Systematic Review of Chemical Constituents in the Genus *Lycium* (Solanaceae)

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Abstract: The *Lycium* genus is widely used as a traditional Chinese medicine and functional food. Many of the chemical constituents of the genus *Lycium* were reported previously. In this review, in addition to the polysaccharides, we have enumerated 355 chemical constituents and nutrients, including 22 glycerogalactolipids, 29 phenylpropanoids, 10 coumarins, 13 lignans, 32 flavonoids, 37 amides, 72 alkaloids, four anthraquinones, 32 organic acids, 39 terpenoids, 57 sterols, steroids, and their derivatives, five peptides and three other constituents. This comprehensive study could lay the foundation for further research on the *Lycium* genus.

Keywords: *Lycium* genus; chemical constituents; goji berry; Lycii cortex

1. Introduction

*Lycium* is one of the genera in the Solanaceae family, comprising 80 species, seven of which are found in China [1]. These species are all deciduous shrubbery, possessing a highly similar morphology and structure. The *Lycium* genus has been an important source of medicines and nutrient supplements for thousands of years in Southeast Asia, especially in China. Two species in particular, *Lycium barbarum* and *Lycium chinense*, have been widely used as traditional Chinese medicinal herbs for centuries and *L. barbarum* is currently widely cultivated in China.

Goji berries (Chinese name Gouqizi), which are derived from the fruits of *Lycium* Linn, have been used as traditional herbs for a long time in China for their benefits of replenishing vital essence to improve eyesight, nourish the liver and kidneys. Lycii cortex is a “heat cleansing” drug that is derived from the root bark of *L. chinense* and *L. barbarum* [2]. Goji berries and Cortex Lycii have demonstrated good therapeutic effects in some chronic diseases such as hectic fever, night sweats, cough, hemoptysis, and diabetes. Recently, medical research has indicated that these fruits and root bark have many pharmacological functions, such as antiglaucoma, immunoregulatory, antitumor, antioxidant, antiaging, neuroprotective, and blood sugar level reducing activities [3–10].

Traditionally, the berry and root bark available have been used as medicinal sources, as well as important components in some traditional Chinese patent medicines. They are not only famous medical herbs, but are also functional foods widely consumed in health-preserving cuisines, i.e., soups, congee, herbal tea, etc. People also eat the fresh leaves as vegetables. In particular, goji berries have become increasingly popular for improving overall well-being and as an anti-aging remedy. There are many goji derived-products on health food market, such as dried fruits, juice, goji wine and goji
Two valuable medicinal herbs, namely *L. barbarum* and *L. chinense*, have received remarkable attention due to their effective clinical therapy, especially in the anti-aging category. In addition, there are increasing numbers of publications about several other *Lycium* plants, i.e., *Lycium ruthenicum* [15,16]. Many researchers have focused great attention on the *Lycium* genus in recent years, and many chemical components from this genus have been isolated. Therefore, a comprehensive and systematic review on the chemical constituents of the *Lycium* genus is much needed.

Most of the published reviews not only covered chemical composition, but also summarized the pharmacology, clinical studies, safety, toxicology and adverse actions of *L. barbarum* or *L. chinense* [17–19]. The aim of this review was to focus on chemical constituents in different parts of plants from different species in *Lycium* genus, especially small molecular compounds with updated research reports. This paper comprehensively summarizes the reports of constituents from the genus *Lycium*. Up to 2016, at least 355 constituents were reported from different species in the *Lycium* genus and different parts (fruits, root bark, leaves, seeds, and flowers) of the plant. This review describes the advances in the phytochemistry of the genus *Lycium* from 1975 to 2016, based on the 142 cited references. The reported constituents can be classified as glycerogalactolipids, phenylpropanoids, coumarins, lignans, flavonoids, amides, alkaloids, anthraquinones, organic acids, terpenoids, sterols, steroids, peptides, and other constituents. The aim of this review is to illustrate the recent advances in the characterization of the *Lycium* genus. The results, based on these phytochemical studies, could lay a solid foundation for better understanding of pharmacological activities of *Lycium* and quality assessment.

**2. Constituents**

Until now, other than polysaccharides, more than 355 compounds have been isolated and identified from the *Lycium* genus. The small molecules can be assigned to various classes of glycerogalactolipids, phenylpropanoids, coumarins, lignans, flavonoids, amides, alkaloids, anthraquinones, organic acids, terpenoids, sterols, steroids and their derivatives, and peptides. Beyond that, other groups of compounds have also been reported. The proportion of different compounds of the *Lycium* genus is show in Figure 1. Their structures are shown below, and their names and corresponding plant sources are included in this paper.

![Figure 1. Different subtype comparison of the 355 constituents reported from *Lycium* genus.](image-url)
2.1. Macromolecules in the Lycium Genus

Polysaccharides

Polysaccharides are the most important group of substances in the goji berry, which are estimated to comprise 5–8% of the dried fruits [20], 1.02–2.48% of the raw material [21–23]. More than 40 polysaccharides, with a molecular weight range of 8–241 kDa, were isolated from the fruit of *L. barbarum*, *L. chinense* and *L. ruthenicum*. Two, LRLP4-A and LBLP5-A, were isolated from the leaves of *L. ruthenicum*. The polysaccharides share a glycan-O-Ser glycopeptide structure and contain galacturonic acid, 18 amino acids, and nine monosaccharides, namely, xylose (Xyl), glucose (Glc), arabinose (Ara), rhamnose (Rha), mannose (Man), galactose (Gal), fucose (Fuc), galacturonic acid (GalA), glucuronic acid (GlcA) [24]. The molar ratios of the polysaccharides are shown in Table 1. The polysaccharides can be isolated and purified by water extract alcohol precipitation, DEAE ion-exchange cellulose, gel-permeation chromatography, high performance liquid chromatography (HPLC). Sevage method and organic reagents were used to remove proteins, pigments and other impurities. The structural composition of a LBP can be studied by SDS-PAGE gel electrophoresis, high performance size exclusion chromatography (HPSEC), gas-chromatographic–mass-spectrometry (GC-MS), nucleic magnetic resonance (NMR), and matrix-assisted laser desorption ionization-time of flight-mass spectrometry (MALDI-ToF-MS) [18,21,25].

| LBPs | Molar Ratio | Source | Reference |
|------|-------------|--------|-----------|
| LbGp1 | Ara:Gal:Glc = 2.5:1.0:1.0 | *L. barbarum* | [26] |
| LbGp2 | Ara:Gal = 4:5 | *L. barbarum* | [27] |
| LbGp3 | Ara:Gal = 1:1 | *L. barbarum* | [28,29] |
| LbGp4 | Ara:Gal:Rha:Glc = 1.5.2.5.0.43:0.23 | *L. barbarum* | [28,30] |
| LbGp5 | Rha:Ara:Yxl:Gal:Man:Glc = 0.33:0.52:0.42:0.94:0.85:1 | *L. barbarum* | [28] |
| LbGp5B | Rha:Ara:Glc:Gal = 0.1:1:1:2.0:3 | *L. barbarum* | [31] |
| LBP3p | Rha:Ara:Yxl:Gal:Man:Glc = 1.25:1.10:1.76:1:1.95:2.12 | *L. barbarum* | [32] |
| LBPc2 | Xyl:Rha:Man = 8.8:2.3:1 | *L. barbarum* | [33] |
| LBPc1 | - | *L. barbarum* | [33] |
| LBP1a1 | heteroglycan | *L. barbarum* | [33] |
| LBP1a2 | - | *L. barbarum* | [34] |
| LBP3a-1 | Glc | *L. barbarum* | [34] |
| LBP3a-2 | GalA | *L. barbarum* | [34] |
| LBPF1 | - | *L. barbarum* | [35] |
| LBPF2 | - | *L. barbarum* | [35] |
| LBPF3 | - | *L. barbarum* | [35] |
| LBPF4 | - | *L. barbarum* | [35] |
| LBPF5 | Ara, Man, Xyl, Glu, Rha | *L. barbarum* | [35,36] |
| LBPF6 | - | *L. barbarum* | [36] |
| LBPF4 | - | *L. barbarum* | [37] |
| LBPF1 | Rha:Ara:Yxl:Gal:Man:GalA = 1:7.85:0.37:0.65:3.01:8.16 | *L. barbarum* | [22] |
| WSP1 | Rha:Fuc:Ara:Yxl:Man:Gal:Glc = 1:6.0:2:51.4:48:8:1.2:25:9:7.3 | *L. barbarum* | [23] |
| AGP | Rha:Ara:Yxl:Gal:Glc:GalA = 3.3:42.9:0.3:44.3:2.4:7.0 | *L. barbarum* | [38] |
| LPB-IV | Rha:Ara:Yxl:Glc:Gal = 1.61:3.82:3.44:7.54:1.00 | *L. barbarum* | [39] |
| LbGp1 | Ara:Gal = 5.6:1 | *L. barbarum* | [40] |
| LBP-s-1 | Rha:Ara:Yxl:Man:Glu:Gal:GalA = 1:00:3.4:1.25:1.26:1.91:7.05:15.28 | *L. barbarum* | [41] |
| p-LBP | Rha:Fuc:Ara:Gal:Glc:Yxl:GalA = 1:00:6.44:54.84:22.98:4.05:2.95:136.98:3.35 | *L. barbarum* | [42] |
| Cp-2-A | Ara:Gal:Man:Rha:Glu = 6:0.2:2.71:1:00:0.70:0.67 | *L. chinense* | [43,44] |
| Cp-2-B | Ara:Gal = 1:0.96 | *L. chinense* | [43,44] |
| Hp-2-A | Ara:Gal = 5:2:1 | *L. chinense* | [43,44] |
| Hp-2-B | Ara:Gal = 7:9:1 | *L. chinense* | [43,44] |
L. barbarum, illustrated in Figure 2, were isolated from the root bark of L. chinense.

### 2.2. Glycerogalactolipids

#### 2.2.1. Glycerogalactolipids 1–22

At present, 17 compounds of this type, a series of glycerogalactolipids 1–17, listed in Table 2, have been isolated and identified. Compounds 1–15 have been isolated and identified from the fruits of *L. barbarum* [52], whereas 16 and 17 were isolated from the fruits of *L. chinense* [53]. Compounds 18–22, illustrated in Figure 2, were isolated from the root bark of *L. chinense* [54,55].

#### Table 2. Chemical structures of compounds 1–17.

| No. | Compounds                        | R₁         | R₂            | R₃            | Source               |
|-----|----------------------------------|------------|---------------|---------------|----------------------|
| 1   | Glycerogalactolipids A           | Palmitoyl  | Linolenoyl    | Linolenoyl    | *L. barbarum*        |
| 2   | Glycerogalactolipids B           | Palmitoyl  | Linolenoyl    | Linoleoyl     | *L. barbarum*        |
| 3   | Glycerogalactolipids C           | Palmitoyl  | Linolenoyl    | Palmitoyl     | *L. barbarum*        |
| 4   | Glycerogalactolipids D           | Palmitoyl  | Linoleoyl     | Palmitoyl     | *L. barbarum*        |
| 5   | Glycerogalactolipids E           | Palmitoyl  | Palmitoyl     | Palmitoyl     | *L. barbarum*        |
| 6   | Glycerogalactolipids F           | Palmitoyl  | Palmitoyl     | H             | *L. barbarum*        |
| 7   | Glycerogalactolipids G           | Linolenoyl | Linolenoyl    | H             | *L. barbarum*        |
| 8   | Glycerogalactolipids H           | Linolenoyl | Linoleoyl     | H             | *L. barbarum*        |
| 9   | Glycerogalactolipids I           | Palmitoyl  | Linolenoyl    | H             | *L. barbarum*        |
| 10  | Glycerogalactolipids J           | Palmitoyl  | Linoleoyl     | H             | *L. barbarum*        |
| 11  | Glycerogalactolipids K           | Palmitoyl  | Oleoyl        | H             | *L. barbarum*        |
| 12  | Glycerogalactolipids L           | Stearoyl   | Linoleoyl     | H             | *L. barbarum*        |
| 13  | Glycerogalactolipids M           | Palmitoyl  | Linolenoyl    | –             | *L. barbarum*        |
| 14  | Glycerogalactolipids N           | Palmitoyl  | Linoleoyl     | –             | *L. barbarum*        |
| 15  | Glycerogalactolipids O           | Palmitoyl  | Oleoyl        | –             | *L. barbarum*        |
| 16  | Glycerogalactolipids P           | Linolenoyl | Linolenoyl    | –             | *L. chinense*        |
| 17  | Glycerogalactolipids Q           | Linoleoyl  | Linolenoyl    | –             | *L. chinense*        |
2.2.2. Phenylpropanoids 23–51

Four phenylpropanoids 23–26, namely E-cinnamic acid (23), E-ferulic acid (24), E-coniferol (25) and isoscopoletin (26) are obtained from wolfberries [56–58]. Four phenylpropanoids, namely scopolin (27), fabiatrin (28), lyciumin (29), and 9-O-(β-D-glucopyranosyl)lyoniresinol (30) are obtained from the root bark of L. chinense [59–61]. 1-O-Methyl-4-O-p-E-coumaroyl-α-L-rhamnopyranoside (31) is obtained from the fruits of L. ruthenicum [62]. The chemical structures of compounds 23–33 are listed in Table 3 and Figure 3. In 2016, 11 phenylpropanoids 32–42 were isolated for the first time by Zhou et al. from Lycium [56], including 1-O-E-feruloyl-6-O-β-D-xylopyranosyl-β-D-glucopyranoside (32), 6-O-E-feruloyl-2-O-β-D-glucopyranosyl-α-D-glucopyranoside (33), 1-O-E-feruloyl-β-D-glucopyranoside (34), ethyl-4-O-β-D-glucopyranosyl-E-ferulate (35), ethyl E-ferulate (36), E-sinapinic acid (37), syringenin (38), Z-ferulic acid (39), phloretic acid (40), dihydroferulic acid (41), and ethyl dihydroferulate (42), along with the nine new lycibarbarphenylpropanoids A–I (compounds 43–51) listed in Table 4.

Table 3. Chemical structures of compounds 26–28.

| No. | Compounds     | R₁(R)        | R₂        | Source       |
|-----|---------------|--------------|-----------|--------------|
| 26  | Isoscopoletin | OCH₃         | OH        | L. barbarum  |
| 27  | Scopolin      | O-β-D-Glc    | OCH₃      | L. chinense  |
| 28  | Fabiatrin     | O-β-D-Glc⁵,β-D-Xyl | OCH₃ | L. chinense  |
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2.2.3. Coumarins 52–61

Nine coumarins, namely E-p-coumaric acid (52), Z-p-coumaric acid (53), fabiatrin (55), scopolin (56), and scopoletin (57), have been reported, and three new coumarins, 6-O-E-p-coumaroyl-2-O-β-D-glucopyranosyl-α-D-glucopyranoside (58), ethyl-4-O-β-d-glucopyranosyl-E-p-coumarate (59), ethyl E-p-coumarate (60) and lycibarbarcoumarin A (61), have been obtained from the fruits of L. barbarum in 2016 [56]. Compounds 55 and 56 were isolated from the root bark and fruits of L. chinense [61], while 52—54 and 57 were isolated from the fruits of L. barbarum [63]. The chemical structures of these coumarins are listed in Figure 4 and Table 5.
2.2.4. Lignans 62–74

Eight lignans, including pinoresinol (62), arctigenin (63), arctiin (64), medioresinol (65), syringaresinol (66), 4-O-(β-D-glucopyranosyl)syringaresinol (67), threo-1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (68), and erythro-1,2-bis(4-hydroxy-3-methoxyphenyl)-1,3-propanediol (69), have been isolated from the fruits of *L. barbarum* [56]. (β)-Lyoniresinol 3-O-β-D-glucopyranoside (70), lyciumlignan A (71), lyciumlignan B (72), lyciumlignan C (73), and (7R,8S)-4,9,9′-trihydroxy-3,3′-dimethoxy-7′-en-8,4′-oxyneolignan-7-O-β-D-glucopyranoside (74) were obtained from the root bark of *L. chinense* [54,60,64]. Among them, 65–70 were first isolated from the fruits of *L. barbarum* in 2016 [56]. The chemical structures of these lignans are listed in Figure 5 and Table 6.

**Table 6. Chemical structures of compounds 62 and 65–67.**

| No. | Compounds                  | R₁ | R₂ | R₃ | R₄ | Source          |
|-----|----------------------------|----|----|----|----|-----------------|
| 62  | Pinoresinol                | H  | OH | H  | H  | *L. barbarum*   |
| 65  | Medioresinol               | H  | OH | OCH₃| OCH₃| *L. barbarum*   |
| 66  | Syringaresinol             | OCH₃| OH | OCH₃| OCH₃| *L. barbarum*   |
| 67  | 4-O-(β-D-glucopyranosyl)syringaresinol | OCH₃| O-β-D-Glc | OCH₃| OCH₃| *L. barbarum*   |
2.2.5. Flavonoids 75–106

Twenty-seven flavonoids 75–101 have been reported from the genus Lycium, are listed in Tables 7 and 8 and Figures 6 and 7. Compound 75 was isolated from the flowers of L. barbarum [58], while 76–83 were identified from the fruits of L. barbarum [62,65–69]. Compound 84 was isolated from the fruits of L. chinense [70], whereas 85–91 were isolated from the leaves of L. chinense [62,66,68,71]. Compound 92 and 93 were isolated from the leaves of L. halimifolium [72]. Compounds 94–98 were isolated from the fruits of L. ruthenicum [16,62]. Compounds 99–101 were isolated from the root bark of L. chinense [54,73,74]. Additionally, Zhou et al. isolated five isoflavonoids, namely derrone (102), alpinumisoflavone (103), auriculasin (104), maackinan (105) and maackiain (106) from the fruits of L. barbarum [56,75,76].

Table 7. Chemical structures of compounds 75–80, 82–83, 85–87 and 89–93.

| No. | Compounds | R₁ | R₂ | R₃ | Source |
|-----|------------|----|----|----|--------|
| 75  | Quercitrin | OH | OH | OH | – | L. barbarum |
| 76  | Kaempferol | OH | OH | OH | – | L. barbarum |
| 77  | Quercetin | OH | OH | OH | – | L. barbarum |
| 78  | Rutin | OH | OH | OH | – | L. barbarum |
| 79  | Narcissoside | OH | OH | O-β-D-Glc | – | L. barbarum |
| 80  | 7-O-(β-D-Glucopyranosyl)-rutin | O-β-D-Glc | OH | O-β-D-Glc | – | L. barbarum |
| 82  | 7-O-(β-D-Glucopyranosyl)-nicotifolin | O-β-D-Glc | O-β-D-Glc | – | L. barbarum |

Figure 5. Chemical structures of compounds 63–64 and 68–74.
Table 7. Cont.

| No. | Compounds                                                                 | \( R_1 \)       | \( R_2 \)       | \( R_3 \)       | Source          |
|-----|---------------------------------------------------------------------------|-----------------|-----------------|-----------------|----------------|
| 83  | 7-O-(β-D-Glucopyranosyl)-3-O-[β-D-glucopyranosyl]-{1 → 2}-β-D-galactopyranosyl | O-β-D-Glc       | O-β-D-Glc       | –               | L. barbarum    |
| 85  | Luteolin                                                                 | OH              | OH              | OH              | L. chinense    |
| 86  | Acacetin                                                                 | OH              | H               | OCH\(_3\)        | L. chinense    |
| 87  | 7-O-(β-D-Glucopyranosyl)-3-O-[β-D-glucopyranosyl]-{1 → 2}-β-D-galactopyranosyl | O-β-D-Glc       | OH              | O-β-D-Glc\(_2\)-β-D-Glc | L. chinense    |
| 89  | 7-O-[α-L-Rhamnopyranosyl]-{1 → 6}-β-D-glucopyranosyl]-acacetin | O-β-D-Glc\(_2\)-α-L-Rha | H              | OCH\(_3\)        | L. chinense    |
| 91  | Apigenin                                                                | OH              | H               | OH              | L. chinense    |
| 92  | Isoquercitrin                                                            | OH              | OH              | O-β-D-Glc       | L. halimiifolium |
| 93  | Nicotiflorin                                                            | OH              | O-β-D-Glc\(_2\)-α-L-Rha | –               | L. halimiifolium |

Figure 6. Chemical structures of compounds 81, 84, 88 and 94.

Table 8. Chemical structures of compounds 95–98.

| No. | Compounds                                                                 | \( R_1 \)       | \( R_2 \)       | Source          |
|-----|---------------------------------------------------------------------------|-----------------|-----------------|----------------|
| 95  | 5-O-(β-D-Glucopyranosyl)-3-O-[4-O-p-E-coumaroyl-α-L-rhamnopyranosyl]-{1 → 6}-β-D-glucopyranosyl]-peonidin | H               | OH              | L. ruthenicum   |
| 96  | 5-O-(β-D-Glucopyranosyl)-3-O-[4-O-p-E-coumaroyl-α-L-rhamnopyranosyl]-{1 → 6}-β-D-glucopyranosyl]-peonidin | OH              | OH              | L. ruthenicum   |
| 97  | 5-O-(β-D-Glucopyranosyl)-3-O-[4-O-p-Z-coumaroyl-α-L-rhamnopyranosyl]-{1 → 6}-β-D-glucopyranosyl]-malvidin | OCH\(_3\)       | OH              | L. ruthenicum   |
| 98  | 5-O-(β-D-Glucopyranosyl)-3-O-[4-O-p-E-(β-D-glucopyranoside)-coumaroyl-α-L-rhamnopyranosyl]-{1 → 6}-β-D-glucopyranosyl]-peonidin | OH              | O-β-D-Glc       | L. ruthenicum   |
2.2.6. Amides 107–143

Sixteen amides 107–122 have been isolated from the root bark of *L. chinense* [9,54,60,77–80], 19 amides (123–141) have been isolated from the fruits of *L. barbarum* [81–88]. Meanwhile, two cerebrosides 142 and 143 have been obtained from fruits of *L. chinense* [89]. The chemical structures of these amides are shown in Figure 8.
Aurantiamide acetate

(E)-N-(4-Acetamidobutyl)-2-[4,5-dihydroxy-2-[3-[2-(4-hydroxyphenyl)ethylamino]-3-oxopropyl]-phenyl]-3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enamide R=H

(E)-N-(4-Acetamidobutyl)-2-[4,5-dihydroxy-2-[3-[2-(4-hydroxyphenyl)ethylamino]-3-oxopropyl]-phenyl]-3-(4-hydroxy-3,5-dimethoxyphenyl)prop-2-enamide R=OCH3

(1R,2S)-1-(3,4-Dihydroxyphenyl)-7-hydroxy-N2,N3-bis(4-hydroxyphenethyl)-6,8-dimethoxy-1,2-dihydro-naphthalene-2,3-dicarboxamide

(1S,2R)-N3-(4-Acetamidobutyl)-1-(3,4-dihydroxy-phenyl)-7-[((E)-3-[((E))-3-((4-hydroxyphenethyl)-amino]-3-oxoprop-1-en-1-yl}-2,3-dihydro-naphthalene-2,3-dicarboxamide

(2,3-E)-3-{(2,3-E)}-2-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-2,3-dihydrobenzo[6][1,4]dioxin-6-yl}-N-(4-hydroxyphenethyl)-acrylamide

(2,3-E)-3-{(2,3-E)}-2-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-2,3-dihydrobenzo[6][1,4]dioxin-6-yl}-N-(4-hydroxyphenethyl)-acrylamide

(2,3-E)-3-{(2,3-E)}-2-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-2,3-dihydrobenzo[6][1,4]dioxin-6-yl}-N-(4-hydroxyphenethyl)-acrylamide

Indole glycoside

Figure 8. Cont.
Figure 8. Cont.
2.2.7. Alkaloids 144–215

To date, 72 alkaloids have been identified, which can be classified into five categories: nortropane, imidazole, piperidine, pyrrole, spermine, tropane, and other alkaloids.

Nortropane Alkaloids

Fourteen nortropane alkaloids 144–157, shown in Figure 9, have been isolated from the root bark of *L. chinense* [90].

![Figure 8. Chemical structures of compounds 107–143.](image)

![Figure 9. Cont.](image)
Imidazole Alkaloids

Six imidazole alkaloids 158–162 were detected in the leaves of L. cestroides [91]: Meanwhile, one imidazole, Na-[(E)-cinnamoyl]histamine (163), was obtained from the leaves of L. barbarum [66], listed in Figure 10.

Piperidine Alkaloids

5-hydroxy-2-pyridylmethyl ketone (164), methyl 5-hydroxy-2-pyridinecarboxylate (165), fagomine (166), and 6-deoxyfagomine (167), listed in Figure 11, have been isolated and identified from the genus Lycium; among them. Compounds 164 and 165 are from the fruits of L. barbarum [92], and 166 and 167 are from the root bark of L. chinense [90].

Pyrrole Alkaloids

Thirteen pyrrole alkaloids 168–180 have been isolated from the fruits of L. chinense [93–95]. Likewise, 2-formyl-5-hydroxymethylpyrrole (181) and 2-formyl-5-methoxymethylpyrrole (182) were isolated from the fruits of L. barbarum [92]. Two pyrrolidine alkaloids, alkaloid I (183) and alkaloid II (184), are obtained from the root bark of L. chinense [96]. The chemical structures of these pyrrole alkaloids are listed in Figure 12.
Spermine Alkaloids

Nineteen spermine alkaloids have been found in the genus *Lycium*. Kukoamines A (185) and kukoamines B (186) are from the root bark of *L. chinense* [97,98], while *N*1-*caffeoyl*-N3-*dihydrocaffeoyl* spermidine (187) and lyrium spermidine A (188) are from the fruits of *L. ruthenicum* [62,99], listed in Figure 13. Another 15 spermine alkaloids, lycibarbarspermidine A–O (189–203), listed in Tables 9 and 10 and Figures 13–15, are from *L. barbarum* [100].
Figure 13. Chemical structures of compounds 185–188.

Table 9. Chemical structures of compounds 189–193.

| No.  | Compounds                        | R₁ | R₂    | R₃    | R₄    | Source       |
|------|----------------------------------|----|-------|-------|-------|--------------|
| 189  | Lycibarbarspermidine A           | H  | β-D-Glc | H     | H     | L. barbarum |
| 190  | Lycibarbarspermidine B           | H  | H     | β-D-Glc | H     | L. barbarum |
| 191  | Lycibarbarspermidine C           | β-D-Glc | H     | H     | H     | L. barbarum |
| 192  | Lycibarbarspermidine D           | H  | H     | H     | β-D-Glc | L. barbarum |
| 193  | Lycibarbarspermidine E           | H  | β-D-Glc | β-D-Glc | H     | L. barbarum |

Figure 14. Chemical structures of compounds 194 and 195.
Tropane Alkaloids

As we know, the genus *Lycium* has been used as both a medicine and a food for a long time in Asia, particularly in China. However, the safety of *Lycium* has been questioned for some time, especially after the detection of the three tropane alkaloids atropine (204), hyoscyamine (205), and scopolamine (206) [101]. Atropine and hyoscyamine were identified from the fruits of *L. barbarum* gathered in India, while scopolamine was identified from *L. halimifolium* at concentrations higher than the toxic dose. However, another scholar, seeking to verify these reports, demonstrated that the atropine content of *L. barbarum* from different sources was just 3.0 ppb—far below the poisoning dose [102]. It was demonstrated that none of the toxic compounds were detected in fruits, leaves, stems and roots of three *L. barbarum* varieties (‘No. 1’, ‘New Big’ and ‘Amber Sweet Goji’) by densitometric TLC analysis [103]. Through field investigation and model specimen inspections, the above three tropane alkaloids were determined to be from *Lycium europaeum* rather than the *L. barbarum*. Thus, the genus *Lycium* is likely non-toxic, and consumers can rest assured that its use is safe [104].

Other than the alkaloids that have been already mentioned, there are nine others that have been obtained from this genus, including 9-formylharman (207), 1-(methoxycarbonyl)-β-carboline (208), perlyrline (209), choline (210), 1β-amino-3β,4β,5α-trihydroxycycloheptane (211), betaine hydrochloride (212), nicotianamine (213), betaine (214), and melatonin (215). Compounds 207–209 were isolated from the fruits of *L. chinense* [105], while 210–212 were isolated from the root bark of *L. chinense* [90]. Compound 213 was isolated from the leaves and flowers of *L. chinense* [106], and 214 was isolated from the stem of *L. chinense* [107].

Table 10. Chemical structures of compounds 196–200.

| No. | Compounds             | R<sub>1</sub> | R<sub>2</sub> | R<sub>3</sub> | R<sub>4</sub> | Source               |
|-----|-----------------------|---------------|---------------|---------------|---------------|----------------------|
| 196 | Lycibarbarspermidine H | H             | H             | H             | β-D-Glc       | *L. barbarum*        |
| 197 | Lycibarbarspermidine I | H             | β-D-Glc       | H             | H             | *L. barbarum*        |
| 198 | Lycibarbarspermidine J | H             | H             | β-D-Glc       | H             | *L. barbarum*        |
| 199 | Lycibarbarspermidine K | β-D-Glc       | H             | β-D-Glc       | H             | *L. barbarum*        |
| 200 | Lycibarbarspermidine L | H             | β-D-Glc       | H             | β-D-Glc       | *L. barbarum*        |

Figure 15. Chemical structures of compounds 201–203.
and 215 were isolated from the fruits of *L. barbarum* [107,108]. The chemical structures of these tropane alkaloids are listed in Figure 16.

![Chemical structures of compounds 204–215.](image)

**Figure 16.** Chemical structures of compounds 204–215.

### 2.2.8. Anthraquinones 216–219

Four anthraquinones: emodin (216), physcion (217), 6-hydroxyrubiadin (218), and 3-O-(2-O-α-L-rhamnopyranosyl-6-O-acetyl-β-D-glucopyranosyl)-6-hydroxy-rubiadin (219), listed in Figure 17, have been obtained from the root bark of *L. chinense* [61,109].

![Chemical structures of compounds 216–219.](image)

**Figure 17.** Chemical structures of compounds 216–219.

### 2.2.9. Organic Acids 220–251

To this point, 32 organic acids, listed in Figure 18, have been identified from the genus *Lycium*, which can be classified into two groups: aliphatic acids 220–238 and aromatic acids and their derivatives 239–251. Compounds 220–225 and 240–244 were isolated from the fruits of *L. barbarum* [56,63,65,107,110–112]; 239 and 245 were isolated from the leaves of *L. barbarum* [66];
was isolated from the root of *L. chinense* [113]; 227, 248 and 249 were isolated from the fruits of *L. chinense* [70,114]; 228–233 and 248 were isolated from the leaves of *L. chinense* [115]; 234, 235, and 249–251 were isolated from the root bark of *L. chinense* [53,78,93,116,117], and 236–238 were isolated from the fruits of *L. urcomanicum* [118,119].

Figure 18. Chemical structures of compounds 220–251.
2.2.10. Terpenoids 252–290

Thirty-seven terpenoids, listed in Figures 19–21 and Tables 11 and 12, have been found in the genus *Lycium*, mainly including monoterpenes 252–256, sesquiterpenes 257–263, diterpenoids 264–274, and carotenoids 275–290. Among them, carotenoids are one of the more important constituents of the *Lycium* fruits. Thus compounds 256 and 275–286 were isolated from the fruits of *L. barbarum* [120–123]; 253, 254, 258, 259 and 287–290 were isolated from the fruits of *L. chinense* [120,121,124–126]; 252 and 264–272 were isolated from the leaves of *L. chinense* [127,128]; 255 and 273–274 were isolated from the root bark of *L. chinense* [80,116]; 260 and 261 were isolated from the leaves of *L. halimifolium* [23]; and 262 and 265 were isolated from the leaves of *L. barbarum* [129].

![Chemical structures of compounds 252–263, 266.](image-url)
Table 11. Chemical structures of compounds 264–265, 267–270 and 272–273.

| No. | Compounds          | R₁   | R₂      | Source       |
|-----|--------------------|------|---------|--------------|
| 264 | Lyciumosides I     | Glc  | Glc     | L. chinense  |
| 265 | Lyciumosides II    | Glc²-Glc | Glc     | L. chinense  |
| 267 | Lyciumosides IV    | Glc  | Glc⁴-Rha| L. chinense  |
| 268 | Lyciumosides V     | Glc⁶-Rha | Glc     | L. chinense  |
| 269 | Lyciumosides VI    | Glc⁶-Rha | Glc⁴-Rha| L. chinense  |
| 270 | Lyciumosides VII   | Glc²-Rha⁶-Glc | Glc | L. chinense  |
| 272 | Lyciumosides IX    | Glc  | 6-O-malonyl-Glc | L. chinense |
| 273 | Capsianoside II    | Rha⁴-Glc⁶-Rha | Glc²-Glc | L. chinense  |

Figure 20. Chemical structures of compounds 271 and 274.

Table 12. Chemical structures of compounds 275–282.

| No. | Compounds          | R₁   | R₂      | Source       |
|-----|--------------------|------|---------|--------------|
| 275 | β-Carotene         | H    | H       | L. barbarum  |
| 276 | β-Cryptoxanthin    | OH   | H       | L. barbarum  |
| 277 | Zeaxanthin         | OH   | OH      | L. barbarum  |
| 278 | Zeaxanthin monopalmitate | OCO(CH₂)₁₄CH₃ | OH | L. barbarum  |
| 279 | Zeaxanthin dipalmitate | OCO(CH₂)₁₄CH₃ | OCO(CH₂)₁₄CH₃ | L. barbarum  |
| 280 | Zeaxanthin monomyristate | OH | OCO(CH₂)₁₂CH₃ | L. barbarum  |
| 281 | Zeaxanthin dimyristate | OCO(CH₂)₁₂CH₃ | OCO(CH₂)₁₂CH₃ | L. barbarum  |
| 282 | β-Cryptoxanthin palmitate | OCO(CH₂)₁₄CH₃ | H | L. barbarum  |
Figure 21. Chemical structures of compounds 283–290.

2.2.11. Sterols, Steroids, and Their Derivatives 291–347

Fifty-seven sterols, steroids, and their derivatives 291–347, listed in Figure 22, have been identified from the genus *Lycium*, mainly from the seeds and the fruits. Compounds 293 and 343 were identified
from the flowers of *L. barbarum* [130], 291–292; 295, 298, 319–324 and 337–339 were identified from the fruits of *L. chinense* [23,35,52,63,107,131]; 341 342, 346 and 347 were identified from the leaves of *L. chinense* [132,133]; 336 and 340 were identified from the root bark of *L. chinense* [80,121]; 294 was identified from the seed of *L. ciliatum* [66]; all others were identified from the seed of *L. chinense* [134–137] 344 and 345 were identified from the seeds of *L. barbarum* [138].

![Diagram of sterols, steroids, and their derivatives](image-url)
Figure 22. Cont.
2.2.12. Peptides 348–352

Five peptides have been isolated from the root bark of *L. chinense* [80,139], including one dipeptide, lyciumamide (348), and four octapeptides, called lyciumins A–D (compounds 349–350), illustrated in Figure 23.
3. Discussion

Other than what has already been mentioned, a few other chemical constituents, listed in Figure 24, were also isolated from the genus *Lycium*. Digupigan A (353), 2-O-(β-D-glucopyranosyl)ascorbic acid (354) and p-hydroxybenzaldehyde (355) also have been obtained from the root bark of *L. chinense*, the fruits of *L. chinense*, and the fruits of *L. barbarum* [75,76,121,137,140,141], respectively. Many minerals, amino acids, and proteins have also been found in the genus *Lycium*, such as Ca, Mg, Zn, Fe, aminoethanesulfonic acid, γ-aminobutyric acid (GABA), Mn-SOD, etc. [121,142,143].

![Chemical structures of compounds 348–352.](image)

**Figure 23.** Chemical structures of compounds 348–352.

**Figure 24.** Chemical structures of compounds 353–355.

3. Discussion

*Lycium* species are of valuable medicinal, nutritional and functional significance, and have been studied in terms of their chemical compounds. Phytochemical investigations on eight different species, have resulted in the isolation of at least 355 constituents up to July of 2016. Research on chemical...
compounds has concentrated mainly on L. barbarum and L. chinense. Therefore, future phytochemistry research should be focused on the other species in Lycium genus. In addition, diverse plant parts (i.e., the flowers, leaves, seeds) have also been testified to contain new constituents, most of which possess the novel chemical structures. Polysaccharides play a particularly significant role in exerting pharmacological actions. A specific class of polysaccharides, abbreviated as LBP, is used as biomarker in the 2015 Chinese Pharmacopoeia as a measure by which wolfberry is qualified. At present, LBP in products or in pharmacological studies usually are polysaccharide mixtures with heterogeneity and polydispersity. On the other hand, development of new separation, detection techniques will greatly benefit the phytochemical isolation and structural elucidation of LBP. There is a growing recognition that not only the LBP, but also the plant secondary metabolites may have the potential active ingredients, while most of the research on goji berry was LBP rather than small molecule substances, so more intensive studies of goji berry are required to shed some light on these compounds.

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