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REVIEW

The medicinal plant *Buddleja asiatica* and its relation to the welfare of local people in the Pan-Himalayan region: Past, present, and future perspectives

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Societal Impact Statement

Globalization and rapid shifts in culture and economy threaten indigenous and local knowledge (ILK) systems, and large intergenerational gaps in this knowledge already exist. *Buddleja asiatica* is a deciduous shrub or small tree with traditional medicinal applications but is currently largely overlooked as a medicinal resource. This study investigates the traditional uses of *B. asiatica* in indigenous communities in the Pan-Himalayan region through ethnobotanical field surveys, with a view to preserving cultural heritage and strengthening economic resilience in these communities, as well as developing *B. asiatica* as a medicinal resource. Prioritizing the well-being of mountain communities, this study aims to bridge community development with nature.

Summary

Buddleja asiatica Lour. (Scrophulariaceae) is widely distributed across the Pan-Himalayan region. It has traditional medicinal applications and cultural value, as well as ecological significance. We conducted an ethnobotanical study combining field surveys from Nepal and Xizang, China with a literature review using Web of Science (WoS) to review the ethnobotanical, phytochemical, and pharmacological aspects of this species. Our study highlights the cultural significance of *B. asiatica* within indigenous communities and, in particular, the use of the leaves to make a starter culture for the preparation of wine. However, an evident intergenerational gap in knowledge transfer exists. The phytochemical investigation revealed the presence of various chemical classes (carbohydrates, terpenoids, flavonoids, saponins, esters, steroids, glycosides, and fatty acids), of which 15 phytoconstituents were first reported from various parts of *B. asiatica*. The potential medicinal properties of these chemicals include anti-inflammatory, antioxidant, cytotoxic, antihepatotoxic, antimicrobial, and cholinesterase activities. We combine these lines of evidence to show the prospects for the livelihoods of local people across this region and propose future research directions.

KEYWORDS

Buddleja asiatica, cultural significance, ethnobotany, Pan-Himalayan, pharmacological activities, phytochemistry

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1 | INTRODUCTION

Plants have nutritional, ornamental, and cultural significance for humans (Schaal, 2019). Moreover, traditional medicinal systems, such as Ayurveda, Traditional Chinese Medicine (TCM), and other holistic systems, have used plants as medicines to treat a variety of conditions for thousands of years (Fitzgerald et al., 2020; Teixidor-Toneu et al., 2018). Modern drug discovery is often informed by studies of ethnobotany, and in many cases the empirical wisdom passed down between generations has been corroborated by scientific research and the compounds responsible have been identified (De Luca et al., 2012; Wurtzel & Kutchan, 2016).

The Pan-Himalayan region is a fascinating biocultural hotspot, making it an area of significant interest for biological and ethnographic research (Dhyani et al., 2010; Li et al., 2020; Shrestha & Medley, 2017). This area is home to various minorities and indigenous groups, each with a unique culture deeply connected to the natural environment. Nepal has over 120 ethnic groups, with the Indo-Aryans being the largest and other significant indigenous groups including the Newar, Gurung, Rai, Limbu, Tharu, Tamang, and Sherpa (Bista, 2004). Meanwhile, in the Mêdog county of Xizang, China, the main ethnic groups are the Monpa and Lhoba (Eberhard et al., 2023). Certain indigenous ethnic groups of Nepal (the Gurung, Rai, Limbu, Tamang, and Sherpa) as well as the Monpa and Lhoba tribes of Xizang, China share a common ancestry and Tibeto–Burman origin (Liu et al., 2022; Sagart et al., 2019).

These ethnic communities have a strong connection to their natural environment and often have an intricate understanding of the regional plants and their diverse applications. This offers opportunities for ethnobotanical exploration. However, rapid population growth in recent decades has led to extensive anthropogenic disturbances, resulting in habitat loss and significant threat to numerous non-human species (Hautier et al., 2015).

The preservation of biodiversity is of paramount importance, not only for the health of the environment but also for human well-being, and indeed many local communities in the Himalayas rely on diverse plant species for sustenance, medicines, and cultural practices (Kunwar et al., 2022). Sustainable resource management is also vital for community development, and improving human quality of life through sustainable development initiatives can mitigate the pressure on natural resources. Integrated efforts that prioritize both environmental and social well-being are essential to ensure coexistence of the people of the Himalayas and their unique biodiversity (Shrestha & Medley, 2017). Investigating the ethnobotany of this region therefore not only promises insights into traditional healing practices but also has implications for species conservation, the sustainable utilization of natural resources, and the preservation of cultural heritage (Dhyani et al., 2010; Shrestha & Medley, 2017).

Buddleja (Scrophulariaceae) is a cosmopolitan genus of flowering plants encompassing about 90 species widely distributed in the tropical, sub-tropical, and warm-temperate regions of Africa, Asia, and the Americas (Chau et al., 2017; Li & Leeuwenberg, 1996; Norman, 2000). *Buddleja* species have a diversity of life forms (shrubs, trees, and lianas) and wide ecological preferences, and are commonly known as butterfly bushes (Norman, 2000). The genus originated in southern Africa and later expanded into the mountains of eastern Africa, the Arabian Peninsula, and Madagascar (Chau et al., 2017). The majority of *Buddleja* species are found in the Americas (Norman, 2000) with the second highest concentration found in Asia in the eastern Himalayas–Hengduan Mountains region, which extends from the western Himalayas to Japan and Southeast Asia (Li & Leeuwenberg, 1996). The study of *Buddleja* diversity in the Sino-Himalayan region, which is the heart of Asian *Buddleja* distribution, is therefore particularly important.

Buddleja species are known for their medicinal applications, aesthetic value, and ecological significance. The leaves and flowers of *Buddleja globosa* are used in Chile for washing wounds and treating ulcers (Houghton, 1985). "*Mi-meng-hua*," prepared from the flowers of *Buddleja officinalis*, is a traditional Chinese medicine used for the treatment of conjunctival congestion and clustered nebulae (Jiangsu New Medical College, 1977). The Madagascan endemic *Buddleja madagascariensis* is used to treat asthma, coughs, and bronchitis (Standley, 1924), and, similarly, *Buddleja saligna* leaves are used as a cough and cold remedy in South Africa (Watt & Breyer-Brandwijk, 1962). *Buddleja americana* has been used to treat cirrhosis and improve biliary function (Diaz, 1976). *Buddleja davidii*, which is known for its fragrant and attractive flowers, was a once popular choice for gardens in Europe, the Americas, Australia, and New Zealand (Tallent-Halsell & Watt, 2009). The yellow flowers of *Buddleja paniculata* have been used for dyeing hemp fabric (Yan et al., 2021) and as food colorants (Aoki et al., 2001), even though it was misidentified as *B. officinalis* (Yang et al., 2023). Some species of *Buddleja* (*B. paniculata*, *B. asiatica*, *Buddleja alternifolia*, *Buddleja cordata*) have been used in vegetation recovery modeling (Huang et al., 2017), ecosystem restoration (Mendoza-Hernandez et al., 2013), and phytoremediation (Sun et al., 2022).

B. asiatica, commonly known as Asian butterfly bush or dogtail in English, is a deciduous shrub with a wide distribution across Afghanistan, Pakistan, India, Nepal, and China into Southeast Asia, including the Philippines. This species has been used traditionally in various indigenous systems of medicine (Houghton, 1985; Pande et al., 2007). Beyond its medicinal uses, this plant holds cultural significance (personal observation) and can play a vital role in ecological restoration efforts (Gong et al., 2020; Waranusantigul et al., 2008). The species also supports many pollinating insects, in particular bumble bees and honey bees (Gong et al., 2015).

The present review aims to (1) conduct ethnobotanical fieldwork across the Pan-Himalayan region, encompassing Nepal and Xizang, China; (2) review the published literature describing the ethnobotany, phytochemistry, and pharmacology of this species and to investigate the significance of *B. asiatica* in local cultures, traditional medicine, ecology, and other aspects; (3) provide recommendations for sustainable development, culture preservation, and ecological conservation in the region; and (4) explore potential future prospects for the utilization of *B. asiatica* to improve the livelihoods of local people. We hope that through this research, we can contribute to the protection of the

rich botanical and cultural heritage in the Himalayan region, promote the sustainable utilization of plant resources, and enhance the health and well-being of the local ethnic minorities.

2 | LITERATURE SURVEY

We conducted a thorough literature search using Web of Science (WoS) and later cross-checked our results with those from other electronic databases including ResearchGate, PubMed, and Google Scholar to compile a comprehensive and unbiased selection of articles. We searched the databases using the keywords "*Buddleja asiatica*" to retrieve relevant articles ($n = 121$, including one book and 64 patents). Of the 56 retrieved journal articles, 50 were recorded in the WoS core collection between 1949 and 2023, and 28 of these were related to ethnobotany, phytochemistry, or pharmacology, 10 were related to ecology, and the remaining articles addressed different subjects. These studies were published in 42 different scientific sources and had an average citation rate of 16.62. A total of 170 authors contributed to papers related to *B. asiatica*. The first journal article was published in 1949 by Moore, R.J. in the *American Journal of Botany* (Moore, 1949).

2.1 | Taxonomy of *B. asiatica*

The genus *Buddleja* was first described by Linnaeus in 1737, as a tribute to Reverend Adam Buddle, the vicar of Farmbridge (Essex, UK) and an amateur botanist. Over time, there have been eight different variant spellings used, including *Buddlea*, *Buddleia*, *Buddleja*, *Buddleya*, *Budlaea*, *Budleia*, and *Budleja*. Linnaeus' spelling, *Buddleja*, is the botanically correct one, as acknowledged in the International Code of Nomenclature (May et al., 2019); however, the common name is often spelled *Buddleia*. In 1830, Bartling and others initially included the tribe *Buddlejeae* within the Scrophulariaceae. Bentham and Hooker moved it to the Loganiaceae in 1876, while Norman established the Buddlejas as a separate family (the Buddlejaceae) (Norman, 2000). However, modern phylogenetic studies have confirmed that the tribe belongs in the Scrophulariaceae (Olmstead et al., 2001; Oxelman et al., 2005) and the *Buddlejeae* has been redefined as monogeneric (Chau, 2017).

Chau (2017) suggest that *Buddleja* is likely to have originated around the early Miocene period (~20 Mya) in southern Africa. Subsequently, during the mid to late Miocene, *Buddleja* species dispersed from Africa to the New World, Asia, and Madagascar. It is likely that *Buddleja* initially arrived in North America before expanding into South America on multiple occasions. The primary mechanisms driving these expansions from Africa to the New World, Asia, and Madagascar are believed to be long-distance dispersal and movement facilitated through migration corridors along high-latitude pathways.

The Sino-Himalayan region is a center of Asian *Buddleja* species diversity, and is home to 25 of the 27 Asian *Buddleja* species (excluding *Buddleja curviflora* and *Buddleja japonica*) (Yang et al., 2023). Within the Asian *Buddleja* species in this region, there is a significant variation in ploidy levels, which seems to be linked to the geological uplift of the Himalayan Mountains (Chen et al., 2007). More recently, Yang et al. (2023) uncovered evidence of reticulation within the Asian *Buddleja* clade, suggesting six hybridization events and two periods of rapid diversification (8–10 and 0–3 Mya) which potentially align with the final uplift of the Hengduan Mountains and fluctuations in Quaternary climate, respectively.

Chen et al. (2010) examined the taxonomic relevance of leaf epidermal features in various *Buddleja* species. This analysis revealed that *B. asiatica* and *Buddleja bhutanica* share similar ploidy levels ($2n = 38$), as indicated by their stomatal dimensions. Additionally, phylogenetic investigations (Chau, 2017; Yang et al., 2023) suggested a close evolutionary relationship between *B. asiatica* and *B. bhutanica*, with these two species together forming a distinct clade. Consequently, study of the evolutionary link between these species has the potential to shed light on the speciation process and on the endemism of *B. bhutanica*.

2.2 | Distribution and description

B. asiatica is a shrub or small tree adapted to diverse environments, including forest edges, thickets, grasslands, rocky slopes, and river banks from sea level to 2800 m. Plants of the World Online (POWO) lists 17 synonyms of *B. asiatica* (POWO, 2023), most of which were published in the early 1800s and have not been challenged by modern phylogenetic studies.

The leaf margins are either smooth-edged (entire) or slightly and shallowly toothed (subentire). The flowers are grouped in inflorescences at the tips of branches and/or in the junctions between a leaf and stem (terminal and axillary). Multiple flower clusters, numbering 1 to 3, are arranged in a slightly branching manner (racemose cymes), appearing either in compact clusters or less commonly, with some gaps in between (clustered or occasionally interrupted). The corolla tube is about 1.2 times as wide as it is long, measuring 1.2 × 3–6 mm with the corolla lobe 1–2 × 1–2.5 mm while the calyx, which encloses the developing flower, varies in size from 1.5 to 4.5 mm. The stamens are inserted above the middle of the corolla tube, extending almost to its opening. The tiny white flowers are sweetly scented and appear in late winter and early spring (Li & Leeuwenberg, 1996).

2.3 | Biology of *B. asiatica*

Pollination syndromes refer to specific floral characteristics, such as scent and flower morphology, believed to have evolved to cater to the needs of particular pollinators. Chen et al. (2012) utilized the volatile compounds found in floral scents to anticipate the types of pollinators that are attracted to specific plants. Subsequently, Gong et al. (2015) demonstrated that *B. asiatica* predominantly relies on bumblebees and honeybees for pollination.

B. asiatica produces numerous small, winged seeds that are dispersed naturally by the wind. However, accidental introductions may

occur through transportation by vehicles, construction equipment, and the movement of ornamental plants and their soil. There have also been reports of intentional introductions in Hawaii, Vanuatu (GBIF, 2023; POWO, 2023), and New Zealand (GBIF, 2023), possibly as ornamental plants because of the fragrant flowers. However, *B. asiatica* is not widely used as an ornamental plant, and its medicinal uses are relatively unknown, lowering the risk of its introduction to new areas. However, a risk assessment for Hawaii conducted by PIER (2015) rates the risk of *B. asiatica* introduction as high, with a score of 9. In its native habitat, *B. asiatica* coexists with other *Buddleja* species including *Buddleja crispa*, *Buddleja macrostachya*, *Buddleja myriantha*, and *B. paniculata* (Schreiter et al., 2011). Hybridization within the genus is common (Liao et al., 2021) and can be induced artificially for horticultural purposes (Renfro et al., 2007). Because of its wide distribution, *B. asiatica* is currently categorized as Least Concern (LC) on the International Union for Conservation of Nature (IUCN) Red List of Threatened Species (IUCN, 2023).

B. asiatica is potentially a useful plant in vegetation restoration (Marliana & Rühe, 2014) and phytoremediation (Waranusantigul et al., 2008). Gong et al. (2020) found that *B. asiatica* contained high superoxide dismutase (SOD) and peroxidase (POD) activities. These enzymes are crucial for detoxifying the plants when they face oxidative stress, which is common in polluted environments. This suggests that *B. asiatica* has great potential as a Cd-hypertolerant plant for use in phytoremediation.

3 | PAN-HIMALAYAN STUDY: PEOPLE AND PERSPECTIVES

3.1 | Study system and design

The ethnobotanical study was designed to investigate the cultural and historical ethnobotanical practices involving *B. asiatica* across the Pan-Himalayan region. The study system was designed to encompass diverse ecological and cultural contexts and to capture a broad spectrum of traditional knowledge and practices related to this plant. Data collection from September 2022 to July 2023 involved structured questionnaires, semi-structured interviews, and informal group discussions. Stratified sampling ensured representation from various altitudinal gradients, allowing for insights into the different uses across ecological zones.

The questionnaires (Notes S1) were carefully designed to introduce a wide range of topics related to *B. asiatica*, including the local name, traditional uses, preparation methods, medicinal properties, cultural importance, and socio-economic aspects of the plant. The demographic survey included questions about the respondent's age, gender, occupation, ethnicity, and educational background. The team included bilingual researchers to ensure effective communication and cultural sensitivity. Collaborative partnerships were fostered with local communities, traditional healers, and knowledgeable individuals, ensuring their active participation and contribution to the study. The proper approvals were obtained in advance, and respect for local customs and practices was maintained at all times.

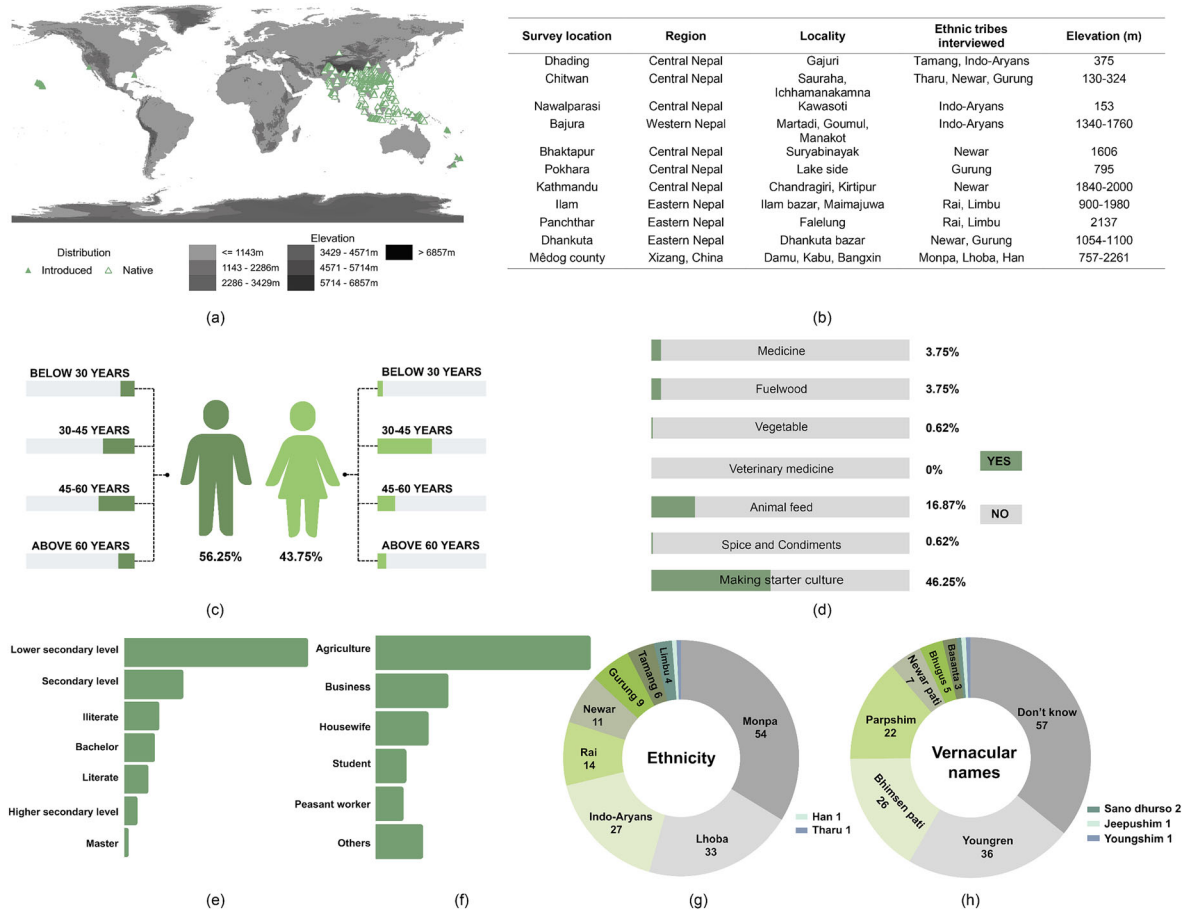
The data were analyzed using both quantitative and qualitative methods. Quantitative data provided insights into the prevalence and distribution of traditional uses of *B. asiatica* across the study region, while qualitative analysis focused on interpreting the narratives, traditional beliefs, and cultural significance of the plant as reported by the local communities.

3.2 | Ethnobotanical practices

The study was centralized in 18 places of four different regions (western, central, and eastern Nepal and Motuo, Xizang, China) along an altitudinal gradient of 130 (Chitwan) to 2261 m (Mêdog county, Xizang, China) (Figure 1b). The survey involved 160 informants, including 90 males and 70 females, representing various occupations (48.13% in agriculture, 16.25% in business, 11.88% are housewives, 6.88% are students, 6.25% are peasant workers, and 10.61% in other occupations), age groups ranging from 18 to 75 years with the mean age being 44 years, ethnicities (the Rai, Gurung, Tamang, Limbu, Newar, Indo-Aryans, Monpa, and Lhoba), and different education status highlighting a balanced and inclusive representation across different demographic factors (Figure 1).

3.2.1 | Ethnomedicine

B. asiatica is used in traditional medicinal systems to treat various ailments, including skin pruritus, headache, pain, diarrhea, fever, hypotension, and respiratory conditions, as well as for inducing abortion. The plant's flowers, leaves, roots, and whole plant have all been utilized in traditional medicinal practices. In TCM, *B. asiatica* has been used to treat skin pruritus and respiratory conditions such as asthma and bronchitis, fever, aches, and diarrhea (Kunming Botanic Institute & Jiangsu Botanic Institute, 1991) as well as cancer (Hu et al., 2001) and articular rheumatism (Jiangsu New Medical College, 1977). In India, the plant has been used as an abortifacient (Houghton, 1985), as well as to treat skin complaints (Pande et al., 2007). A decoction of the leaves is also used as an abortifacient in Nepal (Nepal, 1970). In Myanmar, a paste of *B. asiatica* roots is used as a tonic when mixed with rice water (Gage, 1904). The leaves have been used variously as a fish poison and to treat headaches in Vietnam (Houghton, 1985). The roots and leaves of *B. asiatica* have been utilized to treat head tumors (Hartwell, 1970), and an infusion of roots has been employed in the treatment of malaria (Reis & Von, 1973). *B. asiatica* leaves were found to exhibit a hypotensive effect on cats and dogs, likely because of alpha-adrenoceptor blocking activity (Singh et al., 1980). An essential oil extracted from *B. asiatica* leaves demonstrated antifungal and antibacterial activities (Garg & Dengre, 1992), and the flowers have been found to treat cystitis (Lee et al., 2008) and edema (Zheng & Xing, 2009). Recently, Inta et al. (2023) revealed the maximum



Survey location	Region	Locality	Ethnic tribes interviewed	Elevation (m)
Dhading	Central Nepal	Gajuri	Tamang, Indo-Aryans	375
Chitwan	Central Nepal	Sauraha, Ichhamanakamna	Tharu, Newar, Gurung	130-324
Nawalparasi	Central Nepal	Kawasoti	Indo-Aryans	153
Bajura	Western Nepal	Martadi, Goumul, Manakot	Indo-Aryans	1340-1760
Bhaktapur	Central Nepal	Suryabinayak	Newar	1606
Pokhara	Central Nepal	Lake side	Gurung	795
Kathmandu	Central Nepal	Chandragiri, Kirtipur	Newar	1840-2000
Ilam	Eastern Nepal	Ilam bazar, Maimajuwa	Rai, Limbu	900-1980
Panchthar	Eastern Nepal	Falelung	Rai, Limbu	2137
Dhankuta	Eastern Nepal	Dhankuta bazar	Newar, Gurung	1054-1100
Mêdog county	Xizang, China	Damu, Kabu, Bangxin	Monpa, Lhoba, Han	757-2261

FIGURE 1 Demographic and ethnobotanical characteristics of *Buddleja asiatica*. (a) Map showing the distribution of both native and introduced *B. asiatica*, (b) details of field survey conducted, (c) age groups interviewed, (d) mentioned uses of *B. asiatica*, (e) education grade of interviewees, (f) occupation status of interviewees, (g) ethnic groups interviewed, and (h) vernacular names for *B. asiatica* used across the Pan-Himalayan region.

consumption of *B. asiatica* as a traditional medicinal plant among Tibeto–Burman women in Thailand.

Our investigation revealed that nowadays, *B. asiatica* has only limited use for medicinal purposes, primarily in the treatment of skin conditions (Figure 1d). This suggests that the local people are relying on modern medicine, rather than their traditional ethnomedical practices. This can be attributed to factors including standardization and regulation, accessibility of information, and cultural shift. Where ethnobotanical practices are low, there tend to be limited access to information about traditional plant-based treatments. This, coupled with the allure of modern medicine backed by scientific research, often turns individuals away from the practices embedded in their cultural heritage. Moreover, contemporary medicine is often perceived as being more effective because of its standardization and extensive documentation.

This is a trend that has been observed with other medicinal plant species (Gureje et al., 2015). Integrating traditional ethnomedicine with modern medical practices can, however, prove to be beneficial (Yuan et al., 2016). By conducting thorough scientific research on the efficacy of medicinal plants, we can offer a bridge between traditional wisdom and modern standards of evidence. This, in turn, could help rekindle trust in ethnomedicine among the locals, empowering them to make informed choices regarding their health care.

3.2.2 | Cultural significance

Indigenous and Local Knowledge (ILK) systems intertwine the "knowledge-practice-belief" complex (Sõukand et al., 2023), reflecting community beliefs, experiences, and spirituality, and shaping traditions over time. *B. asiatica* has different cultural meanings in different ethnic tribes. For example, the female relatives of the groom wear necklaces made of *B. asiatica* flowers during wedding ceremonies in the Thangmi ethnic community of Nepal (Turin, 2003). During our surveys, we found that ethnic tribes including the Newar, Rai, and Limbu communities of central and eastern Nepal also leave flowers and leaves as offerings to their gods and goddesses (Figure 2).

The fatty acids found in *B. asiatica* exhibit low thermal stability, and the plant is therefore unsuitable as a human food (Ali, Ali,



FIGURE 2 Utilization of *Buddleja asiatica* by locals as revealed by our field survey. Locals in various regions of Nepal grow and utilize *B. asiatica*, (a) outside their houses to honor deities and (b) in temple gardens. (c) Locals making starter culture from rice grains in Panchthar, Nepal, (d) starter culture ready for drying, (e) dried starter culture in Panchthar, Nepal and (f) in Mêdog, Xizang, China.

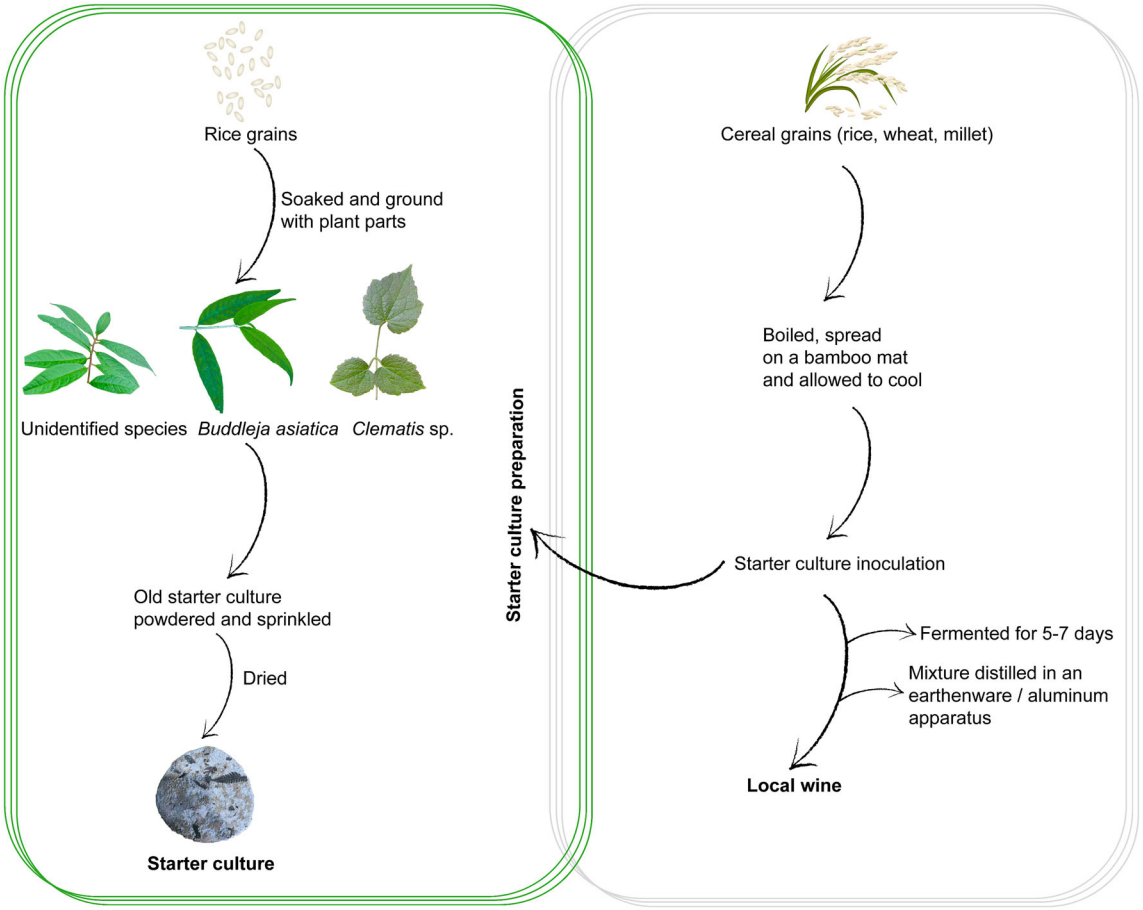


FIGURE 3 General process of making local wine as reported from the eastern part of Nepal during our field investigation; preparing the starter culture (green box) and brewing the liquor (gray box).

et al., 2013); indeed, our surveys revealed no local usage of the plant as a food. However, we found that Tibeto–Burman origins Rai and Limbu communities living in the eastern regions of Nepal and Monpa and Lhoba ethnic groups of Mêdog county, Xizang, China used leaves of *B. asiatica* to create a fermentation starter culture for making local rice wine, an integral part of their culture and traditions (Figure 2). This rice wine preparation involves two key steps: preparing the starter culture and brewing the liquor (Figure 3).

The starter culture, referred to as the rice cake, "*marcha*" or "*murcha*" in Nepali and "*prom*" in Lhoba, is a traditional amylolytic

starter. In Nepal, this is a mixture of local rice (*Oryza sativa*), the roots of an unidentified species, (*Watihangma* in Limbu), the leaves and twigs of *B. asiatica*, and whole *Clematis* sp. plant along with trace amounts of dry red chili (*Capsicum annuum*) and ginger (*Zingiber officinale*) (reported from our field investigation in eastern Nepal). The roots of *Watihangma*, leaves of *B. asiatica* and the *Clematis* plant, are cut into small pieces and dried in the sun. Local rice is then soaked in water until it has softened. The ingredients are then ground using a wooden mortar and pestle. A little water is added to create a paste, which is then shaped into cakes of appropriate sizes (5- to 7-cm radius, weighing 80–100 g). An old rice cake, a mother culture (15–20 g), is sprinkled over the new ones. Subsequently, the cakes are dried suspended below the kitchen ceiling on a platform made up of bamboo strips and bedded with fresh bracken fern fronds (*Pteridium aquilinum*) for at least 24 h. Once hardened, the cakes are stored in a dry place for several months.

The preparation of the starter culture in Mêdog, Xizang, China differed from that described above. In Mêdog, *Zanba* (highland barley flour) or corn flour is generally used as a substrate, and *B. asiatica* leaves, sometimes, together with those from other unidentified plants are used. The leaves of *B. asiatica*, in addition to being air-dried before use, are boiled in water for a few minutes. The water in which the leaves are boiled is then used to knead bread dough. Interestingly, in Mêdog, an old starter culture is not added when preparing new batches of starter. Moreover, we found that locals in both Nepal and Xizang can also make a starter culture without using *B. asiatica* leaves.

For brewing the local wine, rice (or any cereal grains) is mixed with water and cooked in a metallic vessel. It is allowed to cool and is then mixed with the crushed rice cakes (one rice cake is sufficient for 20 kg of rice). The mixture is then fermented for 5–7 days. When slightly yellowish juices come out from the fermented mass, the fermentation process is complete. The fermented mixture is then boiled in an earthenware/aluminum apparatus and distilled to produce the local wine. In Mêdog, finger millet (*Eleusine coracana*) is used instead of rice to make the wine, and sometimes the finger millet is mixed with maize. Fermented grains are sealed for storage. Before drinking, cold or hot water is added to the grains, and the beverage is filtered and consumed directly. Unlike the Nepali, people in Mêdog do not use a distillation process for brewing their wine. Notably, we found that this process is exclusively practiced by women and passes from mother to daughter across all of the study areas.

Traditional liquor brewing is a home-based industry run by tribal women employing indigenous knowledge of the fermentation process. However, scientific studies are necessary to elucidate the microorganisms (potential isolates) used in the fermentation process to increase the efficiency of the process. It has been reported that the microflora of these starter-culture rice cakes consists of filamentous molds such as *Mucor circinelloides* and *Rhizopus chinensis*; bacteria such as *Pediococcus pentosaceus* (Tamang & Sarkar, 1995); and yeasts such as *Saccharomyces bayanus*, *Candida glabrata*, *Pichia anomala*, *Saccharomycopsis fibuligera*, *Saccharomycopsis capsularis*, and *Pichia burtonii* (Tamang & Sarkar, 1995; Tsuyoshi et al., 2005) suggesting their involvement in the amylolytic fermentation.

Local wine is consumed at every religious festival and ceremony in an indigenous community (Rawat et al., 2021; Tamang, 2009). Wine is consumed at traditional occasions including weddings, crop celebrations, worship rituals, and commemorations to allow the people to convey emotions of unity, happiness, and sorrow. For instance, freshly prepared *Judima*, a traditional local wine of the Dimasa tribes of Assam, Northeast India, is prepared as an offering to family deities during religious events, weddings, and festivals, and has both cultural and spiritual value (Chakrabarty et al., 2010).

3.2.3 | Cultural evolution

During our ethnobotanical fieldwork, we discovered that different dialects have unique names for fermentation starter culture, such as "*bopkha*" in Rai (eastern Nepal), "*khesung*" in Limbu (eastern Nepal), "*bharama*" in Tamang (central Nepal), "*taepa*" in Gurung (central Nepal), and "*prom*" in Lhoba (Xizang, China). The tradition of making local alcohol was common across the study regions except in western Nepal among Indo-Aryans. However, the practice of using *B. asiatica* leaves to make starter culture was prevalent in eastern Nepal, mainly within the Rai and Limbu communities, as well as in Xizang, China, among the Monpa and Lhoba ethnic communities.

Similar recipes for the utilization of *B. asiatica* leaves in making local wine have been documented from Sikkim and Darjeeling (Tsuyoshi et al., 2005), eastern Nepal (Tamang & Thapa, 2006), the Dimasa tribes in Assam, Northeast India (Arjun et al., 2014), Bhutan (Wangchuk et al., 2017), the Monpa ethnic group in Mêdog county, Xizang and Arunachal Pradesh, India (Li et al., 2020; Namsa et al., 2011), but were not reported from western Nepal (our field investigations) or the western Pan-Himalayan region.

We hypothesized that the cultural distance is directly proportionate to the ancestor origin, specifically Tibeto–Burman origins, in terms of cultural adaptability (Liu et al., 2022; Sagart et al., 2019). This supports the notion of vertical transmission, as the use of *B. asiatica* leaves for starter culture appears to have been inherited and maintained within specific ancestral lineages. Similarly, the geographic proximity indicated that culturally related groups using *B. asiatica* leaves for starter culture are usually close, further reinforcing the evidence for ancestral transmission. This suggests ongoing cultural interaction and the preservation of traditional knowledge within geographically proximate populations.

The hypothesis presented in this study supports the proposition that the use of *B. asiatica* leaves for making starter culture predominately follows a pattern of vertical transmission. This highlights the enduring influence of ancestral knowledge for traditional practices across the eastern Pan-Himalayan region. However, to prove our proposed hypothesis as a pattern of vertical transmission, comparative phylogenetic methods (Teixidor-Toneu et al., 2018) are highly recommended. Alongside this, the collection and mapping of more linguistic, geographical, plant use, and genetic data are essential to explore the macroevolutionary process of plant use across the Pan-Himalayan region.

3.3 | Gaps and actions needed: bridging the knowledge gap and fostering cultural sustainability

Ethnobotanical competence relies on personal interactions, involving oral communication or the imitation of observed behavior. Our research highlighted a concerning gap in intergenerational knowledge transfer within the communities studied. Understanding of the uses of *B. asiatica* was confined to the elder members of each community, while the younger generation showed limited or no engagement with this knowledge (37.5% of individuals under 30 possessed knowledge of this plant, and 15.63% can make starter culture from it), despite a relatively higher educational background (34.37% of the younger generation hold bachelor's degrees). This discrepancy raises serious concerns and emphasizes the urgent need for effective mechanisms of knowledge transmission, especially given the advantage of education.

This challenge is further compounded by the effects of globalization, which have triggered significant cultural and economic changes. Urbanization and road construction are impacting the market share of traditional alcohol. Urban youth is shifting towards branded products because they are more convenient and easily accessible, while making homemade wine demands considerable time and effort. Additionally, young generation's lack of interest and unfamiliarity with traditional values contribute to the steady erosion of this traditional knowledge. Consequently, a gap has emerged, leaving ethnic communities devoid of knowledgeable and experienced individuals.

Understanding how cultural wisdom is maintained, eroded, and disseminated is pivotal in addressing these gaps. Reyes-García et al. (2009) suggest three fundamental processes are involved in acquiring ethnobotanical competence: a temporal learning sequence spanning childhood to adulthood, more efficient knowledge acquisition when individuals can practically apply what they have learned, and the necessity of direct contact with nature.

Strategies to transmit culture between generations are necessary to bridge this knowledge gap. Public education can help to regenerate cultural awareness in a community through hands-on experience, open book programs, and even the promotion of eco-tourism. Moreover, the commercialization of the local wine while ensuring its quality would contribute to the preservation of this tradition. Such initiatives would safeguard the cultural heritage of these indigenous communities and support their sustainable development both culturally and economically.

4 | PHYTOCHEMISTRY

Phytochemistry plays a significant role in the discovery of phytoconstituents and their potential applications in fields including medicine, agriculture, nutrition, and industry. Ethnobotany, however, focuses on the interactions between plants and people within specific and sociocultural contexts. Thus, phytochemistry and ethnobotany are interconnected disciplines that shed light on the chemical composition, therapeutic potential, and cultural significance of plants.

4.1 | Profiling of phytoconstituents

Phytoconstituents or phytochemicals are the naturally occurring bioactive compounds found in plants and that contribute to their medicinal and therapeutic properties. A total of 105 phytoconstituents reported to date from *B. asiatica* are displayed in Table 1.

Phytochemicals have been isolated from the leaves, flowers, and aerial parts of *B. asiatica*, as well as from the whole plant. Many constituents of different chemical classes have been reported, including carbohydrates, terpenoids, flavonoids, saponins, phenylpropanoid esters, steroids, iridoid glycosides, phenolic glycosides, fatty acids, and benzoates. Notably, 15 compounds (Figure 4) have been reported for the first time from this species, namely buddlin (Chen et al., 2005), phenylpropanoid esters of rhamnose asiatisides A–D (Liu, Cai, Li & Luo, 2008), oleanane-type triterpenoids 13,28-epoxy-23-hydroxy-11-oleanene-3-one and 13,28-epoxy-21β,23-dihydroxy-11-oleanene-3-one (Liu, Cai, Du, et al., 2008), buddlejone, dihydrobuddledin A, buddledone B (Ali, Iqbal, et al., 2011), cholinesterase inhibitors asiatoates A and B (Ali, Khan, et al., 2013), 3,4-dihydroxy phenylethyl alcohol 8-*O*[(4'-*O*-feruoyl)-α-L-rhamnopyranosyl-(1″- > 3′)-β-D-glucopyranosyl(1″- > 6′)]-β-D-glucopyranoside (Mohamed et al., 2013), buddlejol (Khan, Khan, et al., 2015), and an iridoid glycoside buddlejasiaside A (Hien et al., 2018).

4.2 | Pharmacological properties

4.2.1 | Anti-inflammatory properties

B. asiatica is known for its anti-inflammatory properties. Studies have reported that various bioactive compounds, including iridoid glycosides, phenolic glycosides, flavonoids, and terpenoids, contribute to its anti-inflammatory effects (Hien et al., 2018; Liao et al., 1999; Mohamed et al., 2013). These compounds act by inhibiting the production of pro-inflammatory mediators, including cytokines and prostaglandins, thereby reducing inflammation (Yoon & Baek, 2005). Cyclooxygenase-2 (COX-2) is an enzyme involved in the inflammatory response and plays a crucial role in the production of inflammatory mediators called prostaglandins (Vane et al., 1998). Liao et al. (1999) reported that chloroform and methanol extracts of *B. asiatica* (mainly comprising terpenoids and flavonoids) showed 81.0 ± 0.3 and 35.6 ± 8.9% of inhibition of COX at 50 μg/mL, respectively, in elicited rat peritoneal leukocytes, suggesting strong cyclooxygenase inhibitory activities. The compound, 3,4-dihydroxy phenylethyl alcohol 8-*O*[(4'-*O*-feruoyl)-α-L-rhamnopyranosyl-(1″- > 3′)-β-D-glucopyranosyl(1″'- > 6′)]-β-D-glucopyranoside which was first reported for this species, along with the previously described compounds *E*-acteoside, *E*-isoacetoside, and rutin isolated from the methanol extract of *B. asiatica* leaves, showed significant cytotoxic activity (IC_{50} = 0.93, 0.8, 0.84, and 1.65 μg/mL) against HepG2 cells. The researchers suggested that the hydroxy groups of the aromatic rings might play a role in the anticancer effect (Mohamed et al., 2013).

TABLE 1 List of phytoconstituents reported from various parts of *Buddleja asiatica*.

S. No.	Chemical class	Phytochemical name	Plant parts used	References
1	Benzoates	Asiatoate A	Whole plant	(Ali, Khan, et al., 2013)
2		Asiatoate B	Whole plant	(Ali, Khan, et al., 2013)
3	Carbohydrates	Mannitol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
4		Sucrose	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
5	Fatty acids	Palmitic acid	Whole plant	(Ali, Ali, et al., 2013)
6		Linoleic acid	Whole plant	(Ali, Ali, et al., 2013)
7		Stearic acid	Whole plant	(Ali, Ali, et al., 2013)
8		Arachidic acid	Whole plant	(Ali, Ali, et al., 2013)
9		Margaric acid	Whole plant	(Ali, Ali, et al., 2013)
10		Lignoceric acid	Whole plant	(Ali, Ali, et al., 2013; Khan, Khan, et al., 2015)
11		Behenic acid	Whole plant	(Ali, Ali, et al., 2013)
12		Cerotic acid	Whole plant	(Ali, Ali, et al., 2013)
13		Montanic acid	Whole plant	(Ali, Ali, et al., 2013)
14		Melissic acid	Whole plant	(Ali, Ali, et al., 2013)
15		Trycosylic acid	Whole plant	(Ali, Ali, et al., 2013)
16	Flavonoids	Diosmin	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
17		Linarin	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
18		Rutin	Leaves	(Mohamed et al., 2013)
19		Luteolin	Leaves	(Mohamed et al., 2013)
20	Monoterpenoids	α-Pinene	Leaves	(Garg & Dengre, 1992; Khan, Jan, et al., 2015)
21		(+)-Camphene	Leaves	(Garg & Dengre, 1992)
22		(+)-Limonene	Leaves	(Garg & Dengre, 1992)
23		β-Pinene	Leaves	(Garg & Dengre, 1992)
24		Δ 3-Carene	Leaves	(Garg & Dengre, 1992)
25		*p*-Cymeme	Leaves	(Garg & Dengre, 1992)
26		1,8-Cineole	Leaves	(Garg & Dengre, 1992; Khan, Jan, et al., 2015)
27		Citronellal	Leaves	(Garg & Dengre, 1992)
28		Linalool	Leaves	(Garg & Dengre, 1992)
29		α-Terpineol	Leaves	(Garg & Dengre, 1992)
30		Geranyl acetate	Leaves	(Garg & Dengre, 1992)
31		Citronellol	Leaves	(Garg & Dengre, 1992)
32		Limonene monooxide	Leaves	(Garg & Dengre, 1992)
33		α-Phellandrene	Whole plant	(Khan, Jan, et al., 2015)
34		α-Thujene	Whole plant	(Khan, Jan, et al., 2015)
35		Terpinen-4-ol	Whole plant	(Khan, Jan, et al., 2015)
36	Diterpenoids	Buddlejone	Whole plant	(Ali, Iqbal, et al., 2011)
37	Triterpenoids	Maslinic acid	Aerial parts	(Liu, Cai, Du, et al., 2008)
38		β-Amyrin	Aerial parts	(Liu, Cai, Du, et al., 2008)
39		Oleanolic aldehyde	Aerial parts	(Liu, Cai, Du, et al., 2008)
40		Oleanolic acid	Aerial parts	(Liu, Cai, Du, et al., 2008)
41		Ursolic acid	Whole plant	(Ali, Iqbal, et al., 2011)
42		7-deoxy-8-epiloganic acid	Whole plant	(Ali, Iqbal, et al., 2011)
43		Taraxerol	Whole plant	(Khan, Khan, et al., 2015)
44		α-Amyrin	Whole plant	(Khan, Khan, et al., 2015)

(Continues)

TABLE 1 (Continued)

S. No.	Chemical class	Phytochemical name	Plant parts used	References
45	Sesquiterpenoids	β-Caryophyllene	Leaves	(Garg & Dengre, 1992)
46		β-Caryophyllene oxide	Leaves	(Garg & Dengre, 1992)
47		γ-Cadinene	Leaves	(Garg & Dengre, 1992)
48		α-Cadinene	Leaves	(Garg & Dengre, 1992)
49		Eudesmol	Leaves	(Garg & Dengre, 1992)
50		α-Cubebene	Whole plant	(Khan, Jan, et al., 2015)
51		12-Nor-preziza-7(15)-en-2-one	Whole plant	(Khan, Jan, et al., 2015)
52		1,10-Seco-1-hydroxycalamenen-10-one	Whole plant	(Khan, Jan, et al., 2015)
53		Isospathulenol	Whole plant	(Khan, Jan, et al., 2015)
54	Oleanane-type triterpenoids	13,28-Epoxy-23-hydroxy-11-oleanene-3-one	Aerial parts	(Liu, Cai, Du, et al., 2008)
55		13,28-Epoxy-21β,23-dihydroxy-11-oleanene-3-one	Aerial parts	(Liu, Cai, Du, et al., 2008)
56		13,28-Epoxy-3β,23-*O*-isopropylidene-11-oleanene	Aerial parts	(Liu, Cai, Du, et al., 2008)
57		13,28-Epoxy-3β,23-dihydroxy-11-oleanene	Aerial parts	(Liu, Cai, Du, et al., 2008)
58		3β,23,28-Trihydroxy-11α-methoxy-12-oleanene	Aerial parts	(Liu, Cai, Du, et al., 2008)
59	Phenolic acids	*p*-Methoxycinnamic acid	Aerial parts	(Liu, Cai, Li & Luo, 2008)
60		Ferulic acid	Aerial parts	(Liu, Cai, Li & Luo, 2008)
61		*o*-Methylferulic acid	Aerial parts	(Liu, Cai, Li & Luo, 2008)
62	Phenylpropanoids	Isoacteoside	Aerial flowering parts and roots	(El-Domiaty et al., 2009; Mohamed et al., 2013)
63		Acetoside	Aerial flowering parts and roots	(El-Domiaty et al., 2009; Mohamed et al., 2013)
64		Eugenol	Whole plant	(Khan, Jan, et al., 2015)
65	Phytosterols	β-Sitosterol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
66		Stigmasterol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
67		Stigmasterol-*O*-glucoside	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
68		β-Sitosterol-*O*-glucoside	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
69		Buddlejol	Whole plant	(Khan, Khan, et al., 2015)
70	Phenylpropanoid esters	Asiatiside A	Aerial parts	(Liu, Cai, Li & Luo, 2008)
71		Asiatiside B	Aerial parts	(Liu, Cai, Li & Luo, 2008)
72		Asiatiside C	Aerial parts	(Liu, Cai, Li & Luo, 2008)
73		Asiatiside D	Aerial parts	(Liu, Cai, Li & Luo, 2008)
74		Buergeriside C1	Aerial parts	(Liu, Cai, Li & Luo, 2008)
75	Saponins	Mimengoside A	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
76	Glycosides	2-Phenylethyl-β-D-glucoside	Whole plant	(Ali, Iqbal, et al., 2011)
77		3,4-Dihydroxy phenylethyl alcohol 8-*O*[(4'-*O*-feruoyl)- α-L-rhamnopyranosyl-(1″- > 3′) – β-D-glucopyranosyl (1″- > 6′)]-β-D-glucopyranoside	Leaves	(Mohamed et al., 2013)
78	Flavonoid glycosides	Scutellarin-7-*O*-β-D-glucopyranoside	Whole plant	(Ali, Iqbal, et al., 2011)
79	Iridoid glycosides	6-O-(3'',4''-Dimethoxycinnamoyl) catalpol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
80		Methylcatalpol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
81		Catalpol	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
82		Aucubin	Aerial flowering parts and roots	(El-Domiaty et al., 2009)
83		Ajugol	Leaves	(Mohamed et al., 2013)
84		Buddlejasiaside A	Aerial parts	(Hien et al., 2018)

TABLE 1 (Continued)

S. No.	Chemical class	Phytochemical name	Plant parts used	References
85		6-*O*-[α-L-(4-isoferuloyl)-rhamnopyranosylcatalpol	Aerial parts	(Hien et al., 2018)
86		Specioside	Aerial parts	(Hien et al., 2018)
87		Verminoside	Aerial parts	(Hien et al., 2018)
88		Minecoside	Aerial parts	(Hien et al., 2018)
89		6-*O*-(*p*-hydroxybenzoyl)-ajugol	Aerial parts	(Hien et al., 2018)
90		6-*O*-caffeoyl ajugol	Aerial parts	(Hien et al., 2018)
91		Litanthosalin	Aerial parts	(Hien et al., 2018)
92		Eurostoside	Aerial parts	(Hien et al., 2018)
93		10-*O*-caffeoylaucubin	Aerial parts	(Hien et al., 2018)
94	Phenolic glycosides	Phlorizin	Aerial parts	(Hien et al., 2018)
95		Garashangin	Aerial parts	(Hien et al., 2018)
96	Triterpenoidal glycosides	1-*O*-β-D-glucopyranosyl2-methoxy-3-(2-hydroxy-triaconta-3,12-dienoate)-glycerol	Leaves	(El-Sayed et al., 2008)
97		3-O-[α-L-rhamnopyranosyl-(1- > 4)-β-D-glucopyranosyl-(1- > 3)]-[β-D-glucopyranosyl-(1- > 2)]-β-D-fucopyranosyl-olean-11,13(18)-diene-3β,23,28-triol	Leaves	(El-Sayed et al., 2008)
98		3-*O*-[α-L-rhamnopyranosyl-(1- > 4)-β-D-glucopyranosyl-(1- > 4)-β-D-glucopyranosyl-(1- > 3)]-β-D-fucopyranosyl-Olean-11,13(18)-diene-3,23,28-triol	Leaves	(El-Sayed et al., 2008)
99		3-O-[α-L-rhamnopyranosyl-(1- > 4)-β-D-glucopyranosyl-(1- > 3)]-[β-D-xylopyranosyl-(1- > 2)]-β-D-glucuronopyranosyl-acid-olean-11,13(18)-diene-3β,23,28-triol	Leaves	(El-Sayed et al., 2008)
100	Others	Buddlin	Whole plant	(Chen et al., 2005)
101		Dihydrobuddledin-A	Whole plant	(Ali, Iqbal, et al., 2011)
102		Buddledone-B	Whole plant	(Ali, Iqbal, et al., 2011)
103		Furan, 2-(1-pentenyl)- (E)	Whole plant	(Khan, Jan, et al., 2015)
104		Bicyclo[5.1.0]octane, 8-(1-methylethylidene)	Whole plant	(Khan, Jan, et al., 2015)
105		β-Sinensal	Whole plant	(Khan, Jan, et al., 2015)

Furthermore, Hien et al. (2018) reported that various bioactive compounds, including iridoid glycosides such as buddlejasiaside A, 6-*O*-[α-L-(4-isoferuloyl)-rhamnopyranosylcatalpol, litanthosalin, and 10-*O*-caffeoylaucubin, contribute to its anti-inflammatory effect. This effects result from inhibitions of nitrate production in LPS-stimulated BV2 microglia, with IC_{50} values ranging from 43.5 to 79.6 μM. Inhibition of nitric oxide (NO) production is considered to be a therapeutic approach for the treatment of neuro-inflammatory disorders. Nitric oxide, a pro-inflammatory mediator, is synthesized by induction of the enzyme nitric oxide synthase (iNOS) in response to the presence of stimuli in macrophages (Cinelli et al., 2020). However, while the above-mentioned studies have shown promise, it is imperative to conduct further research to investigate the mechanisms underlying these activities, and to optimize dosages and investigate the toxicology profiles of the relevant chemicals to ensure safety.

4.2.2 | Antimicrobial activity

Several studies have indicated the antimicrobial properties of *B. asiatica* extracts (Ali, Ali, et al., 2011; Ali, Iqbal, et al., 2011; Garg & Dengre, 1992; Khan, Jan, et al., 2015), and different extracts have shown activity against various bacteria, including both gram-positive and gram-negative strains, and fungi. Garg and Dengre (1992) extracted essential oils from the leaves of *B. asiatica* by hydrodistillation. Using the filter paper disk agar diffusion method, these essential oils (specifically β-caryophyllene oxide, citronellol, and β-caryophyllene) were shown to have in vitro inhibitory potential against certain pathogenic bacteria, including *Salmonella* sp., *Salmonella paratyphi* strains, *Salmonella typhi* H, *Shigella flexneri*, *Shigella shiga*, and *Vibrio cholerae*, and fungi such as *Aspergillus flavus*, *Aspergillus fumigatus*, *Curvularia parasadii*, *Trichoderma viride*, and *Trichophyton rubrum*.

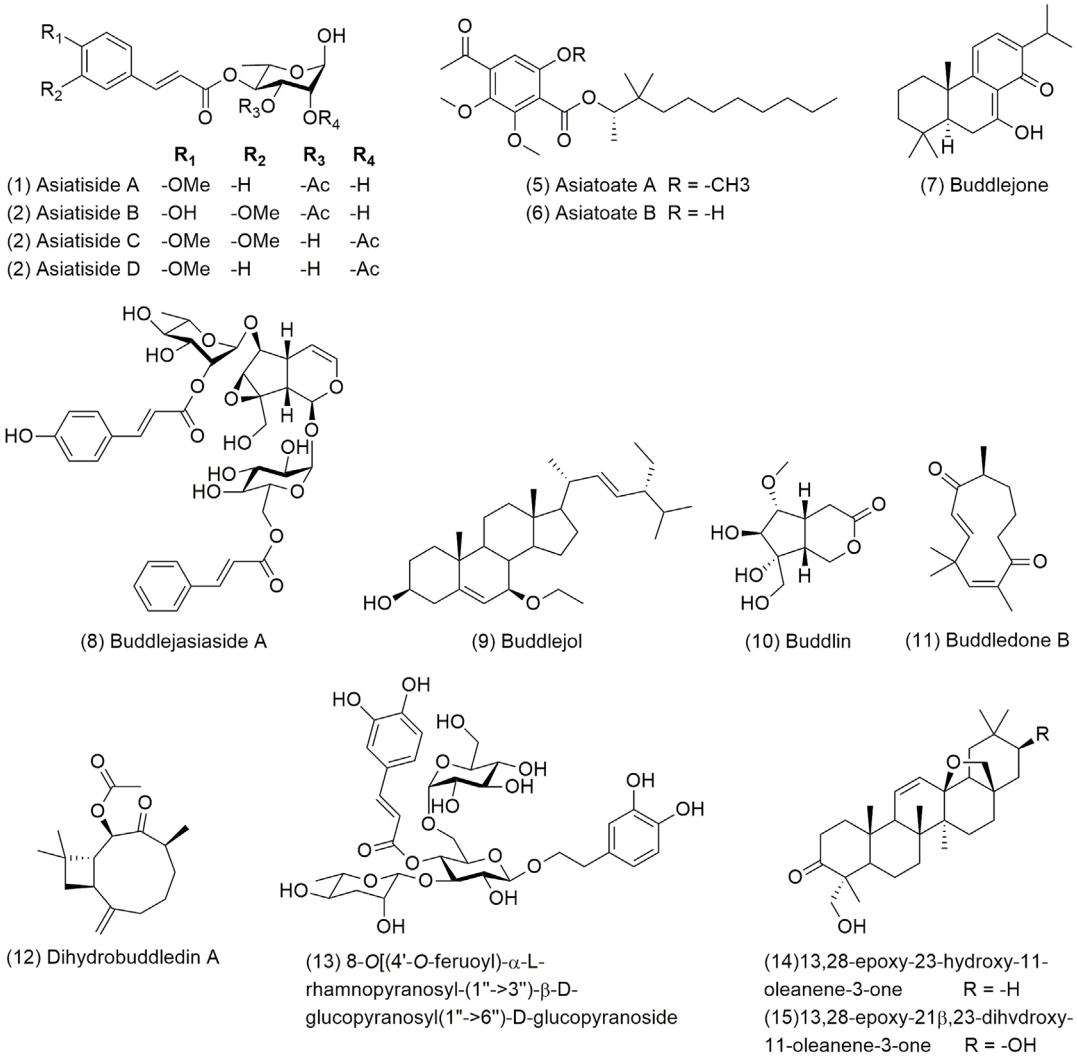


FIGURE 4 Chemical structures of phytoconstituents first reported from various parts of *Buddleja asiatica*. These phytoconstituents were phenylpropanoid esters, oleanane-type triterpenoids, diterpenoids, benzoates, glycosides, phytosterols, and iridoid glycosides.

Bioactive compounds isolated from the chloroform soluble fraction, including 2-phenyl-β-D-glucoside with a zone of inhibition ranging between 17 and 25 mm, 7-deoxy-8-epiloganic acid with an inhibitory zone ranging from 17 to 24 mm, and scutellarin-7-*O*-β-D-glucopyranoside with a range of 17–25 mm, exhibited significant antimicrobial activity against *Proteus vulgaris*, *S. typhi*, *Escherichia coli*, *Trichophyton longifusus*, *Candida albicans*, *Microsporum canis*, *Candida glaberata*, *Fusarium solani*, and *A. flavus* (Ali, Iqbal, et al., 2011). Tetracycline, the standard drug for bacteria, showed a zone of inhibition ranging from 29 to 32 mm, while miconazole, the standard drug for fungi, exhibited a zone of inhibition ranging from 25 to 30 mm (Ali, Iqbal, et al., 2011). Similarly, crude extracts from *B. asiatica* and its chloroform, ethyl acetate, and *n*-butanol fractions showed significant antibacterial and antifungal activities against bacteria with a zone of inhibition ranging from 3 to 29 mm, including *E. coli*, *S. flexneri*, and *Sternostoma boydi*, and against different fungi with a linear growth ranging from 25 to 80 mm, including *A. flavus*, *F. solani*, and *T. longifusus* (Ali, Ali, et al., 2011). Imipenem, the standard drug for bacteria, showed a zone of inhibition ranging from 25 to 34 mm, while miconazole and amphotericin-B, the standard drug for fungi, exhibited linear growth ranging from 30 to 105 mm (Ali, Ali, et al., 2011). In both antimicrobial studies, the zone of inhibition was measured using an agar-well diffusion method. Essential oils (1,8-cineole, β-sinensal, 1,10-seco-1-hydroxy-calamenen-10-one, and α-phellandrene) extracted from *B. asiatica* leaves using hydrodistillation have also shown strong antibacterial activity (66% zone of inhibition) against *Shigella boydii* and outstanding inhibition (79% zone of inhibition) against *A. flavus* in fungicidal assays (Khan, Jan, et al., 2015).

It is evident from various antimicrobial studies that in vitro assays lack specificity, and it is therefore difficult to assess the effectiveness of compounds against various microorganisms. While crude extracts and some bioactive compounds have shown a strong degree of inhibitory activity against *S. boydii*, *E. coli*, and *A. flavus*, the zone of inhibition is still lower than the standard drug (Ali, Ali, et al., 2011; Ali, Iqbal, et al., 2011; Khan, Jan, et al., 2015. This suggests that the use of

B. asiatica compounds as antimicrobials may have limited potential. While the Minimum Inhibitory Concentration (MIC) test is a valuable tool for assessing the effectiveness of antimicrobial agents, it does have limitations, particularly concerning the variability in diffusion rates and potential chemical interactions with the growth medium, which can affect the interpretation of results. These limitations should be carefully considered while conducting antimicrobial studies. One alternative method that could complement MIC testing is the disc diffusion method, which offers advantages such as simplicity, cost-effectiveness, and the ability to test multiple agents simultaneously. However, it also has its own set of limitations related to subjective interpretation, qualitative data, and limited sensitivity. We therefore suggest carefully evaluating different methods and considering incorporating complementary approaches to gain a more comprehensive understanding of the antimicrobial activity of the compounds under investigation. Additionally, we recommend utilizing an integrated panel of pathogens in antimicrobial testing, employing accessible standard in vitro experimental protocols, defined endpoint criteria, and efficacy assessments (Cos et al., 2006).

4.2.3 | Antioxidant effects

B. asiatica contains bioactive compounds, including flavonoids and phenolic compounds, which have antioxidant properties. These secondary metabolites play a crucial role in combating oxidative stress and preventing cellular damage caused by free radicals (Zeb, 2020). Extracts from *B. asiatica* leaves show antioxidant activity in different in vitro antioxidant tests, including the 1,1–diphenyl–2–picrylhydrazyl (DPPH) free radical scavenging assay, total antioxidant capacity (the phosphomolybdenum method), and the hydrogen peroxide (H_2O_2) scavenging method (El-Sayed et al., 2008; Karki & Sapkota, 2022; Sai et al., 2019; Sundararajan & Ilengesan, 2018a). El-Sayed et al. (2008) isolated four non-phenolic antioxidant compounds that showed significant free radical scavenging activity towards DPPH (SC_{50} = 43.08–60.83 μg/mL) and H_2O_2 (SC_{50} = 18.39–32.68 μg/mL) in in vitro antioxidant tests. In addition, methanolic and *n*-butanolic extracts showed free radical scavenging activities with SC_{50} = 16.28 and 18.54 μg/mL and hydrogen peroxide scavenging with SC_{50} = 23.17 and 18.54 μg/mL, respectively.

Similarly, Sundararajan and Ilengesan (2018a) performed ten different in vitro free radical scavenging assays, including DPPH (IC_{50} = 15 μg/mL), nitric oxide scavenging activity (96.2 μg/mL), H_2O_2 scavenging activity (35.2 μg/mL), hydroxyl radical scavenging activity (52.2 μg/mL), superoxide anion radical scavenging activity (40.98 μg/mL), DMPD (N, N-dimethyl-p-phenylene diamine dihydrochloride) assay (18.02 μg/mL), metal ion chelation assay (43.6 μg/mL), xanthine oxidase inhibitory activity (55.6 μg/mL), lipid peroxidation assay (136.2 μg/mL), and CUPRAC (cupric ions reducing) assay (absorbance = 0.567). Based on this reported in vitro antioxidant activity, Sundararajan and Ilengesan (2018b) evaluated the in vivo antioxidant properties of *B. asiatica* through oral administration to healthy rats over 21 days. The results demonstrated that tested doses (250 and 500 mg/kg) of the methanol extract exhibited superior antioxidant effects (p < .05), as evidenced by increased ferric reducing ability of plasma (FRAP), reduced lipid peroxidation, and enhanced activity of antioxidant enzymes, indicating its potential as a potent free radical scavenger. Moreover, crude extracts of *B. asiatica* showed the most potent free radical scavenging activity with an IC_{50} value of 3.04 ± 0.04 μg/mL among several species (*Aeschynanthus parviflorus* [40.26 ± 3.44 μg/mL], *Carica papaya* [41.73 ± 0.07 μg/mL], *Drepanostachyum falcatum* [>100 μg/mL], and *Spondias pinnata* [4.84 ± 0.12 μg/mL]) and control ascorbic acid (IC_{50} = 3.16 ± 0.03 μg/mL) collected from western Nepal (Sai et al., 2019).

However, Chemjong and Subba (2022) reported antioxidant activity from methanolic extract of *B. asiatica* as having an IC_{50} of 26.86 ± 2.00 μg/mL, which is lower than that of *Camellia sinensis* (19.15 ± 4.32 μg/mL) and the standard quercetin (2.36 ± 0.13 μg/mL) in a DPPH assay; this suggests that *B. asiatica* is not particularly promising as an antioxidant. The antioxidants present in *B. asiatica* may acts as scavengers, neutralizing free radicals and preventing their harmful effects on the body. Generally, they donate electrons or hydrogen atoms to stabilize the free radicals and break the oxidative chain reaction (Zeb, 2020). By doing so, they protect cells from oxidative damage, enhancing overall cellular health. Although some studies have reported antioxidant activity in *B. asiatica* extracts, the evidence remains inconclusive because of conflicting results. Therefore, further research in this field is necessary to address this uncertainty and elucidate the antioxidant properties of this species.

4.2.4 | Other activities

Crude extracts from *B. asiatica* flowering parts and roots showed substantial antihepatotoxic activity, resulting in significant reductions (p < 0.05) in the level of alanine aminotransferase (ALT) (29.26 ± 6.56 IU/mL from aerial parts, 37.9 ± 6.7 IU/mL from roots) and aspartate aminotransferase (AST) (594.73 ± 13.9 and 611.9 ± 12.2 IU/mL) in adult male cirrhotic rats compared to the control treated with silymarin (25.73 ± 6.3 and 522.2 ± 63.16 IU/mL) (El-Domiaty et al., 2009). This pronounced antihepatotoxic effect can be attributed to the flavonoids (especially linarin), iridoids (aucubin and catalpol derivatives) and phenylpropanoid glycosides reported from the species. Indeed, phenylpropanoid glycosides, which contain a caffeic acid moiety, are known for their liver-protective properties (Lee et al., 2004). *B. asiatica* can therefore be considered a new promising candidate for putative hepatoprotection drugs. The progress in developing natural compounds as hepatoprotective agents has been limited, but this research suggests that further study in this area might be beneficial.

The ethanolic extracts of *B. asiatica* leaves and bark also showed in vivo antinociceptive and muscle relaxant effects (Ullah et al., 2016). Moreover, bioactive compounds, asiatoates A and B, exhibited mild inhibitory effect on acetylcholinesterase (AChE) and butylcholinesterase (BChE) with IC_{50} value of 5.54 and 8.34 μM against AChE while

30.94 and 35.94 μM against BChE, respectively (Ali, Khan, et al., 2013). Essential oils also showed moderate in vitro acetylcholinesterase (IC_{50} 5.2 μM) and butyrylcholinesterase inhibitory effects (IC_{50} 27.9 μM) (Khan, Jan, et al., 2015). However, bioactive compounds like nonyl benzoate and hexyl p-hydroxycinnamate identified from *B. crispa* also showed weak inhibition against both AChE and BChE (Ahmad et al., 2005), suggesting that these compounds may not be effective candidates for enzyme inhibition.

4.2.5 | Looking forward

The utilization and, at times, overreliance on in vitro tests has become increasingly prevalent because of ethical and economical constraints. While in vitro assays offer valuable insights into the pharmacological activities of natural products, their widespread use without robust validation and correlation with ethnopharmacological investigations can lead to potential pitfalls and limitations (Houghton et al., 2007). To date, pharmacological studies and investigations in to the mechanisms underlying the bioactivity of *B. asiatica* components are still very superficial. It would therefore be prudent to establish a stronger in vitro "proof-of-concept" for its pharmacological potential. This review suggests that using this species as a source of antimicrobials or cholinesterase inhibitors is not ideal. However, *B. asiatica* can be considered as an interesting candidate for the discovery of hepatoprotective drugs.

Plant-derived compounds might have potential cytotoxic side effects, which can lead to undesirable outcomes. In addition to this consideration, it is important to highlight the therapeutic potential of various compounds derived from plants. For example, iridoid glycosides, phenolic glycosides, flavonoids, and terpenoids have been shown to exhibit anti-inflammatory effects. Furthermore, flavonoids and phenolic compounds are recognized for their antioxidant properties, although this information is not new. However, the question arises as to why pharmaceutical companies have not explored the potential of widely available plant species such as *B. asiatica*.

Moreover, it is essential to acknowledge the significant gap between in vitro and in vivo data and the preliminary nature of claims regarding the properties of plant isolates. To address this gap, researchers should consider synergistic formulations, bioavailability enhancement techniques, and conducting in-depth pharmacokinetic studies. Additionally, the utilization of computer-assisted drug design approaches (e.g., molecular docking to elucidate and characterize the binding affinities and specific interactions of phytoconstituents with the target protein) is highly encouraged to ensure a more comprehensive understanding of the therapeutic potential of natural compounds derived from plants used in traditional medicinal practices.

At the same time, global climate change and anthropogenic disturbance pose a severe threat to medicinally important plant species, including the risk of extinction. Preservation efforts, including habitat conservation and sustainable harvesting practices, are imperative to safeguard the biodiversity of these plants.

5 | CONCLUSION AND FUTURE PERSPECTIVES

B. asiatica, which is distributed across the Himalayan region, offers a glimpse into the local cultures and the challenges faced by people living in mountainous regions. This review sheds light on *B. asiatica* by integrating ethnobotanical insights, a critical literature review of the phytochemistry, and pharmacological properties.

We captured a broad spectrum of traditional knowledge and practices, revealing the enduring significance of *B. asiatica* over time in the eastern Pan-Himalayan region. This significance may stem from ancestral connections, cultural influences, and the surrounding environment. However, this knowledge is primarily held by the elderly, and younger people do not have the same ethnobotanical competence. Globalization and evolving cultural and economic paradigms thus pose a threat to the preservation of this knowledge, and safeguarding these traditions from extinction is becoming crucial. Knowing of how traditions are transmitted across generations and the implementation of strategies allowing this is necessary to keep these traditions alive.

Our review also identifies a diverse array of phytochemicals with medicinal potential from *B. asiatica*. However, our pharmacological understanding of these bioactive constituents remains limited, and further investigations into their mechanisms of action are needed.

Future research directions are suggested:

1. Community-driven development: The development of health care while maintaining a balance among economic growth, nature conservation, and the preservation of cultural heritage will improve the well-being of the people of the Himalayas. Our research reveals that despite the existence of studies highlighting the medicinal values of *B. asiatica*, its use as a medicine in traditional practices is relatively limited in the Himalayan region, possibly due in part to the accessibility of modern medicines.
   However, bringing health care to mountainous areas is challenging, and the general lack of public knowledge regarding health necessitates greater public health education. Simultaneously, promotion of the commercial development of local beverage production, such as wine made from *B. asiatica* leaves, represents a possible way to balance economic progress and the preservation of indigenous culture. However, a thorough assessment of local wine production is imperative to ensure safety, considering the potential for hazardous compounds in homemade wine. Research elucidating the possible isolates and optimizing the harvesting process is recommended. Public outreach programs, educational initiatives, and collaborative efforts are needed to raise awareness among local communities about the cultural significance and potential benefits of this plant. This might propel the communities forward while respecting their rich heritage and unique traditions.
2. Ecological recovery of the Himalayan Mountains: With the continuous development of human communities in the Himalayan region, environmental challenges including loss of biodiversity, soil

erosion, and other pressing issues pose a threat to the delicate ecosystem. Many *Buddleja* species, including *B. asiatica*, exhibit high resistance and are commonly used in ecological restoration (Gong et al., 2020; Huang et al., 2017). Giving the pressing environmental challenges, utilizing *B. asiatica* as an ecological model plant holds great promise. Through vegetation restoration (Marliana & Rühe, 2014), phytoremediation (Gong et al., 2020; Waranusantigul et al., 2008), and landslide control, *B. asiatica* not only helps to preserve the unique biodiversity of the Himalayas but also addresses the aforementioned environmental challenges head-on. In a region grappling with deforestation, soil contamination, and landslide hazards, this species can thrive in challenging mountainous terrain, aiding in the restoration of native vegetation, stabilization of soil, and the absorption of heavy metals from polluted soils. The adaptability and beneficial properties of this plant can contribute significantly to the sustainable restoration and conservation efforts in this fragile mountain ecosystem.

3. Investigation of the evolution of Asian *Buddleja* species: *B. asiatica* has high phylogenetic value in the study of Asian *Buddleja* species (Yang et al., 2023), because of its basal position in the Asian *Buddleja* clade. This taxon allows researchers to investigate the evolutionary history, genetic diversity, and adaptations of Asian *Buddleja* species. Moreover, previous research has indicated a high proportion of the aroma component linalool, which exceeds 90% in the floral scent of *B. asiatica* (Gong et al., 2015). Conducting genomic studies on this species is imperative to unravel the metabolic pathways responsible for this floral scent, allowing better understanding and utilization of this early-spring flowering plant as a source of nectar and as an ornamental plant.

In conclusion, despite being an unassuming plant, *B. asiatica* emerges as a symbol of cultural resilience and an opportunity for sustainable development rooted in indigenous wisdom. It is imperative that we recognize and appreciate the inherent value of this remarkable plant, harnessing its potential to safeguard traditions, empower communities, and forge a harmonious balance between cultural heritage and scientific progress.

AUTHOR CONTRIBUTIONS

Conceptualization: Jia Ge and Gao Chen; *Investigation*: Bishal Gurung, Jia Ge, Fengmao Yang, and Gao Chen; *Analysis*: Bishal Gurung; *Supervision*: Jia Ge and Gao Chen; *Writing and review*: Bishal Gurung, Jia Ge, and Gao Chen.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the Supporting Information of this article.

ETHICS STATEMENT

For the questionnaire, we followed the Code of Ethics of the International Society of Ethnobiology (International Society of Ethnobiology, 2006), prioritizing the well-being and consent of our participants. Our research was deemed low risk and aligned with regional and national policies, where formal approval was not mandatory. Verbal prior informed consent (PIC) was documented with local representatives present, respecting the cultural norms and ensuring participant understanding and voluntary agreement. All activities, including the use of photographs and conducting ethnobotanical surveys, were also recorded.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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