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Medicinal plant profile

The nature and status of *Fritillaria cirrhosa*: A key source of '*a bi sa*' in Sowa Rigpa Medicine in Nepal

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Abstract

Sowa Rigpa, also known as Tibetan or Amchi medicine, is one of the traditional systems of medicine practiced across an extensive region of South, Central, and East Asia. Sowa Rigpa pharmacopeia is based on plants, animals, minerals, and other natural substances. Among the plant-based ingredients, *a bi sa* is derived from different Himalayan species belonging to the family Liliaceae. The most commonly used plant species as a source of *a bi sa* in Nepal is *Fritillaria cirrhosa*. However, *F. cirrhosa* is highly threatened throughout the Himalayas mainly due to the overharvesting of its underground bulbs to meet the increasing global demand for these bulbs in the herbal market. Conservation of remaining *F. cirrhosa* populations in the wild is immediately needed, which requires measures such as the prevention of illegal harvesting, protection of natural habitats, promotion of sustainable harvesting practices, and implementation of enrichment planting and *ex-situ* conservation strategies. The current review provides an overview of the taxonomy, morphological variability, ecology, and ethnomedicinal importance of *F. cirrhosa*; and highlights its socio-cultural, economic, and conservation importance.

Keywords: Conservation, Himalayas, Liliaceae, Nepal, sustainable harvest, trade, Tibetan medicine.

Introduction

Sowa Rigpa, also known as Tibetan or Amchi medicine, is a comprehensive and holistic medical tradition practiced across the Himalayas, Tibetan Plateau, Mongolia, and China over centuries (Gurmet 2004). This ancient practice combines public healthcare, ethnoecological knowledge, and cultural heritage, serving as a dynamic medico-cultural system in these regions. Sowa Rigpa has also gained worldwide recognition as an alternative and complementary medical system (Craig 2012; Kloos 2020). An extensive body of scholarly knowledge and practices exist on which the Sowa Rigpa system depends, most of these are derived from the core texts known as the Four Treatises (Gurmet 2004). These texts exist in both Bön (*bum bzhi*) and Buddhist (*rgyud bzhi*) versions and form the theoretical and practical foundation of Sowa Rigpa (Gurmet 2004; Ghimire *et al.* 2021a). The Sowa Rigpa pharmacopeia is based on plants and different nature-based components including minerals, precious stones, and animal parts/products (Gonpo 2008). Raw materials derived from plants play a pivotal role in the tradition and practice of Sowa Rigpa.

Previous research identified 570 species and infraspecific taxa of biological groups, including fungi, lichens, pteridophytes, gymnosperms, and angiosperms used in Sowa Rigpa in Nepal (Ghimire *et al.* 2021a). However, while most of the *Materia Medica* elements, which are the sources used in Sowa Rigpa, remain abundant, some rare ingredients derived from threatened species face regulatory constraints at national or international levels, threatening the sustainability of this tradition. Among such rare substances, derived from threatened plant species is *a bi sa*, which is extensively used in various Sowa Rigpa formulations. *A bi sa* is primarily sourced from the Himalayan plant species of the family Liliaceae, particularly members of the genus *Fritillaria*. This review focuses on *F. cirrhosa*, one of the sources of *a bi sa* in Nepal. Besides its medicinal value, *F. cirrhosa* is also highly important from socio-cultural, economic, and conservation perspectives. The main topics presented in this paper are Sowa Rigpa classification, taxonomy and morphology, distribution and ecology, traditional uses, phytochemistry, pharmacology, and the conservation status of this herb.

Sowa Riga classification

A bi sha, alternatively spelled as *a bhi sha* or *a bhi kha*, literally translates to 'without poison'. It belongs to the *Materia medica* class of 'herb medicine'. In the Himalayas and China, two species, namely *Fritillaria cirrhosa* D.Don (Norbu 2016; Ghimire *et al.* 2021a) and *F. delavayi* Franch. (Gawa Dorje 1995; Arya 1998;

Drungtso and Drungtso 2005; Gonpo 2008; Wangchuk *et al.* 2008, 2009; Norbu 2016), are commonly identified as sources of *a bi sha*.

F. cirrhosa is distributed across the Himalayas, China, and Myanmar; while *F. delavayi* is confined to the Eastern Himalayas (Sikkim and Bhutan), Tibetan Plateau, and South-Central China (Chen and Mordak 2000; POWO 2024). In Sowa Rigpa literature, *F. delavayi* is considered the superior type, referred to as *a bi sha mchog*, and *F. cirrhosa* is regarded as the inferior type, known as *a bi sha dmanpa* (Norbu 2016). The former type is also known by various names, including *a'u tsi*, *dkar po chig thub*, *dug med*, and *klu bdud nag po* (Arya 1998; Wangchuk *et al.* 2009; Norbu 2016). The latter type is commonly mentioned in literature as *a'u tsi* (Gawa Dorje 1995; Arya 1998; Drungtso and Drungtso 2005), but other names like *tshan a'u rtsi* (Arya 1998; Drungtso and Drungtso 2005) and *klu bdud dorje nag po* (Ghimire *et al.* 2001) are also used.

Nepali amchi (practitioners of Sowa Rigpa) recognize both *F. cirrhosa* and *F. delavayi* as the superior type, while *Lilium nanum* Klotzsch is categorized as inferior (Ghimire *et al.* 2021a). Most amchi in Nepal primarily use *F. cirrhosa*, resorting to *Lilium nanum* only when the former species becomes scarce or unavailable. However, *F. delavayi* is employed by some practitioners in Mustang, Kathmandu, and other regions, often sourced from Tibet, India, or Bhutan (Ghimire *et al.* 2021a).

Taxonomy and morphology

The genus *Fritillaria* Tourn. ex L. comprises about 130 species distributed across temperate regions of the Northern Hemisphere, including Asia, North Europe, the Mediterranean region, and North America (Stevens 2001 onwards; Chen and Mordak 2000; POWO 2024). In Nepal, the genus includes two native species: *F. cirrhosa* D.Don, and *F. crassicaulis* S.C.Chen (Paudel *et al.* 2021; Rana and Ghimire 2024).

F. cirrhosa and *F. crassicaulis* are similar but differ in their leaf number, leaf shape, and minor differences in their reproductive traits (Chen and Mordak 2000). In *F. crassicaulis*, stems are white farinose distally; leaves number 10–18, are oblong-lanceolate to lanceolate, more than 1 cm wide, with an acuminate apex. In *F. cirrhosa*, stems are non-farinose; leaves number 7–11, are linear to linear-lanceolate, up to 7 mm wide, with an acuminate to cirrhose or filiform apex (Chen and Mordak 2000).

Fritillaria cirrhosa D.Don, Prodr. Fl. Nepal.: 51 (1825).

Fritillaria cirrhosa subsp. *roylei* (Hook.) Ali; *Fritillaria roylei* Hook.; *Lilium bonatii* H.Lév.

Chinese: *Chuan Bei Mu*.

Dotelī: घाँडे विष *Ghānde vish*, पोड्या *Podyā*.

English: Yellow Himalayan fritillary.

Hindī/local dialects: *Kākolī*, *Chichaor*, *Dharru ghanti*

Khām (Dolpa, Nepal): *Ghā*.

Nepālī: वन लसुन *Ban lasun*, काकोली *Kākolī*.

Sanskrit: काकोली *Kākolī*, क्षीरकाकोली *Kshīrakākolī*.

Sherpā: *Pāngo*, *Tak tak*.

Sowa Rigpa: ཨ་བི་ཤ་མཆོག་ *a bi sha mchog*, ཨའུ་ཙི་ *a'u tsi*, ཚན་ཨའུ་རྩི *tshan a'u rtsi*, ཀླུ་བདུད་ནག་པོ་ *klu bdud nag po*, ཀླུ་བདུད་རྡོ་རྗེ་ནག་པོ་ *klu bdud dorje nag po*.

Tāmāng: *Takhtachawā*.

DESCRIPTION

Perennial bulbous herbs, 13–75 cm tall (Plate 1). Bulbs sub-globose or ovoid, 1.5–3 cm in diameter; scales 2, thick, fleshy, covered with a whitish, papery tunic. Stem erect, unbranched, glabrous, often white-spotted, leafy on upper half. Leaves cauline, 7–11, sessile, scattered; lower ones paired, opposite; upper leaves in whorls of 3 or 4 or few alternate or opposite; lamina linear to linear-lanceolate or narrowly oblong, usually up to 1.2 cm in length and 7 mm wide, apex obtuse to acute or acuminate, often curved to cirrhose or filiform, margin entire. Flowers terminal, solitary or 2–3 in raceme, dropping, campanulate; pedicel much shorter than flower; bracts usually 3, leaf-like. Tepals 6, light green, yellow or yellowish-green, often lightly to densely brown or purple spotted or chequered, oblanceolate or oblong-elliptic, often unequal, inner slightly broader than outer, 3–5.5 × 1.2–2.5 cm, basal nectaries elliptic to ovate. Stamens 6, inserted; filaments slightly papillose. Capsule erect or ascending, oblong to broadly oblong, 1.5–3.5 × 1.5–2.5 cm, triloculed, longitudinally 6-winged, transversely striated; wings narrow, 1.5 mm or less broad. Seeds many, triangular-rotund, narrowly winged.

Plate 1. *Fritillaria cirrhosa* with a yellow, chequered flower in shades of brown to purple; and bracts and leaves curved to slightly cirrhose at the apex (near Bagar, between Deurali and Machhapuchhre Base Camp, Annapurna Conservation Area, Kaski, northcentral Nepal; open meadow, amongst small forbs, grasses, and sedges; 3450 m, May 25, 2016, © S.K. Ghimire).

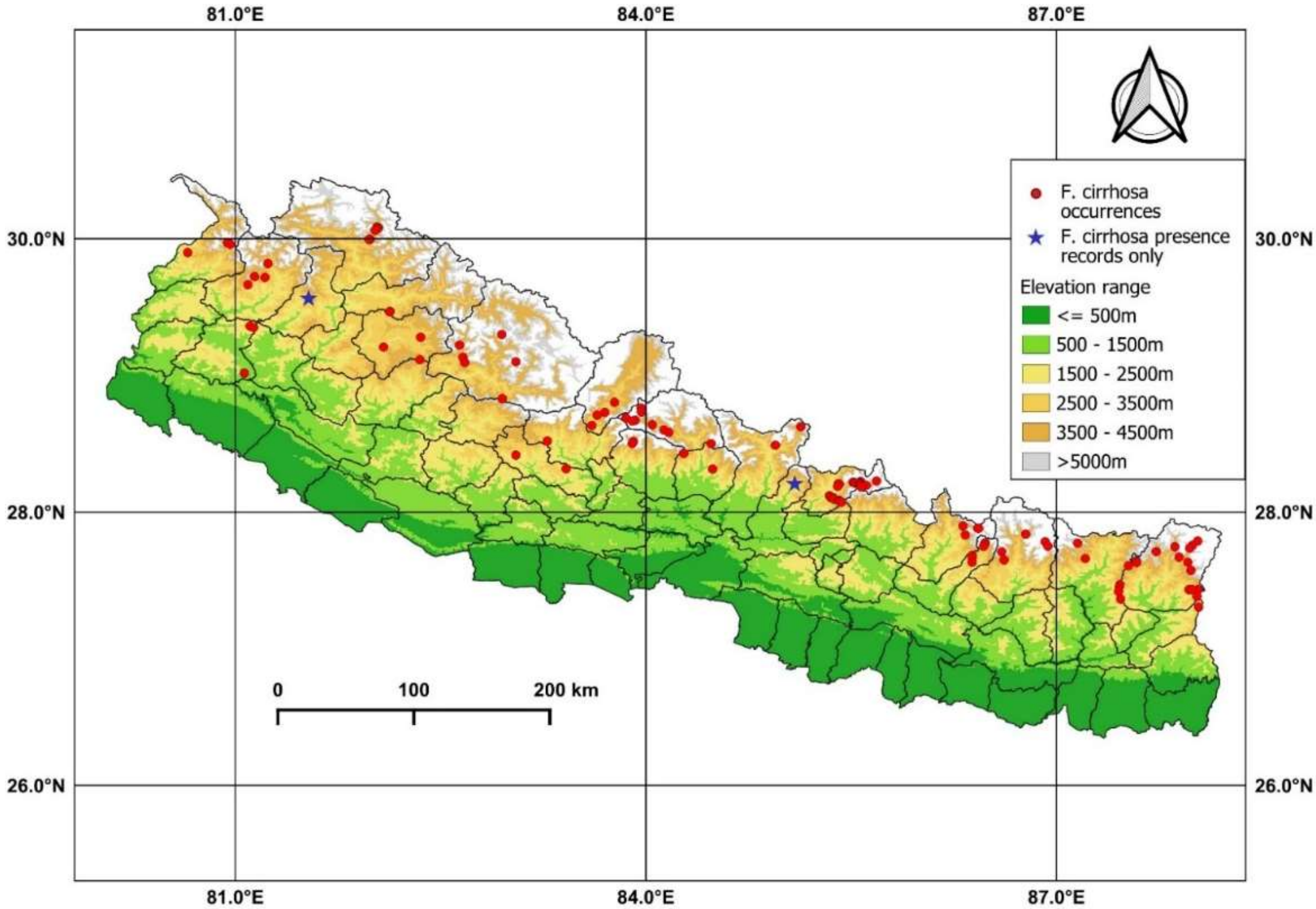

Figure 1. Distribution of *Fritillaria cirrhosa* in Nepal based on locality data from the first author's fieldwork and specimens housed at various herbaria (closed circles) and literature (asterisks). Specimen records were searched on online databases of A (Kennedy 2024), BM (Natural History Museum 2024), E (RBGE 2024), MO (Teisher and Stimmel 2024), NL (Bijmoer *et al.* 2024), NY (Ramirez *et al.* 2024), O (University of Oslo 2024), P (MNHN 2024), RSA (Rancho Santa Ana Botanic Garden 2024), and US (Orrell T, Informatics and Data Science Center - Digital Stewardship 2024), all assessed via the Global Biodiversity Information Facility (GBIF) portal (https://gbif.org/). In addition, specimen records of KATH (National Herbarium and Plant Laboratories 2020–2024) and TI (Society of Himalayan Botany 2013–2024) were assessed from their respective online portals: https://plantdatabase.kath.gov.np/ and https://umdb.um.u-tokyo.ac.jp/DShokubu/. The herbarium acronyms are based on Thiers (2024).

MORPHOLOGICAL VARIABILITY

Studies have reported considerable morphological and genetic variation in *F. cirrhosa* as it has a broad range of geographical distribution with a wide elevation range, and also because of diverse habitat conditions where it grows (Dasgupta and Deb 1986; Luo and Chen 1996; Zhang *et al.* 2010; Wu *et al.* 2020; Huang *et al.* 2024). *F. cirrhosa* shows variations in plant and bulb size, number and shape of leaves, the presence or absence of cirrhose leaf tips, flower color, capsule size, and seed shape and size. These traits are considered to be influenced by geographic and ecological conditions (Dasgupta and Deb 1986; Chandora *et al.* 2023).

Dasgupta and Deb (1986) have reported that plants from the Eastern Himalayas are relatively smaller in size with small bulbs, and linear leaves with cirrhose tips, and these traits gradually change towards the Western Himalayas where plants are bigger, with larger bulbs and broader leaves lacking cirrhose tips. However, Nepali specimens do not consistently follow this pattern. For example, cirrhose leaves are found in specimens observed from both the eastern (e.g., Panchthar) and western (Dolpa) regions of Nepal (Plates 2 & 3), suggesting no clear correlation between morphology and geography.

Distribution and ecology

Fritillaria cirrhosa is found in the Himalayas, East Asia, and Mainland Southeast Asia, covering northern Pakistan (Hazara), India (Jammu-Kashmir, Himachal Pradesh, Uttarakhand, Sikkim), Nepal (western, central, and eastern), Bhutan, parts of China (such as Gansu, Qinghai, Sichuan, Xizang, Yunnan); and Myanmar (Chen and Mordak 2000; Ali 2007; Chauhan 2022; POWO 2024). Information in the herbarium and other sources indicates that the species is almost continuously found from northwest to northeast Nepal. The occurrence of the species has been determined in 24 northern mountain and high Himalayan districts (Figure 1): Bajhang, Bajura, Darchula, and Doti in Sudur Paschim Province; Dolpa, Humla, Jajarkot, Jumla, and Mugu in Karnali Province; Baglung, Gorkha, Kaski, Lamjung, Manang, Mustang, and Myagdi in Gandaki Province; Dhading, Dolakha, Ramechhap, and Rasuwa in Bagmati Province; and Panchthar, Sankhuwasabha, Solukhumbu, and Taplejung in Koshi Province.

The elevation range of the species throughout its distribution range is reported to be between 1500 and 4880 m asl (Noltie 1994; Chen and Mordak 2000; Singh and Sanjappa 2006); and in Nepal, it occurs between 3000 and 4800 m asl (Ghimire *et al.* 2021b; Rana and Ghimire 2024). However, in the Himalayas, most populations have been recorded between 3300 and 4500 m asl, primarily on moist north- or northeast-facing slopes with inclinations ranging from 18° and 37° (Ghimire *et al.* 2001, 2008; Chauhan *et al.* 2011; Lata *et al.* 2023). It prefers slightly acidic substrates (pH ranging from 4.7 to 6.0) rich in organic matter, humus, and essential macronutrients (Chauhan *et al.* 2011; Chandora *et al.* 2023).

Fritillaria cirrhosa thrives in diverse habitats, such as thickets, evergreen broad-leaved and needle-leaved forests, moist open grassy slopes, moist alpine meadows, rocky slopes, and flood plains (Noltie 1994; Chen and Mordak 2000; Ghimire *et al.* 2008; Chauhan *et al.* 2011; Wang *et al.* 2017). It grows in association with forbs, grasses, and dwarf shrubs. The latter chiefly belong to the genera *Berberis*, *Caragana*, *Cotoneaster*, *Hippophae*, *Juniperus*, *Lonicera, Rhododendron*, and *Salix*. The biotic environment (presence of specific shrub species), climatic factors (precipitation, temperature seasonality, and minimum temperature of the coldest month), and elevation have been identified as the most important variables influencing the distribution and abundance of *F. cirrhosa* (Li *et al.* 2017; Jiang *et al.* 2022; Chandora *et al.* 2023).

The plant performs better in relatively cooler temperatures (Li *et al.* 2008) and areas with high precipitation (Li *et al.* 2017). Greater abundance of *F. cirrhosa* has been recorded in areas with higher annual precipitation (Li *et al.* 2017). Cooler temperature, and humid conditions resulting from increased precipitation, have also been identified as crucial for seeds, such as those of *F. cirrhosa*, requiring an after-ripening period (Chen *et al.* 1993; Li *et al.* 2017). According to Chen *et al.* (1993), *F. cirrhosa* seeds, during the initial stages of morphological development, require an optimal temperature of 15°C for embryo after-ripening. But in later stages, seeds prefer slightly cooler temperatures of around 10°C.

The presence of specific associated species, particularly woody and thorny shrubs with dense branches, has been shown to enhance the availability and survival of *F. cirrhosa* (Li *et al.* 2017). Through their nursing effects, such shrubs probably improve the microenvironment by providing partial sheds and also protect herbaceous plants from direct human harvesting, livestock grazing, and other disturbances. Particularly, shading has been shown to increase the survival rate of young-sized individuals of *F. cirrhosa* (Li X. *et al.* 2009).

Plant regeneration occurs both by vegetative and sexual means. Vegetative propagation takes place through underground bulbs. Once these bulbs reach maturity and increase in size to over 1 cm diameter, produce 2–3 daughter bulbs (Chauhan *et al.* 2011). These daughter bulbs later separate from the mother bulbs and begin to regenerate by producing aboveground structures in the next growing season, which starts a few days after snow melts. Adequate moisture is required for successful plant regeneration (Chauhan *et al.* 2011). In nature, *Fritillaria* bulbs become dormant and require low temperatures for normal plant development (Marković *et al.* 2020). An appropriately extended growth period of *F. cirrhosa* has been shown to achieve under 15° and 20° C (Li *et al.* 2008).

In the Himalayas, flowering in *F. cirrhosa* occurs from April to July, and fruiting from June to October (Singh and Sanjappa 2006). However, plant phenology is geography-, elevation-, and microhabitat-dependent (Chauhan *et al.* 2011; Ma *et al.* 2022). In China, the whole phenological period of *F. cirrhosa*, from germination to fructescence, is approximately 117 days on average, from late April to mid-August (with 31 days of flowering) (Ma *et al.* 2022). *F. cirrhosa* has been found to favor outcrossing, which is considered the primary adaptive function of its flowers (Ma *et al.* 2022). The flowers are mostly pollinated by bees (Zhang *et al.* 2010). Despite these facts, sexual regeneration in the wild is reported to be very poor, even though seeds show high viability (up to 97%) and germination rate (up to 93%) under controlled laboratory conditions (Chauhan *et al.* 2011). Alpine environments present harsh conditions like short growing periods, extreme fluctuations in temperature, and limited availability of water, which greatly hinder seedling establishment even if seeds exhibit good germination in controlled laboratory conditions (Fernández-Pascual *et al.* 2021; del Alba *et al.* 2025).

Traditional use and practices

SOWA RIGPA

Bulbs, leaves, and fruits of *F. cirrhosa* are the main parts used in Sowa Rigpa medicines. These are described as having a bitter and sweet taste, with a cool potency. The plant is considered non-toxic (Ghimire *et al.* 2021a).

In Nepal, the plant is used by amchi to treat fractured skull bones, poisoning, fever, and respiratory ailments including cough, cold, and asthma (Ghimire *et al.* 2021a). Bulbs and/or fruits are used as a tonic to improve memory and reduce mental disorders (Ghimire *et al.* 2001, 2021a). In other Sowa Rigpa literature, *a bi sha* sourced either from *F. cirrhosa* or *F. delavayi* is mentioned as useful for healing damaged cranial bones, and for treating infectious fevers, burns, swellings, poisonings, menstrual bleeding, cough due to wind (*rlung*) disorder, and as a blood purifier (Gawa Dorje 1995; Arya 1998; Drungtso and Drungtso 2005; Gonpo 2008; Wangchuk *et al.* 2008, 2009).

Leaves and fruits are harvested in July and August, while bulbs are harvested in September and October. After collection, the plant parts are thoroughly washed, shed- or sun-dried, and stored in airtight containers made of cloth, metal, skin, or plastic. The plant parts are typically used in the form of dried powder mixed with other ingredients. In Dolpa, Nepal, amchi practitioners mix the powder prepared from fresh fruits and bulbs with nine other unspecified herbal ingredients to create small pills with honey, and this mixture is used for the treatment of poisoning, as well as respiratory and mental disorders (Ghimire *et al.* 2001).

AYURVEDA

F. cirrhosa has been referenced under different names in contemporary literature dealing with Ayurveda. It has been identified by some scholars as a source of *kākolī* (e.g., Warrier 1995; Singh 2006; Dhyani *et al.* 2010), but others consider it to be *kshīrakākolī* (Khare 2007; Sagar 2014; Vij *et al.* 2019; Kaur 2021; Gupta *et al.* 2023). Both *kākolī* and *kshīrakākolī* are described in Ayurveda as components of *ashthavarga* – a group of eight

Plate 2. *Fritillaria cirrhosa* from east (A, B) and central (C, D) Nepal. A. Plant with light yellow flower; upper leaves and bracts curled to slightly cirrhose at apex (Phaleke, Singalila Ridge, Panchthar, Nepal-Sikkim border; amongst forbs, sedges and grasses in shrubland, 3600 m; 15 June 2010). B. Plant with dark chequered flowers; upper leaves and bracts curled and not cirrhose at apex (Pahade Megu, Panchthar, Nepal; amongst forbs, sedges, and grasses on open slopes, 3900 m; 18 June 2010). C. Plant with light yellow and less chequered flower; leaves and bracts not cirrhose at apex (Milarepa Cave, Manang, Nepal; amongst dwarf shrubs, mainly *Lonicera* sp., 3800 m; 10 June 2009). D. Plant with densely chequered flowers; leaves and bracts not cirrhose at apex (Cholangpati, Langtang National Park, Rasuwa, Nepal; in shrubland, 3700 m; 20 July 2008). ©S.K. Ghimire.

Plate 3. *Fritillaria cirrhosa* from west Nepal. A. Plant with densely chequered flowers; and leaves and bracts curled at apex (above Tugling, Changla Khola Valley, Dozam, Humla, Nepal; on dry grassy slopes, 3580 m; 23 May 2010). B. Plant with densely chequered flowers; and distinctly cirrhose to curled leaves and bracts (Kyaglafak, near Kagmara, Dolpa, Nepal; open slopes, 4200 m; June 2000). ©S.K. Ghimire.

medicinal ingredients, each derived from different plant species – used as a rejuvenator, aphrodisiac, and tonic to strengthen the immune system and treat general debility (Kumar *et al.* 2019; Mishra 2020). In classical Ayurvedic texts, such as 'Bhāvaprakāsa Nighantu', *ashthavarga* is described as having a cold potency and being heavy in post-digestive effect. It is nourishing and enhances bodily tissues, promotes the production of semen, aids in the healing of fractures, increases sexual vigor, strengthens *kapha* (phlegm) and overall bodily strength, and alleviates conditions related to *vāta* (wind), *pitta* (bile), blood disorders, thirst, burning sensation, fever, diabetes (*prameha*), and tuberculosis (*ksaya roga*) (Chunekar 1969).

Both *kākolī* and *kshīrakākolī* are particularly mentioned in literature as useful to alleviate wind disorders (*vāta*), bleeding disorder (*raktapitta*), intermittent fever, burning sensations, chronic rheumatic pain, cough, asthma, bronchitis, weak ejaculation and general debility (Chunekar 1969; Warrier 1995; Dhyani *et al.* 2010; Ingalhalli *et al.* 2015; Kumar *et al.* 2019; Srivastava *et al.* 2019; Vij *et al.* 2019).

However, the identification of *F. cirrhosa* as a source of *kākolī* or *kshīrakākolī* has been questioned by many scholars (e.g., Singh 2006; Khare 2007; Dhyani *et al.* 2010; Acharya *et al.* 2012; Ingalhalli *et al.* 2015; Srivastava *et al.* 2019; Marde and Mishra 2019). According to Bhāvaprakāsa Nighantu the tuber of *kṣīrakākolī* has a pleasant fragrance, exudes a milky substance when cut, and resembles *shatāvarī* in morphology (Chunekar 1969). *Kākolî* is similar in nature to *kshīrakākolī*, but differs from the latter about its somewhat darker (blackish) color (Chunekar 1969; also reviewed in Kumar *et al.* 2019; Marde and Mishra 2019). Consequently, in modern literature, *kākolī* is most commonly referred to as *Roscoea purpurea* Sm. (Khare 2007; Acharya 2012; Acharya *et al.* 2012; Sagar 2014; Ingalhalli *et al.* 2015; Kumar *et al.* 2019; Marde and Mishra 2019; Srivastava *et al.* 2019), though other species of the genus *Roscoea*, such as *R. capitata* Sm. and *R. alpina* Royle, are also frequently mentioned (reviewed in Kumar *et al.* 2019; Marde and Mishra 2019). Similarly, *kshīrakākolī* of Ayurveda has been mostly attributed to *Lilium polyphyllum* D.Don. (Singh 2006; Khare 2007; Dhyani *et al.* 2010; Acharya *et al.* 2012; Ingalhalli *et al.* 2015; Srivastava *et al.* 2019), a species native to the Western Himalayas. Some literature even suggests that the bulbs of *Fritillaria cirrhosa* can be used as a substitute for *kshīrakākolī* (Srivastava *et al.* 2019; Vij *et al.* 2019). Thus, the identification of *F. cirrhosa* as *kākolī* or *kshīrakākolī* remains an unresolved mystery. Further research is needed to clarify its precise role in Ayurveda.

USE IN OTHER MEDICAL SYSTEMS

In traditional Chinese medicine (TCM), *Fritillaria* bulbs involving at least nine species, including *F. cirrhosa*, have been used for over 2000 years as remedies for conditions such as cough, asthma, bronchitis, pneumonia, lung injuries, and fever (Li *et al.* 2006; Wu *et al.* 2022). In Tibetan folk medicine, a decoction prepared from the bulbs of *F. cirrhosa* is used to treat colds and coughs (Guo *et al.*

2022a). Bulbs boiled in water are also administered to treat colds and tracheitis (Guo *et al.* 2022b). The bulbs are also used in veterinary medicine by locals in the Gyirong Valley of Tibet (Guo *et al.* 2022a).

In Indian folk medicine, *F. cirrhosa* bulbs are traditionally used to treat respiratory disorders, including cough, asthma, bronchitis, and tuberculosis (Ambasta *et al.* 1986). In the Kashmir Himalayas, dried bulbs are ground and consumed with water to treat tuberculosis, abdominal pain, other stomach disorders, and even cancer (Haq *et al.* 2023; Manzoor *et al.* 2023). Additionally, roasted fruits are used to treat gynecological and dermatological disorders, and cancer (Bhat *et al.* 2021). In Uttarakhand, a decoction prepared from the bulbs is used to treat asthma and tuberculosis, while powdered bulbs are consumed to treat fever (Thapliyal *et al.* 2024).

In Nepali folk medicine, a paste made from *F. cirrhosa* bulbs is applied to cuts and wounds to stop bleeding and promote the healing process (Bhattarai 1997; Manandhar 2002; Adhikari *et al.* 2021). The paste is also used to treat pimples (Manandhar 2002). In different regions of Nepal, roasted bulbs are eaten to treat asthma, bronchitis, and coughing with bleeding, possibly caused by tuberculosis (Manandhar 2002). In Rolwaling, central Nepal, Sherpa people consume the bulbs to reduce stomach pain (Sacherer 1979). Similarly, Tamang people in Rasuwa employ the juice obtained from whole plants to treat gastrointestinal disorders, such as stomach pain and gastritis (Uprety *et al.* 2010; Shrestha *et al.* 2014). In Humla, northwestern Nepal, a powder made from the tuber is taken orally to treat headaches (Rokaya *et al.* 2010). In northern far-west Nepal, roasted bulbs are eaten to treat respiratory and gastrointestinal disorders, as well as to act as a general tonic (Ghimire *et al.* 2021b). Additionally, tender shoots are sometimes cooked as vegetables in various parts of Nepal (Ghimire *et al.* 2001; Pradhan *et al.* 2020).

Phytochemistry and pharmacology

CHIEF CONSTITUENTS

F. cirrhosa contains over 100 phytoconstituents (Bhat *et al.* 2022). Isosteroidal alkaloids are the major compounds identified in the crude extracts of its bulbs (Li *et al.* 2000, 2006, 2009; Chen *et al.* 2020; Dong *et al.* 2022; Bora *et al.* 2025). In addition, *F. cirrhosa* bulbs also contain steroidal alkaloids, saponins, terpenoids, organic acids, sterols, and nitrogenous bases and their glycosides (Li *et al.* 2006; Chen *et al.* 2020; Wang *et al.* 2021).

More than 40 different alkaloids have been reported in *F. cirrhosa* bulbs. Among these, cevanine-type isosteroidal alkaloids, such as 3β-acetylimperialine, chuanbeinone, imperialine (or sipeimine), peimine (or verticine), peiminine (or verticinone), peimisine (or ebeiensine), puqiedine and puqiedinone (or delavinone, sinpeinine A) are reported as the major compounds with significant pharmacological activities (Li H.J. *et al.* 2009; Li S.L. *et al.* 2000, 2001; Wang *et al.* 2011, 2021; Wu *et al.* 2022; Bhat *et al.* 2024). Recently, Dong *et al.* (2022) isolated 16 new cevanine-type isosteroidal alkaloids, cirrhosinones A–N and cirrhosinols A-B; and Bora *et al.* (2025) isolated dongbeinine-A, yibeinone G, and tortifoline A as new isosteroidal alkaloids in *F. cirrhosa* bulbs. The steroidal alkaloids present in *F. cirrhosa* bulbs are of two types: verazine type, including puqietinone, cirrhosinine A, cirrhosinine B, and delavidine; and solanidine type, including demissidine, solanidine, and its glycoalkaloids (Wang *et al.* 2021; Qu *et al.* 2022).

Pai *et al.* (2023) recorded the total alkaloid concentration in *F. cirrhosa* bulbs to be 45.54 ± 0.03%. However, in an earlier study, Li *et al.* (2013) found quite low value of total alkaloids (0.094 ± 0.01%) in the bulbs of cultivated *F. cirrhosa* and reported that the content of total saponins (3.436%) to be far greater than total alkaloids. The saponin content in *F. cirrhosa* has been reported to be the highest and alkaloid content the lowest among the nine cultivated taxa under the genus *Fritillaria* (8 species and 1 variety) compared (Li *et al.* 2013). Due to this reason, Chen *et al.* (2020), in their review, argued that saponins may also be one of the active ingredients responsible for the pharmacological activities of *F. cirrhosa*. However, to our knowledge, no study has elucidated the nature of saponins present in *F. cirrhosa* and their biological activities. About 39 different steroidal saponins have been reported in other species of the genus *Fritillaria* (see Wang *et al.* 2021 for a comprehensive review and list of metabolites).

BIOLOGICAL ACTIVITIES

Recent pharmacological studies have shown that crude bulb extracts of *F. cirrhosa* and alkaloids isolated from these bulbs exhibit considerable antitussive, expectorant, anti-asthmatic, and anti-inflammatory activities, and these help in inhibiting cough frequency, reducing acute lung injury and preventing pulmonary fibrosis (Lin *et al.* 2006; Wang *et al.* 2011, 2016 a & b, 2021; Wu *et al.* 2022; Pai *et al.* 2023). In addition, bulb extracts of *F. cirrhosa* and its alkaloids also show hypotensive, analgesic, antiplasmodial, antioxidant, antiviral, antitumor, and anticancer activities (Chen *et al.* 2020; Bhat *et al.* 2022; Wu *et al.* 2022; Bora *et al.* 2023).

Particularly, imperialine, 3β-acetylimperialine, and sinpeinine A from *Fritillaria* have been reported to have antimuscarinic (anticholinergic) activities on tracheal smooth muscles of guinea pigs, indicating their effectiveness in the treatment of asthma (Lin *et al.* 2006). In another study, imperialine reduced the functional and morphologic alterations in the lungs due to chronic obstructive pulmonary disease in rats (Wang *et al.* 2016b). Isosteroid alkaloids have also been reported to inhibit cigarette smoke-induced oxidative stress by activating the Nrf2-mediated antioxidant pathway (Liu *et al.* 2020).

Bora *et al.* (2025) demonstrated that the isosteroidal alkaloids in *F. cirrhosa* inhibit acetylcholinesterase activity, suggesting their potential therapeutic effects on age-related neurodegenerative diseases, such as Alzheimer's. In their earlier study, Bora *et al.* (2023) demonstrated significant antiplasmodial activity of the chloroform and alkaloid-enriched fractions of *F. cirrhosa* bulbs. They identified peimine, peimisine, puqiedinone, and puqiedine as marker compounds responsible for this activity, thus providing scientific evidence to support the traditional use of *F. cirrhosa* in treating fever-related conditions.

F. cirrhosa has also been reported to be potentially effective in treating lung, colorectal, liver, breast, and ovarian cancers, among others (Chen *et al.* 2020; Wu *et al.* 2022; Bhat *et al.* 2024). In several *in vitro* and *in vivo* studies, aqueous extract of *F. cirrhosa* bulbs and its alkaloids exhibited such activities (e.g., Wang *et al.*

2015; Li *et al.* 2020). In their *in vitro* study, Kavandi *et al.* (2013) found that *F. cirrhosa* at higher doses inhibits the proliferation of ovarian and endometrial cancer cells. Li *et al.* (2020) investigated the anticancer mechanisms of *F. cirrhosa* bulb and found that its aqueous extract induces cellular apoptosis through immune regulation. This effect is mediated by the signal transducer and activator of transcription (STAT) pathway, providing insights into its potential therapeutic role in cancer treatment (Li *et al.* 2020). In addition, Wang *et al.* (2015) demonstrated significant *in vitro* antiproliferative activity of the chloroform extracts of *F. cirrhosa* bulbs and the purified total alkaloids of the plant. The purified total alkaloids also showed *in vivo* antitumor activity by inhibiting tumor angiogenesis and inducing apoptosis through enhanced expression of caspase-3 (Wang *et al.* 2015). Among the phytoconstituents isolated from *F. cirrhosa* bulbs, peiminine, imperialine, imperialine-3-β-glucoside, and chuanbeinone show significant anticancer effects (Wu *et al.* 2022; Bhat *et al.* 2024). Bhat *et al.* (2024) explained the molecular basis underlying the therapeutic potential of *F. cirrhosa* constituents in treating breast cancer. The active compounds were reported to deactivate many gene targets and pathways, particularly the PI3K-Akt signaling pathway, suggesting their role in cancer progression inhibition (Bhat *et al.* 2024). These findings suggest that the alkaloids of *F. cirrhosa* hold promising potential for development as antitumor drugs.

TOXICITY

F. cirrhosa is generally regarded as a nontoxic or low-toxic herb (Chen *et al.* 2020; Qu *et al.* 2022) compared to other allied species (Xu *et al.* 2019). In Sowa Rigpa, where only minimal quantities of the bulbs are used, the plant is generally considered safe. In an acute oral toxicity study, Xu *et al.* (2019) determined the maximum feasible dose value of *F. cirrhosa* crude bulb extract in mice to be 452.14 g/kg. Administration of this maximum feasible dose of crude bulb extract for 14 days led to no mice death throughout the test period, but the extract resulted in liver cell edema (Xu *et al.* 2019). However, recent *in vitro* studies suggest potential cytotoxic effects of the aqueous bulb extracts (80 and 160 mg/mL for 72h) of *F. cirrhosa* in human colon epithelial cells causing mitotic aberrations, genomic instability, and cytokinesis failure (Guo *et al.* 2017, 2020). While these findings suggest potential toxicity under specific conditions, further research is needed to fully assess the safety profile of *F. cirrhosa* and its extracts.

VARIATION IN PHYTOCHEMICAL CONSTITUENTS

The concentrations of bioactive alkaloids in *F. cirrhosa* have been shown to vary with plant age, reproductive stage, and timing of harvest (Konchar *et al.* 2011; Ma *et al.* 2021). The highest alkaloid concentration has been reported during the early stages of fruit development, the concentration decreases with fruit maturation (Konchar *et al.* 2011). Consequently, the late flowering or early fruiting stage has been recommended as the optimal time for harvesting *F. cirrhosa* bulbs (Wu *et al.* 2022) during which period there is the highest content of total alkaloids ranging from 0.088% to 0.218% (Ma *et al.* 2021). However, harvesting at this stage negatively impacts the plant's sexual reproduction cycle, as it prevents full seed production and maturation. Alkaloid content has also been shown to be affected based on the processing methods applied. Ma *et al.* (2021) demonstrated that alkaloid levels are higher when bulbs are oven-dried after washing compared to sun-dried bulbs.

Various studies have investigated the effects of environmental factors, artificial lighting, and fertilizer application on the phytoconstituent contents of *F. cirrhosa* (Li *et al.* 2008; Chen *et al.* 2020; Jiang *et al.* 2024). Among environmental factors, relatively lower temperatures have been found to increase alkaloid content in *F. cirrhosa* (Li *et al.* 2008). Fertilizer application, particularly nitrogen, has been shown to influence both yield and alkaloid concentration. Nitrogen application at the rates of 60–120 kg and 60 kg ha^{-1} has been shown to increase bulb yield by 22.47 %–40.69% and boost the concentration of alkaloids (sipeimine and peimine) by 8.01–11.23%, respectively (Jiang *et al.* 2024).

Threats and status

THREATS

Across its distribution range, *F. cirrhosa* faces increasing pressure from unsustainable commercial harvesting (Zhang *et al.* 2010; Konchar *et al.* 2011; Li *et al.* 2017; Cunningham *et al.* 2018; Shafi *et al.* 2018; Mathela *et al.* 2021; Chauhan 2022; Guo *et al.* 2022). The raw underground bulbs of *F. cirrhosa* are the primary commodities involved in trade (see Plate 3). Tender shoots of *F. cirrhosa* are also collected mainly for consumption as a vegetable (Plate 3). In addition to unsustainable harvesting, the populations of *F. cirrhosa* face significant threats from degradation and loss of suitable habitats. Key drivers include deforestation, overgrazing, tourism activities, and human-induced wildfires, all of which contribute to the decline of suitable habitats.

High harvesting pressure has been attributed to escalating demand from herbal industries, resulting in a significant increase in market price – rising over nine-fold between 2002 (USD 60 per kg) and 2017 (USD 560 per kg) (Cunningham *et al.* 2018). This demand has led to widespread premature harvesting due to high competition among harvesters. The annual global demand for *Fritillaria* bulbs is estimated to be between 3000 and 5000 tons (Cunningham *et al.* 2018). While precise figures related to the trade volume of *Fritillaria* bulbs originating in Nepal are unavailable, preliminary estimates suggest an annual volume of about 5–15 metric tons over the past few decades (Tandon *et al.* 2001). Based on information collected from local traders, Pyakurel *et al.* (2018) estimated that 1.5 metric tons of *F. cirrhosa* bulbs were traded alone from the Darchula District in northwest Nepal in the fiscal year 2014/2015. However, an official report from the Api Nampa Conservation Area in Darchula indicated a total volume of 5.2 tons of bulbs traded from the area in the fiscal year 2017/2018 (ANCA n.d.). A significant portion of these collections is exported, whether through legal or illegal channels, to China (Pyakurel *et al.* 2018).

CONSERVATION STATUS

As per the IUCN Red List (https://iucnredlist.org/), the current global status of *F. cirrhosa* is vulnerable. In the past, several

Plate 3. Freshly harvested shoots (A) and bulbs (B) of *Fritillaria cirrhosa*: A. between Machhapuchhre Base Camp and Deurali, Annapurna Conservation Area, Kaski, northcentral Nepal, open slopes among herbs and grasses, 3450 m, 24 May 2016. B. Pilkanda, Api Nampa Conservation Area, Darchula, northwest Nepal, open grassy slopes, 3800 m; 25 July 2016. Both photos ©S.K. Ghimire.

assessments were carried out to evaluate the status of the species in different countries and regions. In the year 1997, the species was categorized as critically endangered for the Indian Himalayas during the Conservation Assessment and Management Planning (CAMP) workshop held in Lucknow, India, using IUCN criteria (Molur and Walker 1998). Subsequent assessments during the CAMP workshop in Kullu, India in 1998 classified the species as critically endangered in Jammu and Kashmir and endangered in Himachal Pradesh (Ved and Tandon 1998). In Sikkim, the species was assigned the status of vulnerable (reviewed in Chauhan 2022). In Nepal, the CAMP workshop held in Pokhara in 2001 reviewed the status of the species within the country and assigned it to be vulnerable (Tandon *et al.* 2001). A recent global assessment has similarly classified the species under the vulnerable category of the IUCN Red List (Chauhan 2022). In China, *F. cirrhosa* is rated Grade III protected species owing to its widespread harvesting, thus placing a premium on the conservation of the species for the future (Zhang *et al.* 2010; Cunningham *et al.* 2018). This comprehensive history highlights the consistent concern for the conservation of *F. cirrhosa* throughout its range.

POPULATION TREND

Some recent reports have highlighted that the species faces continuous overharvesting pressure resulting in the rapid decline of its wild populations (Cunningham *et al.* 2018; Mathela *et al.* 2021; Chauhan 2022). However, the magnitude of this decline is not precisely known as there is no baseline data available for the species covering its wide distribution range to compare with the current population data. A study conducted in the north-western Indian Himalayas, however, showed that the density of *F. cirrhosa* has declined by 58–77% over the past few years, based on data from three populations (Chauhan *et al.* 2011).

In the Indian Himalayas, the current population densities that vary considerably across the region are considered to be very low (Chandora *et al.* 2023). For example, in Himachal Pradesh, the densities have been reported to range from 0.03 to 0.87 individuals m^{-2} (Chandora *et al.* 2023) and 0.33 to 2.30 individuals m^{-2} (Lata *et al.* 2023). In Uttarakhand, the densities were reported to be slightly higher and ranged from 0.4 to 4.2 individuals m^{-2} (Chauhan *et al.* 2011). In China, even reduced population density values have been reported, which ranged from 0.05 to 3.00 individuals m^{-2} among five sites in Sichuan, and 0.15 to 0.23 individuals m^{-2} among three sites in Yunnan (Wang *et al.* 2017). Similarly, the resource density (i.e., weight of bulbs in g m^{-2}) has been reported to range from 2.95 to 17.22 g m^{-2} in Sichuan and 8.69 to 16.52 g m^{-2} in Yunnan (Wang *et al.* 2017). In Nepal, there is no recent population data available. However, an earlier study conducted in Dolpa showed the densities to be 0.05–3.0 individuals m^{-2} (Ghimire *et al.* 2001). Trade-induced overharvesting has been identified as a more critical factor than climatic and biotic conditions in determining the abundance of *F. cirrhosa* (Li *et al.* 2017; Chauhan 2022).

Overharvesting has been shown to affect the bulb and fruit morphology, where the bulbs became thinner and longer, and the fruits thicker and shorter due to the pressure of overharvesting (Li *et al.* 2017).

Conclusions

Fritillaria cirrhosa is highly valued in traditional medical systems, such as Sowa Rigpa under which it is often utilized as a panacea for a wide variety of ailments. Recent pharmacological investigations support its ethnomedicinal use, as it has shown efficacy and low toxicity. Due to these reasons, there is increasing global demand for *F. cirrhosa* bulbs in the international herbal market, which led to overharvesting pressure threatening the long-term viability of its populations. In addition, the species' specific ecological requirements and intrinsic biological traits have made it highly vulnerable to overharvesting and habitat degradation. The large-scale harvesting of the plant driven by the commodification of herbal products has also increasingly threatened the local practices in the Himalayas where *amchi* practitioners and villagers traditionally use the plant in very small quantities. Recent studies highlight the need for broad-scale population assessments and monitoring across its distribution range. Effective conservation measures will be needed to ensure the sustainability of *F. cirrhosa* populations. These measures may include preventing illegal harvesting, protecting natural habitats, promoting sustainable harvesting practices, and implementing enrichment planting and *ex-situ* conservation strategies.

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