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**Review**

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Review

# Genus *Barleria* L. (Acanthaceae): a review of its taxonomy, cytogenetics, phytochemistry and pharmacological potential

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## Abstract

**Objectives** *Barleria*, a large genus of the Acanthaceae family, comprises more than 300 species with diverse taxonomy, cytogenetics, phytochemistry and pharmacological potential. Therefore, the aim of this review is to critically assess the research on *Barleria* and provide guidance for future investigations.

**Methods** The data were obtained from different sources, such as books, theses, journals and some of the websites and internet-based searches, published from 1901 to 2020. Data obtained from PubMed, Google Scholar, ScienceDirect, online electronic journals, SpringerLink, Wiley, etc. have also been used.

**Key findings** The species of this genus exhibit considerable medicinal properties. Cytogenetical data are scantily available with chromosome counts available for only 24 species. The most common chromosome number is $2n = 2x = 40$. So far, 187 compounds are reported from *Barleria* species. The active principles, their uses, toxicity and pharmacological effects are discussed. Essential oils, flavones, flavonoids, glycosides, terpenes and terpenoids form the major compounds.

**Summary** It is highly recommended that the pharmacological and economic potential of *Barleria* species should be exploited and more detailed studies and attention be geared towards its utilization and conservation. In addition, to ensure maximum pharmacological benefits and sustainable use, it is necessary to have empirical information explaining its ethnobotanical values as well as commercial potential.

**Keywords chromosomes; chemistry; ethnomedicine; pharmacology; taxonomy**

## Introduction

*Barleria* L. is a speciose genus of the Acanthaceae Juss., that is, herbs, shrubs and rarely climbers.[1–3] Recently, Darbyshire and Luke[4] described an arborescent species (*B. mirabilis* I. Darbysh. & Q. Luke) from western Tanzania. Recent classification of *Barleria* split it into subgenera, viz. *Barleria* and *Prionitis* (Ness) C.B. Clarke.[3] The subgenus *Prionitis* comprises three sections, *Prionitis* (Ness) Lindau, *Somalia* (Oliv.) Lindau and *Stellatohirta* M. Balkwill.[3]

Flowers of the genus are large, showy, colourful (with usually pink, purple, white and yellow corollas) and have ornamental potential.[5] For example, *Barleria repens* Nees, an African species with red corollas is a common ornamental grown in India and Africa (Figure 1). The ornamental potential of the genus and amenable size of its chromosomes have led to cytogenetic and hybridization studies in the genus.[5]

*Barleria* species have also been used in folk medicine to cure cough and bronchitis.[6] Phytochemicals isolated from various species show many biological activities such as antioxidant, acetylcholine esterase inhibition, anti-inflammatory, antibacterial, antifungal, hepatoprotective, antiulcer and nephroprotective activity.[7–13] Most of the pharmacological evaluation of *Barleria* species has been performed on Indian taxa. Extensive pharmacological research exists on certain species, namely *B. prionitis* L., *B. cristata* L., and *B. lupulina* Lindl. This might be due to their wide geographical distribution and cultivation and hence, easy availability.

Although there are some reviews that focus on individual species, none of these brings together and analyses data available for all the species of *Barleria*. Here, we review for the first time taxonomy, cytogenetics, phytochemistry, traditional uses and pharmacological properties of *Barleria*. We also discuss the gaps in these areas of research and provide scopes for future investigations on genus *Barleria*.

## Methods

This review provides insights into a huge collection of data published from 1901 to 2020 on the genus *Barleria*. The data were obtained from different sources, such as books,

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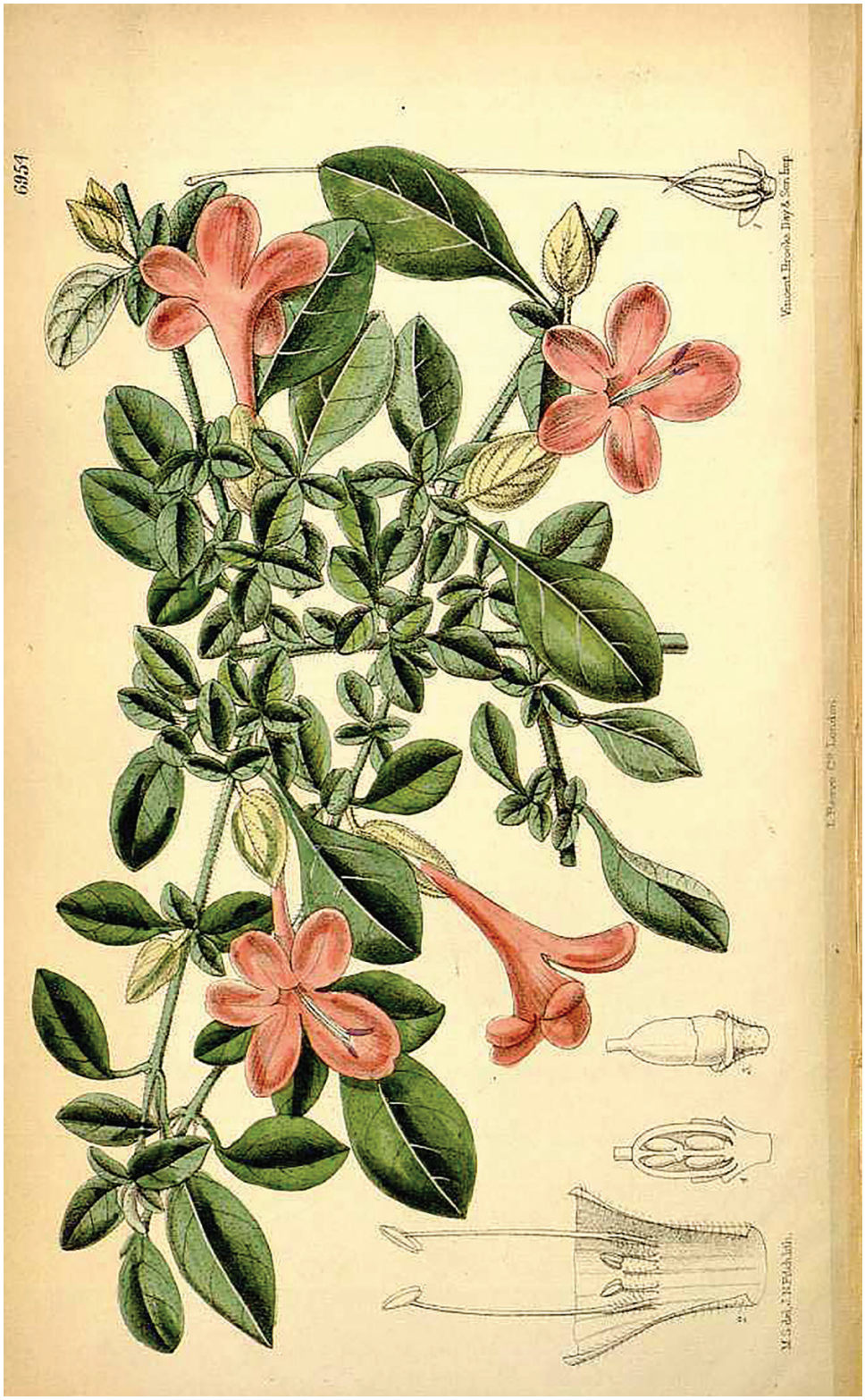



**Figure 1** *Barleria repens* (Bot. Mag. 113: t. 6954). 'Image from the Biodiversity Heritage Library. Contributed by [Missouri Botanical Garden, Peter H. Raven Library]. www.biodiversitylibrary.org' .

theses and peer-reviewed journals. The data published on PubMed, Google Scholar, ScienceDirect, online electronic journals, SpringerLink, Wiley, etc. were included. For information on chromosomes, the database by Rice et al.[14] was also consulted. The literature search was carried out using the keywords *Barleria*, *chromosomes*, *karyotype*, *phytochemistry*, *pharmacology*, *traditional uses*, etc. Additionally, individual species names were used as keywords. The publications in which the keywords appeared were analysed at the full-text level. All the articles published pertaining

to *Barleria* during the said period were examined thoroughly. The results obtained were critically compiled, analysed and presented in this review. Moreover, the data were synthesized and presented in the form of illustrations and tables for a proper understanding of the topics among the readers.

## Taxonomy and Biogeography

The genus *Barleria* was described by Linnaeus[15] with the type species *B. cristata* (Figure 2). *Barleria* can be identified based on the presence of three characteristics, that is, a calyx with two outer segments large and two inner ones smaller, globose honey-comb pollen and the epidermal cells with double cystoliths[1] (Figure 3). The geographical distribution of the genus is depicted in Figure 4. In order to understand the relationships of taxa within the genus infrageneric classification of *Barleria* have been contributed greatly by Nees von Esenbeck,[16] Clarke,[17–19] Lindau,[20] Obermeijer[21] and Balkwill and Balkwill[1, 22] classified the genus on the basis of morphological characters. In a very comprehensive work, Balkwill and Balkwill[22] studied about 240 species and provided an infrageneric classification. This classification utilized morphological traits such as spine systems (present or absent), corolla configuration, stigma structure, androecium composition (number of stamens, their size, staminodes, etc.), capsule morphology, seed number, the nature of the fruit wall and seeds (hygroscopic hairs present or absent). They


**Figure 2** *Barleria cristata* (Bot. Repos. 10: t. 625). 'Image from the Biodiversity Heritage Library. Contributed by [California Academy of Sciences, California Academy of Sciences Library]. www.biodiversitylibrary.org'.


**Figure 3** Some diagnostic features of the genus *Barleria*. (a) Mitotic metaphase of *B. lavaniana* showing 2*n* = 40 chromosomes (scale bar = 5 µm), (b) a pair of cystoliths on the epidermal surface of leaf of *B. cuspidata* (scale bar = 10 µm), (c–f) morphological variation in corolla (scale bars = 1 cm): (c) five-lobed corolla with all lobes similar (*B. morrisiana*), (d) corolla with 2 + 3 configuration (*B. acuminata*), (e) corolla with 4 + 1 configuration (all lobes attached at same level) (*B. sepalosa*), (f) corolla with 4 + 1 configuration (4 lobes attached at upper position remaining one far below from other) (*B. courtallica*), (g) four partite calyx, 2 outer large and 2 inner smaller (*B. cristata*) (scale bar = 1 cm), (h) honey-combed pollen grain (*B. lavaniana*) (scale bar = 20 µm). Arrow depicts inner sepals and arrowhead bracteoles.

grouped *Barleria* into two subgenera, *Barleria* and *Prionitis*. The former with sections, *Barleria* and *Chrysothrix* M. Balkwill and the latter, *Cavirostrata* M. Balkwill, *Fissimura* M. Balkwill, *Prionitis*, *Somalia* and *Stellatohirta*.

Darbyshire et al.[3] recently updated the infrageneric classification of *Barleria*. This forms the first comprehensive phylogenetic analysis of *Barleria*. The authors analysed 53 species of *Barleria*, mostly from Africa, based on *trn*S-G and *ndh*F-*rpl32-trn*L (UAG) (plastid intergenic spacers) and the internal transcribed spacer (ITS) (nuclear) region. The classification is useful for understanding the origin and trend of morphological variations that exist in *Barleria*. *Chrysothix* and *Fissimura*, the sections belonging to subgenera *Barleria* and *Prionitis*, in the classification of Balkwill and Balkwill[22] were subsumed under subgenus *Barleria* (for details, see Darbyshire et al.[3]). Similarly, the section *Cavirostrata* of subgenus *Prionitis* was subsumed under section *Somalia*.[3] However, the phylogenetic results of Darbyshire et al.[3] were not able to clarify relationships in some studied taxa and indicated the need for additional sampling of the species from the Indian landmass and Madagascar as well as the use of restriction site-associated DNA sequencing data to resolve the relationships and recent radiation of *Barleria*. Recently, Patil et al.[23] described a new species of *Barleria* that belonged to the subgenus *Barleria*. The study was based on plastid DNA sequences (*rbc*L and *mat*K). The genus at present comprises 331 taxa (310 species, 14 subspecies and 7 varieties).[24]

Van der Bank et al.[25] were the first to note that allozymes provide valuable information for delimiting *Barleria* species. Allozyme variation in *Barleria* species has been studied by Makholela et al.[26, 27] Analysis of ITS and *trn*L-F, *rps16* and *trn*S-G sequences revealed that *B. oenotheroides* had undergone ancient long-distance dispersal from the Old World to the New World, possibly during the Pliocene or upper Miocene.[28] DNA data on Indian taxa are scanty. Baskaran and Karthikeyan[29] for the first time provided *rbc*L gene sequences of *B. longiflora* from India.

Corolla morphology of *Barleria* species is highly variable. Most of the species have five distinct corolla lobes; however, some species such as *B. lugardii* and *B. rehmanii* have a 4-lobed corolla wherein the adaxial pair of corolla lobes is fused, representing an advanced condition.[22] Other species of the genus have remarkably larger corolla tubes. *B. grandiflora* with a corolla tube 14–15 cm long, probably has one of the largest corollas in the genus. Other species with considerably long corolla tubes are *B. lavaniana* (12–13.5 cm), *B. speciosa* (11.2–12.5 cm), *B. longiflora* (9–11 cm) and *B. illicifolia* (7.7–10 cm).[23, 30–32] All species with a slender white corolla fall under the subgenus *Barleria* except *B. grandiflora* which belongs to the section *Somalia* of subgenus *Prionitis*. The presence of a long and slender corolla tube with white lobes could be an adaptation for moth pollination. Moth pollination has been reported to occur in *B. acanthoides*, *B. capitata* and *B. noctiflora*.[30]

*Barleria* species possess some unique and extreme traits such as the presence of five fully fertile stamens and corolla rotate with five equal lobes that cannot be neglected from the evolution point of view. One of the striking characters is the presence of five or four fully fertile stamens. Generally, the corolla has two abaxial fully fertile stamens with three much-reduced stamens with antherodes of which some without thecae are called staminodes.[33] Surprisingly, *B. morrisiana* has all five fertile stamens with three subequal sets, one stamen shorter and included while the remaining four are longer and extend beyond the mouth of the tube, of which one pair is slightly longer than the other. *B. ovata* has four fertile stamens along with a staminode. *B. deserticola* has four didynamous stamens with much-reduced single staminode.

The centres of diversity and endemism are in Tanzania, Angola, Madagascar and India.[3] A maximum number of endemics (31–40 species) are confined to Tanzania and Madagascar, followed by Angola and India (21–30 species each).[3] The genus shows high rates of local endemism. For example, in west Tanzania, several taxa, including *B. diplotricha*, *B. griseoviridis* and *B. mpandensis*, are narrowly

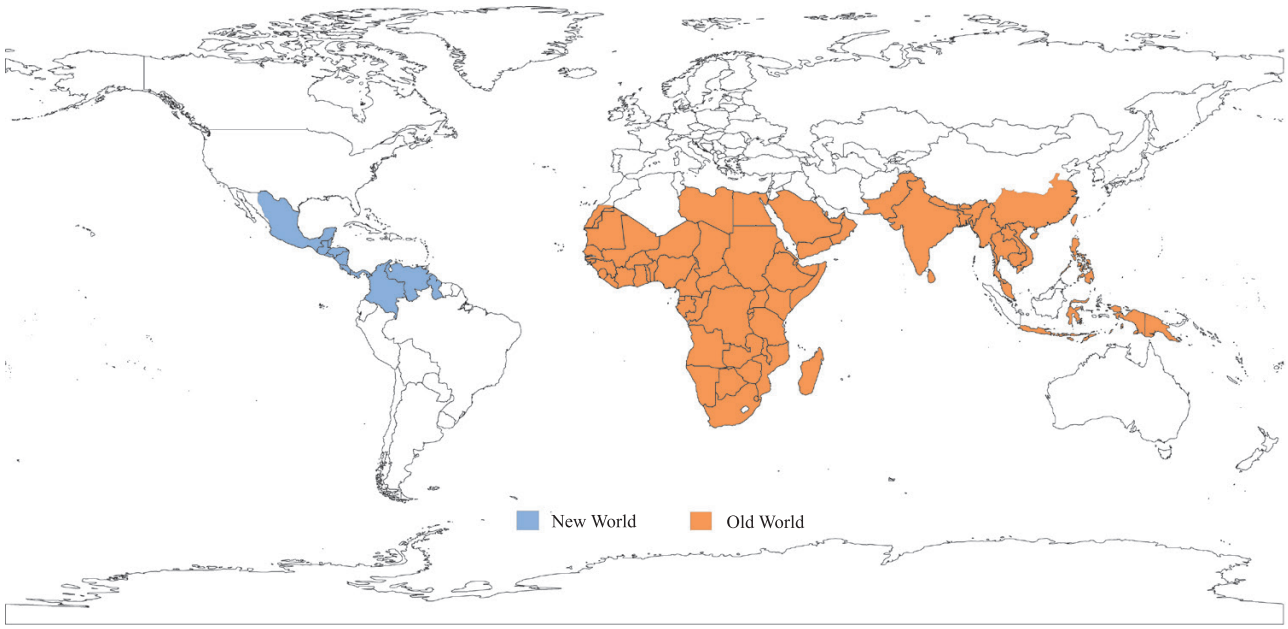



**Figure 4** Geographical distribution of *Barleria*.[24]

endemic. Several species described during the study of the *Barleria* as a part of Flora of Tropical East Africa are known from only one or two collections.[4] Similarly, Indian species, *B. morrisiana* and *B. durairajii* are known from type locality only. Contrastingly, *Barleria* species, viz. *B. cristata* and *B. prionitis sensu stricto* are widespread in tropical Asia.[2] *B. prionitis sensu lato* has been separated into several species.[2] Earlier, Wood et al.[34] followed a broad concept of *B. prionitis* and circumscribed it with eight subspecies across tropical Asia and Africa.

## Cytogenetics

Cytogenetic studies on *Barleria* are far from complete. Chromosome data exist only for 27 taxa (7% of the total taxa). In the centres of diversity (Africa and Madagascar), there are only two species, *B. senensis* and *B. oenotheroides* that have known chromosome numbers (Table 1). *B. candida*, an Arabian species, is also cytogenetically known (Table 1). Most of the cytogenetic work emanates from the species of the Indian subcontinent (Table 1). In the Indian subcontinent, 21 species have been studied from a cytogenetic point of view. So far, chromosome data are lacking for nine species, viz. *B. durairajii*, *B. hochstetteri*, *B. montana*, *B. morrisiana*, *B. nitida*, *B. pilosa*, *B. prattensis*, *B. stocksii* and *B. vestita*.[5]

The most frequent chromosome number $2n = 40$ in the genus is based on $x = 10$ and hence, the species are tetraploids.[37] The lowest chromosome count, that is, $2n = 24$ is reported in *B. noctiflora*[45] and the highest ($2n = 44$) in *B. grandiflora*.[5] Some counts, such as $2n = 30$, 32, 34, 36, 38 and 42, which deviate from the common count ($2n = 40$) have been reported in different horticultural varieties of *B. cristata* on account of hybridization or as a result of aneuploid alteration.[36] The lowest count of $2n = 24$ in *B. noctiflora* has been confirmed as $2n = 40$ by Ranganath and Krishnappa.[36] The earlier count ($2n = 24$) could be an error as there are no instances within the genus where this count is reported. Ranganath and Krishnappa[36] studied karyotype features for six species and found that all the species exhibited $2n = 40$ chromosomes. They noted the shortest chromosome in *B. acuminata* (1.73 µm) and the longest (7 µm) in *B. involucrata* var. *elata*. Devi and Mathew[37] also studied karyotypes of eight *Barleria* species. Karyotypes of most of the species were found to be symmetrical (2b Stebbins' karyotype asymmetry) with a predominance of m-type chromosomes. *B. acuminata* with sm, st and t-type chromosomes had an asymmetrical karyotype. Recent karyotype analyses of *B. lawii* and *B. sepalosa* exhibited 4b category and m-type chromosomes[5]). Patil et al.[23] studied karyotype features of *B. lavaniana* and *B. longiflora* and found that karyotypes of both the species occupied Stebbins' 3b category of karyotype asymmetry, the former with 10 m and 10 sm and the latter with 6 m and 14 sm type chromosomes and had $2n = 40$ chromosome numbers. *B. sepalosa* with m-type chromosomes fell in 4b category and has advanced karyotype when compared with other species.[5]

Meiotic studies in *Barleria* are fewer when compared with mitosis. Only 16 species have been studied for their meiotic behaviour so far.[5, 35, 37, 44, 48, 50, 52] Meiosis of five species was mostly normal except for *B. courtallica* which showed multivalent associations indicating its autopolyploid nature.[5, 23, 37, 44]

As *Barleria* is ornamentally important, cytogenetics and breeding are of utmost significance for developing horticultural varieties. Krishnaswami and Menon[47] carried out hybridization experiments in *Barleria*. They tried six combinations between *B. cristata* and *B. mysorensis* and *B. cristata* and *B. noctiflora*. One interspecific hybrid (*B. prionitis* × *B. noctiflora*) was obtained. The interspecific hybrid was more vigorous and produced flowers and profuse branches but did not set seeds.[47] Natural hybridization between *Barleria* species (*B. obtusa* and *B. bremekampii*) has been illustrated using the allozyme data by Van der Bank et al.[25]

## Phytochemistry

Phytochemical studies in *Barleria* species have revealed the presence of many biologically active compounds in leaves,

**Table 1** *Barleria* species and their diploid chromosome numbers (2*n*).

| Sr. No. | Species | 2*n* | Author(s) |
|---|---|---|---|
| 1. | *B. acanthoides* Vahl | 40[1] | [35] |
| 2. | *B. acuminata* Wight | 40 | [36] |
| 3. | *B. buxifolia* L. | 40 | [36] |
| 4. | *B. courtallica* Nees | 40 | [37] |
| 5. | *B. candida* Nees | 32 | [38] |
| 6. | *B. cristata* L. | 40 | [37] |
| | (white-flowered) | 34 | [39] |
| | | 40[1] | [40] |
| | (pink-coloured) | 36 | [39] |
| | | 40[1] | [40] |
| | | 40 | [41] |
| | | 38 | [42] |
| | (striped flowers) | 38 | [39] |
| | (blue-flowered) | 40 | [39] |
| | *B. cristata* var. *dichotoma* (Roxb.) Prain | 42 | [41] |
| | | 32 | [43] |
| 7. | *B. cuspidata* Heyne ex Nees | 40 | [37] |
| 8. | *B. gibsonii* Dalzell | 40 | [36] |
| 9. | *B. grandiflora* Dalzell | 44 | [44] |
| 10. | *B. involucrata* Nees | 40 | [45] |
| | *B. involucrata* var. *elata* (Dalzell) C.B. Clarke | 40 | [36] |
| 11. | *B. lawii* T. Anderson | 40 | [5] |
| 12. | *B. longiflora* L.f. | 40 | [23, 45] |
| 13. | *B. lavaniana* S.S. Patil, S.R. Yadav & Lekhak | 40 | [23] |
| 14. | *B. lupulina* Lindl. | 40 | [41, 46] |
| 15. | *B. mysorensis* B. Heyne ex Roth | 40 | [47] |
| 16. | *B. noctiflora* L. | 24, 40 | [36, 45, 47] |
| 17. | *B. oenotheroides* D. Cours. | 40 | [48, 49] |
| 18. | *B. prionitis* L. | 40 | [37] |
| | *B. prionitis* subsp. *pubiflora* (Benth. ex Hohen.) Brummitt & J.R.I. Wood | 32 | [43] |
| | | 30 | [39] |
| | | 40 | [37] |
| 19. | *B. repens* Nees | 40[1] | [48] |
| 20. | *B. sepalosa* C.B. Clarke | 40 | [5] |
| 21. | *B. senensis* Klotzsch | 32[1] | [50] |
| 22. | *B. strigosa* Willd. | 40 | [36, 37] |
| 23. | *B. terminalis* Nees | 40 | [51] |
| 24. | *B. tomentosa* Roth. | 40 | [37] |

[1]Gametophyte count converted to sporophytic count.

stems and roots. However, these studies pertaining to phytochemical investigations are limited only to nine species of *Barleria*, viz. *B. cristata*, *B. courtallica*, *B. coriacea* subsp. *dinteri*, *B. lupulina*, *B. montana*, *B. noctiflora*, *B. prionitis*, *B. strigosa* and *B. trispinosa*. A variety of phytoconstituents were recorded from different plant parts using various solvents (ethanol, methanol, water, hexane, chloroform, ethyl acetate, butanol, acetone, petroleum ether, dichloromethane, etc.). Various phytochemical extraction methods such as soxhlet extraction, refluxing into respective solvents from 12 h to 18 h, sequential extraction, etc. have been employed. These extracts were either concentrated or evaporated to dryness and the final dried extract was used for further purification and characterization. For purification and concentration of the extracts, various chromatographic separation techniques like adsorption and partition chromatography such as silica gel column chromatography have been used. Characterization of various phytoconstituents has been reported by high-performance liquid chromatography (HPLC), Fourier transform infrared spectroscopy (FTIR), gas chromatography–mass spectroscopy (GC-MS) and nuclear magnetic resonance (NMR) spectrum. Broadly, these compounds can be grouped as acrylic acids, alkynes, amines, cinnamic acid and its derivatives, fatty acids and waxes, flavones and flavonoids, furans, glycosides, hydroquinones, iridoid glycosides, phenolics, phenolic glycosides, phenyl ethanoid and phenylethanoid glycosides, phytols, phytosterols, sulfur compounds, terpenes and terpenoids. These compounds, their sources (species and plant part/s used) and physiological effects are summarized in Table 2.

Some of the common phytochemicals occurring in *Barleria* species, such as acrylic acids, alkynes, amines, cyclopentanone, cinnamic acids and their derivatives have been reported from the acetone, ethanol and methanolic extracts of leaves stems and aerial parts.[54–57] Extensive studies were conducted on the extraction and characterization of essential oils, fats and waxes from the members of the genus *Barleria*. A total of 46 compounds belonging to this class were analysed and reported by various researchers working in the field from all the plant parts of *Barleria*.[54–56, 59, 61, 68] A total of 31 flavones and flavonoids were recorded in *Barleria* species.[55, 56, 61, 70–72, 74, 75] Various studies have recorded the presence of 11 glycosides,[10, 69, 76, 77] 19 iridoid glycosides,[9, 71, 76, 80–82, 87, 88] 8 phenolic glycosides[72, 73, 76, 84, 90, 91] and 6 phenylethanoid and phenylpropanoid glycosides.[9, 72, 93–95] Besides these, 4 phytols,[56, 59] 4 phytosterols[10, 56, 61, 69, 97] and 27 terpenes and terpenoids were reported from *Barleria*.[10, 54–56, 59, 61, 69, 77, 89, 99–103]

Structures of some of the important compounds that are specific to genus *Barleria* and related genera are depicted in Figure 5. These compounds are p-hydroxy cinnamic acid, 3-methoxy quercetin, 6-O-α-l-rhamnopyranoside quercetagetin, 6-O-α-l-rhamnopyranoside-3,7,3′-O-trimethylated-8-hydroxyquercetin, 7-methoxy luteolin, apigenin 7-O-α-l-rhamnosyl-(1→6)-O-β-d-glucoside, apigenin 7-O-glucoside, gossypetin, luteolin, megastigmatrienone, nicouline, quercetagetin, quercetin, tamarixetin, (3R)-1-octen-3-yl-β-primeveroside, balarenone, forsythoside B, prioniside A, prioniside B, prioniside C, (+)-lyoniresinol 3a-O-β-d-glucoside, 10-O-*trans*-coumaroyl-eranthemoside, 6-O-acetylshanzhiside methyl ester, 6,8-O,O-diacetylshanhiside methyl ester same (acetyl barlerin), 6-α-l-rhamnopyranosyl-8-O-acetylshanzhiside methyl ester, 6-O-*cis*-p-coumaroyl-8-O-acetylshanzhiside methyl ester, 6-O-*trans*-p-coumaroyl-8-O-acetylshanzhiside methyl ester, 8-O-acetyl-6-O-*trans*-p-coumaroylshanzhiside, barlerin, lupulinoside, saletpangponoside A, saletpangponoside B, saletpangponoside C, shanzhiside methyl ester, acteoside (verbascoside), decaffeoylverbascoside, desrhamnosyl acteoside, dimethoxyverbascoside, ipolamiide, ipolamiidoside, isoverbascoside, phlorigidoside B, 4-hydroxyphenylethyl 4-O-β-d-glucopyranosyl-(1yl 4O-α-l-rhamnopyranoside (strigoside), parvifloroside A, parvifloroside B, barlerinoside and poliumoside.

**Table 2** Phytochemicals isolated from *Barleria* species and their biological activities

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| Acrylic acid/propenoic acid | | | | | | | |
| 1. | Propenoic acid | $C_3H_4O_2$ | *B. lupulina* | Antimicrobial | Leaves, stem | Acetone, methanol | [53, 54] |
| Alkynes | | | | | | | |
| 1. | 3-Eicosyne | $C_{20}H_{38}$ | *B. lupulina* | Antibacterial, cytotoxic | Leaves, stem | Acetone, ethanol, methanol | [54, 55] |
| Amines | | | | | | | |
| 1. | 1H-Tetrazole | $CH_2N_4$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 2. | *N*,*N*-Dimethylglycine | $C_4H_9NO_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| Cinnamic acid and its derivatives | | | | | | | |
| 1. | 2-Propenal, 3-phenyl | $C_9H_8O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 2. | 2-Propenoic acid, 3-(3,4-dimethoxyphenyl)-, methyl ester | $C_{12}H_{14}O_4$ | *B. noctiflora* | Antihistamine, antimicrobial, antioxidant | Leaves | Methanol | [56] |
| 3. | *p*-hydroxy cinnamic acid | $C_9H_8O_3$ | *B. montana* | Antimicrobial, hepatoprotective | Aerial parts | Methanol | [57] |
| Cyclic ketone | | | | | | | |
| 1. | Cyclopentanone | $C_5H_8O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| Essential oils, fatty acids and waxes | | | | | | | |
| 1. | 1,3,5,7-Cyclooctatetraene | $C_8H_8$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 2. | 1-Hexadecanol, 2-methyl- | $C_{17}H_{36}O$ | *B. prionitis* | Antifungal, catalytic | Leaves | Water | [58, 59] |
| 3. | 1-Octen-3-ol | $C_8H_{16}O$ | *B. prionitis* | Antioxidant, catalytic | Leaves | Water | [59, 60] |
| 4. | 1,4-Methanoazulene-9-methanol, decahydro-4,8,8-trimethyl-[1S-(1α,3aβ,4α,8aβ,9R*)] | $C_{15}H_{26}O$ | *B. courtallica* | Analgesic, antibacterial, anti-inflammatory, antitumour, fungicide, sedative | Stem | Ethanol | [61] |
| 5. | 1,7-Octanediol, 3,7-dimethyl | $C_{10}H_{22}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 6. | 2-Hexadecanol | $C_{16}H_{34}O$ | *B. prionitis* | Antimicrobial, catalytic | Leaves | Water | [59, 62] |
| 7. | 2-Isopropyl-5-methyl-1-heptanol | $C_{11}H_{24}O$ | *B. prionitis* | Antimicrobial, catalytic | Leaves | Water | [59, 62] |
| 8. | 2-Methylhexacosane | $C_{27}H_{56}$ | *B. courtallica* | Antimicrobial, decrease blood cholesterol | Root, stem | Ethanol | [61, 63] |
| 9. | 3,7,11,15-Tetramethyl-2-hexadecen-1-ol | $C_{20}H_{40}O$ | *B. courtallica* | Antimicrobial | Leaves, root, stem | Ethanol | [61] |
| 10. | 5-Nonadecen-1-ol | $C_{19}H_{38}O$ | *B. courtallica* | Antimicrobial | Stem | Ethanol | [61, 64] |
| 11. | 9,12,15-Octadecatrienoic acid, 2,3-dihydroxypropyl ester, (Z, Z, Z) | $C_{21}H_{36}O_4$ | *B. courtallica* | 5-α reductase inhibitor, antiacne, antiandrogenic, antiarthritic, anticoronary, antieczemic, antihistaminic, insectifuge, hepatoprotective, hypocholesterolemic, nematicide | Leaves | Ethanol | [61] |
| 12. | 9,12-Octadecadienoic acid | $C_{18}H_{32}O_2$ | *B. courtallica*, *B. lupulina* | Antimicrobial | Leaves, stem | Acetone, ethanol, methanol | [54, 61] |
| 13. | 9,12-Octadecadienoic acid (Z, Z)-, methyl ester | $C_{19}H_{34}O_2$ | *B. courtallica* | 5-α reductase inhibitor, antiacne, antiandrogenic, antiarthritic, anticoronary, antieczemic, antihistaminic, hepatoprotective, hypocholesterolemic, insectifuge, nematicide | Leaves, stem | Ethanol | [61] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 14. | 9-Octadecenamide, (Z)- | $C_{18}H_{35}NO$ | *B. courtallica* | Anti-inflammatory, antimicrobial | Leaves, root, stem | Ethanol | [61] |
| 15. | 9-Octadecenoic acid (Z)-, methyl ester | $C_{19}H_{36}O_2$ | *B. courtallica* | 5-α reductase inhibitor, anemiagenic, antiandrogenic, anticancer, anti-inflammatory, antioxidant, choleretic, dermatitigenic, hypocholesterolemic, insectifuge | Leaves | Ethanol | [61, 65, 66] |
| 16. | Acetic acid, 4-methyl-3-oxopent-1-enyl ester | $C_8H_{12}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 17. | Bicyclo[4.4.0]dec-2-ene-4-ol, 2-methyl-9-(prop-1-en-3-ol-2-yl)- | $C_{15}H_{24}O_2$ | *B. courtallica* | Antibacterial | Leaves | Ethanol | [61, 67] |
| 18. | Bis(2-ethylhexyl phthalate) | $C_{24}H_{38}O_4$ | *B. lupulina* | Apoptosis inhibitor | Leaves, stem | Acetone, methanol | [54] |
| 19. | *cis*-1-Chloro-9-octadecene | $C_{18}H_{35}Cl$ | *B. prionitis* | Antimicrobial | Leaves | Water | [59] |
| 20. | Curan, 16,17-didehydro-, (20.xi.)- | $C_{19}H_{24}N_2$ | *B. courtallica* | Antimicrobial | Root, stem | Ethanol | [61] |
| 21. | Cyclohexene, 4-ethenyl-4-methyl-3-(1-methylethenyl)-1-(1-methylethyl)-, (3R-*trans*)- | $C_{15}H_{24}$ | *B. courtallica* | Analgesic, antibacterial, anti-inflammatory, antitumour, fungicide, sedative | Leaves, root | Ethanol | [61] |
| 22. | Decane, 2,3,5,8-tetramethyl | $C_{14}H_{30}$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 23. | Dibutyl phthalate | $C_{16}H_{22}O_4$ | *B. courtallica* | Anti-inflammatory, antimicrobial | Root, stem | Ethanol | [61] |
| 24. | Di-ethyl phthalate | $C_{12}H_{14}O_4$ | *B. courtallica*, *B. lupulina* | Antimicrobial, antifouling | Leaves, root, stem | Acetone, ethanol, methanol | [54, 61] |
| 25. | Dodecyl *cis*-9,10-epoxyoctadecanoate | $C_{30}H_{58}O_3$ | *B. courtallica* | Antimicrobial | Leaves, root, stem | Ethanol | [61] |
| 26. | Eicosane, 7-hexyl- | $C_{26}H_{54}$ | *B. courtallica* | Antimicrobial | Leaves, root, stem | Ethanol | [61] |
| 27. | Ethyl oleate | $C_{20}H_{38}O_2$ | *B. courtallica* | 5-α reductase inhibitor, anemiagenic, antiandrogenic, anticancer, anti-inflammatory, choleretic, dermatitigenic, hypocholesterolemic, insectifuge | Root, stem | Ethanol | [61] |
| 28. | Heptacosane | $C_{27}H_{56}$ | *B. courtallica*, *B. prionitis* | Antimicrobial, catalytic, cytotoxic | Leaves, root, stem | Ethanol, water | [59, 61, 68] |
| 29. | Heptadecane, 2,6,10,15-tetramethyl | $C_{12}H_{44}$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 30. | Heptadecanoic acid, 16-methyl-, methyl ester | $C_{19}H_{38}O_2$ | *B. courtallica* | Antimicrobial | Leaves | Ethanol | [61] |
| 31. | Hexadecane | $C_{16}H_{34}$ | *B. lupulina* | Antibacterial, cytotoxic | Leaves | Ethanol | [55] |
| 32. | Hexadecane, 1,1-bis (dodecyloxy) | $C_{40}H_{82}O_2$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 33. | Hexadecanoic acid | $C_{17}H_{34}O_2$ | *B. lupulina* | Antibacterial, cytotoxic | Leaves, stem | Acetone, ethanol, methanol | [54, 55] |
| 34. | Hexadecanoic acid, 15-methyl-, methyl ester | $C_{18}H_{36}O_2$ | *B. noctiflora* | Antihistamine, antimicrobial, antioxidant | Leaves | Methanol | [56] |
| 35. | Isoaromadendrene epoxide | $C_{15}H_{24}O$ | *B. courtallica* | Analgesic, antibacterial, anti-inflammatory, antitumour, fungicide, sedative | Leaves | Ethanol | [61] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 36. | Octadecane, 3-ethyl-5-(2-ethylbutyl)- | $C_{26}H_{54}$ | *B. courtallica* | Antimicrobial | Leaves, root, stem | Ethanol | [61] |
| 37. | Pentadecanoic acid, 14-methyl-, methyl ester | $C_{17}H_{34}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 38. | Pentanal | $C_5H_{10}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 39. | Propanoic acid, 2-methyl-, 3-hydroxy-2,4,4-trimethylpentyl ester | $C_{12}H_{24}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 40. | tert-Hexadecanethiol | $C_{16}H_{34}S$ | *B. prionitis* | Antiproliferative, catalytic | Leaves | Water | [59] |
| 41. | Tetracosane, 11-decyl- | $C_{34}H_{70}$ | *B. courtallica* | Antimicrobial | Leaves, root, Stem | Ethanol | [61] |
| 42. | Tetradecane | $C_{14}H_{30}$ | *B. lupulina*, *B. prionitis* | Antibacterial, antioxidant, catalytic, cytotoxic | Leaves | Ethanol, water | [55, 59] |
| 43. | Tetradecane, 2,6,10-trimethyl | $C_{17}H_{36}$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 44. | Undecanoic acid, 10-methyl-, methyl ester | $C_{13}H_{26}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 45. | Urs-12-en-28-oic acid, 3-hydroxy-, methyl ester, (3β)- | $C_{31}H_{50}O_3$ | *B. courtallica* | Anti-inflammatory, antimicrobial, cytotoxic | Root | Ethanol | [61] |
| 46. | Z,Z-3,15-octadecadien-1-ol acetate | $C_{20}H_{36}O_2$ | *B. courtallica* | Antimicrobial | Leaves, root, stem | Ethanol | [61] |
| Flavones and flavonoids | | | | | | | |
| 1. | 1-(3,6,6-Trimethyl-1,6,7,7a-tetrahydrocyclopenta[c]pyran-1-yl) ethenone | $C_{13}H_{18}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 2. | 1,1,3-Triethoxypropane | $C_9H_{20}O_3$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 3. | 2-(1-Oxobut-2-ynyl) cyclohexanone) | $C_{10}H_{12}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 4. | 2(4H)-Benzofuranone | $C_{11}H_{16}O_2$ | *B. lupulina* | Antibacterial, antioxidant | Leaves, stem | Acetone, methanol | [54] |
| 5. | 2,5-Dimethyl-4-hydroxy-3(2H)-furanone | $C_6H_8O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 6. | 2-Cyclopenten-1-one, 2-hydroxy | $C_5H_6O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 7. | 2-Methylbenzofuran | $C_9H_8O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 8. | 2-Pentadecanone, 6,10,14-trimethyl | $C_{18}H_{36}O$ | *B. prionitis* | Anti-inflammatory, catalytic | Leaves | Water | [59] |
| 9. | 2(3H)-naphthalenone, 4,4a,5,6,7,8-hexahydro-1-methoxy- | $C_{11}H_{16}O_2$ | *B. courtallica* | Antimicrobial | Leaves | Ethanol | [61] |
| 10. | 3-Buten-2-one, 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)- | $C_{13}H_{20}O$ | *B. courtallica* | Antimicrobial | Leaves | Ethanol | [61] |
| 11. | 3-Methoxy quercetin | $C_{16}H_{12}O_7$ | *B. cristata* | Antibacterial, anticancer, antioxidant, neuroprotective | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 12. | 3-Penten-2-one, 3-ethyl-4-methyl | $C_8H_{14}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 13. | 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl | $C_6H_8O_4$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 14. | 6-O-α-l-rhamnopyranoside quercetagetin | $C_{21}H_{20}O_{11}$ | *B. cristata* | Antibacterial | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 15. | 6-O-α-l-rhamnopyranoside-3,7,3′-O-trimethylated-8-hydroxyquercetin | $C_{27}H_{30}O_{15}$ | *B. cristata* | Antibacterial | Bark | Chloroform, ethanol, ethyl acetate | [70] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 16. | 7-Methoxy luteolin | $C_{16}H_{12}O_6$ | *B. cristata* | Antioxidant | Leaves | | [71] |
| 17. | Apigenin 7-O-α-Lrhamnosyl-(1→6)-O-β-d-glucoside | $C_{21}H_{20}O_{10}$ | *B. strigosa* | Antidiabetic, antipyretic, remedy in stomach disorders | Whole plant | Methanol | [72] |
| 18. | Apigenin 7-O-glucoside | $C_{21}H_{20}O_{10}$ | *B. cristata* var. *alba* | Antidiabetic, antipyretic, remedy in stomach disorders | Aerial parts | Ethyl acetate | [73] |
| 19. | Benzofuran | $C_8H_6O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 20. | Benzofuranone | $C_8H_6O$ | *B. lupulina* | Antibacterial, cytotoxic | Leaves | Ethanol | [55] |
| 21. | Delphinidin 3,5-diglucoside chloride | $C_{27}H_{31}ClO_{17}$ | *B. montana* | Antioxidant | Leaves | Methanol | [74] |
| 22. | Furan, 2,3-dihydro-2,2-dimethyl-3-(1-methylethenyl)-5-(1-methylethyl)- | $C_{12}H_{20}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 23. | Gossypetin | $C_{15}H_{12}O_8$ | *B. cristata* | Antibacterial, antitumour | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 24. | Gossypetin 8-methyl ether | $C_{16}H_{12}O_8$ | *B. cristata* | Antibacterial, antitumour | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 25. | Luteolin | $C_{15}H_{10}O_6$ | *B. cristata* | Antioxidant | Leaves | | [71] |
| 26. | Megastigmatrienone | $C_{13}H_{18}O$ | *B. noctiflora* | Antibacterial, antioxidant | Leaves | Methanol | [56] |
| 27. | Nicouline | $C_{23}H_{22}O_6$ | *B. montana* | Antioxidant, insecticidal, | Leaves | Methanol | [74] |
| 28. | Quercetagetin | $C_{15}H_{10}O_8$ | *B. cristata* | Antibacterial | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 29. | Quercetin | $C_{15}H_{10}O_7$ | *B. cristata* | Antibacterial, anticancer, antioxidant | Bark, leaves | Chloroform, ethanol, ethyl acetate, petroleum ether, water | [70, 75] |
| 30. | Tamarixetin | $C_{16}H_{12}O_7$ | *B. cristata* | Antibacterial, Antioxidant | Bark | Chloroform, ethanol, ethyl acetate | [70] |
| 31. | Tetrahydrocyclopenta[1,3]dioxin-4-one | $C_7H_{10}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| Furan | | | | | | | |
| 1. | Linalool oxide | $C_{10}H_{18}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| Glycosides | | | | | | | |
| 1. | (3R)-1-octen-3-yl-β-primeveroside | $C_{19}H_{34}O_{10}$ | *B. lupulina* | Antimicrobial, antioxidant | Aerial parts | Methanol | [76] |
| 2. | 1,4:3,6-Dianhydro-α-d-glucopyranose | $C_6H_8O_4$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 3. | 1,6:2,3-Dianhydro-4-O-acetyl-α-d-allopyranose | $C_8H_{10}O_5$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 4. | 1,6-Anhydro-β-d-talopyranose | $C_6H_{10}O_5$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 5. | Balarenone | $C_{29}H_{34}O_5$ | *B. prionitis* | Acetylcholine esterase inhibition, antibacterial | Aerial parts, whole plant | Ethanol | [10, 77] |
| 6. | Forsythoside B | $C_{34}H_{44}O_{19}$ | *B. lupulina* | Antimicrobial, antioxidant | Aerial parts | Methanol | [76] |
| 7. | Levoglucosan | $C_6H_{10}O_5$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 8. | Prioniside A | $C_{21}H_{29}O_{10}$ | *B. prionitis* | Antioxidant | Whole plant | Ethanol | [77] |
| 9. | Prioniside B | $C_{21}H_{29}O_9Ac$ | *B. prionitis* | Antioxidant | Whole plant | Ethanol | [77] |
| 10. | Prioniside C | $C_{41}H_{53}O_{24}$ | *B. prionitis* | Antioxidant | Whole plant | Ethanol | [77] |
| 11. | α-d-Glucopyranose, 4-O-β-d-galactopyranosyl- | $C_{12}H_{22}O_{11}$ | *B. courtallica* | Preservative | Root, stem | Ethanol | [61] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| Hydroquinones | | | | | | | |
| 1. | Benzoic acid, 4-methoxy-, methyl ester | $C_{10}H_{12}O_3$ | *B. lupulina* | Antioxidant | Leaves, stem | Acetone, methanol | [54] |
| Iridoid glycosides | | | | | | | |
| 1. | (+)-Lyoniresinol 3α-O-β-d-glucoside | $C_{28}H_{38}$ | *B. lupulina*, *B. strigosa* | Anti-apoptotic, antidiabetic, antimicrobial | Aerial parts, whole plant | Methanol | [72, 76, 78, 79] |
| 2. | 10-O-*trans*-coumaroyl-eranthemoside | $C_{24}H_{28}O_{11}$ | *B. strigosa* | Antioxidant | Whole plant | Methanol | [72] |
| 3. | 6-O-acetylshanzhiside methyl ester | $C_{19}H_{28}O_{12}$ | *B. lupulina* | Acetylcholine esterase inhibition, amelioration of mitochondrial energy metabolism, antifibrinolytic, anti-inflammatory, antinociceptive, attenuation of apoptosis, glutathione S transferase inhibition, radical scavenging activity | Aerial parts | Ethanol, methanol | [76, 80] |
| 4. | 6,8-O, O-diacetylshanhiside methyl ester (acetyl barlerin) | $C_{19}H_{28}O_{12}$ | *B. lupulina*, *B. prionitis*, *B. trispinosa* | Antiviral, antimicrobial, hepatotoxicity | Aerial parts | Ethanol, methanol | ,[9, 76, 80–83] |
| 5. | 6-α-l-rhamnopyranosyl-8-O-acetylshanzhiside methyl ester | $C_{25}H_{38}O_{16}$ | *B. trispinosa* | Acetylcholine esterase inhibition, amelioration of mitochondrial energy metabolism, antifibrinolytic, anti-inflammatory, antinociceptive, attenuation of apoptosis, glutathione S transferase inhibition, radical scavenging activity | Aerial parts | Ethanol | [81] |
| 6. | 6-O-*cis*-p-Coumaroyl-8-O-cetylshanzhiside methyl ester | $C_{19}H_{28}O_{12}$ | *B. prionitis* | Acetylcholine esterase inhibition, amelioration of mitochondrial energy metabolism, antifibrinolytic, anti-inflammatory, antinociceptive, attenuation of apoptosis, glutathione S transferase inhibition, radical scavenging activity | Whole plant | Methanol | [84] |
| 7. | 6-O-*trans*-p-coumaroyl-8-O-acetylshanzhiside methyl ester | $C_{19}H_{28}O_{12}$ | *B. prionitis* | Acetylcholine esterase inhibition, amelioration of mitochondrial energy metabolism, antifibrinolytic, anti-inflammatory, antinociceptive, attenuation of apoptosis, glutathione S transferase inhibition, radical scavenging activity | Whole plant | Ethanol, methanol | [9, 84] |
| 8. | 7-Methoxydiderroside | $C_{20}H_{30}O_{13}$ | *B. prionitis* | Antioxidant | Aerial parts | Ethanol | [9] |
| 9. | 7-O-acetyl-8-epi-loganic acid | $C_{16}H_{24}O_9$ | *B. strigosa* | Aldose reductase inhibitor | Whole plant | Methanol | [72, 85] |
| 10. | 8-O-acetyl-6-O-*trans*-p-coumaroylshanzhiside | $C_{27}H_{32}O_{14}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 11. | 8-O-acetylmussaenoside | $C_{19}H_{28}O_{11}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 12. | Barlerin | $C_{19}H_{28}O_{12}$ | *B. cristata*, *B. dinteri*, *B. lupulina*, *B. montana*, *B. prionitis*, *B. trispinosa* | Antimicrobial, antioxidant, hepatoprotective | Leaves, aerial parts, whole plant | Acetone, dichloromethane, ethanol, hexane, methanol | [9, 57, 71, 80, 81, 84, 86] |
| 13. | Benzyl alcohol b-(20-O-β-xylopyranosyl) glucopyranoside | $C_{18}H_{26}O_{10}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 14. | Cyclopenta (c) pyran-4-carboxylic acid (Dimethoxy) | $C_{11}H_{10}O_3$ | *B. lupulina*, *B. noctiflora* | Antioxidant, antihistamine, antioxidant | Leaves, stem | Acetone, methanol | [54, 56] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 15. | Lupulinoside | $C_{25}H_{38}O_{16}$ | *B. prionitis* | Antioxidant | Aerial parts | Ethanol | [9] |
| 16. | Saletpangponoside A | $C_{34}H_{44}O_{19}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 17. | Saletpangponoside B | $C_{34}H_{44}O_{19}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 18. | Saletpangponoside C | $C_{26}H_{34}O_{13}$ | *B. lupulina* | Antioxidant | Aerial parts | Methanol | [76] |
| 19. | Shanzhiside methyl ester | $C_{17}H_{26}O_{11}$ | *B. cristata*, *B. lupulina*, *B. prionitis*, *B. trispinosa* | Acetylcholine esterase inhibition, amelioration of mitochondrial energy metabolism, antifibrinolytic, anti-inflammatory, antinociceptive, attenuation of apoptosis, glutathione S transferase inhibition, radical scavenging activity | Leaves, aerial parts | Ethanol, methanol | [9, 71, 76, 80–82, 87, 88] |
| Phenolics | | | | | | | |
| 1. | 1,2-Benzenedicarboxylic acid, bis(2-methylpropyl) ester | $C_{16}H_{22}O_4$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 2. | 2,6-dimethoxyphenol | $C_8H_{10}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 3. | 2-Methoxy-4-vinylphenol | $C_9H_{10}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 4. | 2-Propanone, 1-(4-hydroxy-3-methoxyphenyl) | $C_{10}H_{12}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 5. | 4,7,7-Trimethylbicyclo[2.2.1]heptan-2-one O-allyloxime | $C_{13}H_{21}NO$ | *B. courtallica* | Antimicrobial | Root, stem | Ethanol | [61] |
| 6. | 4-Hydroxy-*trans*-cinnamate derivatives | $C_9H_8O_3$ | *B. cristata* | Antifungal, antimicrobial | Whole plant | Methanol | [89] |
| 7. | Androstane-11,17-dione, 3-[(trimethylsilyl) oxy]-, 17-[O-(phenylmethyl)oxime], (3α,5α)- | $C_{29}H_{43}NO_3Si$ | *B. courtallica* | Antiasthma, anticancer, anti-inflammatory, antimicrobial, diuretic, hepatoprotective | Root | Ethanol | [61] |
| 8. | Benzoic acid, 4-ethenyl-, methyl ester | $C_{10}H_{10}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 9. | Benzyl benzoate | $C_{14}H_{12}O_2$ | *B. lupulina* | Antibacterial | Leaves, stem | Acetone, methanol | [54] |
| 10. | Coumarin, 8-acetyl-7-hydroxy-4-methyl- | $C_{12}H_{10}O_4$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 11. | Homovanillyl alcohol | $C_9H_{12}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 12. | Maltol | $C_6H_6O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 13. | Methyl paraben | $C_8H_8O_3$ | *B. lupulina* | Antibacterial | Leaves, stem | Acetone, methanol | [54] |
| 14. | *p*-Hydroxy benzoic acid | $C_7H_6O_3$ | *B. cristata* var. *alba*, *B. montana* | Antimicrobial, antioxidant, oestrogenic, hepatoprotective | Aerial parts | Ethyl acetate, methanol | [57, 73] |
| 15. | *p*-Coumaric acid | $C_9H_8O_3$ | *B. cristata* | Antioxidant | Leaves | | [71] |
| 16. | Phenol, 2,4-bis(1,1-dimethylethyl)- | $C_{14}H_{22}O$ | *B. prionitis* | Antimicrobial, catalytic | Leaves | Water | [59] |
| 17. | Phenol, 2-methoxy- | $C_7H_8O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 18. | Phenol, 4-butyl- | $C_{10}H_{14}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 19. | α-Tocopherol | $C_{29}H_{50}O_2$ | *B. courtallica*, *B. cristata* | Analgesic, antidiabetic, antisterility, antioxidant, antispasmodic, antitumour, hepatoprotective, hypocholesterolemic, hypoglycaemic, vasodilator | Leaves, stem | Ethanol | [61, 71] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| Phenolic glycosides | | | | | | | |
| 1. | Acteoside (Verbascoside) | $C_{29}H_{36}O_{15}$ | *B. cristata*, *B. cristata* var. *alba*, *B. lupulina*, *B. prionitis*, *B. strigosa* | Antibacterial, antimicrobial, antiviral immunomodulating | Aerial parts, callus from aerial shoots, whole plant | Ethanol, ethyl acetate, methanol | [72, 73, 76, 84, 90–92] |
| 2. | Decaffeoylverbascoside | $C_{20}H_{30}O_{12}$ | *B. strigosa* | Antimicrobial | Whole plant | Methanol | [72] |
| 3. | Desrhamnosyl acteoside | $C_{29}H_{36}O_{16}$ | *B. cristata* | Antimicrobial, immunomodulating | Callus from aerial shoots | Ethanol | [90–92] |
| 4. | Dimethoxyverbascoside | $C_{31}H_{40}O_{15}$ | *B. cristata* var. *alba* | Antibacterial, antiviral | Aerial parts | Ethyl acetate | [73] |
| 5. | Ipolamiide | $C_{17}H_{26}O_{11}$ | *B. lupulina* | Antimicrobial, antioxidant | Aerial parts | Methanol | [76] |
| 6. | Ipolamiidoside | $C_{19}H_{28}O_{12}$ | *B. lupulina* | Antimicrobial, antioxidant | Aerial parts | Methanol | [76] |
| 7. | Isoverbascoside | $C_{29}H_{36}O_{15}$ | *B. cristata* var. *alba*, *B. strigosa* | Antibacterial, Antiviral | Aerial parts, whole plant | Ethyl acetate, methanol | [72, 73] |
| 8. | Phlorigidoside B | $C_{19}H_{28}O_{13}$ | *B. lupulina* | Antimicrobial, antioxidant | Aerial parts | Methanol | [76] |
| Phenylethanoid and phenylpropanoid glycosides | | | | | | | |
| 1. | (3R)-1-octen-3-ol-3-O-β-d-xylosyl-(1→6)-β-d-glucoside | $C_{29}H_{36}O_{15}$ | *B. strigosa* | Antimicrobial, antiseptic | Whole plant | Methanol | [72, 93, 94] |
| 2. | 4-Hydroxyphenylethyl 4-O-β-d-glucopyranosyl-(1→3)-O-α-l-rhamnopyranoside(strigoside) | $C_{20}H_{30}O_{11}$ | *B. strigosa* | Antioxidant | Whole plant | Methanol | [72] |
| 3. | Barlerinoside | $C_{42}H_{58}O_{24}$ | *B. prionitis* | Antioxidant | Aerial parts | Ethanol | [9] |
| 4. | Parvifloroside A | $C_{29}H_{36}O_{15}$ | *B. strigosa* | Anti-inflammatory, antioxidant, antiproliferative | Leaves | Methanol | [95] |
| 5. | Parvifloroside B | $C_{29}H_{36}O_{15}$ | *B. strigosa* | Anti-inflammatory, antioxidant, antiproliferative | Leaves | Methanol | [95] |
| 6. | Poliumoside | $C_{35}H_{46}O_{19}$ | *B. cristata*, *B. lupulina* | Antiproliferative | Aerial parts, callus from aerial shoots | Ethanol, methanol | [76, 90, 96] |
| Phytols | | | | | | | |
| 1. | 1-Dodecanol, 3,7,11-trimethyl- | $C_{15}H_{32}O$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 2. | 2-Pentanone, 1-(2,4,6-trihydroxyphenyl) | $C_{11}H_{14}O_4$ | *B. noctiflora* | Antibacterial, antioxidant | Leaves | Methanol | [56] |
| 3. | 3,4-Dimethoxyphenethyl alcohol | $C_{10}H_{14}O_3$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 4. | *trans*-3(10)-Caren-2-ol | $C_{10}H_{16}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| Phytosterols | | | | | | | |
| 1. | 13,14-Seco-stigmasta-5,14-diene-3-α-ol | $C_{29}H_{48}O$ | *B. prionitis* | Acetylcholine esterase inhibition, antibacterial | Aerial parts | Ethanol | [10] |
| 2. | Hexestrol | $C_{18}H_{22}O_2$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 3. | Stigmasterol | $C_{29}H_{48}O$ | *B. courtallica*, *B. montana* | Antiangiogenic, antibacterial, anticancer, antihepatotoxic, anti-inflammatory, antioxidant, antiviral, oestrogenic artemicide, hypocholesterolemic, sedative | Leaves, root, stem | Ethanol | [61, 69, 97] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 4. | β-sitosterol | $C_{45}H_{80}O_2$ | *B. courtallica*, *B. prionitis* | Antiasthma, antiatherogenic, anticancer, antifertility, anti-inflammatory, antimicrobial, antioxidant, diuretic, hepatoprotective | Leaves, root, stem | Ethanol, methanol | [61, 98] |
| Sulfur compounds | | | | | | | |
| 1. | 2-Undecanethiol, 2-methyl- | $C_{12}H_{26}S$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| 2. | Disulfide, di-tert-dodecyl | $C_{24}H_{50}S_2$ | *B. prionitis* | Catalytic | Leaves | Water | [59] |
| Terpenes and terpenoids | | | | | | | |
| 1. | 1, H-3a-7-methanoazulene | $C_{15}H_{24}$ | *B. lupulina* | Antimicrobial, cytotoxic | Leaves | Ethanol | [55] |
| 2. | 1,2-Benzenedicarboxylic acid, butyl 8-methylnonyl ester | $C_{22}H_{34}O_4$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 3. | 1,3:2,5-Dimethylene-l-rhamnitol | $C_8H_{14}O_5$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 4. | 17-Pentatriacontene | $C_{35}H_{70}$ | *B. prionitis* | Antiseptic, catalytic | Leaves | Water | [59] |
| 5. | 2-Hydroxy-6-methylbenzaldehyde | $C_8H_8O_2$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 6. | 3,7,11,15, Tetramethyl-2-hexadecanoic acid | $C_{21}H_{42}O_2$ | *B. lupulina* | Antibacterial, cytotoxic | Leaves | Ethanol | [55] |
| 7. | 3-Buten-2-one, 4-(2,2,6-trimethyl-7-oxabicyclo [4.1.0] hept-1-yl)- | $C_{13}H_{20}O_2$ | *B. noctiflora* | Antioxidant | Leaves | Methanol | [56] |
| 8. | 3-Chloropropionic acid, heptadecyl ester | $C_{20}H_{39}ClO_2$ | *B. prionitis* | Antimicrobial, catalytic | Leaves | Water | [59] |
| 9. | 5,5,8a-Trimethyl-3,5,6,7,8,8a-hexahydro-2H-chromene | $C_{12}H_{20}O$ | *B. noctiflora* | Antihistamine, antioxidant | Leaves | Methanol | [56] |
| 10. | 7-Epi-*cis*-sesquisabinene hydrate | $C_{15}H_{26}O$ | *B. courtallica* | Analgesic, antibacterial, anti-inflammatory, antitumour, fungicidal, sedative | Leaves | Ethanol | [61] |
| 11. | Benzene, (1-methyldecyl) | $C_{17}H_{28}$ | *B. lupulina* | Antibacterial | Leaves, stem | Acetone, methanol | [54] |
| 12. | Bicyclo[2.2.2]oct-7-ene-2,5-dione | $C_8H_8O_2$ | *B. noctiflora* | Antibacterial | Leaves | Methanol | [56] |
| 13. | Caryophyllene | $C_{15}H_{24}$ | *B. courtallica* | Analgesic, antibacterial, anti-inflammatory, antitumour, fungicide, sedative | Leaves | Ethanol | [61] |
| 14. | *cis*-Thiopsine | $C_{15}H_{24}$ | *B. lupulina* | Antibacterial, anti-inflammatory, cytotoxic | Leaves | Ethanol | [55] |
| 15. | Ethyl 9,12,15-octadecatrienoate | $C_{20}H_{34}$ | *B. lupulina* | Antibacterial, anti-inflammatory | Leaves | Ethanol | [55] |
| 16. | Lup-20(29)-en-3-ol, acetate, (3 β)- | $C_{32}H_{52}O_2$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 17. | Lupeol | $C_{30}H_{50}O$ | *B. courtallica*, *B. prionitis* | Analgesic, anticancer, anti-inflammatory, antimicrobial, antioxidant | Aerial parts, leaves, whole plant | Ethanol | [10, 61, 77] |
| 18. | Oleanolic acid | $C_{30}H_{48}O_3$ | *B. cristata* | Antidiabetic, anti-inflammatory, antimicrobial, antioxidant, antitumour | Whole plant | Methanol | [89, 99–103] |
| 19. | Oxiranehexadecyl (phytol) | $C_{20}H_{40}O$ | *B. courtallica*, *B. lupulina*, *B. montana* | Antibacterial, anticancer, anti-inflammatory, antimicrobial, cytotoxic, diuretic | Leaves, stem | Acetone, ethanol, methanol | [54, 55, 61, 69] |
| 20. | p-Cymen-7-ol | $C_{10}H_{14}O$ | *B. courtallica* | Anti-inflammatory, antimicrobial | Root, stem | Ethanol | [61] |
| 21. | Phytol acetate | $C_{22}H_{42}O_2$ | *B. courtallica*, *B. lupulina* | Anticancer, anti-inflammatory, antimicrobial, antioxidant, cytotoxic, diuretic | Leaves, root | Ethanol | [55, 61] |

**Table 2** Continued

| Compound | | Molecular formula | Species | Biological activity | Plant part(s) used | Solvent(s) used | Reference(s) |
|---|---|---|---|---|---|---|---|
| 22. | Pipataline | $C_{19}H_{28}O_2$ | *B. prionitis* | α-Glucosidase inhibitor, antiviral, hyperlipoproteinemic | Aerial parts, whole plant | Ethanol | [10, 77] |
| 23. | Quinic acid | $C_7H_{12}O_6$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 24. | Squalene | $C_{30}H_{50}$ | *B. courtallica*, *B. lupulina* | Antibacterial, antioxidant, antitumour, cancer preventive, chemopreventive, immunostimulant, lipoxygenase inhibitor, pesticidal | Leaves, root, stem | Acetone, ethanol, methanol | [54, 55, 61] |
| 25. | Urs-12-en-24-oic acid, 3-oxo-, methyl ester | $C_{31}H_{48}O_3$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |
| 26. | Ursolic acid | $C_{30}H_{48}O_3$ | *B. montana* | Anti-apoptotic, anticancer, Antimicrobial, antioxidant, antitumour, hepatoprotective | Aerial parts | Methanol | [57, 104, 105] |
| 27. | β-Amyrin trimethylsilyl ether | $C_{33}H_{58}OSi$ | *B. montana* | Antibacterial | Leaves | Ethanol | [69] |

## Toxicity Studies

The available literature on toxicity studies in *Barleria* is very scarce. The studies have been conducted with appropriate biological and non-biological controls. A few studies conducted using extracts of *B. prionitis* and *B. lupulina* had no adverse effect or mortality of rat models.[106–108] In fact, the administration of the extracts has proven to be useful in improving conditions such as hyperglycaemia and inflammation. Alcoholic root and leaf extracts of *B. prionitis* with a dose of 2500 mg $kg^{-1}$ body weight, when administered orally, had no toxic effects in adult albino rats and no death was caused up to 14 days.[106] Similarly, oral administration of the aqueous fraction of *B. prionitis* (3000 mg $kg^{-1}$) rich in iridoid glucoside to mice did not cause any abnormalities or any death up to 15 days. However, the aqueous fraction showed $LD_{50}$ (i.p.) value of 2530 mg $kg^{-1}$ body weight in mice.[108] The $LD_{50}$ value of the methanolic extracts of *B. lupulina* in mice was 4500 mg $kg^{-1}$ body weight (per organism) and 3700 mg $kg^{-1}$ body weight (i.p.). Leaf extract (aqueous) of *B. cristata* showed $LD_{50}$ of higher than 2.0 g $kg^{-1}$ showing the anti-inflammatory action on Wistar albino rats.[107] *B. lupulina* (methanolic extract) at a maximum of 200 mg $kg^{-1}$ body weight showed considerable ($P < 0.01$) anti-hyperglycaemic efficacy in albino rats (from 4 h to 12 h). The group administered with 300 mg $kg^{-1}$ body weight showed high potential of reducing blood glucose (15.35%) after 12 h of administration when compared with glibenclamide (10 mg $kg^{-1}$ body weight), which led to an 18.8% decrease in blood glucose level simultaneously.[109]

## Local and Traditional Medical Uses

Ethnomedical uses of *Barleria* have their roots in Kautilya's Arthasastra.[110] Most of the studies on ethnomedical uses have been concentrated on *B. cristata* and *B. prionitis*. Researchers have used whole plant, roots, leaves, stem, bark, flowers, etc. for the preparation of extracts and have used it in various medical conditions.

*B. cristata* is used in fever, bronchitis, blood diseases and disorders like anaemia, induction of hemostasis during wound healing, etc. Its sap has been found useful in catarrhal affections of the children.[111] In a study by Selvanayagam et al.[112] the root paste of *B. cristata* showed anti-snake venom activity, when administered orally, while in another study the whole plant had been shown to exhibit anti-snake venom activity.[113] Leaves and roots of *B. cristata* are used to reduce swellings, cough whereas the root decoction is used in rheumatism and as a substitute for human breast milk.[113]

*Barleria prionitis* leaf extract has been used to cure skin boils.[114] Its leaves are reported to cure toothache when chewed, and a root decoction is useful in toothache as a mouthwash.[114] Crushed fresh leaves are applied to wounds and pimples. These are also used in rheumatic pain. The leaves and flowering tops are a rich source of Potassium salts and are shown to have diuretic action.[115] The ash of the leaves, when applied on piles, has curative properties whereas the decoction of leaves is given orally to control the irritation.[116] A paste from the roots is applied on swelling and on boils.[113, 114] It works as an antiseptic and the decoction utilized in dropsy for body washings.[114] The leaf sap is used in urinary and stomach disorders as well as paralytic affections. The leaf sap, together with sugar and honey, is also employed for curing catarrhal affections associated with fever and phlegm

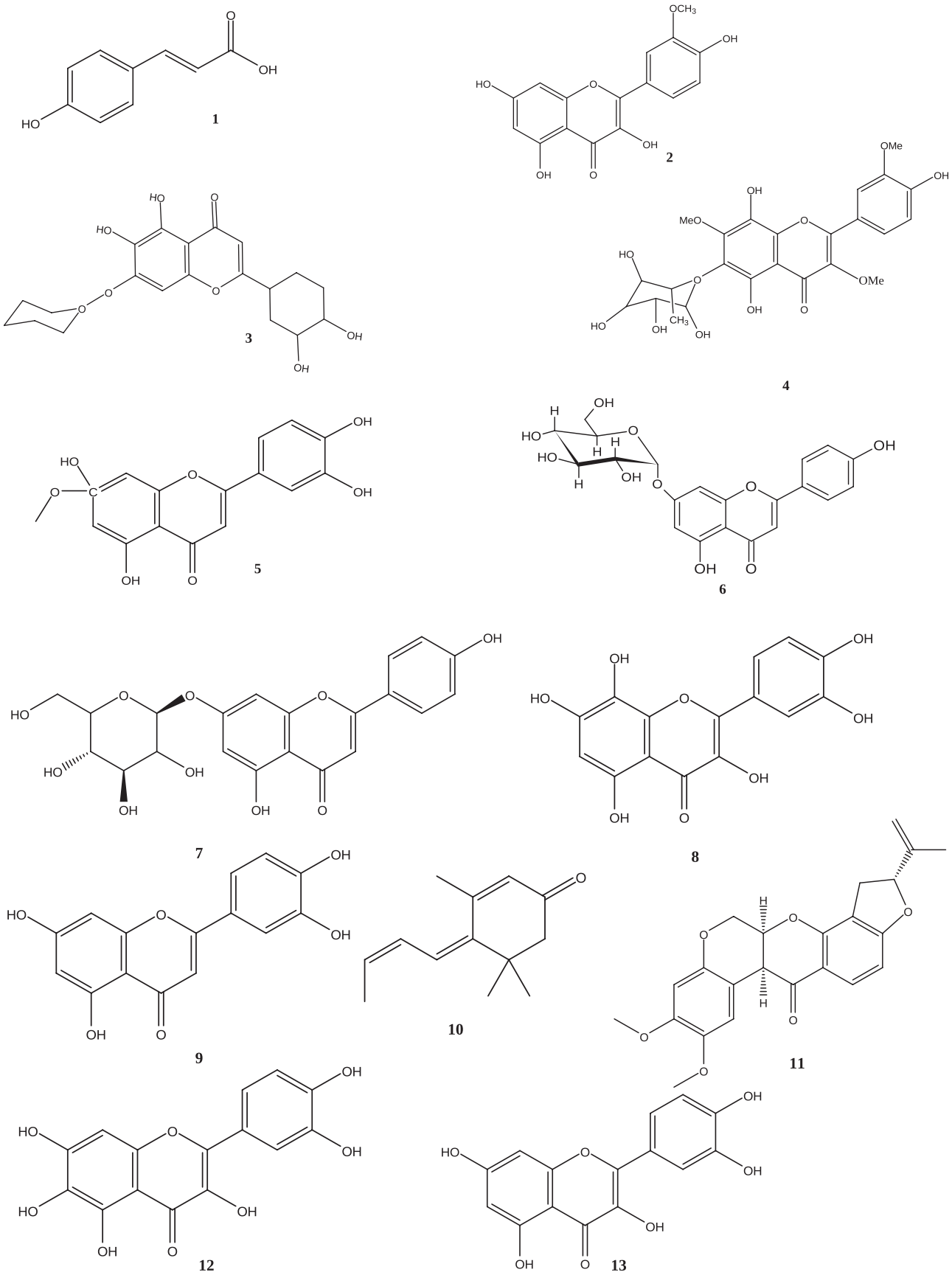
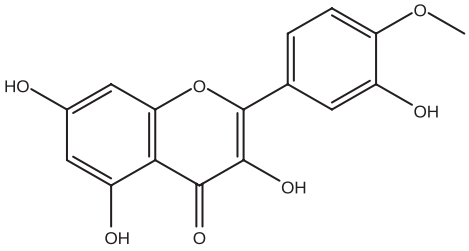


**Figure 5** The chemical structures of some important phytochemicals isolated and identified from *Barleria* species. (1) p-hydroxy cinnamic acid, (2) 3-methoxy quercetin, (3) 6-O-α-l-rhamnopyranoside quercetagetin, (4) 6-O-α-l-rhamnopyranoside-3,7,3′-O-trimethylated-8-hydroxyquercetin, (5) 7-methoxy luteolin, (6) apigenin 7-O-α-l-rhamnosyl-(1→6)O-β-d-glucoside, (7) apigenin 7-O-glucoside, (8) gossypetin, (9) luteolin, (10) megastigmatrienone, (11) nicouline, (12) quercetagetin, (13) quercetin, (14) tamarixetin, (15) (3R)-1-octen-3-yl-β-primeveroside, (16) balarenone, (17) forsythoside B, (18) prioniside A, (19) prioniside B, (20) prioniside C, (21) (+)-lyoniresinol 3α-O-β-d-glucoside, (22) 10-O-*trans*-coumaroyl-eranthemoside,



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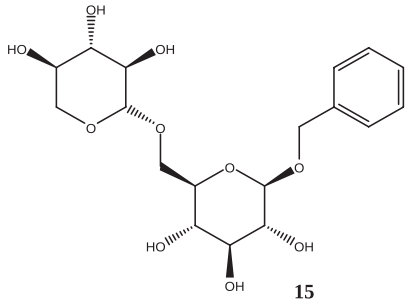

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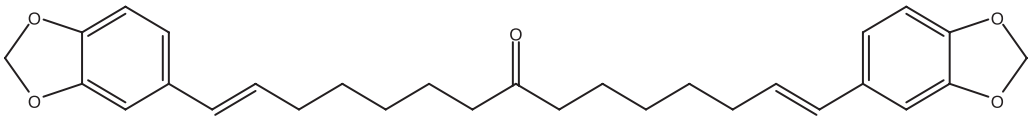

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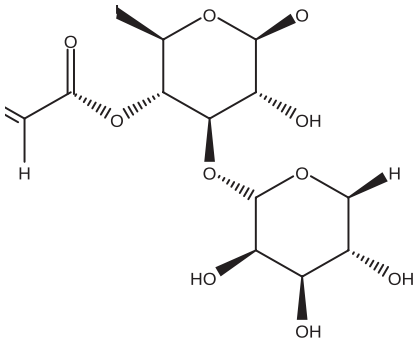

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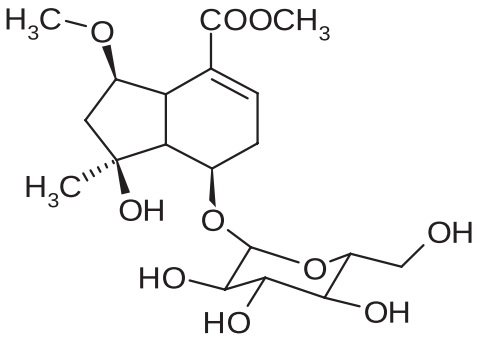

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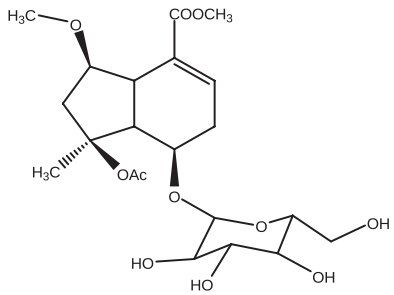

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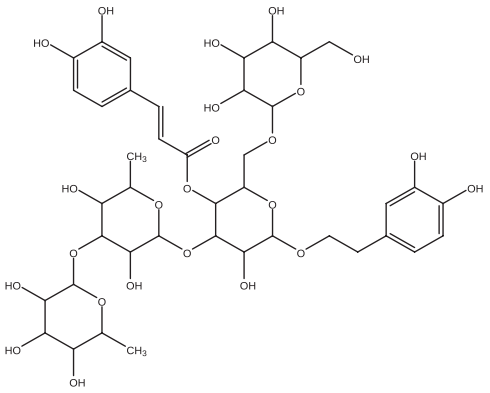

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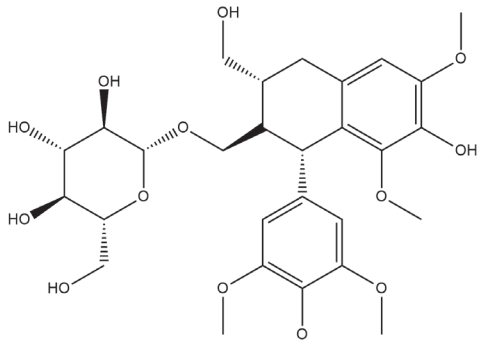
(23) 6-O-acetylshanzhiside methyl ester, (24) 6,8-O,O-diacetylshanhiside methyl ester same (acetyl barlerin), (25) 6-α-l-rhamnopyranosyl-8-O-acetylshanzhiside methyl ester, (26) 6-O-*cis*-p-coumaroyl-8-O-acetylshanzhiside methyl ester, (27) 6-O-*trans*-p-coumaroyl-8-O-acetylshanzhiside methyl ester, (28) 8-O-acetyl-6-O-*trans*-p-coumaroylshanzhiside, (29) barlerin, (30) lupulinoside, (31) saletpangponoside A, (32) saletpangponoside B, (33) saletpangponoside C, (34) shanzhiside methyl ester, (35) acteoside (verbascoside), (37) decaffeoylverbascoside, (37) desrhamnosyl acteoside, (38) dimethoxyverbascoside, (39) ipolamiide, (40) ipolamiidoside, (41) isoverbascoside, (42) phlorigidoside B, (43) 4-hydroxyphenylethyl 4-O-β-d-glucopyranosyl-(1→gluO-α-l-rhamnopyranoside (strigoside), (44) parvifloroside A, (45) parvifloroside B, (46) barlerinoside, (47) poliumoside.



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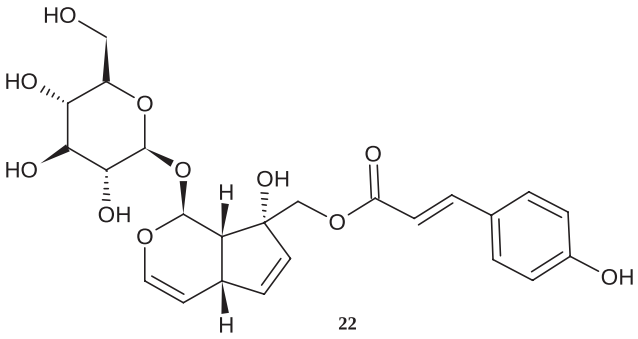

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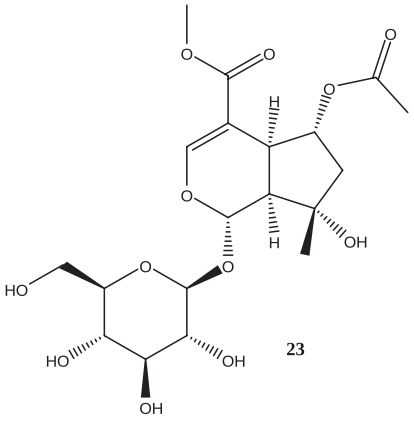

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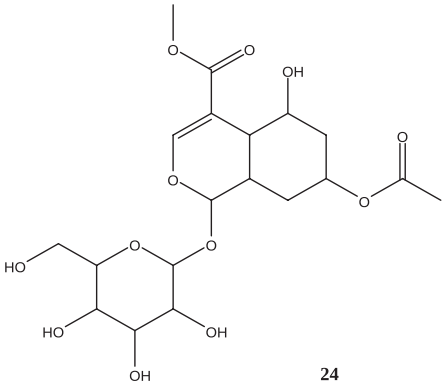

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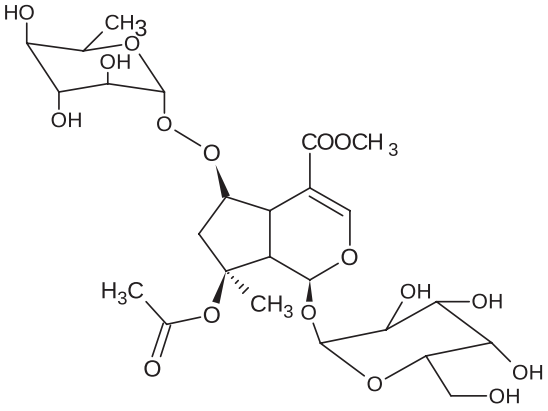

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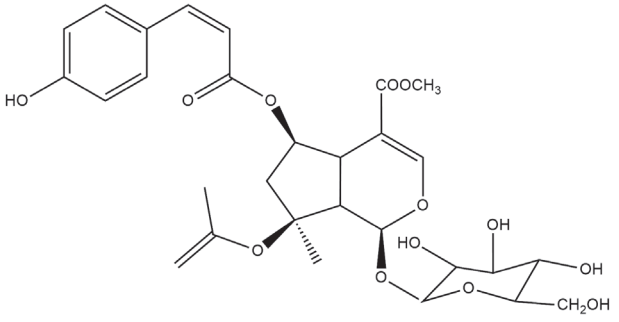

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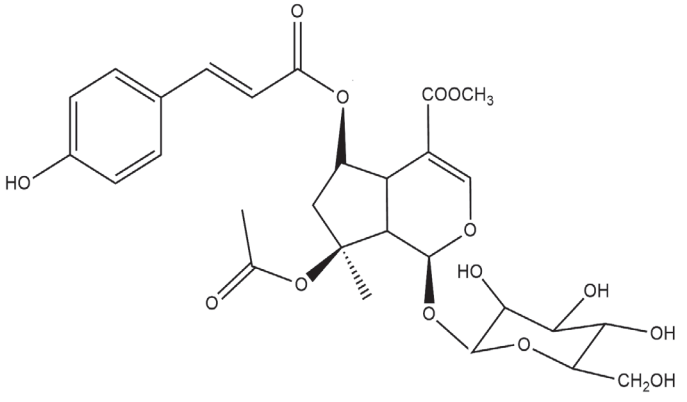

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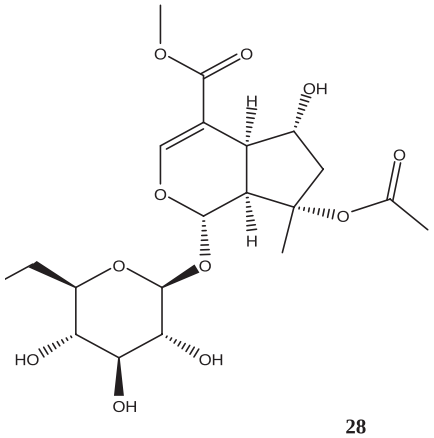

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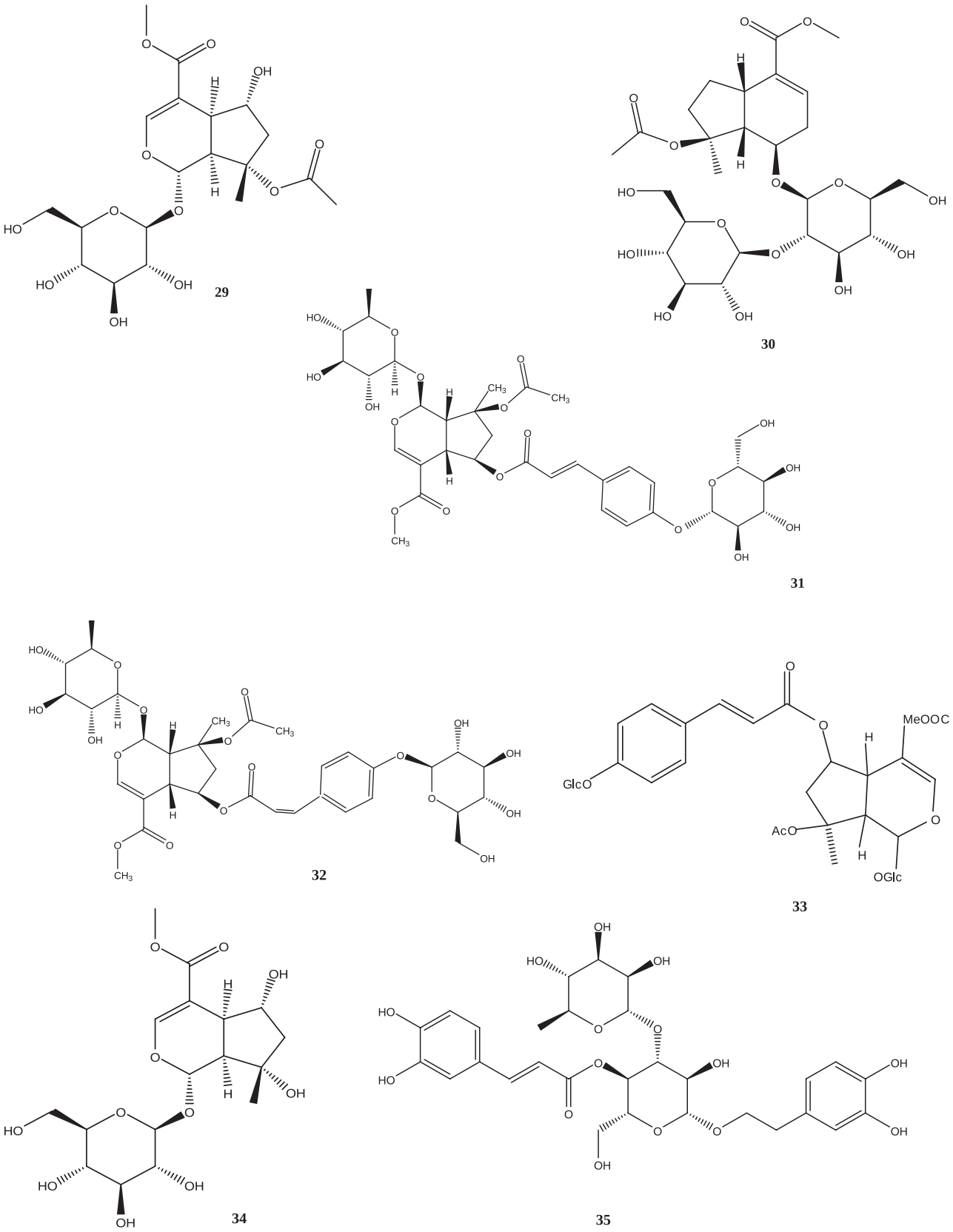


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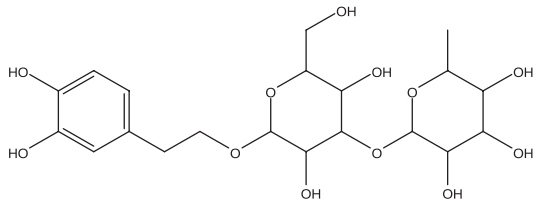

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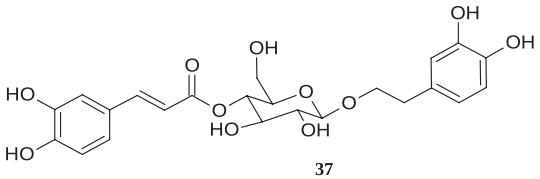

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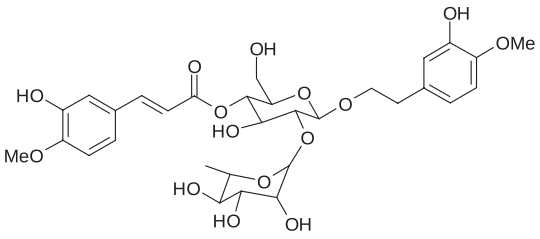

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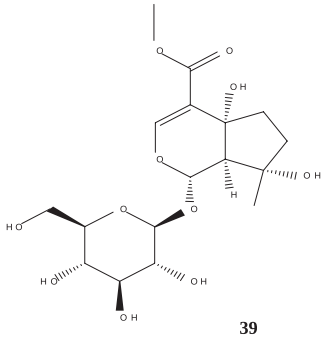

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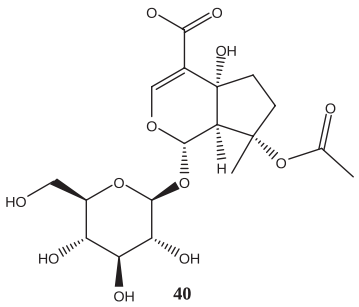

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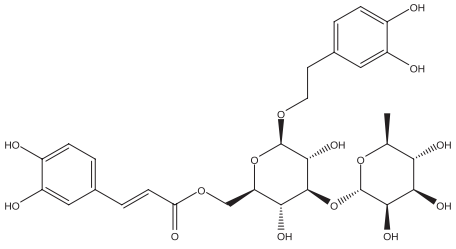

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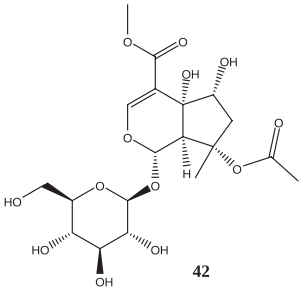

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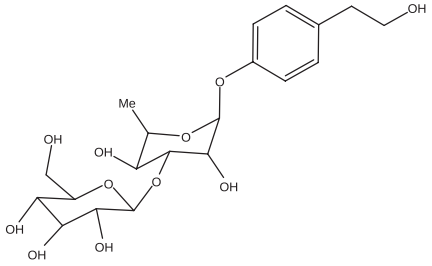

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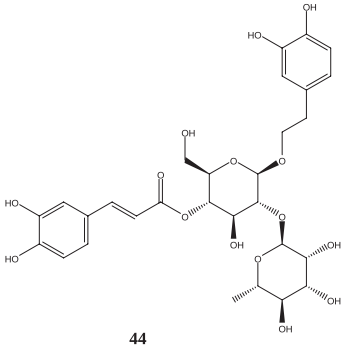

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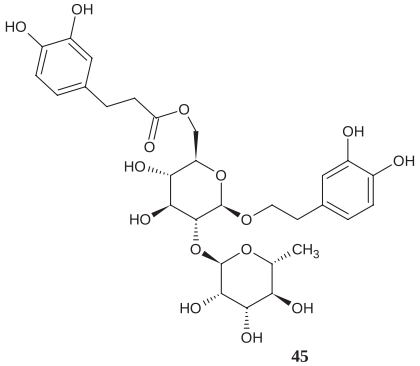

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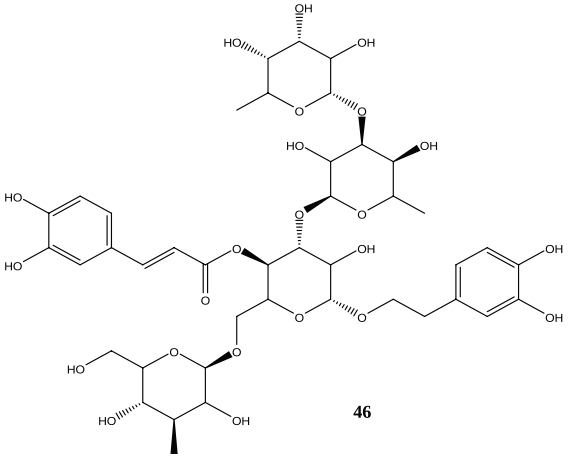

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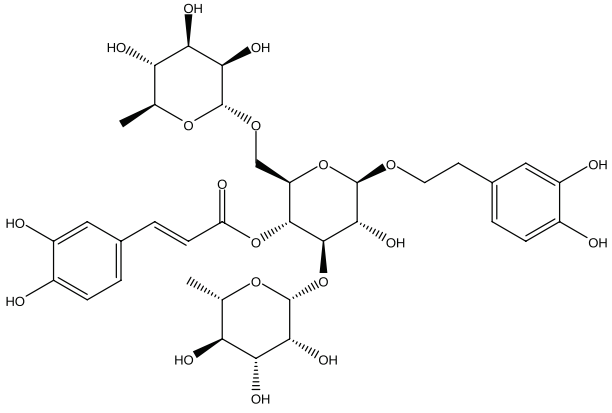

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**Figure 5** Continued

in children. Tribes of the Indian arid zone use the leaf sap to harden the soles of feet. The sap of fresh bark acts as diaphoretic and expectorant. Dried bark powder mixed with honey is used in cough and whooping cough.[115, 117, 118]

Fresh leaves of *B. lupulina* are used to remove warts.[119] They act as anti-inflammatory and analgesic. It stops bleeding from wounds.[119] Traditionally, *B. lupulina* is a diuretic, antiamoebic and anti-inflammatory against insect and snake bites in Thai folk medicine. It has shown antiviral potential against *Varicella zoster*, *Herpes simplex* and *Herpes zoster*.[76, 120, 121]

*Barleria strigosa* leaf sap is given in diarrhoea and the fruit prescribed in gingivitis and as an expectorant.[122] Powdered seeds are emetic and expectorant whereas root paste is an antidote for snake bites.[123]

Three species of *Barleria*, viz. *B. micrantha*, *B. opaca*, *B. taitensis* are a part traditional African medicine system. Aerial parts of *B. micrantha* have been used as a laxative as well as to cure haemorrhoids. Leaves of *B. opaca* were found to be useful as laxative, in the treatment of haemorrhoids, cerebromalaria and snakebite.[124–126] Leaves and stem of *B. taitensis* were reported to have anti-inflammatory properties.[126, 127]

## Pharmacological Effects

*Barleria* species have been evaluated for different pharmacological activities. Natural bioactive compounds in *Barleria* species pose minimum side effects to the patients and thus can be used as potent drugs instead of synthetic drugs.[128] Various extracts (from leaves, bark, stem, root and whole plant) obtained from different species of *Barleria* have shown pharmacological activity. The activities can be broadly grouped as anticancer, anticataract, anti-inflammatory, antimicrobial, antioxidant, antiparasitic, antiulcer, enzyme inhibition, hepatoprotective and wound healing. In-vivo as well as in-vitro experimental studies have been used to evaluate activities. Few of the animal models were used to evaluate the various biological activities, including rats, mice, Tilapia fish, goat lenses, etc. Table 2 summarizes the biological activities of *Barleria* species. The biological activities exhibited by *Barleria* species are depicted in Figure 6 and described below:

### Antiarthritic

The studies on antiarthritic activity in *Barleria* have been limited to *B. lupulina* and *B. prionitis*.

Antiarthritic activity of *B. lupulina* leaf extract (methanolic) (300 and 600 mg $kg^{-1}$ body weight) was assessed in various rat models such as formalin-induced arthritis, adjuvant-induced arthritis, collagen type II-induced arthritis and monosodium iodoacetate-induced osteoarthritis. Considerable inhibition of oedema and myeloperoxidase (MPO) indicated antiarthritic activity.[129] Ethyl acetate fraction of the chloroform extract from *B. prionitis* leaves (125 and 250 mg $kg^{-1}$) showed significant and dose-dependent antiarthritic potential when administered to rats in case of acute non-immunological (formaldehyde-induced) and chronic immunological arthritis (Freund's complete adjuvant-induced).[130]

### Antitumour

Leaf extract of *B. lupulina* has the potential to reduce γ-rays induced tumour (1.2 Gy) by completely decreasing the tumour (ulcer proliferative growth) which occurred near nostril in fresh water Tilapia fish (*Oreochromis mossambicus*) within nine days.[131]

### Anticataract

Cataract, a major cause of blindness all over the world, is an age-related phenomenon.[132] *In vitro* anticataract potential of *Barleria* was determined using ethyl acetate fraction of *B. lupulina* against glucose-induced cataractogenesis using goat lenses. Four groups were made. Group I (normal control) with artificial aqueous humour solution. Group II (control) with artificial aqueous humour solution with 55 mM glucose. Groups III and IV consisted of artificial aqueous humour solution and 55 mM glucose along with 200 and 400 μg $ml^{-1}$ ethyl acetate fraction of *B. lupulina*, respectively. Groups III and IV showed significant anticataract activity against glucose-induced cataractogenesis.[132]

### Anticlastogenic

Sur and Das[131] evaluated the anticlastogenic potential of leaf extract (aqueous) of *B. lupulina* in mice. They divided animals into three sets, sets I and III for pre-treatment and post-treatment of *B. lupulina* plant extract. Set II was kept as control (the entire body of mice was subjected to Cobalt (Co-60) γ-irradiation (1.2 Gy). In set I, mice were injected with aqueous extract at 1 ml 100 $g^{-1}$ body weight, and after 1 h, the whole body was exposed to γ-irradiation (1.2 Gy) from Cobalt (Co-60). In set III, mice were exposed to γ-irradiation (1.2 Gy) from Cobalt (Co-60) and after 1 h injected with aqueous extract at 1 ml 100 $g^{-1}$ body weight. Chromosome aberration was studied at time intervals of 1, 16, 48 h, 1 and 4 weeks in each set of animals. The frequency of chromosome aberration was found to be increased in control (set II) from first to 48 h (16.63%). Similarly, at the same time interval set I and set III showed 7.53% and 4.62% aberrations, respectively. The percentage aberration was low for set III mice (0.22% with translocation) when compared with set I (0.31%) and control set II (1.93% with chromosome dissociation, 1.92% with chromatid break). The results exhibited that *B. lupulina* aqueous extract had a significant role in radiation protection against γ-rays induced structural chromosomal damage in mice.

### Antifertility

Very few reports are available on the antifertility activity of *Barleria*. The effect of the extracts of *Barleria* on the reproductive system of male rats has been studied.[133–135] Extract of the root of *B. prionitis*, when given through mouth to male rats, decreased their fertility by 100% without any reduction of body weight. The process of spermatogenesis was affected and there was 73.6% reduction in round spermatids, primary and secondary spermatids, Sertoli cells and Leydig cells.[134] Antifertility was also observed due to antispermatogenecity.[97, 136, 137]

### Anti-inflammatory

Inflammation is a defence reaction that controls the spreading of injurious agents. The anti-inflammation potential of root extract of *B. cristata* (250, 500 mg $kg^{-1}$) was evaluated in Swiss albino mice (25–30 g) and Wistar albino rats (180–220 g) of both the sexes by employing an acute inflammatory model, viz. carrageenan-induced paw oedema and chronic model and cotton pellet-induced granuloma.[138] *B. cristata* (methanolic

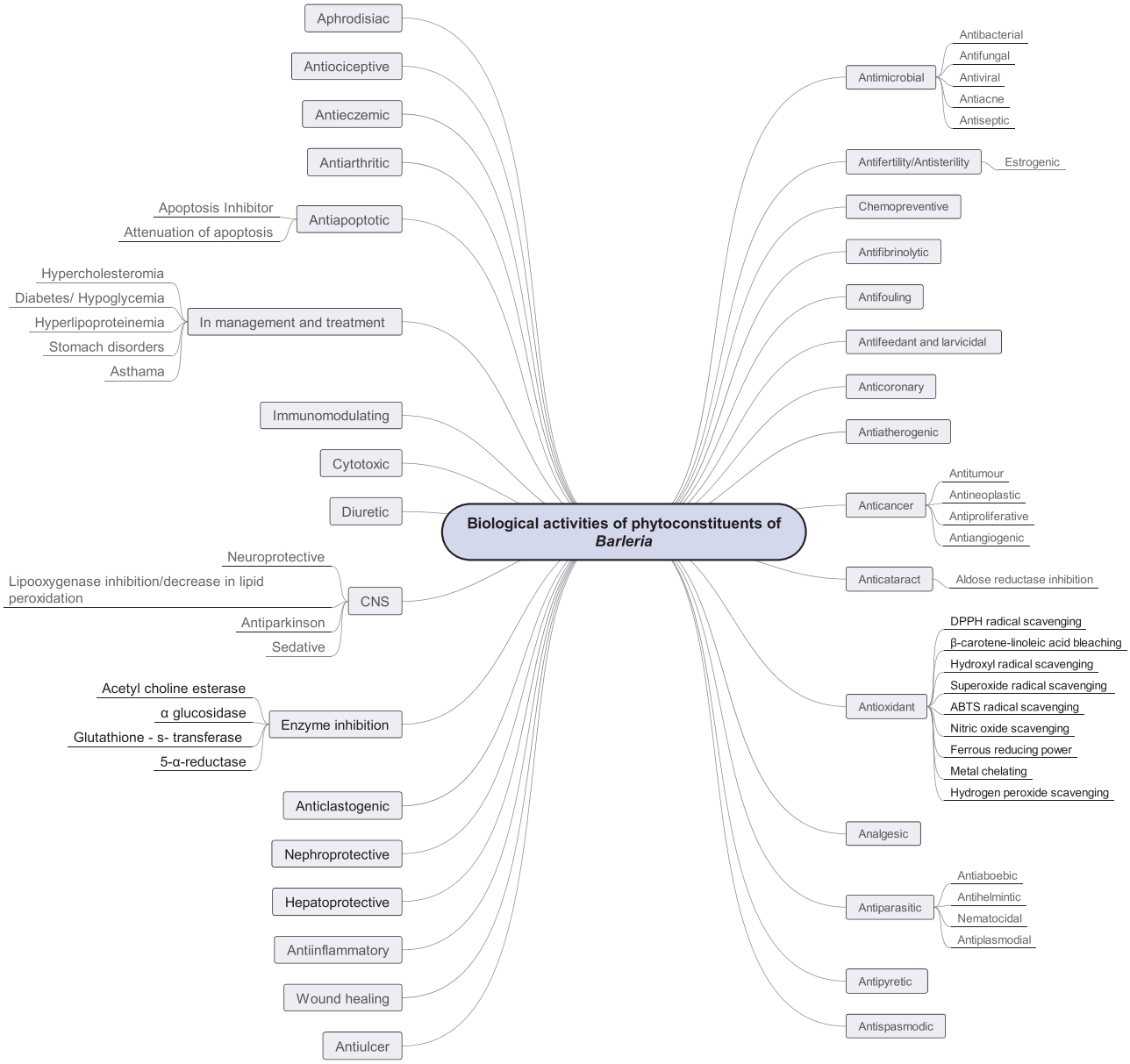


**Figure 6** Biological activities exhibited by *Barleria*.

extract) at 500 mg $kg^{-1}$ body weight inhibited 51% of oedema while 64% inhibition of granuloma was observed. However, the standard (indomethacin) showed 78.67% inhibition. Suba et al.[139] assessed the anti-inflammatory activity of *B. lupulina* (methanolic extract of aerial parts at 200, 300 mg $kg^{-1}$ body weight) in acute and sub-acute inflammation model albino rats (180–200 g) and Swiss albino mice (20–25 g) of both the sexes. The highest inhibition (41.93%) of oedema was observed at 300 mg $kg^{-1}$ methanolic extract of *B. lupulina* after 4 h in serotonin-induced paw oedema. The same concentration extract of *B. lupulina* showed 40.19% inhibition after 5 h in paw oedema caused by carrageenan. The study revealed the potential of the plant to exhibit significant inhibition of dose-dependent paw oedema caused by carrageenan and serotonin.[140] *B. lupulina* extracts showed dose-dependent inhibition in both carrageenan and ethyl phenyl propiolate-induced rat paw oedema by inhibiting the MPO activity in the inflammed tissue and is suggestive of reduced neutrophil migration towards the site of inflammation, without any effect on neutrophil viability and apoptosis.[141] Similar types of results were reported in carrageenan-induced rat paw oedema with the *B. prionitis* extract (500 mg $kg^{-1}$) in methanol. Moreover, inhibition of lipooxygenase led to the inhibition of paw oedema induced by carrageenan in rats.[142] Chloroform extract showed 88.31% inhibition of ear oedema caused because of Croton oil when different extracts (200–400 mg $ml^{-1}$) of *B. cristata* and *B. prionitis* were tested for topical anti-inflammatory activity in female rats.[143] Maji et al.[144] validated the anti-inflammatory activity of *B. prionitis* extract (entire plant). The hydroalcoholic extract obtained from *B. prionitis* (entire plant) stabilized mast cells by inhibiting mast cell degranulation in a dose-dependent manner.[144] It also inhibited the hypotonic solution-induced haemolysis of rat erythrocytes.[144]

## Antimicrobial

*Barleria* species have been screened for antimicrobial activity. Various solvents, such as hot and cold water, ethanol, petroleum ether, methanol, dichloromethane, acetone, chloroform, dimethyl ether, etc. were used for extraction. Antibacterial activity of *Barleria* species is expressed in terms of inhibition zone (IZ) and minimum inhibitory concentration (MIC). The antimicrobial activities exhibited by *Barleria* species are on account of phenolics, tannins, saponins and various essential oils present in them.[145, 146]

### *Antibacterial*

Various extracts of *Barleria* species have been assessed for their antibacterial potential. The test organisms used in most of the studies include *Bacillus cereus*, *B. pumilus*, *B. subtilis*, *Enterococcus faecalis*, *Propionibacterium acne*, *Staphylococcus aureus*, *S. epidermidis*, *Streptococcus mutans*, *S. pneumoniae*, *S. pyogenes* (Gram-positive bacteria) and *Comamonas acidovorans*, *Enterobacter aerogenes*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *P. vulgaris*, *Pseudomonas aeruginosa*, *P. beteli*, *P. fluorescence*, *P. putida*, *Salmonella enteritidis*, *S. paratyphi*, *S. typhi*, *Serratia marcescens*, *Shigella dysenteriae*, *Vibrio cholerae* (Gram-negative bacteria.[8, 54, 55, 69, 70, 86, 145–160] Antibacterial activity of various solvent extracts prepared from various parts of *Barleria* was evaluated following agar well diffusion method, micro-dilution bioassay, modified bioautographic procedure, etc. The activities are expressed in terms of zone of inhibition or MIC. Antibacterial studies were performed using extracts prepared in various solvents from various parts of *B. acuminata*,[150] *B. cristata*,[70, 149] *B. prionitis*,[145–148, 151, 157] *B. nitida*,[159] *B. argillicola*,[8, 86] *B. dinteri*,[150] *B. opaca*,[155] *B. montana*[69]) and *B. lupulina*.[54, 55, 152–154, 156, 158, 160]

Saponin fraction from *B. cristata* leaves exhibited significant activity and thus can be a source for the production of potential antimicrobial agents.[161] Balarenone, pipataline and 13,14-seco-stigmasta-5,14-diene-3-β-ol isolated from *B. prionitis* showed antibacterial activity in the case of *B. cereus*, *S. aureus* and *P. aeruginosa*. The highest IZ (25 mm) was observed in 13,14-seco-stigmasta-5,14-diene-3-β-ol against *B. cereus* compared with Ceftriaxone which showed zone of inhibition of 11 mm.[10]

### *Antifungal*

Various methods, such as micro-dilution assay,[7] agar diffusion method, microbroth dilution assay, etc. were used to express the antifungal activity of the crude extracts obtained from different parts (stem, root, leaves) of *Barleria* species. The species explored so far for the antifungal potential include *B. acuminata*, *B. albostellata*, *B. cristata*, *B. eranthemoides*, *B. greenii*, *B. montana* and *B. prionitis*. The fungal species used in most of the studies included *Aspergillus flavus*, *A. fumigatus*, *A. niger*, *A. parasiticus*, *Candida albicans*, *Fusarium moniliforme*, *Penicillium* species, *P. canescens*, *P. chrysogenum*, *Rhizopus stolonifer*, *Saccharomyces cerevisiae* and *Trichophyton* species.

The antifungal activity of *B. albostellata*, *B. greenii* and *B. prionitis* against *C. albicans* was evaluated by broth micro-dilution assay.[7] Extracts (petroleum ether and dichloromethane) of the stem of *B. albostellata* showed lethal activity with the MIC value of 0.780 mg ml$^{-1}$. The highest minimum inhibitory dilution (MID) and minimum fungicidal dilution (MFD) were observed in ethanolic extracts of different parts of all the three species with the highest MID (58.506 g ml$^{-1}$).[7]

Antifungal activity of *B. cristata* against *Aspergillus flavus*, *A. niger*, *Candida albicans*, *Penicillium* species and *Trichophyton* species was documented by Chellathai et al.[162] Antifungal activity of ethanolic extract (1000, 750 and 500 µg ml$^{-1}$) was determined by the agar diffusion method. The largest zone of inhibition (6 mm) was observed in *A. niger* at 1000 µg ml$^{-1}$ whereas the rest of the fungal strains showed moderate susceptibility with an IZ of 3–5 mm. Kumari et al.[163] evaluated the antifungal activity of *B. grandiflora* plant extract (hot and cold water) by using a broth micro-dilution assay. They also studied its effect on the metabolic pathway of *A. fumigatus*. The result showed that *B. grandiflora* extract made in hot water had considerable antimicrobial activity (MIC 0.625–1.25 mg ml$^{-1}$) against eight clinically isolated strains and the standard strain of *A. fumigatus* while lesser activity (MIC 2.5–5.0 mg ml$^{-1}$) was noticed for cold water extract.

Recently, Pal et al.[164] assessed the antifungal activity of natural dye (25, 50, 100, 200, 300, 400 and 500 µg ml$^{-1}$ concentration) extracted from *B. prionitis* (aerial parts) and dyed silk, wool and cotton were assessed against five fungal strains (*A. flavus*, *A. niger*, *A. parasiticus*, *F. moniliforme* and *P. canescens*) and two standards, namely nystatin and griseofulvin. Antifungal activity was dose-dependent and comparable with the standard drug. MIC of natural dye varied from 22.50 to 23.50 µg ml$^{-1}$ against tested fungi. Similarly, dyed fabrics showed significant antifungal efficiency. The study revealed that natural dye obtained from *B. prionitis* is suitable for dyeing textile fabrics with antifungal properties on a large scale.

IZ of 28 mm was observed in leaf and stem ethanolic extract of *B. acuminata* against *C. albicans* and *A. niger*, respectively.[165] In one of the studies by Maregesi et al.[166] leaf extract (methanolic) of *B. eranthemoides* did not exhibit antifungal activity in the case of *A. niger* and *C. albicans*.

Antifungal property of methanolic extract of *B. montana* aerial part has been evaluated against four fungal strains (*A. niger*, *R. stolonifera*, *S. cerevisiae* and *P. chrysogenum*) by Tulliballi and Seru.[57] IZ of 23 mm at 100 mg ml$^{-1}$ and 200 mg ml$^{-1}$ against *R. stolonifera* and *A. niger* was observed, respectively. The study showed that methanolic extract exhibited moderate activity against tested fungi when compared with the standard.

## Antioxidant

For the prevention of oxidative stress which is on account of misproportion of reactive oxygen species, antioxidant substances are produced.[167] So far, 12 species of *Barleria* have been studied for their antioxidant properties *in vitro* by using different assays. These activities include 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging, hydroxyl radical (·OH) scavenging, superoxide radical ($O_2^-$) scavenging, 2,2′-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical cation, nitric oxide scavenging, ferrous reducing power, metal chelating, hydrogen peroxide scavenging and β-carotene linoleic acid bleaching assay. Amoo and Van Staden[8] evaluated the antioxidant activity of *B. argillicola* in the DPPH assay. *B.*

*argillicola* root and aerial part (400 µg ml$^{-1}$) had 72.6% and 47.2% levels of free radical scavenging activity, respectively which was comparable to the reference antioxidant. More or less similar activity (74.9% and 45.6% from root and aerial part of *B. argillicola*, respectively) were found based on β-carotene linoleic acid bleaching. Antioxidant activity of 96.8% and 99.8% were exhibited by butylated hydroxyl toluene (BHT) and ascorbic acid (100 µg ml$^{-1}$), respectively.

Sujatha et al.[168] evaluated in-vitro antioxidant activity of *B. courtallica* using DPPH, ·OH, $O_2^-$, ABTS, nitric oxide scavenging and ferric-reducing antioxidant power (FRAP) assays. The study revealed ethanolic extract showed good antioxidant activity among all the extracts. Strong DPPH radical scavenging activity showed a percentage increase of 141.34% and 42.31 mg ml$^{-1}$ $IC_{50}$ followed by superoxide scavenging activity (percentage increase of 136.92% and 34.56 mg ml$^{-1}$ $IC_{50}$).

DPPH and nitric oxide scavenging activities were performed *in vitro* using ethanolic extract of *B. gibsonii* (EBG) leaves.[169] The study revealed that EBG leaves have potential antioxidant activity. The $IC_{50}$ value of EBG leaves and standard antioxidant (ascorbic acid) was 180 µg ml$^{-1}$ and 170 µg ml$^{-1}$, respectively. Nitric oxide scavenging activity showed a considerable $IC_{50}$ value, that is, 220 µg ml$^{-1}$.[169]

Yadav et al.[170] evaluated antioxidant activity in *B. noctiflora* leaves and roots using seven different in-vitro assays and calculated $IC_{50}$ values. Significant antioxidant capacity was noted in DPPH scavenging assay in methanol extracted roots ($IC_{50}$: 140 µg ml$^{-1}$) and leaf ($IC_{50}$: 150 µg ml$^{-1}$), followed by ABTS radical cation activity that had an $IC_{50}$ value of 150 µg ml$^{-1}$ in methanol root extract. This study suggested that in comparison to the root extract, leaf extract showed relatively less antioxidant activity.

Kalpana et al.[171] noted the antioxidant activity of *B. longiflora* following the DPPH, FRAP and ABTS assay. The free radicals quenching potential of ethanolic leaf extract (200 µg ml$^{-1}$) of *B. longiflora* was 74.33%. Antioxidant activity of 65.66% was exhibited by ABTS radical cation activity (1000 µg ml$^{-1}$). The maximum antioxidant activity in the ethanol extract ($IC_{50}$ = 38 µg ml$^{-1}$) was found in the FRAP assay.

Ethanol and methanol leaf extracts of *B. buxifolia* were analysed by using three different scavenging assays (DPPH assay, Ferrous reducing power and ABTS radical cation). The highest percentage inhibition (61.72% at 1000 µg ml$^{-1}$ concentration methanolic extract of *B. buxifolia*) was observed against DPPH assay followed by ABTS radical cation assay that showed 60.88% activity with $IC_{50}$ = 717.51 µg ml$^{-1}$ at 1000 µg ml$^{-1}$ concentration[172]).

Aqueous leaf extract of *B. mysorensis* leaves exhibited $IC_{50}$ values of 130.19 µg ml$^{-1}$ and 1824.62 µg ml$^{-1}$ for DPPH and metal chelating assay, respectively. The extract showed a dose-dependent increase in the DPPH scavenging and metal chelating activity.[173]

In another study, DPPH, FRAP and β-carotene linoleic acid assays were performed using extracts of *B. prionitis*, *B. greenii* and *B. albostellata*. The DPPH radical scavenging assay showed $EC_{50}$ values ranging from 6.65 to 12.56 µg ml$^{-1}$ for different parts of *Barleria* species.[7]

The FRAP activity of *B. prionitis* and *B. greenii* (leaf and stem extract) were higher than root extract, suggesting that leaf and stem have potential of plant-part substitution for root. Average β-carotene bleaching rate ranged from 52% to 77% in β-carotene linoleic acid model system. The oxidation rate ratio for the different plant parts was in the range of 0.23–0.48. The lowest oxidation rate ratio equal to BHT was observed in *B. prionitis* roots.

The evaluation of antioxidant activity of *B. dinteri* and *B. prionitis* has been assessed using DPPH assay.[86, 145, 146] Ethyl acetate soluble fraction of whole plant (*B. prionitis*) exhibited 97.20% free radical activity with $IC_{50}$ = 25.22 µg ml$^{-1}$ concentration.[145, 146] *B. dinteri* leaves showed impressive activity with acetone and methanol extracts.[86] Nevertheless, in order to validate therapeutic value extensive research needs to be done under *in vivo* conditions.

## Anti-amoebic

Amoebiasis is an unusual parasitic disease usually found among immunocompromised patients caused by a protozoan, *Entamoeba histolytica*. Patients with HIV are more susceptible to infection than normal persons.[121] Anti-amoebic potential of leaf and stem extracts (methanol, chloroform and water) of *B. lupulina* was studied at 1000 µg ml$^{-1}$ against the strains, viz. HTH-56:MUTM and HM1:IMSS. Considerable inhibition ($IC_{50}$: 78.5 µg ml$^{-1}$) was observed in *E. histolytica* using chloroform extract of *B. lupulina* stem.[121]

## Anthelmintic

Leaf extracts (aqueous and ethanolic) of *B. buxifolia* were studied against *Pheretima posthuma* at (10, 20, 40, 80 and 100 mg ml$^{-1}$ concentrations) to assess anthelmintic activity. Time for paralysis and death was measured and compared with albendazole (10 mg ml$^{-1}$). Results revealed that the ethanolic extract (100 mg ml$^{-1}$) took 37.75 min for paralyzing the *P. postuma* and 89.00 min for death whereas aqueous extract took 64.00 and 150.50 min, respectively.[174]

## Antiulcer

Antiulcer activity of *B. lupulina* and *B. gibsonii* was evaluated by Suba et al.[13] and Tamboli and More.[169] Methanolic extract (200 mg kg$^{-1}$) of *B. lupulina* (aerial parts) when injected in albino rats using various ulcer models (drug-induced, restraint, duodenal and pylorus-ligated ulcers) significantly reduced indomethacin-induced ulcers and severity of ulceration, suggesting the gastroprotective effect on account of acid inhibition and free radical scavenging properties.[13] Ethanolic extract (200, 250 mg kg$^{-1}$) of *B. gibsonii* significantly reduced pylorus ligation-induced ulcers which were comparable to standard omeprazole (20 mg kg$^{-1}$), suggesting the antiulcer potential of *B. gibsonii* leaves.[169]

## Acetylcholinesterase (AChE) inhibition

AChE inhibition activity was reported using petroleum ether, dichloromethane and methanol extracts of *B. argillicola* roots and aerial parts.[7] AChE inhibition was found to be concentration-dependent. Petroleum ether and dichloromethane extracts of roots showed the greatest inhibition when compared with aerial parts of *B. argillicola*.

Methanolic plant extracts of *B. prionitis*, *B. albostellata* and *B. greenii* have been evaluated calorimetrically for AChE inhibition activity using microtitre plate assays.[7] Dose-dependent inhibition was noted for all the extracts. Higher inhibition was observed at the maximum concentration (0.625 mg ml$^{-1}$) in *B. greenii* and *B. prionitis* leaf and stem

extracts than root extract. *B. greenii* leaf extract showed 68% AChE inhibition and leaf extract of *B. albostellata* 22%. Similarly, 38% and 3% inhibition was observed in leaf extracts of *B. greenii* and *B. albostellata* at the least concentration (0.156 mg $ml^{-1}$), respectively. Thus, the study revealed that the leaves of *B. greenii* have potential for inhibition of AChE enzyme and can be used as a substitute for the stem and roots.[7]

## Effect on central nervous system

Different doses (100, 200, 300 mg $kg^{-1}$) of extracts of *B. lupulina* aerial parts in methanol were tested on mice and rats to study the activities, such as general and exploratory behaviour, muscle relaxation, conditioned avoidance response and phenobarbitone sodium-induced sleeping time test.[175] It exhibited considerable motor incoordination and muscle relaxation. General behaviour pattern was reduced (spontaneous activity, alertness, awareness, pain response and touch response) and found to be dose-dependent. A remarkable reduction was observed in the exploratory behavioural profile. All tested doses showed conditioned avoidance response. The study revealed that extract showed significant psychopharmacological activity in the preliminary investigation.[175]

The anti-Parkinson activity of aqueous extract of *B. prionitis* was similar to that of the standard (Levodopa) in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine and Rotenone-induced mouse and rat models, respectively. These models showed high neurotransmitter level. These activities may be attributed to the decrease in lipid peroxidation as various phytochemicals such as flavonoids, polyphenols and glycosides are present in the extract.[176]

## Hepatoprotective

Lakshman et al.[11] assessed the paracetamol (PCT)-induced hepatotoxicity in Wistar albino rats (150–200 g) at 200–400 mg $kg^{-1}$ doses of aqueous ethanolic extract of aerial parts of *B. gibsonii*. Advanced levels of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), serum bilirubin (SB) were used as markers for liver injury in rats. The study showed that the raised level of above-mentioned enzymes in hepatotoxicity control (PCT-treated rats) (SGOT – 652.3 ± 14.43 IU $L^{-1}$, SGPT – 210.4 ± 8.732 IU $L^{-1}$, ALP – 292.8 ± 17.45 IU $L^{-1}$ and SB – 2.62 ± 2.04 mg $dl^{-1}$) compared with normal control rats (SGOT – 325.0 ± 18.60 IU $L^{-1}$, SGPT – 65.25 ± 4.22 IU $L^{-1}$, ALP – 210.6 ± 4.72 IU $L^{-1}$ and SB – 1.21 ± 1.18 mg $dl^{-1}$) and rats treated with 200 and 400 mg $kg^{-1}$ aqueous EBG (SGOT – 355.5 ± 1.9 IU $L^{-1}$, SGPT – 75.63 ± 3.73 IU $L^{-1}$, ALP – 270.4 ± 14.3 IU $L^{-1}$ and SB – 2.27 ± 3.70 mg $dl^{-1}$) and (SGOT – 337.3 ± 10.8 IU $L^{-1}$, SGPT – 71.50 ± 5.103 IU $L^{-1}$, ALP – 236.7 ± 7.2 IU $L^{-1}$ and SB – 1.81 ± 1.16 mg $dl^{-1}$), respectively. The results obtained were comparable with silymarin (standard drug) and aqueous EBG had significant activity against hepatotoxicity and can be used as analgesic and antipyretic.

*B. montana* aerial plant parts were extracted with methanolic extract and evaluated for hepatoprotective activity in carbon tetrachloride ($CCl_4$)-treated Wistar albino rats (150–200 g) at 200, 400, 800 mg $kg^{-1}$ doses.[57] The increased levels of SGOT, SGPT, ALP, total bilirubin (TBL), cholesterol (CHL), total protein (TPTN) and albumin (ALB) were used to study liver injury in rats. *B. montana* (methanolic extract) (800 mg $kg^{-1}$) considerably brought down the elevated levels of SGOT (109.5 ± 2.05 IU $L^{-1}$), SGPT (105.6 ± 2.01 IU $L^{-1}$), ALP (244.1 ± 3.18 IU $L^{-1}$), TBL (1.69 ± 0.17 mg $dl^{-1}$) and CHL (154.8 ± 3.20 mg $dl^{-1}$) and increased levels of TPTN (5.46 ± 0.18 g $dl^{-1}$) and ALB (3.64 ± 0.17 g $dl^{-1}$) compared with normal control rats (SGOT – 104.3 ± 2.31 IU $L^{-1}$, SGPT – 93.90 ± 3.32 IU $L^{-1}$, ALP – 213.50 ± 1.86 IU $L^{-1}$, TBL – 1.19 ± 0.10 mg $dl^{-1}$, CHL – 103.6 ± 2.21 mg $dl^{-1}$, TPTN – 5.70 ± 0.21 g $dl^{-1}$ and ALB – 3.06 ± 0.493 g $dl^{-1}$) and $CCl_4$-treated rats (SGOT – 304.2 ± 11.79 IU $L^{-1}$, SGPT – 236.6 ± 4.04 IU $L^{-1}$, ALP – 423.1 ± 22.47 IU $L^{-1}$, TBL – 3.11 ± 0.34 mg $dl^{-1}$, CHL – 263.7 ± 10.19 mg $dl^{-1}$, TPTN – 2.85 ± 0.28 g $dl^{-1}$ and ALB – 1.62 ± 0.12 g $dl^{-1}$). The results indicated the potential of *B. montana* ethanolic extract in reducing the enzymes responsible for liver damage.

## Immunomodulating

The iridoid fraction of *B. prionitis* (mainly containing shanzhiside methyl ester and barlerin) stimulated specific and non-specific immune mechanisms both *in vivo* and *in vitro*.[177] *In vitro* immunomodulatory activity was studied by nitroblue tetrazolium (NBT) test and neutrophils candidacidal assay where the intracellular killing activity of stimulated neutrophils was considerably increased.

Dose-dependent rise in the antibody titres and augmentation in the effect of delayed-type hypersensitivity reaction induced by sheep red blood cells in mice was recorded when iridoid fraction of *B. prionitis* was administered orally. As a result, the humoral immune response was elevated. Further, the macrophage phagocytic activity, amelioration of red blood cells, total white blood cells and platelets count and haemoglobin concentration were increased. There was a restoration of cyclophosphamide-induced myelosuppressive effects. Further, it showed a considerable increase in neutrophil percentage and their adhesion to nylon fibres.[177]

## Nephroprotective

Effect of ethanolic extract of *B. longiflora* (entire plant including root) (200 and 400 mg $kg^{-1}$ body weight) in male albino Wistar rats (150–200 g) was evaluated for nephroprotective activity by determining serum and kidney antioxidant markers.[12] The effect of the ethanolic extract on serum markers and antioxidant markers against gentamicin-induced nephrotoxicity was found to be comparable. Increased levels of blood urea, serum creatinine and uric acid (53.66, 0.78 and 3.72 mg $dl^{-1}$, respectively) due to gentamicin-induced nephrotoxicity were reduced to 37.50, 0.28 and 1.83 mg $dl^{-1}$, respectively, in 400 mg $kg^{-1}$ body weight dose. Plant extract showed similar results in the case of kidney antioxidant markers.

## Wound healing

Excision and incision wound models of male inbred albino rats (150–180 g in weight) were used to evaluate wound healing activity of methanolic extract of *B. cuspidata* leaves (10% and 15% w/w) with a reference drug, nitrofurazone ointment (0.2% w/w).[178] Lesser wound enclosure time with more percentage of wound contraction (18 days for 100% contraction) was observed with 15% w/w extract, which was more or less similar to that of the standard drug. Tensile strength of 15% w/w extract-treated group was comparable

to nitrofurazone ointment-treated group. However, significant wound contraction was observed in 10% w/w extract-treated group (100% contraction in 20 days). Significant increase in tensile strength was noted in groups treated with the same extract, though lesser compared with the control groups.

Arumugam et al.[179] found that ethyl acetate extract of *B. noctiflora* (aerial parts) exhibited wound healing activity within 16 days in diabetic rat wound models. Similarly, results for 5% and 10% w/w ethanolic aqueous fraction of *B. noctiflora* showed 95.8% and 96.6% wound closure, respectively, on the same day whereas the standard drug showed complete epithelialization (99%). This study signifies the applicability of *B. noctiflora* ethyl acetate extract in the management of wound healing in diabetic rats.

## Miscellaneous Applications

### Antifeedant and insecticidal

Jeyasankar et al.[6] evaluated the antifeedant potential of crude leaf extract of *B. buxifolia* against *Helicoverpa armigera* and *Spodoptera litura*. The highest antifeedant activity, that is, 78.5% against *S. litura* and 75.4% against *H. armigera* from different crude extracts (hexane, chloroform and ethyl acetate) at different concentrations (0.625%, 1.25%, 2.50% and 5.0%) was observed in ethyl acetate extract at 5% concentration. Chennaiyan et al.[180] obtained similar results for crude leaf extract of *B. longiflora* in the case of *S. litura* and *H. armigera* (larvae, pupa and adult). Higher antifeedant activity was observed in ethyl acetate extract. At 5% concentration, it was 79.40% and 77.36% in the case of *S. litura* and *H. armigera*, respectively, whereas at the same concentration insecticidal activity was 70.96% and 68.70% for *S. litura* and *H. armigera*, respectively. The larvicidal activity may be due to the arrest in metabolic pathways in larvae which would have prevented their moulting.[181]

### Fodder value

Three species of *Barleria*, namely *B. acanthoides*, *B. eranthemoides*, *B. proxima* have been reported as a food for camels and goats whereas sheep and cattle gave less preference as food to these species.[182]

### Heavy metal tolerance/accumulation

*B. variabilis* Oberm. (a synonym of *B. spinulosa* subsp. *kirkii* (T. Anderson) I. Darbysh.) is reported to grow on Cu-rich soil where the parent material is granite.[183] *B. aromatica* and *B. kirkii* (a synonym of *B. spinulosa* subsp. *kirkii*) have been shown to accumulate Cr, Ni, Co and Cu.[184]

## Conclusions and Future Perspectives

The genus *Barleria* comprises herbs, shrubs, or more rarely climbers and tree species. The species are important plants from an ornamental and medicinal point of view. Both flowers and foliage of the species can be used for ornamental purposes. The colours of *Barleria* flowers are due to the presence of a variety of pigments. Evaluation of extracted pigments from flowers is required so that they can be used as natural colours in the food industry. As the flowers come in different colours, cytogenetics and hybridization studies can play a pivotal role in developing improved horticulture varieties that can be used in gardens. Chromosome data in conjunction with taxonomic information on the genus form the very basis of designing/planning interspecific hybridization among the species of *Barleria*. In addition to being horticulturally superior, these hybrids can be raised *in vitro* under the influence of various plant growth regulators (PGRs) or stress factors to enhance the quantity of their active principles. Alternatively, polyploidy can be induced in the hybrids under *in vitro* conditions that may make them phytochemically superior to their diploid parental species.

Based on the phytochemical and pharmacological studies conducted on *Barleria*, it is evident that *Barleria* has tremendous potential to be used as medicine for curing various acute and chronic ailments. Although pharmacological and medicinal uses of some species are well documented since ancient times, the scientific information on many species is scanty. Of the 300 species only nine, viz. *B. cristata*, *B. courtallica*, *B. coriacea* subsp. *dinteri*, *B. lupulina*, *B. montana*, *B. noctiflora*, *B. prionitis*, *B. strigosa* and *B. trispinosa* have been studied by researchers for their phytochemical constituents. Thus, extensive studies need to be conducted for the exploration of novel medicinally important phytoconstituents, their isolation, characterization, biological activities, mechanism of action and their applicability to mankind. The medicinally important anticancer phytochemicals, such as ethyl oleate, phytol, β-sitosterol, quercetin and its derivatives and stigmasterol need to be scaled up by means of *in vitro* cultures. In this regard, explant selection, manipulation of the type and concentration of different PGRs will play an inevitable role in mass propagation of *Barleria* species and stimulation of phytochemical content. In addition, extensive molecular-based approaches as well as classical breeding approaches will also enhance the biomass yield and variety of *Barleria* species as a potential source for the production of bioactive compounds. Furthermore, the commercialization of these products as modern drugs needs to be done.

There is a huge gap between the phytochemical investigations and pharmacological studies in *Barleria*. Though only nine species of *Barleria* have been explored for their phytoconstituents, the biological and pharmacological activities of many species are reported. However, these studies were mainly conducted using crude solvent extracts of *Barleria* plant/plant parts. The bridging of the gap between these studies can be achieved by a thorough investigation of these species for their phytoconstituents. In-depth understanding of the mechanism of action of phytochemicals occurring in *Barleria* will pave a way for its applicability in modern medicine and important drugs can be formulated against specific diseases. Thus, there is a tremendous scope in conducting *in vivo*, *in vitro* as well as *in silico* studies using specific pure compounds such as barlerin, verbascoside, poliumoside, etc. occurring in the genus. These studies will open up future avenues for research in drug designing and formulation. Similarly, scientific studies on the toxicity of extracts and the isolated and purified phytochemicals need to be conducted for a better understanding of their use in medicine.

Some *Barleria* species, viz. *B. acanthoides*, *B. aromatica* and *B. eranthemoides* have been reported as a food for animals. On a similar line, other species can also be assessed for their fodder value. Heavy metal accumulation potential of *Barleria* species is also an unexplored aspect that holds great promise for phytoremediation studies.

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## Author Contributions

M.M.L. conceived and supervised the review; S.S.P., U.M.L. and M.M.L. collected the literature and drafted the manuscript; M.M.L., U.M.L., P.V.D., V.K. and A.R. edited the manuscript. All the authors have read and approved the final manuscript.

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## Conflict of Interest

The authors declare no conflict of interest whatsoever.

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