121) [23], squalene (122) [25], 1-octacosanol (123) [24], n-hexacosanoic acid (124) [18, 24], 1,30-triacontanediol (125), tetracosanoic acid (126), n-octane (127), and n-nonane (128) [21] were also isolated from E. alatus. In a study of essential oil from E. alatus by using GC-MS, 56 volatile components were identified. The main volatile components include carboxylic acid, aldehyde, ketone, terpenoid, and derivatives of oxygenated terpenoid. Among these the highest content was hexadecanoic acid (39.69%), followed by wintergreen (5.02%) [30].

3. Antidiabetic Activity

The effects of E. alatus extracts have been tested in vivo. In streptozotocin (STZ) treated diabetic rats, an aqueous extract of E. alatus reduced the body weight, the fasting plasma glucose level, and glucose tolerance. The serum levels of insulin, glucagon, cholesterol, and triglyceride were also reduced [31]. Similar results were obtained in high-fat plus low dose STZ diabetic rats, showing that E. alatus treated rats had lower levels of fasting blood glucose and insulin and decreased levels of blood lipids and inflammatory mediators (TNF-α, C-reactive protein), indicating that E. alatus can improve the glucose-lipid metabolism and insulin resistance in diabetic conditions [32]. Park et al. also demonstrated that an ethanol extract of E. alatus reduced the body weight, increased insulin sensitivity, and corrected the associated hyperinsulinemia and hyperlipidemia in high-fat diet-induced hyperglycemic and hyperlipidemic ICR mice [33].

The antihyperglycemic effect of E. alatus may involve a protection of functional islet β cells since E. alatus treated animals were shown with more positive staining of islet β cells than those in diabetic controls [34]. Other studies in ICR mice indicate that E. alatus may affect glucose and lipid homeostasis via a regulation of hepatic lipogenesis related genes (SREBP1a, FAS, and GAPT) and PPARγ gene expressions in perirenal fat. The plausible mechanism of hypoglycemic and hypolipidemic actions of E. alatus extract is illustrated in Figure 5 [33].

In addition, a study showed that E. alatus protected rats from experimental diabetic nephropathy induced by uninephrectomy plus STZ treatment, with 12-week administration of E. alatus extract and irbesartan (positive control) decreased HbA1c and pathological changes (extracellular matrix expansion and glomerulosclerosis) in kidney and improved blood lipids profile and kidney function; the effect was associated with a downregulation of transform growth factor β1 expression [35]. In addition, E. alatus was shown to inhibit polyol pathway, which is known to be associated with chronic diabetic complications such as neuropathy, nephropathy, and retinopathy [36].

Fang et al. studied the antidiabetic effects of different fractions of E. alatus extracts (including petroleum ether, diethyl ether, ethyl acetate, n-butanol, and water fraction) in alloxan-induced diabetic mice and high-fat diet diabetic mice and found that ethyl acetate fraction significantly reduced plasma glucose and glucose tolerance in both normal and diabetic mice [37] and also reduced total cholesterol and triglyceride contents and increased SOD activity in diabetic mice [37]. Further analysis revealed that the main components in the ethyl acetate fraction were flavonoids and phenolic acids, including quercetin and kaempferol, which were known for their antioxidant activities [37]. In another study, different extract fractions of E. alatus, including aqueous, diethyl ether, and ethyl acetate fractions, were tested in alloxan induced diabetic mice at a dose of 10 g/kg and it was found that the aqueous extract was the most active in decreasing blood glucose and lipid levels and improved glucose tolerance [6]. Thus, E. alatus may contain multiple active antidiabetic constituents. Similarly, a study on the hypoglycemic effects of six fractions of E. alatus extracts (including petroleum ether, ethyl acetate, n-butanol, water, residue, and rectified polysaccharide) in diabetic rats found that the fractions of petroleum ether, water, and ethyl acetate had significant antidiabetic effects. Fractions of n-butanol and rectified polysaccharide reduced blood creatinine, and other fractions reduced urea level. The residue fraction decreased the low-density lipoprotein (LDL) and cholesterol contents. The body weight was increased by the treatment with all fractions except rectified polysaccharide. These results indicate that different active compounds in these fractions may be responsible for the observed effects of E. alatus, including antidiabetic, antihyperlipidemic, kidney function improvement, blood viscosity decrease, and body weight affecting [38], and the active antidiabetic compounds are likely to be from the petroleum ether, water, and ethyl acetate fractions. In another study, an ethyl acetate extract of E. alatus was shown with hypoglycemic effect, and four compounds were isolated from this fraction and identified as p-hydroxybenzoic acid (EA-1), protocatechuic acid (EA-2), 4-hydroxy-3-methoxybenzoic acid (EA-3), and 3, 5-dimethoxy-4-hydroxybenzoic acid (EA-4) [8]. Others reported identification of six compounds with hyperglycemic activity from the 90% ethanol extracts of E. alatus, including armodadendrin, epifriedelanol, protocatechuic acid, β-sitosterol, quercetin, and rutin [39]. The active components in protecting experimental diabetic nephropathy as mentioned above have also been suggested to be concentrated in ethyl acetate and n-butanol fractions [36, 40], though the nature of these compounds is still not identified.

Jeong et al. (2015) studied the inhibitory effects of 23 compounds isolated from E. alatus on protein tyrosine phosphatases 1B (PTP1B) and α-glucosidase activities and found that lupenone, lupeol, taraxerol, p-propropoxybenzoic acid, 1-feruloyl-β-D-glucoside, and 3-hydroxycomarinflavanol exhibited inhibitory activity against PTP1B with IC50 values ranging from 5.6 to 18.4 μM. 24R-methyllophenol, arborinone, and p-propoxybenzoic acid were shown with a similar
Figure 4: Structures of compounds 78–97 isolated from leaves and twigs of *E. alatus*, modified from [29].
| Number | Name                                           | Chemical structure | Reference |
|--------|------------------------------------------------|--------------------|-----------|
| 98     | Usnic acid                                     | ![Usnic acid structure](image) | [24, 48]  |
| 99     | Protocatechuic acid                            | ![Protocatechuic acid structure](image) | [18, 39]  |
| 100    | 2-Hydroxy-4-methoxy-3,6-dimethylbenzoic acid   | ![2-Hydroxy-4-methoxy-3,6-dimethylbenzoic acid structure](image) | [48]     |
| 101    | Benzoic acid                                   | ![Benzoic acid structure](image) | [24, 48]  |
| 102    | Methyl 2,4-dihydroxy-6-methyl benzoate          | ![Methyl 2,4-dihydroxy-6-methyl benzoate structure](image) | [52]     |
| 103    | 2,4-Dihydroxy-3,6-dimethylbenzoate             | ![2,4-Dihydroxy-3,6-dimethylbenzoate structure](image) | [21, 52] |
| 104    | 7-Methoxy-4-methyl phthalide                   | ![7-Methoxy-4-methyl phthalide structure](image) | [52]     |
| 105    | Caffeine                                       | ![Caffeine structure](image) | [25]     |
| 106    | Caffeic acid                                   | ![Caffeic acid structure](image) | [49, 53] |
| 107    | Chlorogenic acid                               | ![Chlorogenic acid structure](image) | [54]     |
| 108    | Vanilllin                                      | ![Vanilllin structure](image) | [52]     |
| 109    | 5-Hydroxymethyl furfural                       | ![5-Hydroxymethyl furfural structure](image) | [25]     |
| 110    | Dulcitol                                       | ![Dulcitol structure](image) | [20]     |
| 111    | Grasshopper ketone                             | ![Grasshopper ketone structure](image) | [49]     |
Table 7: Continued.

| Number | Name      | Chemical structure          | Reference |
|--------|-----------|----------------------------|-----------|
| 112    | Suberone  | ![Suberone Chemical Structure](image) | [18]      |
| 113    | Syringin  | ![Syringin Chemical Structure](image) | [49]      |

Figure 5: Possible mechanism of hypoglycemic and hypolipidemic actions of *E. alatus* ethanol extract, modified from [33].

Studies on kaempferol and quercetin, the active constituents of *E. alatus*, demonstrated that these compounds improved insulin-stimulated glucose uptake in mature 3T3-L1 adipocytes [41]. Kaempferol and quercetin were shown to act as weak partial agonists in the PPARγ reporter gene assay, without inducing differentiation of 3T3-L1 preadipocytes as traditional PPARγ agonists. When kaempferol and quercetin were added together with the PPARγ agonist rosiglitazone, the 3T3-L1 differentiation was inhibited in a dose-dependent manner. Competitive ligand-binding assay confirmed that kaempferol and quercetin competed with rosiglitazone at the same binding pocket site as PPARγ. These compounds were also shown with significant inhibitory effects on NO production in response to lipopolysaccharide treatment in macrophage cells in which the PPARγ was overexpressed. These findings suggest that kaempferol and quercetin may act on multiple targets to ameliorate hyperglycemia [41].

Ivorra et al. studied the effects of daucosterol (β-sitosterol 3-β-glucoside) and its aglycone (β-sitosterol) on plasma insulin and glucose levels in normo- and hyperglycemic rats and found that oral administration of daucosterol or β-sitosterol increased the fasting plasma insulin levels. In addition, both compounds improved the oral glucose tolerance and increased glucose-induced insulin secretion [42].

3.1. Clinical Evidence. There have been limited clinical studies, mostly case reports, on the antidiabetic actions of *E. alatus* containing formulae (Table 8). In addition, a controlled trial, involving two groups of patients (40 patients in each group) with impaired glucose tolerance, showed that the group treated with diet and exercise intervention plus *E. alatus* formula for 1 month had significantly reduced blood glucose levels, compared to that in the diet and exercise control group. The effective rate was 80% in the *E. alatus* treatment group, compared to that of 55% in the control group [47]. It should be pointed out in most of these studies that *E. alatus* was not used alone, but in combination with other herbs; thus it is not clear if the observed effects are due to *E. alatus* or through interactions with other herbs. Thus, there may be potential bias in these findings. The current evidence for the clinical efficacy for treating diabetes is still weak. Nevertheless, these findings warrant further studies.

4. Conclusion

There is an increasing interest in *E. alatus* as a potential antidiabetic agent. More than 100 chemical constituents have been isolated and identified from *E. alatus*. The main chemical classes include flavonoids, terpenoids, steroids, phenylpropanoids, cardenolides, phenolic acids, and alkaloids. *E. alatus* has been demonstrated with hyperglycemic activity in vivo. The hypoglycemic activity of *E. alatus* may be related to its effects on insulin signaling and glucose metabolism, including stimulating insulin secretion, improving affinity
Table 8: Clinical studies of *E. alatus* for diabetic conditions.

| Number of patients | Preparation/compound | Treatment | Outcome measures/outcome | Reference |
|--------------------|----------------------|-----------|--------------------------|-----------|
| 57                 | *E. alatus* formula containing other herbs | Oral, daily per dose, for 3 months | Fasting blood glucose and 24 h urine glucose levels 30 cases with marked improvement 19 cases improved 8 cases no effect Total effective rate: 86% | [55] |
| 58                 | *E. alatus* formula containing other herbs | Oral, daily per dose, average medication for 37.2 days. | Fasting blood glucose level 21 cases remarkable effect 28 cases effective 9 cases no effect Effective rate: 84.4% | [56] |
| 100                | *E. alatus* formula containing other herbs | Oral, daily per dose, for 4 months | Fasting blood glucose and urine glucose levels, clinical symptoms 40 cases showed remarkable effect 51 cases effective 9 cases failed Total effective rate: 91% | [57] |
| 1                  | *E. alatus* decoction | Oral, daily per dose, for 20 days | Hypoglycemic effects Reduced blood and urine glucose and increased body weight | [58] |
| 80                 | *E. alatus* formula containing other herbs | Oral, daily per dose, for 30 days | Fasting blood glucose, 2 h postprandial blood glucose values Treatment group: 32 cases effective (80%) and 8 cases no effect (20%) Control group: 22 cases effective (55%) and 18 cases no effect (45%) | [47] |

of insulin and receptor, increasing insulin sensitivity and tolerance, and reducing insulin resistance. It may also act as PPARγ agonist and aldose reductase inhibitor. Further study on the bioactive compounds of *E. alatus* and its pharmacology may help to develop new agents for treating diabetes and diabetic complications.

**Abbreviations**

AR: Aldose reductase  
DPP-IV: Dipeptidyl peptidase IV  
*E. alatus*: Euonymus alatus  
GC-MS: Gas chromatography-mass spectrometry  
LDL: Low-density lipoprotein  
NO: Nitric oxide  
PPARγ: Peroxisome proliferator activated receptor gamma  
PTP1B: Protein tyrosine phosphatase 1B  
SOD: Superoxide dismutase  
STZ: Streptozotocin  
TNF-α: Tumor necrosis factor-alpha.

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**Competing Interests**

The authors declare that they have no competing interests.
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