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REVIEW ARTICLE

Taxonomic diversity, distribution, biochemical, molecular and pharmacological potential of *Paris* L. (Melanthiaceae): a review

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Abstract

The genus *Paris* L. belonging to the family Melanthiaceae is one of the important monocot angiosperms with wide range of medicinal and pharmacological potentials. In the recent decades, a surging popularity and demand for dried rhizomes of *Paris polyphylla* Sm. have been witnessed in the international herbal market which is mainly due to the *Rhizoma Paridis* based anti-oxidant and anti-cancer herbal drug products of Traditional Chinese Medicine (TCM) rich in bioactive steroidal saponins emanating from China. This has triggered rampant wild collection and pushed the natural population of *P. polyphylla* on the verge of extinction in the Indian Himalayas, Northeast India, Bhutan, Nepal and China. The present review highlights current taxonomic diversity and nomenclatural status, biosystematics, ethnobotany and traditional uses, global distribution and endemism range, molecular phylogeny and evolution, biochemical profiles, pharmacological activities including anti-microbial, cytotoxicity, anti-inflammatory, anti-tumour, and anti-aging potential, mineral ion deposits, tissue culture, trade and commerce, and conservation aspects of *Paris* L. in a regional and global perspectives. The present review revealed 36 taxa (at species and varietal level) of *Paris* L. published in various literatures including Flora of China, and now some of the varieties have been found synonymized and merged into 27 species reported as accepted names now found updated in POWO (2022). The Chinese species and varieties of *Paris* L. have been found extensively studied to date for their medicinal and pharmacological potential. However, there is a need for detail taxonomic and biochemical studies on Indian species of *Paris* L. including *P. polyphylla* to unveil their correct taxonomic status, and population status in natural habitats, bioactive phytochemicals, pharmacological potential, cultivation and conservation, sustainable harvesting and value addition, trade and commerce. This article is expected to help researchers, traders and conservationists in realizing the taxonomic diversity, ecological, economic, medicinal and pharmacological importance of the genus *Paris* L.

Keywords: *Paris* L.; Taxonomic Diversity; Medicinal Importance; Bioactive Phytochemicals; Molecular Phylogeny; Pharmacological Potential; Trade and Commerce; Conservation

1. Introduction

The sacred *Vedas* of India and Traditional Chinese Medicines of China have the references of several medicinal plants and their various uses in traditional medicines for promoting health and wellbeing. The *Virikshayurveda,* which is considered one of the oldest works in traditional herbal medicine in India which were compiled even before the beginning of the Christian era is reported as a basis for the evolution of pharmacological science in ancient India (Chopra et al., 1956; Zhao, 2004; Phurailatpam and Choudhury, 2022). The genus *Paris* L. was first described and published by Linnaeus in *Species Plantarum* 367 (1753), and its native range is reported to be Eurasian to Eastern China, Himalaya and Eastern Himalaya, and North Myanmar. At present, *Paris* L. has 27 accepted species updated in POWO (2022), and 6 heterotypic synonyms are also available for the genus *Paris* L. circumscribed under the family Melanthiaceae (POWO, Govaerts, 2011; Ji, 2021). In Flora of China, Liang et al (2000) reported 22 species and 16 varieties of *Paris* L. found widely distributed in China. Among these, the *Paris polyphylla* Sm. has garnered significant global attention in the last few decades due to its immense medicinal potential as an anti-cancer and anti-oxidant drugs popular in the international herbal market. *Paris polyphylla* Sm. was first described by a British botanist Sir James Edward Smith published in A.Rees (ed.) Cycl. 26:n.2 (1813) (Smith, 1813). The etymology of the genus *Paris* L. is derived from '*pars*' referring to the symmetry of the plant and '*polyphylla*' meaning many leaves. Earlier, the *P. polyphylla* Sm. has been reported with several varieties such as *P. polyphylla* var. *polyphylla*, *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *stenophylla* which have been mainly reported from India, China, Nepal, Bhutan, Burma, Thailand, Mexico, Honduras, Brazil and Indo-China countries (Liang et al., 2000; Kress et al., 2003; Ji et al., 2006a).

Paris quadrifolia is found distributed in Russian provinces namely, Siberia, East Asian countries like Mongolia and parts of temperate Europe such as Ireland and Western Europe, North of Spain and Portugal (Farmer, 2006; Jacquemyn et al., 2008). States of North East India such as Arunachal Pradesh, Meghalaya, Manipur and Nagaland, which is reported as a hub of *Paris* species, and have been identified as focal corridor for an unorganized trading route for the costly *Paris* rhizome sold in South East Asian countries (Tag, 2013; Roy et al., 2018). *P. polyphylla* has been investigated for its pharmacological potential, including antitumor, anti-inflammatory, antioxidant, anthelmintic, and antimicrobial properties (Cunningham et al., 2018; Debmalya et al., 2021). In the last two decades, several review and research articles have been published on *Paris* L. which has thrown light on its taxonomic diversity, nomenclatural status, distribution range, habitat ecology and medicinal potential (Shah et al., 2012; Lalsangluaii et al., 2013; Sharma et al., 2015; Tariq et al., 2016; Yang et al., 2016; Mayirnao and Bhat, 2017; Cunningham et al., 2018; Pei et al., 2019). The present review highlights current status of the *Paris* L. which would provide deep insight into its current taxonomic diversity and nomenclatural status, distribution and endemism range, biochemical profile, pharmacological potentials, medicinal uses, conservation, trade and commercial prospects in regional and global perspectives.

2. Taxonomic diversity, nomenclatural status and biosystematics

2.1. Taxonomic diversity and nomenclature

Taxonomic studies of *Paris* L. including its rhizome, leaf morphology and seed anatomy have been studied for the last 80 years. Initially, the genus *Paris* L. Sp. Pl. (1753: 367) was placed under Liliaceae (Melchior, 1964) and later it was transferred to Trilliaceae and then subsequently placed under the family Melanthiaceae in APG-III (2009) classification system. In APG III & IV systems, *Paris* L. is placed under the order Liliales within clade monocot of angiosperm. It was bifurcated into 02 genera based on floral merosity where Paris showed variable floral merosity (Li, 1984; Li et al., 1998; Zomlefer et al., 2006). However, further revision of the family Trilliaceae using molecular phylogenetic approaches led to the placement of the genus in Melanthiaceae (Ji et al., 2006a; APG-III, 2009; Chase et al., 2016; Kim et al., 2016). Earlier, the genus *Paris* L. had earned 6 other heterotypic synonyms (Govaerts, 2011; Ji et al., 2021), namely, *Alopicarpus* Neck. in Elem. Bot. 2: 369 (1790), Aloaceae
Cartalinia Szov. ex Kunth in Enum. Pl. 5: 119(1850), Trilliaceae,
Daiswa Raf. in Fl. Tellur. 4: 18(1838), Trilliaceae,
Demidovia Hoffm.in Hort.Mosq.: 2(1808), Liliaceae,
Euthyra Salisb. in Gen. Pl.: 41(1866), Trilliaceae
Kinugasa Tatew. & Sutô in Trans. Sapporo Nat. Hist. Soc. 14: 34 (1935), Trilliaceae, all of them are now available in the recent (2022) version of POWO website. The majority of the *Paris* species have been reported from China with 22 species and 16 varieties which are found mentioned in FOC Vol. 24, pp. 88-95 (Liang et al., 2000). Some of the important taxa reported from China are *Paris tengchongensis* Y.H. Ji, C. J. Yang & Y.L. Huang, now a synonym for *Paris forrestii* (Takht). H. Li from Yunnan Tengchong County, Houqiao township China (Li et al., 2017), *Paris caobangensis* Y. H. Ji, H. Li & Z. K. Zhou from Cao Bang, Northern Vietnam (Ji et al., 2006b), *Paris stigmatosa* Shu-dong Zhang, now a synonym for *Paris mairei* H. Lev. from Northeastern Yunnan (Shu-Dong et al., 2014), *Paris nitida* G.W.Hu, Z.Wang & Q.F.Wang, now a synonym for *Paris caobangensis* Y. H. Ji, H. Li & Z. K. Zhou from Jiugongshan Mountain, South Central China (Wang et al., 2017), *Paris qiliangiana* H. Li, J. Yang & Y. H. Wang from Hubei Province (Yang et al., 2017) and *Paris vaniotii* H. Lev. from Yunnan, China (Xu et al., 2019). Similarly, *Paris rugosa* H. Li & Kurita, now a synonym for *Paris forrestii* (Takht.) H. Li was reported for the first time in the Upper Dibang Valley district of Arunachal Pradesh (India) based on the morphological evidences (Lidén and Adhikari, 2019). Further, in Flora of China (Vol. 24, pp.88-95), 08 varieties of *Paris polyphylla* Sm. have been reported, namely, *P. polyphylla* var. *latifolia* F.T. Wang & C. Yu Chang, *P. polyphylla* var. *minor* S.F. Wang, *P. polyphylla* var. *pseudothibetica* H. Li, *P. polyphylla* var. *kwantungensis* (R. H. Miao) S. C. Chen & S. Yun Liang, *P. polyphylla* var. *yunnanensis* (Franchet) Handel-Mazzettii, *P. polyphylla* var. *alba* H. Li & R.J Mitchell, *P. polyphylla* var. *chinensis* (Franchet) H. Hara, *P. polyphylla* var. *nana* H. Li, *P. polyphylla* var. *stenophylla* Franchet. The *P. polyphylla* var. *polyphylla* has been reported exotic to Asia (FOC Vol.24, p. 90) but native of Mexico, Honduras and Brazil. Till 2022, a total of 27 accepted names (at species level) of *Paris* L. have been mentioned in POWO supported through backbone literatures of Zhenyi and Raven (2000) and Ji (2021) which is presented in Table 1 while the majority of the total 36 species and varieties mentioned in FOC Vol. 24, pp.88-95 (Liang et al., 2000) and other literature sources are now declared synonyms of the 27 taxa (Table 1) reported as accepted names (Ji, 2021; Kress et al., 2003) updated in POWO (2022) (Table 2).

Table 1: Checklist of 27 taxa reported as accepted names (at species level only) of the *Paris* L. found updated in POWO (Plants of the World Online) website till 2022 with their native range which is based on backbone *Paris* literatures (Liang et al., 2000 in Zhenyi and Raven (2000) Ed. FOC, Vol. 24, pp. 88-95; Kress et al., 2003; Li and Lei, 2017; Ji, 2021).

SN	Accepted Name & Author citations	Native Range (Liang et al., 2000; Kress et al., 2003; Ji, 2021; POWO, 2022)
1	*Paris bashanensis* F.T.Wang & Tang	South – Central China (Sichuan, Chongqing, W. Hubei).
2	*Paris caobangensis* Y.H.Ji, H.Li & Z.K.Zhou	China (Hubei to Guangxi) to N. Indo-China.
3	*Paris chinensis* Franch.	S. China to Indo-China, Taiwan.
4	*Paris cronquistii* (Takht.) H.Li	S. Central China (to SW. Guangxi) to N. Vietnam.
5	*Paris delavayi* Franch.	China South-Central, China Southeast
6	*Paris dunniana* H.Lév.	China (Guizhou, Guangxi) to Hainan.
7	*Paris fargesii* Franch.	Eastern Himalaya, Arunachal Pradesh, North East India to S. China and N. Indo-China.
8	*Paris forrestii* (Takht.) H.Li	W. Nepal, Assam (Manipur) to China (Sichuan, Yunnan) and N. Myanmar.
9	*Paris incompleta* M.Bieb.	North Caucasus, Transcaucasus, Turkey
10	*Paris japonica* (Franch. & Sav.) Franch.	Japan (N. & Central Honshu).
11	*Paris lancifolia* Hayata	China North-Central, China South-Central, China Southeast, Taiwan.
12	*Paris liana* Y.H.Ji	China South-Central, China Southeast (Yunnan, Guizhou, Guangxi).
13	*Paris luquanensis* H.Li	China South-Central (S. Sichuan, N. Central Yunnan).
14	*Paris mairei* H.Lév	China South-Central, Tibet (SE. Tibet to S. Central China).
15	*Paris marmorata* Stearn	China South-Central, East Himalaya, Nepal, Tibet [Central Himalaya to China (Sichuan, Yunnan)].
16	*Paris polyphylla* Sm.	Himalaya to Central China and N. Myanmar (Assam, Bangladesh, China North-Central, China South-Central, East Himalaya, Myanmar, Nepal, Qinghai, Tibet, West Himalaya).
17	*Paris qiliangiana* H.Li, Jun Yang bis & Y.H.Wang	China North-Central, China South-Central (Sichuan to Shaanxi).
18	*Paris quadrifolia* L.	Eurasia to Mongolia.
19	*Paris taiwanensis* S.S.Ying	Taiwan
20	*Paris tetraphylla* A.Gray	S. Korea to Japan
21	*Paris thibetica* Franch.	Nepal to Central China (China North-Central, China South-Central, East Himalaya, Myanmar, Nepal, Qinghai)
22	*Paris vaniotii* H.Lév.	S. Central China (to Hunan) to N. Myanmar.
23	*Paris verticillata* M.Bieb.	N. Kazakhstan, Inner Mongolia to Siberia and Japan.
24	*Paris vietnamensis* (Takht.) H.Li	China (Yunnan, Guangxi) to N. Indo-China (China South-Central, China Southeast, Laos, Vietnam).
25	*Paris xichouensis* (H.Li) Y.H.Ji, H.Li & Z.K.Zhou	China (SE. Yunnan) to N. Vietnam.
26	*Paris yanchii* H.Li, L.G.Lei & Y.M.Yang	China (W. Yunnan).
27	*Paris yunnanensis* Franch.	E. Himalaya to S. China and N. Myanmar (East Himalaya, Arunachal Pradesh, Assam, China South-Central, China Southeast, Myanmar, Tibet)

Table 2: Checklist of some of the *Paris* species and varieties (Melanthiaceae) with their current nomenclatural status and synonyms with global distribution range as mentioned in POWO- Plants of the World Online (http://www.plantsoftheworldonline.org/) updated by Govaerts (2011) and eFlora of China (www.eFloras.org) confirmed through backbone literatures of Liang et al (2000) in Zhengyi and Raven (2000) Ed. FOC Vol.4, pp-88-95, Kress et al (2003 and Ji (2021) and other relevant *Paris* literatures. A total of 36 taxa were found reported under *Paris* and out of which 17 taxa including at varietal have been reported synonyms and 19 taxa as accepted names at species level.

SL	Scientific Name (Liang et al., 2000; Kress et al., 2003 and other literatures)	Current Nomenclatural Status as per Ji (2021) and POWO (2022)	Global Distribution Range (FOC, 2000; Ji, 2021; POWO, 2022)
1.	*Paris axialis* H.Li	Heterotypic synonym of *Paris vaniotii* H.Lév.	Forests floor; 700-3000 m. Sichuan, North-East Yunnan.
2.	*Paris bashanensis* F.T.Wang & Tang	Accepted name	Moist and shady places in forests; 1400-4300 m. Western Hubei, Sichuan, China.
3.	*Paris caobangensis* Y.H.Ji, H.Li & Z.K.Zhou	Accepted name	Cao Bang, Northern Vietnam, China
4.	*Paris cronquistii* (Takht.) H.Li	Accepted name	Evergreen forests on limestone slopes, ravine forests, mossy forests; 900-2100 m. South-West Guangxi, Guizhou, Sichuan, South-East Yunnan, China
5.	*Paris cronquistii* var. *xichouensis* H.Li	Homotypic synonym for *Paris xichouensis* (H.Li) Y.H.Ji, H.Li & Z.K.Zhou	South East Yunnan, China to Northern Vietnam.
6.	*Paris daliensis* H.Li & V.G.Soukup	Heterotypic synonym of *Paris yunnanensis* Franch.	Forests; ca. 2600 m. Western Yunnan (Dali Xian), China
7.	*Paris delavayi* Franch.	Accepted name	Forests, bamboo forests, thickets; 1300-2000 m. Guizhou, Hubei, Hunan, Jiangxi, Sichuan, Yunnan (Vietnam).
8.	*Paris dulongensis* H.Li & Kurita	Heterotypic synonym of *Paris forrestii* (Takht.) H.Li	Thickets along ravines; 1500-1600 m. North-West Yunnan, China.
9.	*Paris dunniana* H.Lév.	Accepted name	Forests floor, near sea level to 1100 m. Guizhou, Hainan, Yunnan, China.
10.	*Paris fargesii* Franch.	Accepted name	Forests, shady places; 500-2100 m. Guangdong, Guangxi, Guizhou, Hubei, Hunan, Jiangxi, Sichuan, Yunnan (Vietnam).
11.	*Paris fargesii* var. *petiolata* (Baker ex C.H.Wright) F.T.Wang & Tang	Homotypic synonym of *Paris fargesii* Franch.	Shady places in forests; 1200-2000 m. Guangxi, Guizhou, Jiangxi, Sichuan, China.
12.	*Paris forrestii* (Takht.) H.Li	Accepted name	Alpine coniferous forests, evergreen broad-leaved forests; 1900-3500 m. South-East Xizang, Western Yunnan (Myanmar).
13.	*Paris guizhouensis* S.Z.He	Heterotypic synonym of *Paris vaniotii* H.Lév.	Guizhou Province in South-West China.
14.	*Paris incompleta* M.Bieb.	Accepted name	Caucasus-Europe to Eastern Asia also distributed in Georgia and Turkey
15.	*Paris japonica* (Franch. & Sav.) Franch.	Accepted name	Restricted to Japan, where it grows in the Central and Northern Mountains of Honshu Island.
16.	*Paris luquanensis* H.Li	Accepted name	Forests, thickets; 2100-2800 m. NC Yunnan (Luquan Xian), China.
17.	*Paris mairei* H.Lév.	Accepted name	Forests, thickets, alpine grassy slopes; 1800-3500 m. Guizhou, W Sichuan, Northern Yunnan, China.
18.	*Paris marmorata* Stearn	Accepted name	Broad-leaved forests; 2400-2800 m. Sichuan, S Xizang, Yunnan (Bhutan, Northern India, Nepal).
19.	*Paris polyandra* S.F.Wang	Heterotypic synonym of *Paris cronquistii* (Takht.) H.Li	Moist and shady places along valleys; 1200-1600 m. South-West Sichuan, China.
20.	*Paris polyphylla* Sm.	Accepted name	Forests, bamboo forests, thickets, grassy or rocky slopes, streamsides; 100-3500 m. Anhui, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Henan, Hubei, Hunan, Jiangsu, Jiangxi, Shaanxi, Shanxi, Sichuan, Taiwan, Xizang, Yunnan, Zhejiang (Bhutan, India, Laos, Myanmar, Nepal, Sikkim, Thailand, Vietnam).
21.	*Paris polyphylla* var. *alba* H.Li & R.J.Mitchell	Heterotypic synonym of *Paris polyphylla* Sm.	Sichuan, South Central China
22.	*Paris polyphylla* var. *chinensis* (Franch.) H.Hara	Homotypic synonym of *Paris chinensis* Franch.	Central China, South China to Indo-China, Taiwan.
23.	*Paris polyphylla* var. *latifolia* F.T.Wang & C.Yu Chang	Heterotypic synonym of *Paris lancifolia* Hayata	Forests, streamside; 300-2300 m. Anhui, Henan, Hubei, Jiangxi, Shaanxi, China.
24.	*Paris polyphylla* var. *stenophylla* Franch.	Heterotypic synonym of *Paris lancifolia* Hayata	Forests, rocky slopes; near sea level to 3500 m. Anhui, Fujian, Gansu, Guangxi, Guizhou, Hubei, Hunan, Jiangsu, Jiangxi, Shaanxi, Shanxi, Sichuan, Taiwan, Xizang, Yunnan, Zhejiang (Bhutan, India, Myanmar, Nepal, Sikkim).
25.	*Paris polyphylla* var. *yunnanensis* (Franch.) Hand.-Mazz.	Homotypic synonym of *Paris yunnanensis* Franch.	Broad-leaved or coniferous forests, bamboo forests, thickets, grassy slopes; 1400-3100 m. Guizhou, Sichuan, South-East Xizang, Yunnan (India, Myanmar).
26.	*Paris quadrifolia* L.	Accepted name	Boreal and temperate areas of Europe and extends eastwards to western Asia, Western Siberia and the Himalayas.
27.	*Paris rugosa* H. Li & Kurita	Heterotypic synonym of *Paris forrestii* (Takht.) H.Li	North-West Yunnan, China.
28.	*Paris stigmatosa* Shu D. Zhang	Heterotypic synonym of *Paris mairei* H.Lév.	Yunnan, China
29.	*Paris tetraphylla* A.Gray	Accepted name	South Korea, Japan.
30.	*Paris tetraphylla* var. *penduliflora* J.Murata & T.Yamanaka	Heterotypic synonym of *Paris tetraphylla* A.Gray	Higashi-Akaishi Mountains, Japan.
31.	*Paris thibetica* Franch.	Accepted name	Forests, forest margins; 1400-3800 m. South Gansu, Guizhou, Sichuan, South Xizang, North-West Yunnan (Bhutan, Myanmar, Sikkim).
32.	*Paris thibetica* var. *apetala* Hand.-Mazz.	Heterotypic synonym of *Paris thibetica* Franch.	Eastern Himalayas to South Central China.
33.	*Paris undulata* H.Li & V.G.Soukup	Heterotypic synonym of *Paris vaniotii* H.Lév.	Central Sichuan (Emei Shan), China.
34.	*Paris vaniotii* H.Lév.	Accepted name	Shady and moist places in forests. Guizhou, Hunan, Yunnan (Myanmar).
35.	*Paris verticillata* M.Bieb.	Accepted name	Forests, thickets, grassy and shady places, hillsides along ravines; 1100-3600 m. Anhui, Gansu, Hebei, Heilongjiang, Jilin, Liaoning, Nei Mongol, Shaanxi, Shanxi, North-West Sichuan, Zhejiang [Japan, Korea, Mongolia, Russia (Siberia)].
36.	*Paris vietnamensis* (Takht.) H.Li	Accepted name	Evergreen broad-leaved forests; 1200-1900 m. Guangxi, Yunnan (Vietnam).

2.2. *Diagnostic characters*

Paris L. (Melanthiaceae) is a perennial rhizomatous geophytic herb preferably grow in subtropical and temperate forests. Rhizome slender and thickened, stem simple and erect; leaves 4 – 7 to many, rarely 3; flower bisexual, solitary, terminal and pedunculate while tepal 3-8, found in two whorl, free, outer tepal green, ovate-lanceolate, inner tepal linear; stamen 8-24 or more, filaments narrow and flat, elongated in some species, anther basifixed, often with convex connective, at apex; carpel 4 – 10 lobes stigmas, (4-5 in *Paris polyphylla* Sm.), stigma brown in case of *Paris polyphylla*, style short, ovary subglobose, 1 locule with parietal placentation or 4-10 locule with axile placentation. Fruit berry, capsule berry, orange yellow, indehiscent or loculicidal, seeds many, red when

matured and white during immature stage [Liang et al (2000) in Zhengyi & Raven (2000) Ed. FOC Vol. 24, pp.89-95)]. For our taxonomic studies, we collected the tubers of *Paris polyphylla* Sm. collected from the Arunachal Himalayan region and brought to RGU Campus Rono Hills, Doimukh, Arunachal Pradesh and then planted in pots filled with soil rich in organic content and grown in shade. The reproductive characters were investigated by the present authors (Hui Tag & Debmalya Das Gupta during in 2021) at RGU campus which is provided in in Figure 1A-E. It was observed that the new stem and leaf appear from the tubers during the month of April and flowering starts in May and ends in June. Fruits matured by August-September.

2.3. *Biosystematics*

Paris L. is a very slow-growing herb which almost takes a year to increase its rhizome size from one node to another and this is one important reason for the fast disappearance of this species from their natural habitat (Kress et al., 2003; Ji, 2021; Phurailatpam and Choudhury, 2022). About fourteen seedlings of *P. quadrifolia* and *P. polyphylla* were studied at various stages of development which revealed that the anatomy is quite simple and the *Paris* seedlings develop slowly due to slow germination rate (Boyd, 1930; Li, 1998; Lepcha et al., 2019). Studies on different types of heterochromatin and its distribution in the genus have led to the findings that the *P. polyphylla* Smith chromosomes (2n = 10, 20) are the largest in the plant kingdom having distinct fine banding along with large regions of low-intensity fluorescence (Filion and Vosa, 1980). It was also observed that the metacentric pattern of chromosomes is similar for *P. polyphylla* var. *stenophylla* and *P. polyphylla* var. *yunnanesis* and the Japanese species of *Paris* viz. *P. japonica, P. tetraphylla* and *P. verticillata* showed proximal bands (Miyamoto et al., 1992). Some species of this genus namely, *P. delavayi* and *P. thibetica* have been subjected to taxonomic revisions and reduced as synonyms of the existing species (Ji et al., 2007).

Another study in *P. polyphylla* var. *yunnanensis* has found sun light, relative humidity, and rainfall factors to play a crucial role in the opening and closing of anther along with improving the male fitness in this species (Wang et al., 2009). Studies on the leafy sepals of *P. polyphylla* var. *yunnanensis* have shown that photosynthates produced by sepals are involved in seed development and fruit growth, and they compete for the photosynthates exported by the leaves. Hence, the removal of sepal leads to reduced fruit size and a decline in rhizome biomass (Yu et al., 2013). Microscopic methods have been developed for distinguishing 11 *Paris* species in China both for rhizomes as well as for crude drugs to check adulteration while selling a particular species as well as for the authentication and quality control (Xue et al., 2009).

3. Ethnobotany and traditional uses

3.1. *Vernacular names*

The genus *Paris* L. is primarily found in the wild and is mostly native to India, China and the South East Asian Region of the world and have several vernacular names available for the species. These include Himalayan Paris, Love Apple, Daiswa Paris (English), Dudhibauj (Hindi) Hemawati Bacha, Svetavaca (Sanskrit), Thoksam (Bhutanese), Satuwa, Thoksampa, Bako (Nepali), Sinpan (Manipuri), Naga Ginseng, Pekhiepoh, (Poumai dialect, Nagaland), Jyuro (Japanese) Chang Lou, Qi ye yi zhi hua, dian chong lou, hua chong lou (Chinese), trọng lâu nhiều lá (Vietnamese), Khambal (Mizo). In Arunachal Himalayan Region of India, the *Paris* L. is named differently among various tribes such as Orpo, Nyomrang Takeng and Kangkom Oying (Adi), Nyoro-enyii (Nyishi), Morey-enge (Apatani), Ratena (Idu-Mishmi), Mungong (Monpa), Kekuak (Nocte) and Aii-changmu (Sherdukpen) (Haridasan et al., 1995; Liang et al., 2000; Maity et al., 2004; Pei et al., 2019; Lalsangluaii et al., 2013; Deb et al., 2015; Paul et al., 2015; Jambey et al., 2017; Cunningham et al., 2018; Wangpan et al., 2019).

3.2. *Traditional uses*

The rhizome of *Paris polyphylla* Smith has been reported to be traditionally used as an analgesic agent, removes heat, antispasmodic, antitussive, depurative, snake bites, boils and ulcers, diphtheria and epidemic Japanese B encephalitis, stomach ache, appendicitis, tonsils, insect bites and boils. It also has anti-tumour actions (Zhang et al., 2007; Jambey et al., 2017; Deki et al., 2018; Cunningham et al., 2018; Pei et al., 2019). The Chinese varieties of *Paris polyphylla* var. *yunnanensis* and *Paris polyphylla* var. *chinensis* are reported as important raw materials for the herbal formulation of Traditional Chinese Medicine (TCM) (Wang et al., 2009). They have also been reported as the main ingredients of some of the patented Chinese herbal formulations such as “Biyan Qing Keli” which has immense medicinal utility against the treatment of chronic rhinitis and nasopharyngeal cancer (Guo et al., 2006; Han et al., 2009; Xiao et al., 2009a). In Traditional Chinese Medicine (TCM), the Chinese varieties of the *Paris* species are reported as useful for treating boils, severe abscesses, throat infection carbuncles, poisonous snakebites, traumatic pain, countering fever, parotitis, alexipharmic, detumescent, demulcent, hemostatic, hepatopathy, lung and throat related cancer, especially that of the larynx (Yan et al., 2008; Man et al., 2009a; Wang et al., 2013; Commission CP, 2015). The dried rhizomes of *P. polyphylla* var. *yunnanensis* is mainly used to prevent bleeding, treatment of fractures, and antidote for snakebites and abscess (Liu et al., 2016). In the Darjeeling Himalayan region of India, traditional healers namely, Lepchas, Bhutias and Nepalese communities use infusion of the rhizome of *P. polyphylla* against gastritis (Bhandari et al., 2021). In the Nepali folklore, the rhizomes of *P. polyphylla* are reported to be used as a vermifuge, and anti-helminthic agent and the rhizome juice is taken with boiled milk to get relief from intoxication (Devkota et al., 2007; Pande and Tiwari, 2007; Uprety et al., 2010; Chhetri et al., 2013; Thapa, 2013; Liu et al., 2014).

The fresh rhizomes are reported to be used against fever whereas the fresh rhizomes (*Nyomrang Takeng*), fruits and leaves (*Kangkom Oying*) of the *Paris polyphylla* are also reported as consumable in the form of paste among the Adi tribe of the Upper Siang district of Arunachal Himalayan Region of India. The Sherdukpen tribe of the West Kameng district of Arunachal Pradesh (India) use the paste of the rhizome against snakebites (Sharma et al., 2015; Jambey et al., 2017).

4. Distribution and endemism range

The genus comprises more than 27 accepted species which are found distributed in Bhutan, China, India, Japan, Korea, Laos, Mongolia, Myanmar, Nepal, Russia, Thailand, Vietnam and Europe. The highest number of *Paris* species were reported from China (22 species and 16 varieties) with 12 species endemics to China (Liang et al., 2000, Ji et al., 2021, POWO, 2022). Different species and varieties of *Paris* along with its geographical location are listed in Tables 1 and 2. In India, the genus is represented by 2 species, namely, *P. polyphylla* and *P. thibetica* with about 6 intraspecific taxa distributed in the Indian Himalayan region (Phurailatpam and Chowdhury 2022). The maximum species diversity of *Paris* has been reported from Yunnnan-Guizhou Plateau in Southwest China (Li, 1984). Among the Chinese species, 15 species are reported to be endemic to China, and 04 species are found harboured in the Gaoligong Mountains region of China (Shi and Yang, 2008). The species of *Paris* have been reported from 09 Indian States where maximum species diversity was observed in Anjaw, Changlang, Kamle, Kurung Kumey, Lohit, Lower Dibang Valley, Lower Subansisri, Pangin, Siang, Tirap, Upper Siang and West Kameng districts of Arunachal Pradesh (Paul et al., 2015; Sharma et al., 2015; Phurailatpam and Chowdhury 2022). The current distribution range of *P. polyphylla* in the Indian Himalayan Region and North East India is shown in the map (Figure 1).

5. Habitat ecology

Ecological and phytogeographical studies have confirmed that *Paris* L. species prefers temperate biome and thrive in the slightly moist and shady habitat of subtropical and cold temperate forests of India, Bhutan, Myanmar, China, Nepal, Europe and the Indo-China and temperate Eurasian region. It prefers to grow in moist soil with high organic nutrient content under natural forest floors. The minimum and maximum temperature regimen for seed germination and growth has been recorded to be 10 – 25 ^{o}C. The young tubers appear between March to May and flowering and fruiting in May - September. *Paris polyphylla* Sm. (Love Apple), commonly called Satuwain in Nepal has shown low population density (Oliya et al., 2022). In Nepal, this plant is mainly distributed in an altitudinal range of 1500–4500 m above mean sea level from east to west Nepal within the geographical coordinates between 27° -30.18° N Latitude and 80.7° -88° E Longitude (Oliya et al., 2022). Water and soil moisture content has shown direct relationships with the biomass increment of *P. polyphylla* var. *yunnanensis* whereas the amount of polyphyllin content in the species was reported to be inversely proportional to the soil moisture content (Wu et al., 2019). *P. polyphylla* prefers rich humus soil with an efficient drainage system found along with associated species such as *Aconitum, Abies, Musa, Quercus, Smilax, Taxus, Ilex* etc. (Deb et al., 2015).

In the Arunachal Himalayan Region of India, the presence of *Paris polyphylla* has been recorded from the subtropical-temperate forests of Tawang through East Kameng, Pakke Kessang, Lower Subansiri, Papum Pare, Kurung Kumey, Kamle, Kra Daadi, Upper Subansiri, Siang, Eastern Arunachal Districts namely Dibang Valley, Anjaw and Changlang at elevation ranging between 1500 – 3000 m from mean sea level (Sharma et al., 2015; Debmalya et al., 2021). The temperate forest of the Talley Valley range has been recorded with the highest population density of *Paris polyphylla* whereas the Mayodia range of the Eastern Arunachal Pradesh has been recorded with lowest population density (Paul et al., 2015). There are some potential habitats, mostly the community forest area located in the temperate range with less human interference in the Himalayas, which could serve as an ideal natural habitat for the reintroduction of this threatened species (Jambey et al., 2017; Lepcha et al., 2019). *Paris polyphylla* (Love Apple) has been recently assessed for the IUCN Red List of threatened species and placed under Vulnerable (VU) category under criteria A4cd which need habitat protection for effective conservation and restoration of the globally declining species (Chauhan, 2020).

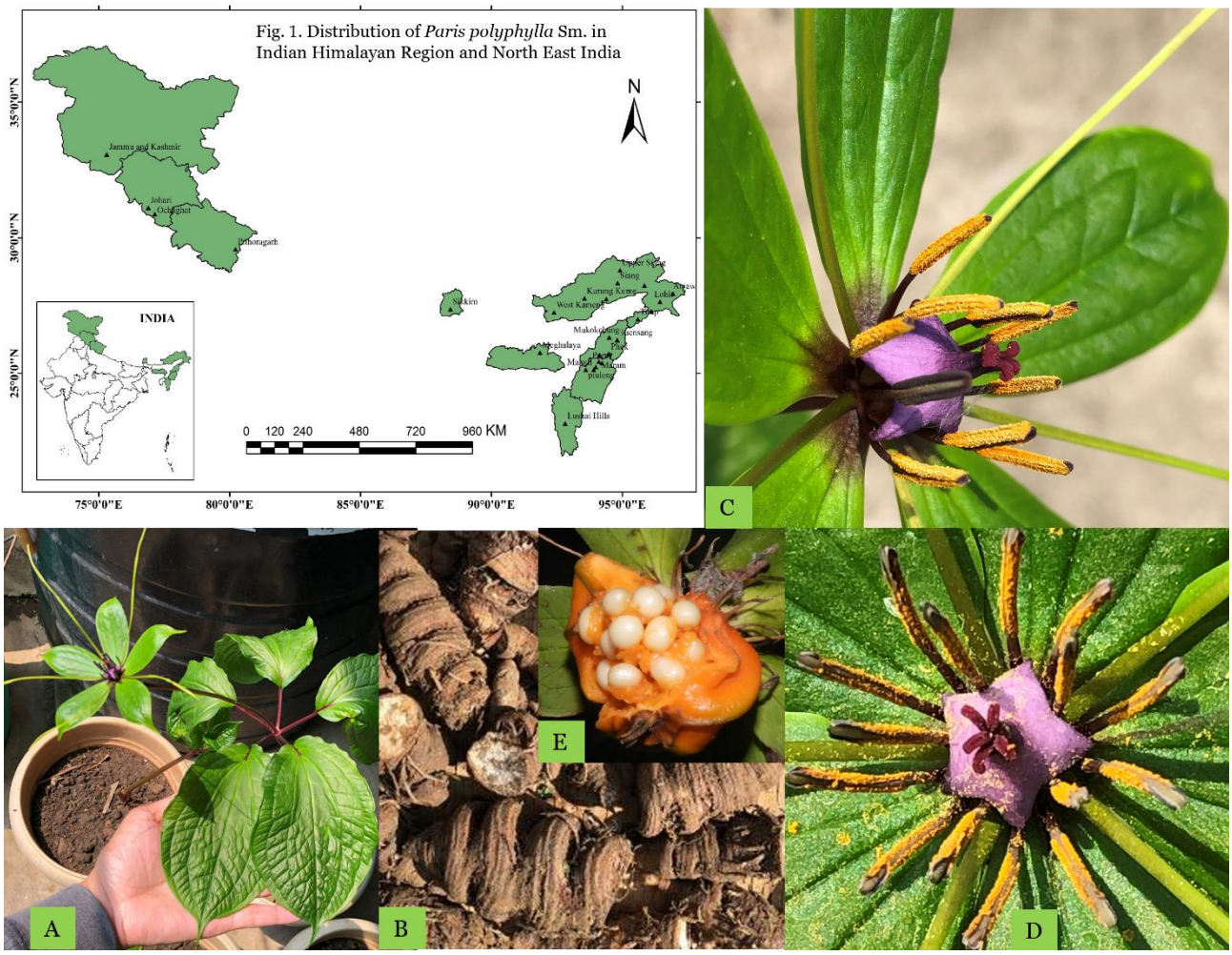

Figure 1. Map (green colour) showing distribution of *Paris polyphylla* Sm. (Melanthiaceae) in the Indian Himalayan Region and North East India. Fig.1A. *Paris polyphylla* Sm. collected from Pangin (Siang District) of Arunachal Pradesh and grown in the Pot under shade condition at RGU campus, Rono Hills, Doimukh, Arunachal Pradesh; Fig.1B. Freshly harvested tuber of *P. polyphylla* grown in pot; Fig.1C-E). Individual flower *of P. polyphylla* grown in pot at RGU Campus and investigated during the month of May 2021 showing stamens with matured pollen grains dehiscing from anther lobes, and the carpel with short and swollen with 4-5 fid stigma (Fig.1C&D) and orange colour fruit (capsule) with immature white seeds (Fig.1E).

6. Molecular phylogeny and evolution

DNA-based molecular markers have been widely used for the assessment of the genetic diversity and genetic structure of *P. polyphylla* and its related species inside and outside the region (Oliya et al., 2022). The molecular tools especially DNA-based markers have been successfully used for establishing molecular phylogeny among the closely related species and varieties of the genus *Paris* (Melanthiaceae). RAPD studies in 04 natural populations of *P. polyphylla* have established a close relationship between the 2 varieties namely, *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *chinensis*. These findings are in agreement with earlier studies based on the gross morphology of these two species (Jin-Yu et al., 2004). DNA sequence data along with generic and infrageneric studies have shown that the genus *Paris* is monophyletic origin and supported the concept that the *Paris* should be treated separately from the other three (03) genera, namely, *Daiswa, Kinugasa* and *Paris sensu tricot* (Ji et al., 2006a). Studies on clonal populations within and among the populations of *P. quadrifolia* using AFLP markers have suggested that under stressful conditions the clonal forest populations can gradually evolve into populations with lower genetic diversity and low sexual reproduction traits. This calls for the urgent conservation of such clonal plant species (Jacquemyn et al., 2006). Genetic diversity studies using ISSR markers among the 08 populations of *P. polyphylla* in Yunnan and Sichuan provinces have indicated *P. polyphylla* var. *yunnanensis* to be phylogenetically closer to the *P. polyphylla* var. *stenophylla* when compared with *P. polyphylla* var. *pseudothibetica* (Jun et al., 2007). Further ISSR studies on 03 natural and 03 cultivated populations of *P. polyphylla* var. *yunnanensis* have demonstrated higher genetic diversity among the cultivated populations when compared with natural populations, which might be due to the introduction, and artificial selection of cultivars from a wider geographical area resulting in higher gene flow (He et al., 2007). RFLP studies of the nuclear internal transcribed spacer (ITS) region have demonstrated *P. polyphylla* var. *yunnanensis* to be different from other *Paris* species (Liu, 2012). SSR-based marker study conducted on 30 natural populations of *P. polyphylla* var. *chinensis* using 12 microsatellite loci from a $(CT)_n$ enriched genomic library have demonstrated a common phenomenon of self-pollination in *P. polyphylla* var. *chinensis*, which accounts for low polymorphism due to heterozygote deficiency caused by inbreeding among the samples (Zheng et al., 2012). Parallel pyrosequencing of *P. polyphylla* var. *yunnanensis* has found involvement of 464 transcripts and 16 genes in phytohormone biosynthesis and catabolism, hormone signal, cell wall growth, circadian rhythms, seed maturation and seed dormancy in *P. polyphylla* var. *yunnanensis* (Qi et al., 2013). Total chloroplast genome sequence data of *P. polyphylla* var. *yunnanensis* have revealed a genome length of 1,57,675 bp having 18,319 bp small single-copy region (SSC) and 84,108 bp large single-copy region (LSC) separated by 27, 624 bp of inverted repeats (Irs). It also contains 115 genes, out of which 81 genes code for proteins, 04 ribosomal RNA genes and 30 tRNA genes. Phylogenetic analysis has established the monophyletic origin of the genus *Trillium, Paris, Fritillaria*, and *Lilium* and also established a close relationship between the genus *Trillium* and *P. polyphylla* var. *yunnanensis* (Song et al., 2017). Chloroplast genomic studies on 11 taxa of *Paris* have also demonstrated similar genomics exception for *P. verticillata* and *P. quadrifolia* (where trnI-CAU is found in triplicates) which failed to resolve the genus into a separate monophyletic group (Huang et al., 2016). Illumina sequencing technology and transcriptome analysis of a 04-year-old root and an 08-year-old root of *P. polyphylla* var. *yunnanensis* revealed approximately 87,577 unique sequences, with an average length of 614 bases. Analysis of the metabolic pathway inferred that 25 unigenes were responsible for the biosynthesis of the saponins steroids which confers future scope for genetic engineering of *P. polyphylla* with saponin-rich active constituents (Wang et al., 2016). Studies on complete transcriptome data of dormant seeds of *Paris polyphylla* var. *yunnanensis* have revealed a total of 1,46,671 unigenes with an average length of 923 bp. Further sequencing of 02 small RNA libraries from respective seeds and seed coats have demonstrated 263 conserved miRNAs belonging to at least 83 families and 768 novel miRNAs in 1174 transcripts which could be a future target for understanding the molecular mechanism of seed dormancy in this species (Ling et al., 2017). Complete sequences of 02 SMT1 genes (PpSMT1-1 and PpSMT1-2) obtained from *P. polyphylla* and studies on its enzymatic activities have revealed that PpSMT1-1 encoded cycloartenol-C24-methyltransferase catalyzes the conversion of cycloartenol to 24-methylene cycloartenol, while the gene PpSMT1-2 lacked this catalytic activity. The 02 isolated SMT genes provided a vision in the biosynthesis pathways of active steroid compounds present in *P. polyphylla* (Guan et al., 2018). DNA barcoding studies along with high-resolution melting analysis (HRM) have successfully generated a distinct melting profile of *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *chinensis* by using internal transcribed spacer 2 (ITS2) barcode of the selected varieties. This study has resulted in a separate molecular identity for the 02 varieties which could be useful for checking adulteration caused by mixing both species in different herbal preparations (Duan et al., 2018). Recently, a new species *Paris lihengiana* has been described from Yunnan Province, China using evidences from both morphological and molecular phylogeny using nuclear ribosomal ITS and 06 plastid-based markers i.e., trnL-trnF, psbA-trnH, rbcL, atpB, ndhF, and matK (Xu et al., 2019). Similarly, a new species *Paris variabilis* was also described from the Wumengshan Mountains, Southwestern China using evidences from morphological and ITS DNA sequence data (Yang et al., 2019a). Studies revealed 57,537 unigenes found involved in the biosynthesis of steroidal saponins from transcriptomes of *Paris polyphylla* var. *chinensis* out of which 56.54% were successfully annotated. Among these, 194 unigenes were coded for terpenoid backbone biosynthesis, 17 unigenes coded for sesquiterpenoid and triterpenoid biosynthesis and 80 unigenes were code for steroid biosynthesis pathways (Yang et al., 2019b).

7. Biochemical profile

The genus *Paris* L. is known to be a rich source of steroidal saponins that possess different glycosidic sugar derivatives. A new saponin-polyphyllin A-H has been isolated from the rhizome of *Paris polyphylla* of which the first six are spirostanol steroidal saponins and the remaining two are furastanol steroidal saponins (Xiao et al., 2014; Ling et al., 2015). A checklist of the compounds and major classes of phytochemicals identified and isolated from different species and varieties of *Paris* L. from 1973 - 2018 are presented in Table 3. However, the majority of the compounds have been isolated from the Chinese species and varieties. Initial studies have revealed that the Chinese varieties of *P. polyphylla* have saponin content in common while other compounds such as pennogenin and dioscin vary among different species. A novel steroidal saponin along with 12 known compounds was separated from *Paris polyphylla* var. *chinensis* (Wang et al., 2013). The novel compound was obtained as an amorphous solid, and the spectral data including two-dimensional NMR showed the structure as 3b,21-dihydroxypregnane-5-en-20S-(22,16)-lactone-1-O-a-L-rhamnopyrnosyl(1®2)-[b-D-xylopyranosyl(1®3)]-b-D-glucopyranoside. The 12 known compounds are known steroids and their structures were identified by 13C NMR spectrum (Singh and Thakur, 1980; Singh and Thakur, 1982a; Wang et al., 2013). The Himalayan varieties of the *Paris polyphylla* have shown a diverse range of compounds such as, diosgenin and its derivatives, different types of polyphyllin viz. furostanol and spirostanol steroidal glycosides (Sogawa and MDP, 1970; Singh and Thakur, 1980; Miyamura et al., 1982; Singh and Thakur, 1982a; Singh et al., 1982b). The novel compound known as 1,5-dihydroxy-7-methoxy-3-methyl-anthraquinone was isolated from the rhizomes of *P. polyphylla* from Parbat district, Nepal which showed strong tyrosinase inhibitory activity (Devkota et al., 2007). The Chinese varieties of the *Paris polyphylla* have been thoroughly investigated and a diverse range of compounds have been reported such as steroidal saponins, phenylpropanoid glycosides, flavonoid glycosides homo-aro-cholestane glycosides and cholestane glycoside (Zhang et al., 2005; Zhou et al., 2007; Wang et al., 2007; Xiao et al., 2009a; Liu et al., 2016). The phytochemical constituents of the Chinese species and varieties of the genus *Paris* have been found extensively screened using sophisticated modern tools and techniques such as combination of HR-ESI-MS, FAB-MS, 1D and 2D Nuclear Magnetic Resonance (NMR) techniques (Zhao et al., 2007), optimized extraction process via ultra-high-pressure extraction (UPE) (Zhang et al., 2007) and Electrospray Ionization Method (ESI) method (Man et al., 2009).

Table 3: List of phytocompounds reported from different species and varieties of *Paris* L. using various screening and isolation tools and methods reported in various literatures from 1973-2018.

Name of the Species	Part used	Name/classes of compounds	References
P. polyphylla	Rhizomes	Diosgenin 3-O-α-L-rhamnopyrosyl-(1→2)-[α-L arabinofuranosyl-(1→4)]-β-D-glucopyranoside, Diosgenin 3-O-α-L-rhamnopyrosyl-(1→4)-α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside, Pregna-5,16-dien-3β-ol-10-one 3-O- β-chacotrioside, Diosgenin 3-O β-chacotrioside	Nohara et al., 1973
P. polyphylla	Tubers	Polyphyllin A, Polyphyllin B, Polyphyllin C, Polyphyllin D, Polyphyllin E, Polyphyllin F, Polyphyllin G, Polyphyllin H	Singh and Thakur, 1980 Wu et al., 2012
P. polyphylla	Tubers	Paristerone	Singh and Thakur, 1982a.
P. polyphylla	Tubers	Polyphyllin C, Polyphyllin D, Polyphyllin E, Polyphyllin F	Singh et al., 1982b.
P. polyphylla	Tubers	Polyphyllin G, Polyphyllin H	Singh et al., 1982c.
P. polyphylla	Rhizomes	(22E, 25R)-22 methoxy furost-5-ene-3, 26-diol 26-O-β-D-glucopyranosides of 3-O-α-L-rhamnpyranosyl-(1→4)-α-L-rhamnpyranosyl-(1→4)-[α-L-rhamnpyranosyl-(1→2)]β-D glucopyranosyl, Pennogenin 3-O- α-L- arabinofuranosyl-(1→4) β-D-glucopyranoside Pennogenin glycosides having 3-O-α-L arabinofuranosyl-(1→4) β-D glucopyranoside sugar moiety, Diosgenin glycosides having 3-O-α-L arabinofuranosyl-(1→4) β-D glucopyranoside having same sugar moiety	Miyamura et al., 1982 Lee et al., 2005.
P. polyphylla var. *yunnanensis*	Rhizomes	Pennogenin 3-O-α-L-rhamnopyranosyl(1→2)-[α-L arabinofuranosyl(1→4)]-β-D-glucopyranoside, Pennogenin 3-O- α -L- rhamnopyranosyl(1→4)- α-L rhamnopyranosyl(1→4)-[α -L-rhamnopyranosyl(1→2)]- β-D –glucopyranoside, Diosgenin 3-O- -L-rhamnopyranosyl(1→2)-[α – L arabinofuranosyl(1→4)]-β-D-glucopyranoside Diosgenin3-O-α-L-rhamnopyranosyl(1→4)-α-L-rhamnopyranosyl(1→2)]- β-D glucopyranoside, Parisaponin I, Trigofoenoside A, Protogracillin	Matsuda et al., 2003
P. polyphylla	Underground parts	3-O-[α-L-rhamnopyranosyl (1→2)]-[β-D-glucopyranosyl(1→3)]-β-D-glucopyranosyl-27-hydroxylpennogenin 3-O-[α-L rhamnopyranosyl(1→2)]-[*β*-D-glucopyranosyl(1→3)]-*β*-D-glucopyranosyl26-O*β*-D-glucopyranosyl cholest-5-ene-16,22-dione	Zhang et al., 2005.
P. polyphylla var. *yunnanensis*	Rhizomes	Saponin A, Saponin B, Saponin C, Saponin D	Zhang et al., 2007.
P. polyphylla var. *yunnanensis*	Rhizomes	(25R)-spirost-5-en-3 β, 7 β -diol-3-O- α -L-arabinofuranosyl-(1→4)-[α-L-rhamnopyranosyl- (1 → 2)]-β-D-glucopyranoside (25R)-spirost-5-en-3β, 7α -diol-3-O- α -L-arabinofuranosyl-(1 → 4)-[α -L-rhamnopyranosyl-(1 → 2)] -β – D- glucopyranoside 26-O-β-D-glucopyranosyl-(25R)-15,6/. 17:20/-dien-16,22-dione-cholestan-3-β,26-diol-3-O-α -L-arabinofuranosyl-(1 → 4)-[α -L rhamnopyranosyl-(1 → 2)]-β –D-lucopyranoside	Zhao et al., 2007
P. polyphylla var. *yunnanensis*.	Rhizomes	Parispolyside F, Parispolyside G	Wang et al., 2007
P. polyphylla	Rhizomes	1,5-dihydroxy-7-methoxy-3-methyl-anthraquinone	Ke et al., 2016
P. polyphylla var. *pseudothibetica*	Rhizomes	Parispseudoside A, Parispseudoside B, Parispseudoside C	
P. polyphylla var. *yunnanensis*	Rhizomes	Polyphyllin D, Formosanin C, Gracillin, Paris H, Paris VII, Dioscin	Man et al., 2009a
P. yunnanensis	Rhizomes	Paris I, Paris II, Paris III, Paris V, Paris VI, Paris VII, Paris H, Gracillin Protodioscin	Man et al., 2010
P. polyphylla var. *yunnanensis*	Rhizomes	Saponin I, Saponin II, Saponin VI, Saponin VII, Saponin H, Pennogenin Diosgenin	Yu et al., 2010 Wu et al., 2012b
P. polyphylla var. *yunnanensis*	Rhizomes	PNA, PNB, PNC, PND, PNE, DSF, DSG, DSH, DSI, DSJ, DSK	Zhang et al., 2010
P. polyphylla var. *chinensis*			
P. polyphylla var. *yunnanensis*	Rhizomes	Turkesterone, 20-Hydroxyecdysone-3-O- β-D glucopyranoside/ecdysone, 25-O- β-D glucopyranoside, Ecdysone / Paristerone/Pinnatasterone, Parisyunnanoside G, Parisyunnanoside H, Parisyunnanoside I Padelaosides B, 3β, 27-diol-pennogenin-3-O- rhamnosyl –β-chacotrioside, 23β, 27-diol-pennogenin-3-O- α-L-rhamnopyranosyl-(1→2)] -β-D glucopyranoside / 23β, 27-diol-pennogenin-3-O- α-L-rhamnopyranosyl-(1→4)- β-D glucopyranoside, Parisyunnanoside J, 3β, 21-diol-pregnane-5-ene-20S-(22,16)-lactone-1-O- α-L-rhamnopyranosyl-(1→2)- [β-D-xylopyranosyl-(1→3)] -β-D glucopyranoside, Tj, Parisyunnanoside A, Te, Th, Parisyunnanoside F, Parispseudoside C, Proto-dioscin, Parisaponin I, Dichotomin, Td, Proto-gracillin, Isomer of parisaponin I, Pseudoproto-Pb, Pseudoproto-dioscin, Parisyunnanoside B, Pseudopro-gracillin, Parisyunnanoside C, Tg, Pennogenin-3-O- β-D-glucopyranosyl-(1→3) [α-L-rhamnopyranosyl-(1→2)] -β-D glucopyranoside, Tc, Chonglouoside H, Isomer of Tg, Tb, Isomer of chonglouoside H, Ypsilandroside G (25S)-Isonuatigenin3-O- β-chacotrioside, Pennogenin-3-O- α-L-rhamnopyranosyl-(1→2)-[α-L-arabinofuranosyl-(1→4)]-β-D glucopyranoside, Isomer of T-c, Parisyunnanoside D/Parisyunnanoside E7/1-hydroxy-isospiroanol-5-ene-3-O- β-D-glucopyranosyl-(1→3) [α-L-rhamnopyranosyl-(1→2)] -β-D glucopyranoside, Parisyunnanoside E/Parisyunnanoside D, Kingianoside K, Loureiroside, Pb, Reclinatoside, Dioscin, Polyphyllin D, Gracillin, Pa, Progenin III, Isomer of Pa, Diosgenin diglucoside, Diosgenin-3-O-S4	Kang et al., 2012a Kang et al., 2012b Yang et al., 2017b
P. polyphylla var. *yunnanensis*	Rhizomes	Paris Ø, Paris H, Formosanin C, Gracillin, Polyphyllin D	Liu et al., 2013

High-performance liquid chromatography coupled with electrospray ionization multi-stage tandem mass spectrometry (HPLC–ESI-MS^n) and triple quadrupole mass spectrometric detection (HPLC–ESI-MS/MS), Microwave-assisted extraction (MAE) coupled with counter-current chromatography using evaporative light scattering detection (ELSD), HPLC-ESI-QTOF-MS/MS, Ultra High-Pressure Liquid Chromatography (UHPLC) has been extensively used for the detection and separation of phytocompounds (Yu et al., 2010; Zhang et al., 2010; Man et al., 2010; Xiao et al., 2014; Ling et al., 2015). UHPLC-UV-MS (Yang et al., 2016), UHPLC-IT-TOFMS (Wang et al., 2017), Ultra Performance Liquid Chromatography-tandem mass spectrometer (UPLC-MS) (Yang et al., 2017) have also been used for the detection of bioactive phytoconstituents of the *Paris* L.

About 98 compounds were identified from *P. polyphylla* var. *yunnanensis* extract which includes 40 furostanol saponins, 50 spirostanol saponins, 02 C-22 steroidal glycosides, 02 ecdysteroid glycosides, and 04 ecdysteroids covering more than 30 types of steroidal aglycones (Kang et al., 2012). Effect of adsorption and desorption studies of *Rhizoma Paridis* saponin on 07 different types of resins showed that a particular type of resin (D101) demonstrated the best adsorption and desorption properties for steroidal saponins besides increasing its content in the product to 4.83 fold with 85.47% recovery yield (Liu et al., 2013). The 03 pennogenin glycosides and the 02 diosgenin glycosides were identified and quantified using specific HPLC conditions in the rhizomes of *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *chinensis*. Results detected 10 saponins from *P. polyphylla* var. *yunnanensis* and 07 saponins from *P. polyphylla* var. *chinensis* respectively including 04 unknown compounds out of which 01 unknown compound was tentatively identified as diosgenin-3-O-α-L-rhamnopyranosyl(1→4)[α–L-rhamnopyranosyl(1→2)]-β-D glucopyranoside and the aglycones of the other 03 new compounds were reported as novel (Zhang et al., 2010).

Table 3: List of phytocompounds reported from different species and varieties of *Paris* L. using various screening and isolation tools and methods reported in various literatures from 1973-2018.....

P. polyphylla var. *yunnanensis*	Stems and leaves	SL (9 - 20), 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside, 26-O-β-D-glucopyranosyl nuatigenin 3-O-a-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside, 26-O-β-D-glucopyranosyl nuatigenin 3-O-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside, Abutiloside L, Diosgenin 3-O-α-L-rhamnopyranosyl- (1→4)-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside, Borassoside B, 7β-hydroxysitosterol-3-O-β-D-glucopyranoside, (23Z)-9,19-cycloart-23-ene-3α,25-diol, Kaempferol-5-O-α-L-rhamnopyranoside, Kaempferol 3-O-β-D-glucopyranosyl- 7-O-α-L-rhamnopyranoside, Kaempferol 3-O-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-7-O-β-D-glucopyranoside, Vanillin	Qin et al., 2013
P. polyphylla var. *yunnanensis*	Leaves	Polysaccharides from leaves of *P. polyphylla* var. *yunnanensis* (PPLPs)	Shen et al., 2014
P. polyphylla	Rhizomes	Polyphyllin VII, Gracillin, Dioscin, Polyphyllin I	Xiao et al., 2014
P. polyphylla	Roots	Parisyunnanoside G, Parisyunnanoside W, Parisvientnaside A Parisvientnaside M, 24-epipinnatasterone, Parisyunnanoside J parisyunnanoside H, Th, Protodioscin, Polyphyllin H, Progracillin Pseudoproto-Pb, (3β,17α,25R)-spirost-5-ene-3,17-diol 3-O- α -L-arabinofuranosyl-(1 → 4)-[α-L-rhamnopyranosyl-(1 → 2)]- β -D-glucopyranoside, (3β,7β,25R)-spirost-5-ene-3,7-diol-3-O- β -D-glucopyranosyl-(1→3)-[α -L-rhamnopyranosyl-(1 → 2)]- β -D-glucopyranoside, Chonglouoside SL-4, Paris saponin VII, Polyphyllin VI, Disoseptemloside E, Pennogenin-3-O- α-L-arabinofuranosyl-(1→4)-β –D glucopyranoside, Parisyunnanoside B, Paris saponin II (3β,25R)-spirost-5-en-3-ol 3-O- α -L-rhamnopyranosyl-(1 → 4)-α -L-rhamnopyranosyl-(1 → 4)- β-D-glucopyranoside, Gracillin, Pa, Dioscin, (3β,25R)-3-hydroxyspirost-5-en-7-one -3-O- α -Larabinofuranosyl-(1 → 4)-[α-L-rhamnopyranosyl-(1 → 2)]- β-D-glucopyranoside, Polyphyllin V, Chonglouoside SL-5, Pariposide E	Ling et al., 2015
P. longistigmata *P. polyphylla* var. *yunnanensis* *P. vietnamensis* *P. polyphylla* *P. axialis*	Whole plant	Chonglou saponins I, Chonglou saponins II, Chonglou saponins V, Chonglou saponins VI, Chonglou saponins VII, Chonglou saponins D, Chonglou saponins H, Dioscin, Gracillin	Chen et al., 2016
P. polyphylla var. *yunnanensis* *P. polyphylla* var. *chinensis*	Rhizomes	Pa, Pb, Polyphyllin VI, Chonglou saponin VII	Yang et al., 2016
P. polyphylla var. *yunnanensis* *P. vietnamensis*	Rhizomes	(23R,25S)-spirost-5-ene-3β,17β,23,27-tetrol-3-O-rha-(1→4)-rha-(1→4)-[rha-(1→2)]-glc 24-O-gal or it isomers, 1β,3β,21,23,24-pentol-5,23-diene-spirost-1-O-rha-(1→2)- [xyl (1→3)]-glc 21-O-gal 24-O-fuc(23S,24S)-1β,3β,21,23,24-pentol-5-ene-spirost-1-O-rha-(1→2)-[xyl-(1→3)]-glc 21-O-gal 24-O-fuc, (23S,24S)-spirost-5,25-diene-1β,3β,21,23,24-pentol-1-O- xyl-rha-(1→2)-[xyl-(1→3)]-glc 21-O-gal 24-O-fuc, (23S,24S)-spirost-5-ene-1β,3β,21,23,24-pentol-1-O-xyl-rha-(1→2)-[xyl-(1→3)]-glc 21-O-gal 24-O-fuc, 1β,3β,21,23,24-pentol-5,24-diene-spirost-1-O-rha-(1→2)- [xyl (1→3)]-glc 21-O-gal 24-O-fuc, (23S,24S)-1β,3β,21,23,24-pentol-5-ene-spirost-1-O-rha-(1→2)-[xyl-(1→3)]-glc 21-O-gal 24-O-fuc, (23S,24S)-spirost-5-ene-1β,3β,23,24-pentol-1-O-rha-(1→2)-glc 24-O-gal, 23β,27-diol-pennogenin-3-O-rha-(1→2)-glc, (23S,24S)-spirost-5-ene-1β,3β,23,24-tetrol-1-O-rha-(1→2)-glc 23-O-gal or its isomer, (23S,24S)-spirost-5-ene-1β,3β,23,24-tetrol-1-O-rha-(1→4)-glc 24-O-gal, 26-O-glc-glc-(25R)-5-ene-furost-3β,17α,22α,26-tetrol-3-O- rha (1→4)-rha-((1→4)-[rha-((1→2)]-glc, (20R)-1β,3β,21-trihydroxy-pregnane-5-ene-(22,16)-lactone-1-O-xyl-rha-(1→2)-[xyl-(1→3)]-glc, (20R)-1β,3β,21-trihydroxy-pregnane-5-ene-22,16-lactone-1-O-rha-(1→2)-[xyl-(1→3)]-glc, (20R)-1β,3β,21-trihydroxy-pregnane-5-ene-(22,16)-lactone-1-O-xyl-rha-(1→2)-[xyl-(1→3)]-glc, (20R)-1β,3β,21-trihydroxy-pregnane-5-ene-(22,16)-lactone-1-O-rha-(1→2)-[xyl-(1→3)]-Glc, 1β,3β-dihydroxy-pregnane-5,20-diene-(22,16)-lactone-1-O-rha-(1→4)-rha-(1→4)-[rha-(1→2)]-glc, 1β,3β-dihydroxy-pregnane-5,20-diene-(22,16)-lactone-1-O-glc (1→3)-[rha-(1→2)]-glc, 26-O-glc-furost-5-en-3β,17α,22,26-tetrol-3-O-glc(1→5)-ara-(1→2)-[rha-(1→2)]-glc, (23S,24S)-spirost-5,25-diene-1β,3β,21,23,24-pentol-1-O-rha-rha-rha-(1→2)- [xyl--(1→3)]-glc or its isomer, 26-O-glc-glc-(25R)-5-ene-furost-3β,17α,22α,26-tetrol-3-O-rha (1→4)-rha-(1→4)-[rha-(1→2)]-glc, (23S,24S)-spirost-5-ene-1β,3β,23,24-tetrol-1-O-rha-(1→2)-glc23,24,27-triol-Pa, 26-O-glc-furost-5,25(27)-en-3β,17α,22,26-tetrol-3-O-rha-(1→2)-glc, 23 (or 27)-O-glc-(23S,25R)-spirost-5-en-3β,23α, 27-triol-3- O-rha-(1→2)-[ara-(1→4)]-Glc, 23 (or 27)-O-glc-(23S,25R)-spirost-5-en-3β,23,27-triol-3- O-rha-(1→2)-[ara-(1→4)]-glc or its isomer, (23S,24S)-spirost-5-en-1β,3β,23,24,27-pentol-1-O-rha-(1→2)-[ara-(1→4)]-glc-rha, 27-O-glc-(23S,25R)-spirost-5-en-1β,3β,27-triol-3-O-glc-(1→3)-[rha(1→2)]-glc, 27-glc-parisverticoside C, Protoloureiroside, 26-O-glc-7β-hydroxy-nuatigenin-3-O-rha-(1→2)-glc, 26-O-glc-glc-5-ene-furost-3β,22,26-triol-3-O-rha-(1→5)- ara-(1→4)-[rha-(1→2)]-glc, Isomer of protoloureiroside, 26-O-glc-glc-5-ene-furost-3β,22,26-triol-3-O-rha-(1→4)- rha-(1→4)-[rha-(1→2)]-glc, Proto-reclinatoside, 5,25(27)-diene-furost-3β,22α-diol-7-one-3-O-rha-(1→2)- [ara-(1→4)]-glc (23S,24S)-spirost-5,25(27)-diene-1β,3β,23,24-tetrol-1-O-glc-(1→3)-[rha-(1→2)]-glc, 26-O-glc-(22R,25R)-nuatigenin-3-O-ara-(1→4)-[rha-(1→2)]-glc, 26-O-glc-nuatigenin 3-O-rha-(1→2))-[ara- (1→4]-glc, 12OH-gracillin, Diosgenin 3-O-rha-(1→2)-[xyl-(1→5)]–ara- (1→4)-glc(1→2)]-glc (Where Xyl: β-D-xylopyranosyl; rha: α-L-rhamnopyranosyl; ara: α-L-arabinofuranosyl; glc: β-D-glucopyranosyl; gal: β-D-galactopyranosyl; fuc: α-L-fucopyranosyl).	Kang et al., 2017
P. polyphylla var. *yunnanensis*	Rhizomes	Paris saponin I, Paris saponin II, Paris saponin VI, Paris saponin VII	Yang et al., 2017b
P. polyphylla var. *yunnanensis*	Whole plant	Paris saponin I, Paris saponin II, Paris saponin V, Paris saponin VI, Paris saponin VII, Paris saponin H, Disocin, Gracillin, 17-Hydroxygracillin	Qin et al., 2018
P. polyphylla var. *yunnanensis*	Roots	Polyphyllin I, Polyphyllin II, Polyphyllin VI, Polyphyllin VII	Wu et al., 2018
P. polyphylla	Leaves	Catechin, Gallic acid, Chlorogenic acid, 4-hydroxybenzoic acid, Caffeic acid	Mohd et al., 2018

Total saponins in different parts of *P. polyphylla* var. *chinensis* were determined using dioscin as standard, revealed that there is a significant difference in saponin content with the rhizome part having the maximum followed by the root while the terrestrial stem and leaves did not show dioscin content (Yang et al., 2014b). Optimization of polysaccharides isolated from the leaves of *P. polyphylla* var. *yunnanensis* was studied by taking different independent variables. The findings revealed extraction temperature to be the most vital factor which influence yield of the polysaccharides, followed by extraction time and the ratio of water to raw material (Shen et al., 2014).

Biochemical profiling of the *P. polyphylla* roots using a fast and efficient HPLC-ESI-QTOF-MS/MS has identified about 30 phytoconstituents of which 02 were reported as novel compounds, namely, parisyunnanoside W and parisvientnaside M (Ling et al., 2015). Studies on *P. polyphylla* var. *yunnanensis* have confirmed that the composition of bioactive constituents of species and varieties are linked with maturation and harvest time (Wu et al., 2017). Further phytochemical screening has revealed that *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *chinensis* have identical content of certain steroidal saponins viz. Pa, Pb, polyphyllin VI and Chonglou saponin VII (Yang et al., 2017a).

Some bioactive spirostanol saponins (PS-I, II, VI, VII) have shown their presence both in rhizomes as well as in the leaves of *P. polyphylla* var. *yunnanensis* with similar pharmacological effects. This indicated that the leaves of *P. polyphylla* also possess active phytoconstituents, which could be investigated and used besides the rhizomes (Qin et al., 2018). A holistic quality control method was standardized using 05 species of *Rhizoma Paridis* by using UHPLC with photodiode array PDA detection. A total of 09 saponins, viz. Chonglou saponins I, II, V, VI, VII, D and H, along with dioscin and gracillin, were successfully determined thereby proving the method to be reliable for quality control (QC) of *Paris polyphylla* ingredients used in Traditional Chinese Medicines (Chen et al., 2016). Sequential window acquisition of all theoretical mass spectra (SWATH-MS), as well as gas chromatography–time-of-flight mass spectrometry (GC/TOF-MS) methods, have been used successfully to discriminate 03 species of *Paris* viz. *P. polyphylla* var. *chinensis*, *P. polyphylla* var. *yunnanensis*, and *P. fargesii* var. *fargesii*. Results revealed 419 proteins and 33 metabolites and it was also found that the pyruvate content and efficiency of acetyl-CoA-utilization in saponin biosynthesis were found higher in *P. polyphylla* var. *chinensis* when compared with other two species of *Paris* (Liu et al., 2019).

However, in the Indian context, little evidence is available to date on biochemical profiling. Rhizomes of *P. polyphylla* collected from the Arunachal Himalayan Region of India has been subjected to phytochemical screening using water, methanol, ethanol, ethyl acetate and chloroform. The chloroform extract has demonstrated maximum yield of secondary metabolites (Rajsekhar et al., 2016). *Paris polyphylla* samples from different parts of North East India viz. Nagaland, Manipur, Meghalaya and Arunachal Pradesh were screened for total steroidal saponin contents. The highest saponin contents were observed for the population group sampled from Meghalaya when compared with the population groups sampled from other North Eastern States of India (Devi et al., 2017). Gas Chromatography-Mass Spectrometry (GC-MS) studies of *P. polyphylla* collected from the Dibang Valley District of Arunachal Pradesh (India) revealed 45 phytocompounds with different biological activities (Payum, 2018). Extraction methods have been optimized for the isolation of polyphenolic compounds from the leaves of *P. polyphylla* collected from Pindar Valley, Uttarakhand (India) using Response Surface Methodology (RSM). It was found that the extraction temperature plays a key role in the variation of polyphenolic and flavonoid content. Further HPLC analysis of the extract detected 05 phenolic compounds i.e., catechin, gallic acid, chlorogenic acid, 4-hydroxybenzoic acid and caffeic acid that could be useful as pharmaceutical drugs (Mohd et al., 2018). Details of different bioactive phytoconstituents isolated from different parts of the genus *Paris* L. using different isolation tools and methods used by different authors with relevant literature references are provided in Table 3 for further consultation and reference.

8. Mineral ion concentration

Trace of toxic elements in *P. polyphylla* samples from China were determined by flame and graphite furnace atomic absorption spectrometry and analysed using chemometric approaches. Results showed *P. polyphylla* to be a rich source of Iron (Fe) and Zinc (Zn) while Manganese (Mn) ion concentration was found to be low. The sample also showed a low level of toxic metal lead (Pb) satisfying the level recommended by World Health Organization. Based on nutritional content, the cluster analysis revealed 05 distinct groups of *P. polyphylla* samples confirmed through chemometric study (Wang et al., 2010). In another study, water extracts of *P. polyphylla* were reported with very negligible amounts of trace metals Mg, Mn, Cu, Zn, Se and Mo (Ravipati et al., 2012).

9. Pharmacological activities

9.1. Antimicrobial activities

The anti-microbial activities, mainly the anti-bacterial and anti-fungal activities of the phytocompounds isolated from *Paris* L. are presented in Table 4 cited from relevant literature sources. Methanol, ethanol and water extracts from the leaves, rhizome and whole plant of *P. polyphylla* showed antifungal and antibacterial activities (Thapa, 2012). The 03 steroidal saponins isolated from the commercial products of the rhizomes of *P. polyphylla* have shown antifungal activities against *Cladosporium cladosporioides* and *Candida* species (Deng et al., 2008). *P. polyphylla* var. *yunnanensis* also reportedly harbours some important endophytic fungal species whose volatile oil possesses important phytoconstituents having strong antibacterial activity against 02 gram-positive and 04 gram-negative bacteria (Zhao et al., 2008). They further isolated 03 steroids and 01 nordammarane triterpenoid viz. helvolic acid for the first time from the endophytic fungus *Pichia guilliermondii* derived from *P. polyphylla* var. *yunnanensis*. Antibacterial assay of these compounds using micro dilution, colorimetric and spore germination assays showed strongest antibacterial activity against bacterial strains by helvolic acid (Zhao et al., 2010).

Pennogenin steroidal saponins from *P. polyphylla* var. *yunnanensis* have also demonstrated moderate antifungal activities against *Saccharomyces cerevisiae* and *Candida albicans* (Zhu et al., 2011). From the stems and leaves of *P. polyphylla* var. *yunnanensis,* 01 sapogenin and 24 steroidal saponins including 06 new glycosides, chonglouosides SL-1to SL-6 were isolated. The 11 selected compounds isolated from *P. polyphylla* were found to demonstrate inhibitory potential against the bacteria *Propionibacterium acnes* (Qin et al., 2012). In another study, the increased saponin content were found in mature rhizomes of *P. polyphylla* which were found to be elevated by the endophytic *Cyanobacteria* and *Proteobacteria* (Yang et al., 2015). *P. polyphylla* is also known to store some rare and novel actinobacterial strains of the genus *Catellatospora* and *Oceanobacillus* in its rhizosphere region of soil as well as roots (Jia et al. 2016; Yang et al. 2016). Some of the fungal strains were also found to occur in the rhizomes of *P. polyphylla* var. *yunnanensis* among which *Fusarium oxysporum* has the highest frequency of occurrence (Liu et al., 2017). Some novel bacterium such as *Ornithinimicrobium flavum* was reported from the surface-sterilized leaf of *P. polyphylla* var. *yunnanensis* and successfully characterized using a polyphasic approach (Fang et al., 2017).

Table 4: Antimicrobial activities of different species and varieties of *Paris* L. against a wide range of bacterial and fungal strains

Name of the Species	Method used	Part used	Compounds tested	Microbial strains used	Reference
P. polyphylla	Cladosporium agar-TLC plate testing Candida agar diffusion susceptibility testing	Rhizomes	(25R)-spirost-5-ene-3β,17-α-diol (pennogenin) 3-O-{O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-xylopyranosyl-(1→5)-α-L-arabinofuranosyl-(1→4)]-β-D glucopyranoside	*Cladosporium cladosporioides* *Candida* species	Deng et al., 2008
P. polyphylla var. *yunnanensis*	Modified broth dilution-MTT assay	Rhizomes	Volatile oil from *Picha guilliermondii*	*Bacillus subtilis Staphylococcus haemolyticus) Escherichia coli, Xanthomonas vesicatoria, Agrobacterium tumefaciens Pseudomonas lachrymans*	Zhao et al., 2008
P. polyphylla var. *yunnanensis*	Microdilution- colorimetric and spore germination assays	Rhizomes	Ergosta-5,7,22-trienol, 5α,8α-Epidioxyergosta-6,22- dien-3β-ol, Ergosta-7,22-dien-3β,5α,6β-triol Helvolic acid	*Agrobacterium tumefaciens* *Escherichia coli* *Pseudomonas lachrymans* *Ralstonia solanacearum* *Xanthomonas vesicatoria* *Bacillus subtilis* *Staphylococcus aureus* *Staphylococcus haemolyticus* *Magnaporthe oryzae*	Zhao et al., 2010
P. polyphylla var. *yunnanensis*	Broth micro dilution method	Roots	Chonglouoside SL-2 Chonglouoside SL-3 Chonglouoside SL-6 Polyphyllin A Polyphyllin V Progenin II Sansevierin A Progenin II Diosseptemloside E	*Propionibacterium acnes*	Qin et al., 2012
P. polyphylla	Agar well diffusion technique (Cup plate technique) two fold serial dilution technique	Aerial parts Rhizomes	petrol ether, chloroform, methanol and water extracts of aerial parts petroleum ether and chloroform extracts of rhizome parts	*Bacillus subtilis* *Staphylococcus aureus* *Pseudomonas aureginosa* *Escherichia coli* *Salmonella flexinerai* *Staphylococcus aureus* *Propionibacterium acnes*	Chhetri et al., 2013
P. polyphylla var. *yunnanensis*	Broth micro dilution method	Stems and leaves	Chonglouoside SL-7. Dumoside		Qin et al. 2013
P. polyphylla	Disc diffusion assay	Rhizomes	Methanolic plant extract	*Escherichia coli* *Staphylococcus aureus* *Aspergillus niger* *Trichoderma reesei*	Mayirnao and Bhat, 2017
P. vietnamensis	Broth micro dilution method	Rhizomes	25(R)-spirost-5-en-3β,17α-diol-3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside 25(R)-spirost-5-en-3β,17α-diol-3-O-α-L-rhamnopyranosyl-(1→3)-β-D-glucopyranoside 25(R)-spirost-5-en-3β,17α-diol-3-O-α-L-rhamnopyranosyl-(1→2)-6-acetyl-β-D-glucopyranoside	*Escherichia coli* *Serratia marvescens* *Bacillus subtilis* *Staphylococcus aureus* *Sarcina lutea* *Lactobacillus. plantanum*	Vu et al., 2019

Methanol and acetone extracts of *P. polyphylla* from Uttarakhand region of Indian Himalaya have been found more effective as antimicrobial agents than the hexane extracts, especially against 02 bacterial strains (*E. coli* and *S. aureus*) and 02 fungal strains (*A. niger* and *T. reesei*). It was observed that the percentage inhibition was highest in the case of *E. coli*, *S. aureus* and *A. Niger* when compared with *T. reesei* (Wu et al., 2018). A detailed study of different bioactive constituents isolated from different parts of the genus *Paris* L. and their antimicrobial assays and the microorganism against which they were effective are presented in Table 4.

9.2. *Anthelmintic activities*

Some literature suggested that *P. Polyphylla* has also demonstrated anthelmintic activity. The evaluation of anthelmintic activity of the methanol extract of *P. polyphylla* rhizome has demonstrated EC_{50} value of 18.06 mg/L (Wang *et al.*, 2010). Polyphyllin D (EC50 of 0.70 mg/L) and dioscin (EC_{50} value of 0.44 mg/L) were extracted from crude methanol extract and showed significant anthelmintic activity when compared with crude methanol extract (Thapa, 2012). Similarly, the methanol extracts of the *P. polyphylla* were used to isolate another 02 bioactive compounds namely, formosanin C and polyphyllin VII. *In-vivo* studies of phytocompounds further confirmed their anthelmintic activity against particular parasite (Li et al., 2013).

9.3. *Antiviral activities*

Aqueous and ethanolic crude extracts of *P. polyphylla* from China have shown potent anti-viral activities against A-type and Asia A-type flu viruses (Fu et al., 2019). Methanol extracts from *P. polyphylla* leaves were found effective against the Chikungunya virus. *P Polyphylla* saponin I derived from *P. polyphylla* was found to have antiviral activity against the influenza A virus (Thapa, 2012). The 95% ethanol extract of *P. polyphylla* has shown antiviral activity against *enterovirus* 71 (EV71) and *coxsackie virus* B3 (CVB3). Besides their anti-viral activity, it has also demonstrated strong correlation between the high amounts of IL-6 induction in the EV71 and CVB3-infected cells (Wang et al., 2011). *Polyphylla* saponin I isolated and purified from Chinese species of *Paris polyphylla* have shown both *in-vivo* and *in-vitro* activities on MDCK cells infected with influenza A virus in rats by decreasing the mortality of influenza A infected mice (Pu et al., 2015).

9.4. Anti-inflammatory activities

Polyphyllin I isolated from *Paris polyphylla* has shown potent *in-vitro* anti-inflammatory activity against *Propionibacterium acnes* (Zhu et al., 2019). Similarly, another steroidal saponin Polyphyllin VII reportedly exerts anti-inflammatory activity in lipopolysaccharide (LPS)- (Zhang et al., 2019). Diosgenin-enriched *Paris polyphylla* extract (DPPE) obtained from *P. polyphylla* landraces of the Arunachal Himalayan region of India demonstrated significant anti-inflammatory and antioxidant activities, and also demonstrated cytotoxicity effects in different cancer cell lines (Debmalya et al., 2021).

9.5. Cytotoxic activities

Acute oral toxicity, sedative–hypnotic activity and gastro-intestinal toxicity tests carried out in the ethanol extract of fresh roots of *P. polyphylla* var. *yunnanensis* have shown a dose-dependent toxicity effects on the normal behaviour and mortality rate of mice (Stefanowicz-Hajduk et al., 2011; Liu et al., 2012). Another study also found that a dose of 350 mg/kg/d of *Rhizoma paridis* saponins in rats causes liver and lung injury through the over-expression of reactive oxygen species (ROS) and pro-inflammatory cytokines, and down-regulating the levels of antioxidant and detoxification enzymes (Li et al., 2012). The sedative, hypnotic and gastrointestinal toxicity effect has been reported for saponins from *Paris polyphylla* rhizome (Liu et al., 2012). Methods for isolation and purification of cytotoxic compounds from the rhizome of *Paris polyphylla* are also reported to be developed (Gajdus et al., 2014). A detail of cytotoxic effects (Huang et al., 2007; Huang et al., 2011) demonstrated by different parts of the *Paris* species and varieties and isolated bioactive compounds, type of cell lines and the mechanism by which they function are presented in Table 5.

9.6. Anti-angiogenic activities

Polyphyllin D from the Chinese varieties of *P. polyphylla* has shown anti-angiogenic effect by showing its inhibitory effects on angiogenesis processes such as proliferation, migration and differentiation when examined in human microvascular endothelial cell line HMEC-1 using MTT assay, scratch assay and tube formation assay respectively. *In vivo* studies using zebrafish embryos further confirmed the said effect (Chan et al., 2011).

9.7. Antioxidant activities

Antioxidants are the chemicals that protect proteins, lipids, DNA, and other molecules within the cells from the scavenging effects of free radicals and oxidative stress. Oxidative stress is reported to enhance fast ageing and chronic ailments such as cancer, heart disease, cognitive decline and immune system decline (Thapa, 2012). The salt extract of *P. polyphylla* has been reported to have shown little ability to remove superoxide anion radicals while the scavenging ability of water extract and alcohol extract were found almost the same (Li et al., 2012). The Chinese varieties of *P. polyphylla* have shown higher antioxidant potential in ethanol extract when compared with water extract (Ravipati et al., 2012). Methanol, ethanol, petroleum ether, water extract and steroidal saponins derived from the rhizome of *P. polyphylla* have demonstrated remarkable antioxidant activity (Thapa, 2012). The methanolic extract of *P. polyphylla* samples from Manipur also showed higher antioxidant potential when compared with aqueous extract in DPPH radical assay (Mayirnao and Bhat, 2017). Ethanolic extract of *P. polyphylla* was found to have an anti-oxidative and protective effect against oxidative damage of Human Umbilical Vein Endothelial Cells (HUVECs) (Gao et al., 2012a).

9.8. Anti-tumour activities

The detailed phytocompounds isolated from *Paris* L., and their anti-cancer activities reported and cited from various relevant literature are provided in Table 5. A quick LC–ESI-MS/MS method with high sensitivity and accuracy was found to be developed for separation as well as determination of 02 potential antitumor active constituents (Wang et al.,2005) namely, Polyphyllin D and *Paris* H in *P.polyphylla* taking ginsenoside Rh2 as the internal standard (IS). The average recoveries of both the separated constituents from rat plasma were above 80% (Wu et al., 2012). *In-vitro* studies on *Paris* saponin, I using diphenyl-tetrazolium bromide assay have demonstrated potent activity in terms of radiosensitivity against gefitinib-resistant lung adenocarcinoma (PC-9-ZD) cells (Jiang et al., 2014; Wang et al., 2018; Chen et al., 2019). The antitumor properties of *P. polyphylla* var. *yunnanensis* was found boosted by aqueous extract of *Curcuma* by causing liver injury in mice bearing tumour cells followed by oxidative stress, separation of thioredoxin (Trx) and thioredoxin-interacting protein (TXNIP), increase in heme oxygenase-1 (HO-1), glutathione S-transferase (GST), and nuclear factor-regulated factor 2 (Nrf2) and inflammation (up-regulation of cyclooxygenase-2 (COX-2), interleukin-1b (IL-1β), and nuclear factor kappa B (NF-ķB) (Man et al., 2013). The saponins present in *P. polyphylla* var. *yunnanensis* were also found to inhibit tumour growth in mouse lung adenocarcinoma via apoptosis and upregulation of TIMP-2 gene expression and downregulation of MMP-2 and MMP-9 genes expression (Man et al., 2009b). Diosgenyl saponins isolated from *P. polyphylla* reportedly elevated phagocytic activity in rats with an increase in the concentration of saponins until a threshold level and then tend to decrease further at higher concentrations. The study also demonstrated glucoside moieties present in diosgenin saponins to play a significant role in the activation of immunological reactions (Zhang et al., 2007).

A recent method of UPLC-MS has been developed which has the potential to quantify a total of 09 saponins from *P. polyphylla* viz. polyphyllin I, polyphyllin II, dioscin, progenin III, polyphyllin VI, polyphyllin VII, polyphyllin H, gracillin and polyphyllin S, and has been recommended for pharmacokinetic studies in rats (Zhang et al., 2016). The serum metabolomics approach has been successfully used to study the antitumor mechanisms of *Rhizoma Paridis* saponins in differently treated mice models. It showed reduced tumour weight which were found linked with down-regulating lactate, acetate, N-acetyl amino acid and glutamine signals, and also found to reverse aerobic glycolysis via activating tumour suppressor p53 and PTEN, and found to suppress FASN to inhibit lipogenesis inducing metabolic changes (Qiu et al., 2016). Polyphyllin I isolated from the rhizomes of *Paris polyphylla* has been reported with higher absorption rat when treated orally in malnourished rats when compared with normal healthy rats suggesting modification in the dosage of PPI during the treatment of cancer patients with protein–calorie malnutrition (PCM) (Yu et al., 2018).

9.9. Anti-ulcer activities

The 04 spirostanol steroid saponins and a new furostanol steroid saponin (*Paris* saponin I), together with 02 known furostanol steroid saponins were obtained from the methanolic extract from the rhizomes of *P. polyphylla* var. *yunnanensis* through bioassay-guided separation. Among them, the spirostanol steroid saponins were found successfully inhibit chemically induced gastric lesions in rats (Matsuda et al., 2003). Total steroidal saponins extracted and subsequently purified from the rhizomes of *P. polyphylla* var. *yunnanensis* have shown to reduce abnormal uterine bleeding in the *in-vitro* estrogen elevated pregnant rats. Pennogenin-3-O-α-L-arabinofuranosyl (1→4) [α-L-rhamnopyranosyl (1→2)]-β-D-glucopyranoside was identified as the principal compound responsible for such activity which is governed by the influx and release of extracellular and intracellular calcium respectively (Guo et al., 2008).

9.10. Antiaging activities

The leaves of *Paris polyphylla* was found to possess homogenous polysaccharide (PPLP) having the backbone of (1→6)-β-D-galactan, and the branched chains consisting of arabinose residues linked to the backbone via (1 → 3) linkages. This polysaccharide has demonstrated anti-ageing activity in the mouse by preventing malondialdehyde (MDA) formation and boosting levels of antioxidant enzymes in the serum and liver (Shen et al., 2018).

10. Tissue culture

The 02 linear oligomers isolated from the aqueous extract of the rhizomes of *P. polyphylla* var. *yunnanensis* showed growth-regulatory activity at low concentrations stimulating shoot formation in a culture medium (Zhou et al., 2003a). The 02 oligosaccharides namely, a heptasaccharide (HS) and an octasaccharide (OS), isolated from *P. polyphylla* var. *yunnanensis* boost the growth, and yield of saponins in hairy root biomass of *Panax ginseng* in tissue culture (Zhou et al., 2007). The oligosaccharides obtained from *P. polyphylla* var. *yunnanensis* were reported to enhance tobacco (*Nicotiana tabacum* L.) seedling growth using tissue-cultured seedlings in a concentration-dependent relationship (Liu et al., 2010). Findings revealed that alcohol disinfection in combination with sterilization by mercuric chloride was very effective. Pre-treatment at a temperature of 4 ^{o}C for 360 minutes followed by soaking in penicillin and nutrient medium supplemented with 3000 mg/L sodium propionate and 20 mg/L sodium benzoate was found to reduce the contamination rate of the explants (Yang et al., 2014a).

In the context of Indian landraces of *P. polyphylla*, somatic embryogenesis protocols have been developed for plant regeneration for the first time taking different hormone regulators, media and other requirements under consideration (Raomai et al., 2014a). They also employed the transverse thin cell layer (tTCL) culture technique, which led to the formation of mini-rhizomes of *P. polyphylla* with a survival percentage of more than 95% under greenhouse conditions with an increase in yield of saponin content. A developed protocol was found to have a low mortality rate and increase in saponin content that could meet the global demands of steroidal saponins production particularly in the pharmaceutical industry (Raomai et al., 2014b). Clonal populations of *P. polyphylla* collected from Nagaland were successfully grown via rhizome splitting and group rhizome fragmentation (Jamir et al., 2015).

11. Trade and commerce

During the last 02 decades, there has been a growing popularity and surging demand for *Paris polyphylla* origin herbal formulations of Traditional Chinese Medicine (TCM) in countries such as Indonesia, Singapore, the United States, Canada, Vietnam, Malaysia, South Africa, Liberia etc. This has led to increased demand for raw materials within the domestic market in China. There was a shortfall in the supply of raw materials within the domestic market in China to meet the surging demand for *P. Polyphylla* rhizome-based TCM formulations in the international herbal market. Such a trend has compelled rapid surge of prices in the domestic market in Nepal, Bhutan, Vietnam and India. It also necessitated the wild collection of larger quantities of rhizomes of *P. polyphylla* by local collectors for export to regional markets in mainland China through Kunming and Chengdu in border trade route through the corridor of Myanmar and Indo-China countries in the South, and the Northern Nepal – Tibet trade Corridor (He et al., 2018). Trade data showed that about 800 – 1050 tonnes of *P. polyphylla* rhizomes were found sold annually in both domestic and international markets (Cunningham et al., 2018). Such rising demand in the international market is very alarming for the countries where the limited population of *P. polyphylla* is found in the wild condition in some of the rich primary forests of Indian Himalayas, China, Nepal, Myanmar, Bhutan and Vietnam. It has been found that during the harvesting process, the whole plant is often uprooted to collect the rhizomes, which leads to the destruction of the gene pool in the natural habitat. This unsustainable harvesting practice, coupled with illegal cross-border trades of rhizomes and habitat destructions were found common in the Indian Himalayas and North East India (Phurailatpam and Choudhury, 2022). It was also observed that unorganized cross-border trade is the main cause of the rapid depletion of the wild populations of *P. polyphylla* in the natural habitat in Bhutan, Nepal and Indian Himalayan Regions in current decades. However, this is not an adequate initiative to check the rapid loss of the natural populations and illegal wild harvest from natural habitats. *Paris polyphylla* tubers were found sold illegally to anonymous buyers at the rate of INR 10,000 – 15,000 per kilogram of tubers in the Arunachal Himalayan region, and the price of the dried tuber (*Rhizoma Paridis*) have been found to be 30-40 times higher in the international market (Tag, 2013).

12. Cultivation and conservation

Paris polyphylla is currently listed under the Vulnerable (VU) category in the IUCN Redlist of Threatened Species 2020 Global but locally found endangered in the Eastern Himalayan Region and has been used as a high-valued medicinal herb in traditional medicine among the folk healers. The natural population is decreasing due to over-exploitation from the wild to meet the demand for traditional medicine (Tag, 2013; Paul et al., 2015; Sharma et al., 2015; Phurailatpam and Choudhury, 2022). It is necessary to conserve the natural population through tissue culture techniques and the production of high-value secondary metabolites in cultured plantlets for sustainable utilization as pharmaceutical drug sources. The genus *Paris* L. has been subjected to rapid loss of natural habitat owing to large-scale demand as well as limited geographic distribution in a few Asiatic countries. In some parts of Vietnam, the species *P. polyphylla* is considered endangered and is enlisted in Vietnam Red Data Book 2007 (Quang Binh Provincial People's Committee, 2012). About 09 species of the genus *Paris* L. are Red-listed and several are threatened while *P. polyphylla* is reported to be cultivated in high-altitude regions of Ludian Yunnan, Sichuan, Guizhou, Hunan and Guangxi provinces of China (Bhattarai et al., 2002; Cunningham et al., 2018). In the Arunachal Himalayan Region of India, a low-income group of local farmers have started cultivation of *P. polyphylla* in the Tawang, Shi-Yomi and Siang Districts from 2013 - 2015 onwards (Tag, 2013; Paul et al., 2015). With funding support from UNDP, the Department of Environment, Forest and Climate Change, Govt. of Arunachal Pradesh (India), and the State Govt. of Uttaranchal (India) has taken the initiative for the conservation of *P. polyphylla* through the establishment of the Medicinal Plant Conservation Area (MPCA) as Forest Gene Bank in the community forests of 07 districts of Arunachal Pradesh in collaboration with local communities covering a total land area of about 12000 hectares (Tag, 2013). However, community sensitization is required to promote medicinal importance, conservation and sustainable harvesting practices of *Paris polyphylla* in their native range of Himalaya and North East India, Indo-China and China.

13. Conclusion and future prospects

In recent years, ethnobotanical studies coupled with the isolation of bioactive compounds from medicinal plants have triggered worldwide interest mainly due to the discovery of novel drugs from indigenous medicinal plants for the treatment of chronic diseases such as oxidative stress, inflammation and cancer, which includes threatened and endangered species (Lalramnghinglova and Jha, 1999; Cunningham et al., 2018). The genus *Paris* L. with 27 species reported to date has been traditionally proven as a valuable medicinal agent with high ethnopharmacological relevance in Asiatic countries. The present review establishes *P. polyphylla* and their varieties as potential sources of bioactive steroidal saponins effective against cancer, inflammation, oxidative stress, microbial infection, anthelmintic, and wound healing properties and are found naturally distributed in the subtropical-temperate range of China, Nepal, Bhutan and the Indian Himalayan Region particularly in Uttaranchal, Sikkim, Arunachal Pradesh, Darjeeling, Nagaland, Manipur and Mizoram. However, for Indian species, proper taxonomic investigation using molecular tools and techniques are recommended to resolve the taxonomic puzzle still persistent at the varietal level. Apart from morphological characters, the power of discrimination of DNA-based and gene-based markers can be effectively used for delimiting closely related taxa at varietal level. Population studies, sequencing and transcriptome analysis are the need of the hour for establishing insight into the molecular phylogeny of these varieties of Indian Himalayan Regions. Literature studies have revealed that *P. polyphylla* and its constituent varieties are popularly used as important ingredients in traditional folk medicines among the tribal communities in Indian Himalaya, Bhutan, Nepal, China and Indo-China countries.

The genus *Paris* L. harbours approximately 126 bioactive constituents although steroidal saponins – Diosgenin, Polyphyllin D, Paris saponin, and Pennogenin have been identified as main active principles that possess anti-oxidant, anti-cancer, anti-inflammatory and wide ranges of medicinal and pharmacological properties (Yang et al., 2016). The elemental analysis has revealed that the rhizome of the *Paris polyphylla* harbours calcium (Ca), potassium (K), magnesium (Mg), iron (Fe), sodium (Na), copper (Cu), manganese (Mn), zinc (Zn) and chromium (Cr) which is within the tolerable limit prescribed by WHO. *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *chinensis* are among the extensively studied varieties which have found their place in Chinese Pharmacopoeia for their immense medicinal values associated with Traditional Chinese Medicines (TCM). However, *P. polyphylla* and its constituent varieties are yet to be enlisted in Indian Pharmacopoeia although this plant has been traditionally used as medicine among the local tribal communities of the Central and Eastern Himalayan region of India for several centuries. The tissue culture of *P. polyphylla* has shown promising results of regeneration and multiplication through micropropagation using specific media conditions and such measures can be applied to curb the rapid decline of natural wild populations. This can serve as both economically and ecologically important tools to conserve the medicinally important *Paris* species in the appropriate agroclimatic zone in the temperate regions of the world. In case of overdose, the Chinese species and varieties of *P. polyphylla* have shown selective cytotoxic activities in mammalian cells. Steroidal saponins extracted from *P. polyphylla* var. *chinensis*, *P. polyphylla* var. *yunnanensis* and *P. polyphylla* var. *stenophylla* have shown promising anti-tumour activities in different carcinoma cell lines. Apart from anti-cancer and anti-tumour activities, the extracts of *P. polyphylla* also demonstrated anthelmintic, anti-microbial, anti-viral, anti-angiogenic, and mild to potent anti-oxidant properties.

In the previous decades, a lack of awareness and understanding of the pharmacological uses and commercial values among the local communities have led to the undervaluation of the *Paris* species. However, the *Paris polyphylla* has garnered the attention of global herbal researchers and local communities of India, Nepal, Bhutan, Myanmar, Japan and China in recent decades due to the surging demand for *Rhizoma Paridis*-based anti-oxidant and anti-cancer herbal products under the brand name of the Traditional Chinese Medicine (TCM) in China. This has triggered rampant illegal wild collection of rhizomes from their native range of Himalaya and found exported to China through the Nepal-Tibet corridor and Indian-Myanmar-Yunnan (China) corridors mostly executed through middlemen. Such indiscriminate extraction of rhizomes from the wild has pushed the 04 species and varieties of the *Paris* L. in the Indian Himalayas, Nepal, Bhutan, Myanmar and Vietnam ranges on the verge of extinction from their native ranges. Large-scale cultivation of *P. polyphylla* as conservation measures are well adopted in China outside of their natural habitat whereas such scientific cultivation measures are still lacking in India, Bhutan, Nepal, Myanmar and Vietnam coupled with the imminent threat of habitat destruction (Shankar and Rawat, 2013; Cunningham et al., 2018). Prospective farmers should be encouraged to cultivate *Paris polyphylla* in suitable agroclimatic zone in their community forest land. This will ensure community livelihood through conservation and sustainable supply of raw materials of *Paris polyphylla* to meet the demand of the herbal industries in future.

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Author's contributions

The first author (HT) contributed to the concept, literature review, develop the draft manuscript, taxonomy and nomenclature section and finalization of the manuscript. The second (DD) and third (DK) also equally contributed in the literature review on phytochemicals and contributed in the development of the manuscript. The fourth author (PKH) contributed in the intellectual approaches and concept, literature review, proofreading and finalized the manuscript.

Conflict of interests

The authors declare that they have no conflict of interest.

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Table 5: Anticancer activity of the phytocompounds of *Paris* L. species and varieties tested on different cancer cell lines.

Name of the Species	Part used	Type of Cell Line studied	Compounds with anti-cancer activity	Class of Compounds	Plausible Mechanism	References
P. polyphylla var. *chinensis*	Rhizomes	Human Promyelocytic Leukemia HL-60 cells	(25R)-spirost-5-en-3β 17α –diol (diosgenin) 3-o-{o- α -L-rhamnopyranosyl-(l→2)-O- β -D-glucopyranoside} Pennogenin 3-o-{o- α -L-rhamnopyranosyl-(l→2) O- β -D -glucopyranoside} Diosgenin 3-o-{o- α -L-rhamnopyranosyl-(l→2)-o-[β -glucopyranosyl-(l--3)]- β -D-glucopyranoside} Pennogenin 3-o-(o-a-L- rhamnopyranosyl-(l→2)-o-[β -D-glucopyranosyl-(1-3)]- β -D-glucopyranoside) Diosgenin 3-o-{o- α -L-rhamnopyranosyl-(l→2)-o-[α -L-arabinofuranosy (1→4)]- β -D-glucopyranoside} Pennogenin 3-o-{o- α -L-rhamnopyranosyl- (1→2)-o-[α -L-arabinofuranosyl-(1→4)]- β -D-glucopyranoside} Diosgenin 3-o- (o- α -L-rhamnopyranosyl-(1 →2)-o-[O- α -L-rhamnopyranosyl-(1 →4)- α -L-rhamnopyranosyl-(l→4)]- β -D-glucopyranoside Pennogenin 3-o-{o- α -L- rhamnopyranosyl-(l→2)-o-[o- α -L-rhamnopyranosyl-(l→4)- α -L-rhamnopyranosyl- (1 →4)]- β -D-glucopyranoside}	Spirostanol Steroidal saponins	Not defined	Mimaki et al., 2000
P. polyphylla	Rhizomes	Human Breast Cancer cells MCF-7 and MDA-MB-231 cells	Polyphyllin D	Steroidal saponins	Polyphyllin D dissipates mitochondrial membrane potential, downregulates anti-apoptopic Bcl-2 expression and upregulates pro-apoptopicBax expression; activates caspase 9	Lee et al., 2005
P. polyphylla	Rhizomes	HeLA cells and L929 cells	Falcarindiol Pennogenin-3-O-α-L-arabinofuranosyl(1→4)-β-D-glucopyranoside Pennogenin-3-O-α-L-arabinofuranosyl(1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside Diosgenin-3-O-β-D-glucopyranoside, diosgenyl-3-O-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranoside Diosgenin-3-O-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside Diosgenin-3-O -α-L-rhamnopyranosyl (1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside	Steroidal saponins	The number of glycoside and their linked position in the structure of saponins strongly influenced their anti-tumor activity	Wang et al., 2005.
P. polyphylla	Underground parts	Liver Cancer Cell Line of BEL-7402	3-O-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranosyl diosgenin 3-O-[α-L- rhamnopyranosyl(1→2)]-[α-L-arabinofuranosyl(1→4)]-β-D-glucopyranosyl pennogenin 3-O-[α-L- rhamnopyranosyl(1→2)]-[β-D-glucopyranosyl(1→3)]-β-D-glucopyranosyl pennogenin 3-O-[α-L- rhamnopyranosyl(1→2)]-[β-D-glucopyranosyl(1→4)]-β-D-glucopyranosyl pennogenin	Steroidal saponins	Not defined	Zhang et al., 2005
P. polyphylla var. *chinensis*	Rhizomes	Human Gastric Cancer Cell Line HepG2, SGC7901, BxPC3.	Diosgenin-3-O-α-L-rhamnopyranosyl(1→2)[α-L-arabinofuranosyl(1→4)]-β-D-glucopyranoside	Steroidal saponins	Not defined	Huang et al., 2007
P. polyphylla var. *chinensis* *P. polyphylla* var. *yunnanensis*	Rhizomes	HepG2 Cells	Rhizoma Paridis Total Saponin (RPTS)	Steroidal saponins	Induction of apoptosis and cell cycle S phase arrest.	Cheng et al., 2008
P. polyphylla var. *yunnanensis*	Roots	Mice Lung Adenocarcinoma Cell Line (LA795)	2-feruloyl-O-α-D-glucopyranoyl-(1′→2)-3,6-O-feruloyl-β-D-fructofuranoside	phenylpropanoid glycosides	Not defined	Yan et al., 2008
P. polyphylla var. *yunnanensis*	Rhizomes	Lung Adenocarcinoma T739 cells	RhizomaParidis Saponins (RPS)	Steroidal saponins	Elicits programmed cell death and inhibits metastases in murine lung adenocarcinoma	Man et al., 2009

P. polyphylla	Roots	K562/R7 Human Leukemic Cells	3-O-Rha (1→2)[Ara (1→4)] Glc-pennogénine Gracillin, Polyphyllin D	Steroidal saponins	Inhibits P-glycoprotein-mediated drug efflux	Xiao et al., 2009a
P. polyphylla var. *chinensis* *P. polyphylla* var. *yunnanensis*	Roots	A549 (Human Lung Adenocarcinoma Cell Line) HepG2 (Hepatocellular Carcinoma Cell Line) CaSki and SKOV3 (Ovarian Cancer Cell Lines) SiHa and HeLa (Cervical Carcinoma Cell Lines) OSE (Ovarian Surface Epithelial Cell Line) and HEC-1A (Endometrial Carcinoma Cell Line)	Paris Saponin I (PSI)	Steroidal saponins	Facilitates G2-M phase arrest and apoptosis in SKOV3 cells; Increased levels of Bax, cytochrome c, Activated caspase-3, active caspase-9, and cleaved poly(ADP-ribose) polymerase and decreased both Bcl-2 expression levels and extracellular signal–regulated kinase-1/2 activity.	Xiao et al., 2009b
P. polyphylla var. *yunnanensis*	Rhizomes	HL-60 Human Promyelocytic Leukemia Cells	Pennogenin-3-O-α-L-arabinofuranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside Tb Pa Prosapogenin A of dioscin	Steroidal saponins	Spirostanol framework of the aglycone and the terminal α-L rhamnopyranosyl with 1→2 linkage to the sugar chain of saponins at C-3 are essential for their high cytotoxicity, whereas the hydroxyl group substitution at C-12 or C-17 of the aglycone causes a reduction in their activity.	Zhao et al., 2009
Paris axialis	Rhizomes	LA795 cells	Diosgenin, Paris saponin V, Paris saponin VI Paris saponin I, Paris saponin H, Paris saponin II Paris saponin VII Luteolin, Luteoloside Isorhamnetin-3-O-α-L-rhamnopyranosyl(1→2)-β-D-glycopyranoside	Steroidal saponins	Not defined	Huang et al., 2011
Paris quadrifolia	Rhizomes	Human Promyelocytic Leukemia (HL-60) Cells, Human Cervical Adenocarcinoma (HeLa) Cells Human Breast Cancer (MDA-MB-468) cells Human Skin Fibroblasts (non-neoplastic control cells)	butanolic fraction (effective against HL-60 and HeLa cells) weakly water-soluble solid residue (effective against all cell lines tested)	Steroidal saponins	Synergistic, additive or antagonistic interactions of many compounds present in the extract	Stefanowicz-Hajduk et al., 2011
P. polyphylla	Herb	SMMC-7721 Liver Cancer Cells	Ethanolic extract of whole herb	Not defined	Apoptosis along with S phase cell cycle arrest, the activation of pro-caspase 3, and a marked increase in Bax/Bcl-2 ratios due to upregulation of Bax and downregulation of Bcl-2 proteins expression by western blotting.	Sun et al., 2011.
P. polyphylla var. *yunnanensis*	Aerial part	HepG2 Cells	Pennogenin-3-O- α-L-rhamnopyrosyl (1→2) - β -D-glucopyranoside Pennogenin-3-O- α-L-rhamnopyrosyl (1→4) - α -L- rhamnopyrosyl	Pennogenin steroidal saponins	Activation of the cell apoptosis process within cancerous cells	Zhu et al., 2011
P. polyphylla	Roots	Human Esophageal Cancer ECA109 Cells	Whole ethanolic extract	Steroidal saponins	Inhibits cell proliferation and induces cell apoptosis	Li et al., 2012
P. polyphylla var. *yunnanensis*	Rhizomes	Human CCRF Leukemia Cells.	Dichotomin, Paris saponin I, Protogracillin, Parisyunnanoside A, Pseudoproto-Pb	Steroidal saponins	Not defined	Kang et al., 2012
P. fargesii var. *brevipetala*	Rhizomes	HepG2, A549, RPE and L929 Cells	Ps H	Steroidal saponins	Not defined	Wen et al., 2012
P. polyphylla var. *yunnanensis*	Rhizomes	Human Nasopharyngeal Carcinoma Epithelial (CNE) Cells	3β -hydroxyoleane-12-en-28-oic acid 3-O-β-D- glucopyranosyl-(1-2)-a-L arabinopyranoside 3β-hydroxyoleane-12-en-28-oic acid 3-O- β-D-glucopyranosyl-(1→2)-β-D-xylopyranoside 3β-hydroxyoleane-12-en-28-oic acid 3-O-β-D xylopyranoside	Triterpenoid saponins	Not defined	Wu et al., 2012a

P. polyphylla var. *yunnanensis*	Rhizomes	Human Nasopharyngeal Carcinoma Epithelial (CNE) Cells	(3 β ,25R)-spirost-5-en-3-ol-3-O- β -D-glucopyranosyl-(1→4)- α -L-rhamnopyranosyl-(1→4)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside (3 β,25R)-spirost-5-en-3-ol-3-O- α -L-arabinofuranosyl-(1→4)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside (3 β ,25R)-spirost-5-en-3-ol-3-O- β -D-glucopyranosyl-(1→3)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside (3 β ,17 α ,25R)-spirost-5-ene-3,17-diol-3-O- α -L-rhamnopyranosyl-(1→4)- α -L-rhamnopyranosyl-(1→4)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside (3 β ,25R)-spirost-5-en-3-ol-3-O- β -D-apiofuranosyl-(1→3)-[α -L-rhamnopyranosyl-(1→2)]- β-D-glucopyranoside (3 β ,17 α ,25R)-spirost-5-ene-3,17-diol-3-O- β -D-apiofuranosyl-(1→3)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside (3β ,17 α ,25R)-spirost-5-ene-3,17-diol-3-O- β -D-glucopyranosyl-(1→5)- α -L-arabinofuranosyl-(1→4)-[α -L-rhamnopyranosyl-(1→2)]- β -D-glucopyranoside	Steroidal saponins	Apoptosis and cell cycle viz. G1 or S phase arrest in CNE cells	Wu et al., 2012b
P. polyphylla var. *chinensis*	Rhizomes	Lewis bearing-C57BL/6 mice & A549 cells	Paris VII, PGRR, Paris VI, Paris H, Paris II, Dioscin, Gracillin, Paris I and Paris V	Steroidal saponins	Paris saponins inhibits via amelioration of inflammation responses, induction of apoptosis, as well as the decrease of ROS.	Li et al., 2013
P. polyphylla var. *yunnanensis*	Rhizomes	Human Cancer Cell Lines (HEK293 and HepG2).	Parisyunnanoside H, Paris saponin I, Trigofoenoside A, Dichotomin, Parisyunnanoside B, Pseudoproto-Pb	Steroidal saponins	Not defined	Wen et al., 2015
P. polyphylla var. *chinensis* *P. polyphylla* var. *yunnanensis*	Rhizomes	Primary Human Umbilical Vascular Endothelial Cells (HUVECs) Human High-Grade Serous Ovarian Cancer SKOV3 Cell Line, SKOV3/IκBαM cells	Paris saponin II (PSII) (formosanin C)	Steroidal saponins	PSII suppressed NF-κB activation due to reduction in IKKβ kinase activity on its substrate IκBα and the expression of IKKβ. It also reduced the expression of NF-κB-downstream targets such as VEGF, Bcl-2 and Bcl-xL resulting in inhibitory effects against human ovarian cancer cell growth in a xenograft mouse model of ovarian cancer.	Yang et al., 2015
P. polyphylla var. *yunnanensis*	Roots and rhizomes	Non-small cell lung cancer (NSCLC) cell line PC-9	Paris saponin I (PSI)	Steroidal saponins	The inhibition rates significantly increased with PSI in combination with hyperthermia at 43˚C causing G2/M phase arrest and significantly induced apoptosis. The expression level of Bcl-2 decreased, while Bax expression and caspase-3 increased resulting in cell death and tumor inhibition.	Zhao et al., 2015
P. polyphylla var. *yunnanensis*	Dried roots	Human Tongue Squamous Cell Carcinoma SCC-15 Cells	(3β,17α,25R)- spirost-5-ene-3,17-diol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside/ PP-22,	Steroidal saponins	PP-22 activated p38, inhibited cdc25B, increased p-cdc2 (Tyr15), and triggered S and G2/M phase arrest, as well as activated p53 through the p38-p53 pathway, inhibited the MAPK/ERK pathway, activated the caspase 8/caspase 3 pathway, and triggered the extrinsic apoptotic pathway in SCC-15	Ke et al., 2016

					cells.	
P. delavayi	Rhizomes	Human Glioblastoma U87MG Human Hepatocellular Carcinoma Hep-G2 Cell Lines	Padelaoside E, Padelaoside F, 25(S)-spirost-5-en-3β,17α,27-triol-3-O-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside 25(S)-spirost-5-en-3β,17α,27-triol-3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside (polyphylloside III)	Furostanol saponins, Spirostanol saponins	Saponins with branched sugar chains shows higher cytotoxic activities compared to saponins having straight sugar chains	Liu et al., 2016 Zhang et al., 2020
Rhizoma paridis	Rhizomes	HepG2 cells	Polyphyllin I, Formosanin C	Steroidal saponins	They in combination increased single G1 phase arrest and mitochondria-dependent apoptotic pathway and reduced the ability of cell migration.	Liu et al., 2016a
P. polyphylla var. *yunnanensis*	Rhizomes	N-nitrosodiethylamine (DEN) induced Liver Cancer in Mice	Rhizoma Paridis Saponins (RPS)	Steroidal saponins	RPS alleviated levels of liver injury through inhibiting liver tissues of malondialdehyde (MDA) and nitric oxide (NO) formation, increasing superoxide dismutases (SOD) production, and up-regulating expression of GST-α/μ/π in DEN-induced rats.	Liu et al., 2017
P. polyphylla	Whole herb	High-Glucose (HG) induced-Human Ovarian Carcinoma Cell Line (OVCAR-3 cells)	Aqueous extract of Paris polyphylla (AEPP)	Steroidal saponins	AEPP reduced the viability of OVCAR-3 cells via induction of apoptosis. This inhibitory potential of AEPP was attenuated by HG induction in OVCAR-3 cells. The levels of estrogen-related receptor (ERR)-alpha activator and peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1 alpha was elevated by HG induction, but were suppressed by AEPP treatment. Down-regulations of cell survival and EMT were oberved in OVCAR-3 cells through suppression of PGC-1alpha by AEPP treatment.	Wang et al., 2016
P. polyphylla	Rhizomes	Human Chronic Myelogenous Leukemia K562 Cells	Polyphyllin D	Diosgenyl saponin	Polyphyllin D induced apoptosis via The mitochondrial apoptotic pathway, as evidenced by the decreased Bcl-2 and Bcr/Abl expression levels, disruption of MMP and increased Bax, cytochrome c and cleaved caspase-3 levels. At low dose, polyphyllin D increased CD14 expression on the surface of K562 cells and induced cells to differentiate into monocytes or mature macrophages.	Yang et al., 2016
P. polyphylla	Rhizomes	Human lung cancer cells (NCI-H460 and A549)	Paris saponin II	Steroidal saponins	PS II induced apoptosis by activating autophagy possibly by activation of JNK and inhibition of PI3K/AKT/mTOR pathways	Zhang et al., 2016

P. chinensis	Herb	Stably transfected Hela cells	Aqueous ethanolic extract of Paris chinensis	Steroidal saponins	The nuclear factor-kappa B(NF-ķB) signalling pathway is affected.	Fan et al., 2017
P. polyphylla	Rhizomes	Human Breast Cancer Cell Line MDA-MB-231 (HTB-26) and MCF-7 (HTB-22)	Polyphyllin I	Steroidal saponins	Polyphyllin I induces mitochondrial translocation of DRP1 by dephosphorylating DRP1 at Ser637, leading to mitochondrial fission, cytochrome c release from mitochondria into the cytosol and, ultimately apoptosis. It also increased the stabilization of full-length PINK1 at the mitochondrial surface, leading to the recruitment of PARK2, P62, ubiquitin, and LC3B-II to mitochondria and culminating in mitophagy.	Li et al., 2017
P. polyphylla	Rhizomes	Human lung adenocarcinoma NCI-H1299 (H1299), human lung squamous cell carcinoma NCI-H520 (H520), human lung large cell carcinoma NCI-H460 (H460) and SCLC NCI-H446 (H446)	Paris saponin I	Steroidal saponins	PSI acts as a chemosensitizer of Camptothecin (CPT)/ 10-hydroxycamptothecin (HCPT) CPT/HCPT that leads to a synergistic inhibition of proliferation and an induction of cell apoptosis by inducing the activation of p38 MAPK/caspase signaling pathway in H1299 cells, and suppression of AKT and ERK pathways activation in H460 cells as well as in H446 cells.	Liu et al., 2017
P. polyphylla var. *yunnanensis*	Rhizomes	N-nitrosodiethylamine (DEN) induced Lung Cancer in Mice	RhizomaParidis Saponins (RPS)	Steroidal saponins	RPS reduced oxidative stress injury through up-regulating activities of CAT and SOD, down-regulating the levels of inflammatory factors, like TNF-α, IL6, COX-2 and PGE2, activation of caspase-3 and up-regulating the pro-apoptotic protein Bax, decreasing the expression of PCNA, depressing the expression of cancer stem cells marker CD133, suppressing aberrant expression of cytokeratin 8 and 18, and inhibiting EGFR/ PI3K/Akt, EGFR/Ras/Erk and NF-κB pathways.	Man et al., 2017
P. polyphylla	Rhizomes	Human Neuroblastoma IMR-32 and LA-N-2 and NB-69 cells	Polyphyllin D	Steroidal saponins	Polyphyllin D-induced cell death in NB-69 cells via apoptosis, whereas cell death in IMR-32 and LA-N-2 cells was caused by necroptosis.	Watanabe et al., 2017 Wu et al., 2012
P. polyphylla var. *yunnanensis*	Rhizomes	Human Nasopharyngeal Carcinoma Epithelial (CNE) cells	(23S,24S)-spirost-5,25(27)-diene-1β,3 β,21,23α,24 α -pentol-1-O-{ α -L-rhamnopyranosyl-(1→2)- [β-D-xylopyranosyl-(1→3)]-β-D-glucopyranosyl}-21-O-β-D-galactopyranosyl-24-O-β-D-galactopyranosyl Parisyunnanoside I	Steroidal saponins	The results indicated that the F ring in steroidal saponins might be the active group against CNE cells. The results indicated that the cytotoxicities of triterpenoid saponins might be related to 28-carboxylic acid	Wu et al, 2017

P. polyphylla var. *yunnanensis*	Roots	Human Nasopharyngeal Carcinoma Epithelial (CNE) cells	(3β,25R)-spirost-5-en-3-ol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside (3β,25R)-spirost-5-en-3-ol 3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside (3β,17α,25R)-spirost-5-ene-3,17-diol 3-O-α-L-rhamnopyranosyl-(1→2)-β-D- glucopyranoside (3β,17α,25R)-spirost-5-ene-3,17-diol 3-O-α-L-arabinofuranosyl-(1→4)-[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside	Steroidal saponins	Sugar units affected cytotoxicities of the compounds a lot	Wu et al, 2017
P. polyphylla var. *yunnanensis*	Rhizomes	Osteosarcoma Cell Line 143B, MG-63, U-2 OS and hFOB1.19 cells	Ethanol extract of whole rhizome	Not defined	Caused apoptosis in 143B cell via caspase activation, increased Bax/Bcl-2 ratio and PARP cleavage. It also induced G2/M phase arrest associated with elevated phosphorylation of CDK1, Cdc25C, Chk2 and down-regulation of cyclin B1, CDK1, Cdc25C expression. Additionally, it inhibited 143B cell migration, invasion and VM formation at non-cytotoxic concentrations through decreasing the expression of FAK, Mig-7, MMP2 and MMP9.	Yao et al., 2017
P. vietnamensis	Rhizomes	Human Glioblastoma U87MG And U251 Cell Lines	25(R)-diosgenin-3-O- α -L-rhamnopyranosyl-(1→2)- α -L-rhamnopyranosyl-(1→3)- β -D-glucopyranoside 25(R)-spirost-5-en-3b, α -O- α -L-rhamnopyranosyl-(1→4)-[α -L-rhamnopyranosyl-(1→2)]-b-D-glucopyranoside, 25(R)-diosgenin-3-O-a-L-rhamnopyranosyl-(1→2)- β -D-glucopyranoside	Spirostanol glycosides	branched trisaccharide chain attached to C-3 of the aglycone, exhibited significant cytotoxicities against the two test tumor cells	Liu et al., 2018
P. polyphylla var. *yunnanensis*	Rhizomes	Lung Adenocarcinoma Cells	Ethanolic extract of whole rhizome	Not defined	Rhizome extract inhibited levels of cytokines or receptors such as VEGFD, VEGFR3, RAGE, IL6R, IL17BR, and CXCL16 which were regarded as the initiators induced tumor cell proliferation, adhesion, angiogenesis, and invasion. It also raised the content of SOD and CAT enzymes and thereby inhibited the aberrantly active NF-jB, and phosphorylation of PI3K/Akt and MAPK (including p38, Erk1/2, and JNK) signalling pathways.	Man et al., 2018
P. polyphylla	Rhizomes	L929 and Hela cells	Falcarindiol Pennogenin-3-O-α -L-arabinofuranosyl(1→4)-β-D-glucopyranoside Pennogenin-3-O-α-L-arabinofuranosyl (1→4)-[α-L rhamnopyranosyl(1→2)]-β-D-glucopyranoside Diosgenin-3-O-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside Diosgenin-3-O -α-L-rhamnopyranosyl(1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside	Steroidal saponins	Not defined	Wang et al., 2018
P. forrestii	Rhizomes	Human Leukemia HL-60, Human Liver Cancer SMMC-7721, Human Lung Cancer A-549 Human Breast Cancer MCF-7 Human Rectal Cancer SW480 Cell Lines	Total saponins, Polyphyllin D, Formosanin C Dioscin, Diosgenin-3-O-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside, Paris saponin H Pennogenin-3-O-α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→4)]-β-D-glu copyranoside	Saponin glycosides	Not defined	Wang et al., 2018b

P. polyphylla	Rhizomes	HT 29 and HCT 116 cells	Paris Saponin II (PSII)	Steroidal saponins	PSII inhibits colorectal carcinogenesis by regulating mitochondrial fission and NF-κB pathway.	Chen et al., 2019
P. polyphylla	Rhizomes	Hepg2 Cells, SMMC 7721, And LO2 Cells	*Paris polyphylla* 26 (PP-26)	Steroidal saponins	PP-26 inhibited proliferation of HepG2 cells in a dose-dependent manner by triggering G2/M-phase arrest and apoptosis of HepG2 cells. Expression levels of apoptosis proteins caspase 9, caspase 3, PARP, Bcl-2, Bcl-xL, and Mcl-1 were downregulated, Expression level of apoptosis protein Bax was upregulated. Expression levels of p-Akt, p-GSK-3b, and p-Foxo3 were downregulated.	Li et al., 2019
P. polyphylla	Rhizomes	Hepatocytes cell lines HL-7702 and HepaRG cells	Rhizomaparidis saponin I	Steroidal saponins	PSI-induced lactate dehydrogenase (LDH) release from HepaRG cells besides enhancing the levels of reactive oxygen species (ROS) and blocked the S and G2 phases of the cell cycle in HepaRG cells. PSI upregulated the protein expression levels of p53, p21, and Fas and induced changes in the p53 protein increased the Bax/bcl-2 ratio, increasing the release of mitochondrial cytochrome c, activation of caspases-3, -8, and -9, poly-ADP ribose polymerase (PARP), and ultimately apoptosis.	Wang et al., 2019
P. polyphylla var. *yunnanensis*	Rhizomes	Nasopharyngeal Carcinoma Cell Line CNE-2	Paris polyphylla 22 (PP-22)	Steroidal saponins	Activates the p38 mitogen-activated protein kinase (MAPK) pathway promoted apoptosis via an intrinsic pathway, including the endoplasmic reticulum stress pathway, in a caspase-dependent manner. Induced apoptosis by downregulating the signal transducers and activators of transcription 3 (STAT3) pathway,	Tan et al., 2019