Medicinal Plants of Himalayan Forests

Sakshi Painuli, Prabhakar Semwal, Natália Cruz-Martins, and Rakesh Kumar Bachheti

Contents

S. Painuli
Department of Biotechnology, Graphic Era University, Dehradun, India

P. Semwal (✉)
Department of Biotechnology, Graphic Era University, Dehradun, India

Uttarakhand State Council for Science and Technology, Dehradun, India

N. Cruz-Martins (✉)
Faculty of Medicine, University of Porto, Porto, Portugal

Institute for Research and Innovation in Health (i3S), University of Porto, Porto, Portugal

Laboratory of Neuropsychophysiology, Faculty of Psychology and Education Sciences, University of Porto, Porto, Portugal
e-mail: ncmartins@med.up.pt

R. K. Bachheti
Department of Industrial Chemistry, College of Applied Sciences, Addis Ababa Science and Technology University, Addis Ababa, Ethiopia

A. Husen et al. (eds.), *Non-Timber Forest Products*,
https://doi.org/10.1007/978-3-030-73077-2_8

1 Introduction

Plants play a vital role in our diet and are an excellent reservoir of proteins, carbohydrates, antioxidants, vitamins, and other important components required for our existence (Vella 1990). Among such important components, secondary metabolites have received increasing attention, as they contain medicinal values with huge therapeutic significance, besides being major contributors to health care improvements (Eloff 1998). Such secondary metabolites are often named active compounds or phytochemicals and display renowned biological effects, such as antimicrobial, antioxidant, antitumor, antidiabetic, antinociceptive, cardioprotective, and immunomodulatory properties, among others. Indeed, the increasing importance on the use of herbal preparations and medicinal plant is that they have low or even no side effects when compared to synthetic drugs and are simultaneously more potent against several diseases and disorders.

From time immemorial, a variety of indigenous and cultivated plants have been exploited for their therapeutic properties, and globally they are analyzed for the assessment of their efficiency as a result of increasing demand by the worldwide population by plant-based medicine. The World Health Organization (WHO) has reported that the business of medicinal plants and herbal medicine and the demand for herbal raw material is increasing annually at a growth rate of almost 15% (Neupane and Lamichhane 2020). However, it is expected that the global market of medicinal or pharmaceutical products extracted from plant sources will surpass $111 billion by the year 2023 (Sofowora et al. 2013; Neupane and Lamichhane 2020). Hence, the research for identifying new species of medicinally important plants and the search for biologically active compounds from them is in progressing phase, due to which the demand for these medicinal plants has increased a lot in the market.

The forest richness of the Himalayan region is inexhaustible with exceptional medicinal flora and incredible economic significance (Pandey 2007). Flora from the Himalayan region is used by native communities for different reasons, including food, fuel, and medicinal purposes (Detwiler and Hall 1988; Bhat et al. 2020). A huge range of Himalayan plants has been cited by researchers around the world, with multiple therapeutic virtues underlined as well as their major role in traditional medicinal systems of different countries.

Currently, numerous herbal medicines and their active components have been used directly or indirectly in the modern medical system. A plethora of biologically important active compounds has been isolated from plant species found in the Himalayan region. Among such active compounds, linoleic acid, quercetin, gallic acid, ascorbic acid, piperine, myricetin, curcumin, taxol, palmitic acid, cinnamaldehyde, nerolidol, taxiresinols, amarogentin, swertiamarin, mangiferin, hesperidin, picroliv, and apocynin have been extracted and/or isolated at considerable amounts from a variety of plants, including *Anogeissus latifolia*, *Justicia adhatoda*, *Curcuma longa*, *Punica granatum*, *Piper nigrum*, *Aegle marmelos*, *Rhododendron arboreum*, *R. campanulatum*, *Podophyllum hexandrum*, *Saussurea obvallata*, *Taxus* *wallichiana*, *Pinus roxburghii*, *Swertia chirayita*, *Picrorhiza kurroa*, etc., to whom excellent therapeutic activities have been attributed, such as antimicrobial, anticancer, anti-inflammatory, antiproliferative, antioxidant, antiatherogenic, anti-asthmatic, antifungal, antidiabetic, immunomodulatory, anti-HIV, anti-Parkinson, and anti-hepatitis effects (Rajeshkumar and Kuttan 2001; Juyal et al. 2014; Painuli et al. 2015; Kumar and Van Staden 2016; Painuli and Kumar 2016; Painuli et al. 2016; Semwal 2017; Adnan et al. 2019; Semwal and Painuli 2019; Soni and Grover 2019). In this sense, this chapter aims to address the important medicinal plants from the forests of the Himalayas and their traditional uses, promising bioactive molecules along with therapeutic potential.

2 From Himalayan Mountain Diversity to New Drug Sources

The Himalaya, a crescent-shaped continuous belt of mountain system located in Asia, is known to be the highest and youngest mountain range worldwide. It extends over about 2500 km from Nanga Parbat in the west to Namja Barwa in the east, ranging up to 350 km of width in the west to 150 km in the east. This mountain belt is mainly distributed across the territories of five countries, namely, Pakistan, India, Nepal, China, and Bhutan (Roy and Purohit 2018). From west to east, the Himalayan belt is sectioned into three well-defined regions: western, eastern, and central Himalayan. With a complex and diverse geological pattern in terms of hydrology, environment, erosion, and mass movement, in the Himalayan belt, there is a marked climate variation at different zones, drifting from the tropical climate at the bottom and everlasting snow at the top of the mountain, with regional ecosystem transformations depending on elevation. In fact, both altitudinal and climatic variations make the Himalayan vegetation extremely rich and broadly distributed in forests and grasslands (Hajra and Rao 1990). Himalaya forest systems vary markedly in their topography, soils, rainfall, and weather, harboring rare and valuable flora and fauna. The variation in Himalayan vegetation ranges from tropical deciduous forests at the lower altitude to temperate forest at middle altitude, while at higher altitudes, coniferous forest, subalpine, and alpine forests are found, ranging from alpine grasslands and meadows to scrublands and permanent snowline.

Among the wide plant biodiversity of the Himalayan forest, which includes medicinal, aromatic, and wild edible plants, orchids, ferns and fern allies, bamboos, and ornamental plants (Hajra and Rao 1990), with increasing elevation, the flora shows even greater diversity profile (Manish and Pandit 2018; Bhat et al. 2020). The major plant species in the Himalayan tropical and subtropical forests include *Acacia catechu, A. procera*, *Albizia lebbeck*, *Bombax ceiba*, *Careya arborea*, *Dalbergia sissoo*, *Duabanga grandiflora*, *Garuga pinnata*, *Gmelina arborea*, *Haldina cordifolia, Kydia calycina*, *Mesua assamica*, *M. ferrea*, *Oroxylum indicum*, *Pinus roxburghii*, *Quercus lamellose*, *Semecarpus anacardium*, *Shorea robusta*, *Terminalia tomentosa*, and *T. bellirica*; however, in the Himalayan temperate forest, species like *Abies delavayi*, *A. densa*, *A. pindrow*, *Acer* spp., *Berberis* spp., *Cedrus deodara*, *Larix griffithii, Lithocarpus pachyphyllus*, *Magnolia* spp., *Picea smithiana*, *Prinsepia utilis, Quercus cerris*, *Q. lamellose*, *Rhododendron* spp., and *Tsuga dumosa* predominate (Manish and Pandit 2018). In the shrubby region, *Artemisia*, *Berberis*, *Cotoneaster,* and *Ephedra* species are major elements, while in subalpine and alpine zones, *Aconitum heterophyllum*, *Aster albescens*, *Anemone*, *Berberis*, *Cotoneaster*, *Geranium*, *Iris*, *Juniperus*, *Lloydia*, *Potentilla*, *Primula*, and *Rhododendron* dominate (Srivastava et al. 2017; Manish and Pandit 2018). Table 1 enumerates the list of some Himalayan plants along with their distribution.

3 Traditional Uses of Himalayan Plants

The traditional system of medicine (TSM) comprises folk knowledge-based medicines, exercises, manual techniques, and spiritual healing along with other medical aspects developed over generations by several communities for diagnosis and prevention of a plethora of diseases. According to the WHO, "*the traditional medicine is the sum total of the knowledge, skills, and practices based on theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in health maintenance as well as prevention, diagnosis, improvement or even treatment of physical and mental illness*" (Che et al. 2017). TSM uses natural compounds, extracted from herbs, animals, organic matter, and minerals, for preventing or curing diseases, with medicinal plants being used for preparing a plethora of herbal drug formulations. TSM, including Ayurveda, Yoga, Unani, Naturopathy, Siddha, Homeopathy, and Chinese medicine system (TCM) used Himalayan medicinal plants as a leading source for efficient and effective herbal drug formulation. Among all, the Ayurvedic medicinal system is the oldest system of medicine developed and is in practice since 1500 BC (Ravishankar and Shukla 2007). These different TSMs are practiced in India, Nepal, Srilanka, Pakistan, Bangladesh, Bhutan, China, and Tibet, among other places (Rosenberg 2012; Samal and Dehury 2016).

Among the renowned plant species that play important roles in these TSM, *Andrographis paniculate*, *Artemisia maritime, Asparagus racemosus*, *Bacopa monnier*, *Barbarea vulgaris, Berberis vulgaris*, *Cedrus deodara*, *Curcuma longa*, *Datura innoxia*, *Dioscorea deltoidea*, *Equisetum arvense*, *Girardinia heterophylla*, *Ocimum sanctum*, *Paeonia emodi*, *Picrorrhiza kurroa*, *Pinus gerardiana*, *Podophyllum hexandrum*, *Rheum emodi*, *Rhododendron arboreum*, *Saussurea obvallata*, *Terminalia chebula*, *Tulipa gesneriana*, and *Withania somnifera* are the most widely recognized (Kurup 2002; Khare 2008; Gautam and Bhadauria 2009). These herbal plants exhibit numerous biological properties and have been used to treat high blood pressure, migraine, parasitic and fungal infections, fever, skin problems, cancer, stomach ache, uterine infection, inflammation, microbial infection, stress, fatigue, liver, and kidney problems (Joshi and Joshi 2013; Chaudhury and Rafei 2002). Some of these traditionally important plants and their traditional uses are mentioned in Table 2.

Table 1 Some popular Himalayan plants and their distribution

Species name	Family	Distribution
Aconitum heterophylloides (Brühl) Stapf	Ranunculaceae	Pakistan, India, Nepal
Aconitum heterophyllum Wall. ex Royle	Ranunculaceae	Pakistan, India, Nepal
Allium carolinianum DC.	Amaryllidaceae	Afghanistan, India, China, Pakistan, Nepal
Allium rubellum M. Bieb.	Amaryllidaceae	Asia, Europe
Anoectochilus roxburghii (Wall.) Lindl.	Orchidaceae	China, Tibet, Japan, Sri Lanka, India, Nepal
Arisaema propinquum Schott	Araceae	Pakistan, India, Nepal, Tibet
Aster falconeri (C.B.Clarke) Hutch.	Asteraceae	Arctic, Africa, Asia, America
Atropa acuminata Royle ex Lindl.	Solanaceae	Afghanistan, Iran, Pakistan, India
Begonia picta Sm.	Begoniaceae	China, India, Nepal, Bangladesh, Myanmar
Berberis aristata DC.	Berberidaceae	Asia, Europe, and America
Berberis lyceum Royle	Berberidaceae	India, Pakistan, Nepal
Bombax ceiba L.	Malvaceae	Asia, Africa, Australia
Calanthe davidii Franch.	Orchidaceae	China, India, Japan, Nepal, Taiwan, Vietnam
Calanthe plantaginea Lindl.	Orchidaceae	India, Nepal, Bhutan
Cardiocrinum giganteum (Wall.) Makino	Liliaceae	India, Pakistan, Nepal
Cicer microphyllum Benth.	Leguminosae	India, Pakistan, Afghanistan, Nepal, Tibet, Bhutan
Colchicum luteum Baker	Colchicaceae	Afghanistan, Turkestan, Pakistan, India
Cymbidium iridioides D.Don	Orchidaceae	Bhutan, India, Myanmar, Nepal, North Vietnam
Cymbidium lowianum (Rchb.f.) Rchb.f.	Orchidaceae	India, China, Japan, Indonesia, Australia
Dactylorhiza hatagirea (D.Don) Soó	Orchidaceae	India, Pakistan, Afghanistan, Nepal, Tibet, Bhutan
Dendrobium heterocarpum Wall. ex Lindl.	Orchidaceae	India, Nepal, Bhutan, Myanmar, Sri Lanka, Pakistan
Dendrocalamus strictus (Roxb.) Nees	Poaceae	India, Peninsula, Bangladesh, Myanmar, Thailand
Dioscorea deltoidea Wall. ex Griseb.	Dioscoreaceae	China, Pakistan, Nepal, Bhutan, India, etc.
Elaeagnus rhamnoides (L.) A.Nelson	Elaeagnaceae	Asia, Europe
Eremurus himalaicus Baker	Xanthorrhoeaceae	Afghanistan, India, Pakistan, Nepal
Euryale ferox Salisb.	Nymphaeaceae	India, Europe, China, Japan
Fraoaria nubicola Lindl. ex Lacaita	Rosaceae	China, Nepal, India, Myanmar
Gentiana kurroo Royle	Gentianaceae	Pakistan, India, Nepal

(continued)

Table 1 (continued)

Species name	Family	Distribution
Hedychium spicatum Sm.	Zingiberaceae	Pakistan, India, Nepal
Hypericum hookerianum Wight & Arn.	Hypericaceae	India, Pakistan, China, Nepal, Bangladesh.
Myrica esculenta Buch.-Ham. ex D Don	Myricaceae	India, Nepal, China, Japan, Pakistan, Singapore
Nardostachys jatamansi (D.Don) DC.	Caprifoliaceae	Afghanistan, China, Tibet, Nepal
Nasturtium officinale R.Br.	Brassicaceae	Asia, Europe, Africa
Nymphaea nouchali Burm. F.	Nymphaeaceae	India, Africa
Nymphoides peltata (S.G. Gmel.) Kuntze	Menyanthaceae	China, India, Nepal
Picrorhiza kurrooa Royle	Scrophulariaceae	Pakistan, India, Nepal
Pinus gerardiana Wall. ex D.Don	Pinaceae	Afghanistan, India, China, Pakistan, Nepal
Podophyllum hexandrum Royle	Berberidaceae	India, Afghanistan, China, Pakistan, Nepal, Bhutan
Primula denticulata Sm.	Primulaceae	Bhutan, India, Myanmar, Nepal, China, Pakistan
Rheum webbianum Royle	Polygonaceae	India, Pakistan, Afghanistan, Nepal, Tibet, Bhutan
Rhodiola imbricata Edgew.	Crassulaceae	China, India, Nepal, Pakistan
Rhododendron arboreum Sm.	Ericaceae	India, Nepal, China, Bhutan, Sri Lanka, Pakistan
Rubus ellipticus Sm.	Rosaceae	China, Nepal, India, Philippines
Saussurea costus (Falc.) Lipsch.	Asteraceae	India, Pakistan, China
Saussurea obvallata (DC.) Edgew.	Asteraceae	India, Pakistan, China, Tibet, Nepal
Sinopodophyllum hexandrum (Royle) T.S.Ying	Berberidaceae	Afghanistan, India, China, Pakistan, Nepal
Taxus baccata L.	Taxaceae	Asia, Europe, America, Iran
Urtica dioica L.	Urticaceae	Africa, America, Asia, Australasia, Europe
Valeriana hardwickii Wall.	Valerianaceae	Afghanistan, India, Pakistan, Myanmar
Valeriana jatamansii Jones	Valerianaceae	Afghanistan, Bhutan, China, India, Pakistan

On the other hand, the TCM system was written around 100 or 200 BC, and the Chinese Materia Medica was published in 1977 (Yuan et al. 2016). Regarding the most frequently used Himalayan medicinal plants in TCM, *Aquilaria sinensis*, *Bergeria purpurascens*, *Cistanche salsa*, *Coptis omeiensis*, *Coptis teeta*, *Cordyceps sinensis*, *Dendrobium* spp., *Dioscorea deltoidea*, *Dioscorea ipponica*, *Dioscorea zingiberensis*, *Dracaena cochinchinensis*, *Ephedra sinica*, *Epimedium brevicornum*, *Erigeron breviscapus*, *Eucommia ulmoides*, *Fritillaria* spp., *Gastrodia alata*, *Gentiana macrophylla*, *Gentiana scabra*, *Glycyrrhiza uralensis*, *Homalomena*

Table 2 Some popular medicinal plants and their traditional uses

Name of the species	Traditional uses	References
Abrus cantoniensis Hance	Chronic hepatitis, rheumatism, traumatic injury	Hong et al. (2015)
Abutilon indicum Linn. Sweet.	Paralysis, cough, chronic cystitis	Khare (2008)
Acanthopanax trifoliatus (L.) Merr.	Rheumatic arthritis, traumatic injury, sciatica, eczema	Hong et al. (2015)
Aconitum heterophyllum Wallich ex Royle	Stomach ache, fever	Uniyal et al. (2006)
Acorus calamus L.	Diarrhea	Hong et al. (2015)
Acorus calamus L.	Skin wounds, cough, cold, roundworm, hookworm	Ambu et al. (2020)
Adenanthera pavonina Linn.	Diarrhea, paralysis, pulmonary affections	Khare (2008)
Aesculus indica (Colebr. ex Cambess) Hook.	Pregnancy food for ladies	Uniyal et al. (2006)
Ajuga bracteosa Wall. ex Benth.	Stimulant, aperient, diuretic, blood purifier, fever	Khare (2008)
Allium humile Kunth	Breathing problem, stomach disease, jaundice	Bano et al. (2014)
Amygdalus persica Linn.	Cough, chronic bronchitis	Khare (2008)
Angelica glauca Edgew	Fever and cold	Uniyal et al. (2006)
Artemisia capillaris Thunb.	Decoction, hepatitis, jaundice	Hong et al. (2015)
Artemisia sieversiana Ehrh.	Pneumonia, joints, boils, wounds, swelling	Bano et al. (2014)
Asparagus racemosus Willd	Immunoregulatory, tonic	Ojha et al. (2020)
Astragalus psilocentros Fisch	Teeth cleaning, stomach problems	Bano et al. (2014)
Berberis asiatica Roxb. ex DC.	Diabetes, Jaundice	Uniyal et al. (2006)
Berberis lycium Royle	Eye disease	Uniyal et al. (2006)
Bergenia ciliata (Haw.) Sternb.	Diarrhea, asthma, urinary problems, ophthalmia	Bano et al. (2014)
Betula utilis D. Don.	Rheumatism, dropsy, stones in the kidneys, eczema	Khare (2008)
Cannabis sativa L.	Paralysis, joint pain, piles	Uniyal et al. (2006)
Cedrus deodara (Roxb.) Loud.	Astringent, antidiarrheal, febrifuge, skin disease	Khare (2008)
Chenopodium album L.	Rheumatism, swollen feet, sunstroke, sunburn	Bano et al. (2014)

(continued)

Table 2 (continued)

Name of the species	Traditional uses	References
Chirita eburnea Hance	Grinding, decoction	Hong et al. (2015)
Citrus hystrix DC.	Gastrointestinal	Ojha et al. (2020)
Dactylorhiza hatagirea (D.Don) Soo	Bleeding, wounds	Ojha et al. (2020)
Dioscorea deltoidea Wall	Could, cough, joint pain, wounds, constipation, etc.	Semwal et al. (2021)
Dioscorea opposita Thunb.	Grinding, decoction, weakness, frequent urination	Hong et al. (2015)
Eclipta prostrata (L.)	Diarrhea, hematuria, hemoptysis, socioeconomic	Semwal et al. (2017)
Ficus benghalensis Linn.	Diabetes, dysentery, wounds	Khare (2008)
Ficus palmate Forsk.	Cuts, wounds	Ojha et al. (2020)
Grewia optiva Drummond ex Burret	Joint pain	Uniyal et al. (2006)
Hedychium spicatum Buch. Ham. ex Smith	Respiratory, intestinal problems, purgative, laxative	Ojha et al. (2020)
Hypericum sampsonii Hance	Traumatic injury, pain, indigestion, chest congestion	Hong et al. (2015)
Jasminum arborescens Roxb.	Astringent, stomachic	Khare (2008)
Juniperus excelsa M. Bieb.	Kidney stone, rheumatism, respiratory disorders	Bano et al. (2014)
Malva parviflora L.	Abortion	Uniyal et al. (2006)
Myrica esculenta Buch.-Ham. ex D. Don	Constipation, diarrhea, asthma, bronchitis	Ambu et al. (2020)
Paeonia emodi Wall. ex Royle.	Nervous affections, uterine diseases, blood purifier	Khare (2008)
Paeonia officinalis Linn	Antispasmodic, sedative, vasodilatory, hypotension	Khare (2008)
Picrorhiza kurrooa Royle ex Benth.	Joint pain, fever	Uniyal et al. (2006)
Podophyllum hexandrum Royle	Dermatological	Ojha et al. (2020)
Polygonum amplexicaule D.Don	Wounds in the eyes	Uniyal et al. (2006)
Quercus leucotrichophora A. Camus	Indigestion, diarrhea, asthma	Semwal et al. (2018)
Rhaphidophora glauca (Wall.) Schott	To promote pregnancy	Ambu et al. (2020)
Rheum australe D.Don	Fractured bone	Uniyal et al. (2006)

(continued)

Table 2 (continued)

Name of the species	Traditional uses	References
Rhododendron arboreum Smith	Nasal bleeding	Uniyal et al. (2006)
Rumex nepalensis Sprengel	Anti-allergic	Uniyal et al. (2006)
Saussurea costus (Falc.) Lipsch.	Joint pain	Uniyal et al. (2006)
Saussurea obvallata (D.C.) Edgew	Paralysis, mental illness, cough, chronic cystitis	Semwal et al. (2020)
Senecio chrysanthemoides DC.	Rheumatic pain, wounds, sore throat	Bano et al. (2014)
Swertia chirayita (Roxb. ex Fleming)	Skin infection in children's	Uniyal et al. (2006)
Swertia petiolata Royle	Opthalmia, liver tonic, stomach inflammation	Bano et al. (2014)
Taxus baccata Linn.	Nervousness, epilepsy, asthma, chronic bronchitis	Khare (2008)
Thalictrum foliolosum DC.	Stomach pain, gastric trouble	Uniyal et al. (2006)
Viola betonicifolia J.E. Smith	Antidote	Ojha et al. (2020)
Viola pilosa Blume	Fever, cold, cough	Uniyal et al. (2006)
Zanthoxylum armatum DC	Respiratory, gastrointestinal, spices, and condiments	Ojha et al. (2020)
Zanthoxylum nitidum (Roxb.) DC.	Ulcer, rheumatism, diarrhea, malaria, chronic gastritis	Hong et al. (2015)
Zingiber officinale Rosc	Cold, cough	Ojha et al. (2020)

occulta, *Panax ginseng*, *Panax pseudoginseng*, *Paris polyphylla* var. *yunnanensis*, *Picrorhiza scorophulariiflora*, *Psammosilene tunicoides*, *Rauwolfia yunnanensis*, *Rheum officinale*, *Salvia miltiorrhiza*, *Saussurea lappa*, *Sinopodophyllum emodi*, *Stephania epigaea*, *Stephania yunnanensis*, *Taxus chinensis*, and *Taxus wallichiana* are the most evident (Shengji et al. 2009). Indeed, the Himalayan flora has a long history in traditional or alternative treatments, and presently researchers are not only searching for new active components but also exploring the mechanism of action of many of these plant-derived extracts and even single components.

4 Plant-derived Bioactive Compounds

Bioactive compounds are essential and nonessential elements extracted from natural sources, especially from plants that help fulfill vital health requirements. Secondary metabolism produces these specialized compounds as a self-defense mechanism, conferring protection against herbivores, insects, pathogen, pests, pathogens, and harsh environmental conditions (Egbuna et al. 2018). These secondary metabolites, also known as phytochemicals, phytoconstituents, or even active compounds, have microbicidal, insecticidal, and pesticidal effects and are also of huge interest for the production of several pharmaceutical drugs. Moreover, they also have numerous biomedicinal properties, such as antioxidant, anti-inflammatory, cardiovascular, anti-allergic, antihypertensive, and anticancer potentialities, being, therefore, a rich source of nutraceutical and pharmaceutical products (Hussein and El-Anssary 2018).

The Himalayan flora are known worldwide for their wide spectrum of biological activities, attributed to the presence of high-valued secondary metabolites (Semwal et al. 2020). The plant species at higher altitudes have high diversity and a significant amount of several phytoconstituents, as they face high radiations, low soil nutrients, moisture stress, harsh temperature, and other adverse environmental conditions (Pandey et al. 2018; Yang et al. 2018). At higher altitude, phytoconstituents also help in pollination and confer protection and defense against several biotic and abiotic stresses (Demasi et al. 2018), with this plant–environmental interconnection being responsible for the unique mixture and composition of active compounds (Yang et al. 2018; Jurić et al. 2020).

Despite being put in the background for several years, today, there has been a growing interest in plant secondary metabolites over synthetic molecules because of several properties, such as low or no side effects, less toxicity, cost-effectiveness, and easy availability (Zeb et al. 2014). Many studies have suggested that natural compounds that are directly or indirectly isolated from plant origin actively participates in the formulation of effective and potent drugs. Currently, the field of synthetic chemistry is well developed yet, with more than 850 plant-derived active molecules being used in pharmaceutical formulations and with more than 100 plant-based compounds/molecules in the phase of clinical trials (Fowler 2006; Katiyar et al. 2012). Aspirin, ephedrine, colchicine, taxol, digoxin, camptothecin, atropine, and artemisinin are some of the plant-based active phytochemicals used in modern medicine (Jan and Abbas 2018; Calixto 2019).

Secondary metabolites are majorly classified into four main groups, such as alkaloids, terpenes, terpenoids, and polyphenolic compounds. Glycosides, tannins, and saponins are part of them, given their specific structure. Alkaloids are well-studied plant metabolites with remarkable anticancer, antimalarial, antihypertensive, antiasthmatic, antimicrobial, analgesic, and vasodilatory activities (Roberts and Wink 1998; Raymond et al. 2010; Cushnie et al. 2014). Terpenes and terpenoids are major constituents of plant essential oil and exhibit great anti-inflammatory, anticancer, and antimicrobial activities (Trombetta et al. 2005; Salminen et al. 2008). Polyphenols are a vast group of phytochemicals, which include flavonoids, phenolic acids, isoflavonoids, lignans, curcuminoids, and tannins, possessing immense biomedicinal potentialities like anticancer, antimicrobial, anti-inflammatory, antioxidant, antidiabetic, neuroprotective, and antiallergic effects, among others (Huang et al. 2010; Ghasemzadeh and Ghasemzadeh 2011; Ferrazzano et al. 2011; Egbuna et al. 2018).

4.1 Alkaloids

Alkaloids are a group of naturally occurring organic compounds obtained from bacteria, plants, and fungi that contain at least one nitrogen atom in their heterocyclic ring (Mueller-Harvey and McAllan 1992). Ancient records have shown that alkaloids have been used for medicinal purposes since 4000 BC and are probably the first natural compounds (e.g., morphine) extracted from plants (Rao et al. 1978; Roberts and Wink 1998). Indeed, the therapeutic use of poppy and opium by Persians, Egyptians, Arabs, Greeks, and Sumerians has been mentioned in various ancient manuscripts.

Although they are known for their exceptional biomedicinal properties, several alkaloids with high toxic effects have been reported to cause death in minor amounts. For example, the evaluation of active compounds from *Kopsia* genus leads to the revelation of various classes of alkaloids, with antitumor, anti-leishmania, and antimitotic properties (Chen et al. 2012). Thus, based on their heterocyclic ring, alkaloids are classified as pyrrolidine alkaloids, pyridine alkaloids, pyrrolidine–pyridine alkaloids, pyridine–piperidine alkaloids, quinoline alkaloids, and isoquinoline alkaloids (Jan and Abbas 2018). These groups are comprised of medicinally important alkaloids, including hygrine, isopelletierine, piperine, coniine, nicotine, myosmine, quinine, taxol, hyoscyamine, scopolamine, papaverine, morphine, codeine, narcotine, and heroine (Saxena et al. 2013). Moreover, some alkaloids, including anabasine and nicotine, have insecticidal properties, while others like tetrahydropalmatine, isoquinoline, zephyrantine, berberine, palmatine, atropine, scopolamine, atropine, quinine, colchicine, ephedrine, hyoscyamine, morphine, taxol, emetine, and narcyclasine glucoside have a long history of medicinal applications and are pharmacologically important (Bribi 2018; Jan and Abbas 2018; Badri et al. 2019).

In general, various therapeutic activities have been reported to alkaloids, such as anticancer, antihyperglycemic, antimalarial, anti-asthmatic, vasodilatory, antiarrhythmic, cholinomimetic, and analgesic effects (Roberts and Wink 1998; Sinatra et al. 2010; Russo et al. 2013; Kittakoop et al. 2014; Cushnie et al. 2014), with Himalayan plants, like *Aconitum balfourii*, *Aconitum heterophyllum*, *Atropa belladonna*, *Berberis asiatica*, *Camellia sinensis*, *Cinchona officinalis*, *Colchicum luteum*, *Corydalis govaniana*, *Datura innoxia*, *Dicentra canadensis*, *Ephedra gerardiana*, *Eupatorium cannabinum*, *Rauvolfia serpentina*, *Saussurea lappa*, *Taxus baccata*, *Thalictrum foliolosum, Valeriana dubia*, *Vinca rosea*, and *Withania somnifera* being extremely rich sources of such class of biologically active molecules (Khare 2008; Sharma and Gaur 2012; Chhetri 2014).

4.2 Terpenes and Terpenoids

Terpenes and terpenoids are one of the most common and diverse groups of plant secondary metabolites, with around more than 22,000 compounds occurring in all plant sorts (Adeyemi 2011). Briefly, terpenes are simple hydrocarbons consisting of five-carbon isoprene units, assembled in thousands of different ways. On the other hand, terpenoids are modified terpenes with different functional groups and oxidized methyl group present or absent at several locations (Tiwari and Rana 2015; Perveen and Al-Taweel 2018). They are the main constituents of essential oils (Joshi et al. 2016), namely, sesquiterpenes, saponins, iridoids, cardiotonic heterosides, alpha-terpineol, γ-terpinene, terpinolene, and terpinen-4-ol (Joshi et al. 2016). Organoleptically, terpenes, and terpenoids are responsible for the aroma and flavoring properties of plants, with compounds like linalool, caryophyllene, menthol, and geraniol being widely renowned for it. They also possess a broad range of pharmacological and biological properties, such as anti-inflammatory, antiparasitic, antioxidant, anticancer, antiviral, antimicrobial, insecticidal, and antihyperglycemic effects (Zhu et al. 2003; Trombetta et al. 2005; Salminen et al. 2008; Hanuš and Hod 2020). Himalayan flora, namely *Abies pindrow*¸ *Achillea millefolium*, *Achyranthes bidentata*¸ *Aconitum chasmanthum*, *Aconitum ferox*, *Aconitum palmatum*, *Adiantum capillus-veneris*, *Andrographis panicultata*, *Artemisia maritima*, *Artemisia vestita*, *Baliospermum montanum*, *Blumea balsamifera*, *Bridelia montana*, *Bupleurum flacutum*, *Callicarpa macrophylla*, *Caltha palustris*, *Cedrus deodara*, *Cetraria islandica*, *Cimicifuga racemose*, *Curcuma angustifolia*, *Daphne oleoides*, *Delphinium denudatum*, *Euonymus tingens*, *Eupatorium cannabinum*, *Galium aparine*, *Inula racemose*, *Juniperus communis*, *Kalanchoe integra*, *Madhuca butyracea*, *Nardostachys jatamansi*, *Perilla frutescens Picea smithiana*, *Quercus incana*, *Rhododendron arboreum*, *Rhododendron campanulatum*, *Rhododendron cinnabarinum*, *Roylea cinereal*, and *Saussurea lappa*, are well recognized for their rich contents in terpenes and terpenoids, with multiple applications in chemical, cosmetic, and pharmaceutical industries (Khare 2008; Painuli et al. 2015; Painuli et al. 2016; Rawat et al. 2019).

4.3 Phenolic Compounds

Polyphenols are widely known for their excellent antioxidant properties and ability to enhance the function of endogenous antioxidants, vitamins, and enzymes to prevent oxidative stress-induced damages by the high amount of reactive oxygen species (ROS). This group of biologically active molecules is considered to have chemical features related to phenolic substances and is composed of various subgroups, namely, phenolic acids, flavonoids, phytoalexins anthocyanins, lignin, tannins, and furanocoumarins (Tsao 2010; Singla et al. 2019). Synthesized by malonic and shikimic acid pathways occurring in plants, there are over 8,000 known structures of phenolics of which more than 4,000 are recognized as flavonoids (Bravo 1998; Harborne and Willians 2000; Cheynier 2005). Polyphenols possess a wide range of biological activities, including antioxidant, antiaging, anticancer, anti-inflammatory, anti-atherosclerotic, anti-apoptotic, cardioprotective, and neuroprotective abilities (Han et al. 2007; Soto-Hernández et al. 2017), with the major groups responsible for such effects being phenolic acids and flavonoids.

Himalayan flora is also a rich source of secondary metabolites and particularly has high contents of polyphenols. Many studies have proved that plant species from higher altitudes contain high and diverse polyphenolic forms. Among the Himalayan plants, *Aegle marmelos*, *Ampelocissus latifolia*, *Artemisia sp.*, *Berberis asiatica*, *Bergenia ciliate*, *Dendrobenthamia capitata*, *Fagopyrum esculentum*, *Ficus palmata*, *Ficus subincisa*, *Grewia optiva*, *Hippophae rhamnoides*, *Hypecoum leptocarpum*, *Hypericum perforatum*, *Leea asiatica*, *Meconopsis aculeata Royle*, *Morus alba*, *Morus serrata*, *Nardostachys jatamansi*, *Paris polyphylla*, *Pinus Species*, *Podophyllum hexandrum*, *Potentilla fulgens*, *Prunus cerasoides*, *Pyracantha crenulata*, *Reinwardtia indica*, *Rubus ellipticus*, *Satyrium nepalense*, *Saussurea obvallata*, *Taxus wallichiana*, *Viburnum mullaha*, *Vitis jacquemontii*, *Ziziphus mauritiana*, *Ziziphus nummularia*, and *Vaccinium glaucoalbum* have been reported to have high polyphenolic content with rich biological activities (Prakash et al. 2007; Kaur et al. 2009; Ratan and Kothiyal 2011; Singh et al. 2015; Kundu et al. 2016; Feng et al. 2017; Mishra et al. 2018; Mohd et al. 2018; Painuli et al. 2018; Bahukhandi et al. 2019; Semwal and Painuli 2019; Singh et al. 2019; Rawat et al. 2019; Belwal et al. 2020; Gauchan et al. 2020; Tewari et al. 2020).

5 Biological Activities

At present, the earth's population exceeds 7 billion and is continuously increasing at the rate of 1.05% per year, and as a consequence, humans have directly or indirectly influenced almost all parts of the planet (Vitousek et al. 1997; Lindahl and Grace 2015). The rise in anthropogenic activities not only influences the planet's environment but also triggers human health problems (Myers and Patz 2009). There are a number of factors, like food and water scarcity, climate change, globalization, urbanization, among others, that are a root cause of diseases and disorders in humans. According to the WHO Report in 2016, ischemic heart disease, stroke, respiratory infections, cancer, diabetes, and tuberculosis are some of the diseases with highest mortality rates. The factors responsible for such disorders can be intrinsic (e.g., genetic disorders, malfunctioning of the immune system, and hormonal imbalance) and extrinsic (e.g., radiations, harmful chemicals, bacteria, viruses, and fungi). Presently, in our day-to-day life, we are more exposed to these external factors, especially harmful radiations, chemicals, and mutated pathogens, like multidrug resistance bacteria and viruses, like severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), due to which we suffer from deadly diseases.

The Himalayan region is one of the major habitats for medicinally important plant species for millennia. Dhar (2002) reported that the Himalayan region has a rich biodiversity, with around 21 vegetation types, 11 forest formations, and 10 forest types. The diverse climatic and geological conditions of the Himalayas are responsible for different types of flora and active compounds found in them, accountable for multiple medicinal properties. As previously referred, Himalayan plant species have remarkable antioxidant, anticancer, antimicrobial, antidiabetic, antiparasitic, analgesic, neuroprotective, antihepatotoxic, antihypertensive, anti-inflammatory, antiallergic, and anti-stress abilities (Khare 2008; Joshi et al. 2016). For example, *Aconitum heterophyllum* possesses antioxidant, anti-inflammatory, alexipharmic, antiflatulent, and analgesic effects, while the diterpenoid alkaloid isolated from the plant shows antioxidant and anticholinesterase properties (Ahmad et al. 2017; Paramanick et al. 2017). On the other hand, *Arctium lappa* is reported to possess anticancer, hepatoprotective, antidiabetic, anti-inflammatory, and antihuman immunodeficiency virus (HIV) properties (Chan et al. 2011; Gao et al. 2018). *Atropa acuminata* ethanol extract has revealed anti-arthritic effects, while the plant-derived phytoconstituents possess anticholinergic, antimicrobial, and anti-inflammatory activities and have wide medicinal uses in cardiology, gastroenterology, and ophthalmology (Rahman et al. 2018). *Berberis aristata* is reported to have antidiarrheal, hepatoprotective, antimicrobial, anticancer, antidiabetic, antiplatelet activating factor (paf), cardiotonic, and anti-inflammatory effects (Potdar et al., 2012). *Dioscorea deltoidea* is used for its prominent therapeutic effects in solving female reproductive system problems, central nervous system (CNS) and skin diseases, autoimmune diseases, oncology, cardiovascular system, bones and joint diseases, and metabolic disorders (Dangwal and Chauhan 2015). *Hedychium spicatum* holds anti-inflammatory, anti-asthmatic, anti-allergic, analgesic, antiulcer, hepatoprotective, antihyperglycemic, anticancer, and cytotoxic effects (Rawat et al. 2018). *Nardostachys jatamansi* is reported to possess antifungal, hepatoprotective, CNS, anticonvulsant, neuroprotective, anti-Parkinson's, and antidiabetic activities (Purnima and Kothiyal 2015). *Picrorhiza kurrooa* has antioxidant, antimicrobial, hepatoprotective, antimutagenic, and anticancer activities (Masood et al. 2015). Podophyllotoxin is an active compound from *P. hexandrum* used in the synthesis of the anticancer drugs etoposide and teniposide (Giri and Narasu 2000). *Rhododendron arboreum* possesses antioxidant, adaptogenic, anti-inflammatory, antinociceptive, hepatoprotective, antidiabetic, cardioprotective, antimicrobial, and immunomodulatory activities (Popescu and Kopp 2013; Painuli et al. 2018). *Swertia chirayita* exhibits a broad range of bio-medicinal properties, like antiviral, antidiabetic, anti-inflammatory, anticancer, antioxidant, and antimicrobial effects (Kumar and Van Staden 2016). In addition, *Artemisia*, *Cinnamomum*, *Cymbopogon*, *Junipers*, *Nepeta*, *Origanum*, and *Valeriana* species are some other important plant genus from the Himalayan region with a wide range of polyphenols and with significant biomedicinal activities (Joshi et al. 2016). Different biological applications of the plants are presented in Fig. 1.

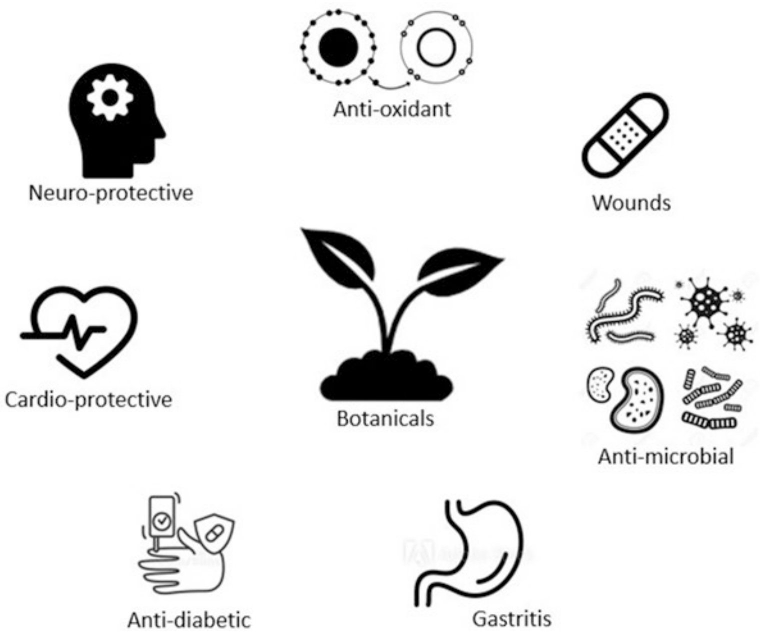

Fig. 1 Different biological applications of the plants

6 Pharmacological Effects of Himalayan Plant-derived Phytochemicals

6.1 Anticancer Activity

Cancer is considered the second major cause of mortality worldwide. Broadly, it not only affects the mental and physiological status of individuals but also has a huge social impact on the worldwide economy. Cancer therapy seems to be difficult, as most existing drugs and treatments are not very potent in conferring complete protection against the disease. The major steps involved in anticancer drug development are to assess both safety and efficacy in human models through clinical trials. Despite the huge amount of molecules with promising potential, from these studies, normally consisting of 4 phases (Phase I, II, III, and IV), unfortunately only one of every 5000–10,000 anticancer drugs get approval from the FDA, and only 5% of oncology drugs enter the phase I clinical trial (Paul et al. 2010; Petsko 2010; Shibue and Weinberg 2017; Bedard et al. 2020). Thus, the developmental cost of synthetic anticancer agents is extremely high; however, it can be reduced by introducing plant-based anticancer agents. Plant-derived active compounds have been detected to be effective in experimental and clinical trials against cancer. For example, the compound genistein (isoflavone) extracted from legumes and used for the treatment of various diseases including breast cancer, osteoporosis, obesity, and menopause reveals to be safe and effective at low cost (Zhang et al. 2020). In addition, Vincristine (*Catharanthus roseus*), Vinblastine (*Catharanthus roseus*), 5-Fluorouracil (*Withania somnifera*), Paclitaxel (*Taxus brevifolia*), Bullatacin (*Annona squamosa*), Theabrownin (*Camellia sinensis*), Solamargine (*Solanum nigrum*), Psoralidin (*Psoralea corylifolia*), Kaempferol galactoside (*Bauhinia variegata*), Skimmianine (*Aegle marmelos*), Podophyllotoxin (*Podophyllum hexandrum*), and Plumbagin (*Plumbago zeylanica*), among others, are some important anticancer phytochemicals extracted from plant species found in the Himalayan region (Ashraf 2020). **Table 3** lists the anticancer effects of some Himalayan plants.

6.2 Neuroprotective Activity

Neurodegenerative diseases comprise an anomalous group of disorders that are described by continuous declining or worsening of the peripheral nervous system or CNS structure and function. These neurodegenerative diseases are basically age dependent (Heemels 2016), with Alzheimer’s disease (AD) and Parkinson's disease (PD) being the most common, despite Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), spinocerebellar ataxias, and frontotemporal dementia being increasingly diagnosed.

AD is a progressive and irreversible brain disorder that gradually damages the memory and thinking skills and eventually results in inability to perform simple tasks. PD is characterized by a continuous loss of dopamine resulting in movement disorder, rigidity, and tremor, as well as neuron demise in cholinergic and catecholaminergic nuclei. Sparreboom et al. (2004) reported that a huge population of Australia, Europe, and North America are using plant-derived medicines for treating such conditions. Although many modern medicines are available in the market for neurodegenerative diseases, plant-based drugs have also left their promising impression in this field. In fact, among the Himalayan flora, *Artemisia absinthium*, *Bergenia ciliate*, *Centella asiatica*, *Crocus sativus*, *Curcuma longa*, *Elaeagnus umbellata*, *Lindera neesiana*, *Myrica esculenta*, *Panax ginseng*, *Swertia chirayita*, *Valeriana officinalis*, and *W. somnifera* are some examples of plants with remarkable neuroprotective abilities (Table 4).

6.3 Antidiabetic Activity

Diabetes is a chronic metabolic disease with a huge public health impact (Modak et al. 2007; Osadebe et al. 2014) that results from either insulin dysfunction or insulin deficiency in the body. Currently, there are three major types of diabetes, type I, type II, and gestational diabetes, which are responsible for sickness and premature fatality rate (Cade 2008). Indeed, diabetes is considered as a fifth leading cause of death in the twenty-first century, and as per data, more than 2.8% of the world’s

Table 3 In vitro and in vivo anticancer effects of plants from the Himalayan region

Plant species and used part	Used Doses	% Inhibition	Used model (In vitro, In vivo)	References
Aconitum heterophyllum Wall.; (Roots, Areal part)	50[a]	12–65, 4–36	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Albizia lebbeck (L.) Benth.; (Leaves)	12.5–200[a]	6–88	In vitro (HT-29, MCF-7)	Aditya et al. (2014)
Annona squamosa L.; (Seed)	33.8[a]	50	In vitro (KB cells)	Biba et al. (2013)
Annona squamosa L.; (Seed)	0.25–13[a]	50	In vitro (A-549, Hela, MCF-7, Hep G2)	Chen et al. (2012)
Arisaema flavum (Forssk.) Schott; (Whole plant)	500[a]	1.2–83	In vitro (MCF-7)	Nisa et al. (2011)
Arnebia euchroma (Royle) I.M. Johnst.; (NA)	2.7–6.8[a]	50	In vitro (A-549, Bel-7402, MCF-7, LLC)	Xiong et al. (2009)
Artemisia argyi H. Lév. & Vaniot; (Leaves)	10[a]	75	In vitro (Hela)	Lee et al. (2005)
Asclepias curassavica L.; (Areal parts)	0.02–0.69[a]	50	In vitro (HepG2)	Li et al. (2009)
Azadirachta indica A. Juss.; (Leaves)	250–500[b]	85	In vivo (Swiss male mice)	Paul et al. (2011)
Azadirachta indica A. Juss; (Leaves)	10[a]	30–60	In vitro (MCF-7)	Bibi et al. (2012)
Berberis lycium Royle; (Areal part)	50[a]	9–81	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Butea monosperma (Lam.) Taub.; (Flowers)	0.1–10[a]	50	In vitro (Huh7, HepG2, AML12 [CRL 2254])	Choedon et al. (2010)
Butea monosperma (Lam.) Taub.; (Flowers)	100–400[b]	80	In vivo (Transgenic mouse model [X15-myc])	Choedon et al. (2010)
Carissa spinarum L.; (Fruits)	200–500[a]	65–99	In vitro (MCF-7)	Sahreen et al. (2013), Nisa et al. (2013)
Centella asiatica (L.) Urb.; (Whole plant)	10–82[a]	25–95	In vitro (MCF-7)	Babykutty et al. (2009)
Centella asiatica (L.) Urb.; (Whole plant)	50[b]	50	In vivo (Swiss male mice)	Jayashree et al. (2003)
Dianthus superbus L.; (Aerial Parts)	20.5–200[a]	50	In vitro (Bel-7402, HepG2, HeLa)	Yu et al. (2007)
Euonymus hamiltonianus Wall.; (Berries, areal part)	50[a]	22–81, 10–75	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Euphorbia wallichii Hook.; (Roots, areal part)	50[a]	24–62, 27–84	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)

(continued)

Table 3 (continued)

Plant species and used part	Used Doses	% Inhibition	Used model (In vitro, In vivo)	References
Ficus carica L.; (Roots)	50[a]	16–87	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Ligustrum lucidum L.; (Berries)	50[a]	1–34	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Semecarpus anacardium L. f.; (Kernels)	0.1–5.9[a]	50	In vitro (CEM, CEM/VLB, MCF-7, MCF-10 A, SW620, SW620Ad300)	Nair et al. (2009)
Semecarpus anacardium L. f.; (Oil)	0.1–100[a]	10–90	In vitro (HL-60, K-562, MCF-7, HeLa)	Chakraborty et al. (2004)
Solanum americanum Mill.; (Fruits)	1.25–100[a]	16–80	In vitro (HeLA Vero, SMMC-7721, HepG2, MCF-7)	Patel et al. (2009), Ding et al. (2012), Son et al. (2003)
Syzygium cumini (L.) Skeels; (Fruits)	100[a]	25–70	In vitro (AML)	Afify et al. (2011)
Taxus wallichiana Zucc.; (Stem bark)	0.063–50[a]	50–90	In vitro (MCF-7, MDA-MB-231, HEK-293, COLO-320, $CaCO_2$)	Reddy et al. (2009)
Taxus wallichiana Zucc.; (Stem bark)	10[b]	60–100	In vitro (Virgin female Sprague Dawley rats)	Reddy et al. (2009)
Viburnum grandiflorum Wall. ex DC.; (Berries)	50[a]	1–19	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Viscum album L.; (Aerial)	50[a]	5–21	In vitro (A-549, MCF-7, MiaPaca, HCT-116)	Mushtaq et al. (2017)
Xanthium strumarium L.; (Roots)	0.161–0.434[a]	13.55–67.93	In vitro (MCF-7, SKMEL cell)	Milton et al. (2013)
Xanthium strumarium L.; (Roots)	20–400[b]	73–92	In vivo (Swiss male mice)	Milton et al. (2013)

[a]Indicates μg/mL
[b]Indicates mg kg^{-1} day^{-1}

population is suffering from diabetes, and it is expected that the number of cases will raise to more than 5.4% by 2025 (Mukesh and Namita 2013; Kazi 2014). Pharmacotherapy, diet therapy, and insulin therapy are the most common modern therapeutic strategies for such conditions. Although modern treatments are available, complete treatment and prevention of diabetes still seem impossible due to some disadvantages, including side effects, drug resistance, and even drug-related toxicity (Kooti et al. 2016). Therefore, plant-based drugs have been highly recommended for the treatment of such affections (Kooti et al. 2015). Phytochemicals, like flavonoids, alkaloids, terpenoids, and glycosides, have shown interesting antidiabetic effects (Afrisham et al. 2015), with some Himalayan plants revealing an interesting potential (Table 5).

Table 4 Bioactive compounds with neuroprotective effects

S.N	Neuroprotective bioactive compounds	References
1	6-MSITC	Morroni et al. (2018)
2	Berberine	Velmurugan et al. (2018), Yuan et al. (2019)
3	Caffeine	Hussain et al. (2018), Pohl and Lin (2018)
4	Cannabidiol	Watt and Karl (2017)
5	Catechin	Hajialyani et al. (2019)
6	Curcumin	Khazdair et al. (2019), Manzinea et al. (2019)
7	Delta-9-tetrahydrocannabinol	Maurya and Velmurugan (2018)
8	Epigallocatechin-3-gallat	Manzinea et al. (2019)
9	Galantamine	Hussain et al. (2018), Libro et al. (2016)
10	Hesperidin	Hajialyani et al. (2019)
11	Huperzine A	Hussain et al. (2018), Libro et al. (2016)
12	Huperzine A	Wang et al. (2005)
13	Isorhynchophylline	Hussain et al. (2018)
14	Moringin	Libro et al. (2016)
15	Morphine	Hussain et al. (2018), Libro et al. (2016)
16	Nicotine	Libro et al. (2016), Hussain et al. (2018)
17	Physostigmine	Omar et al. (2017), Hussain et al. (2018)
18	Piperine	Hussain et al. (2018)
19	Quercetin	Hajialyani et al. (2019)
20	Resveratrol	Colica et al. (2018), Wang et al. (2018)
21	Rosmarinic acid	Fachel et al. (2019)
22	Sulforaphane	Libro et al. (2016), Pohl and Lin (2018)

6.4 Antimicrobial Activity

Worldwide, the burden of infectious diseases is increasing at a frightening rate, causing death in millions (Bhutta et al. 2014). To fight such infectious diseases, many modern medicines have become available in the market, but along with their therapeutic activity, severe side effects have also been reported. In addition, currently, an increasing amount of multidrug-resistant microorganisms (MDRM) have become a key matter of concern. Therefore, it becomes an urgent and important need to develop powerful and safe drugs against microbial diseases at the right time.

Worldwide, many research groups are showing greater interest in developing antimicrobial drugs from plant source as they are more effective against microbial infections and have been safer for both humans and the environment, along with that where existing antibiotics showed no or less activity against multidrug resistance microorganisms (MDRM), plant-based drugs naturally boost immunity and show promising activity against MDRM (Subramani et al. 2017). A wide range of phytoconstituents, such as phenols, flavonoids, tannins, quinine, and coumarins, have been reported with significant antimicrobial activities (Cushnie and Lamb 2005; Kurhekar 2016; Cueva et al. 2010; Al-Majedy et al. 2017; Scalbert 1991; Antika

Table 5 Himalayan plant species with antidiabetic potential

S.N	Species name	References
1	*Ampelopsis grossedentata* (Hand.-Mazz.)	Wan et al. (2017)
2	*Centella asiatica* (L.) Urb.	Abas et al. (2016)
3	*Coptis chinensis* Franch.	Gu et al. (2010)
4	*Curcuma longa* L.	Tranchida et al. (2015)
5	*Gardenia jasminoides* J. Ellis	Shen et al. (2016)
6	*Zanthoxylum armatum* DC.	Khan et al. (2020)
7	*Acacia catechu* (L.f.) Willd.	Rao et al. (2015)
8	*Acacia modesta* Wall.	Jawla et al. (2011)
9	*Acanthopanax senticosus* (Rupr. & Maxim.)	Saito et al. (2016)
10	*Allium sativum* L.	Sudha et al. (2011)
11	*Aloe vera* (L.) Burm.f.	Rashidi et al. (2013)
12	*Amaranthus cruentus* L.	Kunyanga et al. (2012)
13	*Angelica sinensis* (Oliv.) Diels	Zhi (2009)
14	*Artemisia parviflora* Roxb. ex D.Don	Ahuja et al. (2011)
15	*Artemisia princeps* Pamp.	Yamamoto et al. (2011)
16	*Artemisia gmelinii* Weber ex Stechm.	Yuan et al. (2010)
17	*Primula denticulate* Sm.	Singh et al. (2014)
18	*Abrus precatorius* L.	Joshi (2011)
19	*Astragalus membranaceus* (Fisch.) Bunge	Fu et al. (2014)
20	*Berberis aristata* DC.	Khan et al. (2016)
21	*Berberis vulgaris* L.	Rahimi-Madiseh et al. (2017)
22	*Butea frondosa* Roxb.	Kumar and Malik (2012)
23	*Butea monosperma* (Lam.) Taub.	Rao et al. (2015)
24	*Citrus sinensis* (L.) Osbeck	Shakthi Deve et al. (2014)
25	*Curcuma longa* L.	Sukandar et al. (2015)
26	*Dioscorea opposita* Thunb.	Xie and Du (2011)
27	*Embelia ribes* Burm.f.	Ratnasooriya et al. (2011)
28	*Ficus amplissima* Sm.	Arunachalam and Parimelazhagan (2013)
29	*Ficus racemosa* L.	Trinh et al. (2016)
30	*Zaleya decandra* (L.) Burm.f.	Meenakshi et al. (2010)
31	*Viola odorata* L.	Rao et al. (2015)
32	*Ocimum sanctum* L.	Upadhyay (2017)
33	*Paeonia lactiflora* Pall.	Yoon et al. (2014)
34	*Rheum emodi* Wall.	Arvindekar et al. (2015)
35	*Solanum nigrum* L.	Sohrabipour et al. (2014)
36	*Swertia chirayita* (Roxb.) Buch.-Ham.	Kar et al. (2003)
37	*Syzygium jambolanum* (Lam.) DC.	Baliga et al. (2013)
38	*Taxus baccata* L.	Rao et al. (2015)
39	*Terminalia arjuna* (Roxb. ex DC.)	Rafe (2017)
40	*Tinospora cordifolia* (Willd.) Miers	Kar et al. (2003)
41	*Vaccinium bracteatum* Thunb.	Qian et al. (2017)

(continued)

Table 5 (continued)

S.N	Species name	References
42	*Withania coagulans* (Stocks) Dunal	Maurya et al. (2008)
43	*Withania somnifera* (L.) Dunal	Jonathan et al. (2015)
44	*Zanthoxylum armatum* DC.	Thakur et al. (2016)
45	*Zanthoxylum humile* Waterm.	Pamhidzai and Isaac (2013)

et al. 2020). Moreover, from a long back, the Himalayan region communities have been using native plant species to treat different microbial diseases from which some important species are mentioned in Table 6.

6.5 Antioxidant Activity

Recently, more interest has arisen toward natural antioxidants and their role in human health maintenance and disease prevention. Briefly, in healthy individuals, antioxidants regulate the homeostasis between free radicals' production and scavenging; however, antioxidants depletion results in higher production of free radicals triggering oxidative stress, which ultimately leads to several disturbances in the whole organism. As a matter of fact, oxidative stress is responsible for oxidation at both cell and molecular levels and further leads to cells/tissues damage being associated with a plethora of diseases, like neurodegenerative, metabolic, osteoarticular, cardiovascular and immune system disorders, and even cancer (Jonah 2013).

The Himalayan medicinal plants are highly acknowledged for their nutritional phytoconstituents and antioxidant effects. Indeed, phytoconstituents, like flavonoids, lignans, catechins, phenols, coumarins, isocatechins, isoflavones, and anthocyanins, have been widely recognized for their antioxidant properties (Prior 2003; Cai et al. 2004).

The determination of the antioxidant potential of plants, its derived extracts, and even isolated constituents can be analyzed by different in vitro (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid [ABTS], 2,2-diphenyl-1-picrylhydrazyl [DPPH], oxygen radical absorbance capacity (ORAC), thiobarbituric acid reactive substances [TBARS], ferric reducing antioxidant power [FRAP] and Trolox equivalent antioxidant capacity [TEAC] assays) and in vivo methods, with a series of medicinal plants already been studied by different research groups around the world. As some examples, the crude methanol extracts from *Bunium persicum* (seeds), *Dactylorhiza hatageria* (tubers), *Satyrium nepalense* (tubers), *Viscum album* (fruits), and *Urtica dioica* (leaves) have revealed interesting antioxidant effects by the DPPH assay, with IC_{50} values of 0.09, 0.21, 0.04, 0.42, and 0.14 mg/mL, respectively (Kawra et al. 2020). Also, the methanol extracts from *Trillium govanianum* rhizome, leaf, and stem showed maximum DPPH, ABTS, and FRAP activities with 16.06 milli molar ascorbic acid extract/gram fresh weight (mM

Table 6 Antioxidant and antimicrobial studies in different Himalayan regions

S.N	Plant species name	Antimicrobial profiling (ZOI)		Antioxidant profiling		References
1	*Acorus calamus* L.	*Bacillus subtilis*	6–10[a]	NT		Rawat et al. (2016)
		Staphylococcus aureus	7[a]			
		Micrococus luteus	6–9[a]			
		Escherichia coli	6–9[a]			
2	*Acorus calamus* L.	*Escherichia coli*	0.40[b]	DPPH	01.61–02.16[d]	Verma et al. (2021)
		Klebsiella pneumoniae	0.40[b]	FRAP	76.76–91.68[c]	
		Salmonella typhimurium	0.80[b]			
		Staphylococcus aureus	0.40[b]			
		Pseudomonas aeruginosa	0.20[b]			
3	*Bunium persicum* Boiss.	NT		DPPH	0.09[e]	Kawra et al. (2020)
4	*Dactylorhiza hatagirea (D.Don) Soó*	NT		DPPH	0.21[e]	Kawra et al. (2020)
5	*Ficus palmata* Forssk	NT		ABTS	114.03–265.14[f]	Tewari et al. (2020)
				DPPH	80.97–175.08[f]	
				FRAP	139.89–364.84[f]	
				CUPRAC	228.86–344.64[f]	
6	*Fraxinus micrantha* Lingelsh	*Agrobacterium tumefaciens*	16[a]	DPPH	43.93[d]	Kumar and Sati (2020)
		Bacillus subtilis	22[a]	H_2O_2	68.90[d]	
		Erwinia chrysanthemi	19[a]	FRAP	38.27[h]	
		Escherichia coli	18[a]			
		Xanthomonas phaseoli	11[a]			
7	*Habenaria intermedia* D.Don	*Bacillus subtilis*	6–11[a]	NT		Rawat et al. (2016)
		Staphylococcus aureus	6–9[a]			
		Micrococus luteus	6–9[a]			

(continued)

Table 6 (continued)

S.N	Plant species name	Antimicrobial profiling (ZOI)		Antioxidant profiling		References
		Escherichia coli	6–11[a]			
8	*Hedychium spicatum* Sm.	*Bacillus subtilis*	6–7[a]	NT		Rawat et al. (2016)
		Staphylococcus aureus	0[a]			
		Micrococus luteus	6–9[a]			
		Escherichia coli	6–9[a]			
9	*Origanum vulgare* L.	NT		DPPH	5.85–72.70[d]	Bhatt et al. (2020)
				FRAP	45.7–266.0[d]	
				Iron-chelating activity	51.4–146.0[d]	
10	*Pinus gerardiana* Wall. ex D.Don	*Escherichia coli*	15–19[a]	DPPH	54.8–71.2[d]	Sharma et al. (2020)
		Pseudomonas aeruginosa	20–25[a]	NO_2	18.7–76.3[d]	
		Staphylococcus aureus	17–23[a]			
		Klebsiella pneumoniae	17–23[a]			
11	*Pinus roxburghii Sarg.*	*Escherichia coli*	15–18[a]	DPPH	51.7–67.3[d]	Sharma et al. (2020)
		Pseudomonas aeruginosa	17–23[a]	NO_2	59.0–71.2[d]	
		Staphylococcus aureus	17–20[a]			
		Klebsiella pneumoniae	18–22[a]			
12	*Pinus wallichiana A.B.Jacks.*	*Escherichia coli*	13–17	DPPH	58.4–69.8[d]	Sharma et al. (2020)
		Pseudomonas aeruginosa	15–22	NO_2	62.0–73.0[d]	
		Staphylococcus aureus	15–21			
		Klebsiella pneumoniae	15–21			
13	*Rhododendron arboreum*	NT		DPPH	91.67[c]	Painuli et al. (2016)
				ABTS	96.65[c]	
				FRAP	429.07[j]	
				TRP	292.27[k]	
14	*Rhododendron campanulatum*	NT		DPPH	91.27[c]	Painuli et al. (2016)

(continued)

Table 6 (continued)

S.N	Plant species name	Antimicrobial profiling (ZOI)		Antioxidant profiling		References
				ABTS	96.53[c]	
				FRAP	378.73[j]	
				TRP	283.26[k]	
15	*Roscoea procera* Wall.	NT		ABTS	1.47[i]	Rawat et al. (2017)
				DPPH	0.75[i]	
				FRAP	1.01[i]	
16	*Roscoea procera* Wall.	*Bacillus subtilis*	6–9[a]	NT		Rawat et al. (2016)
		Staphylococcus aureus	6–10[a]			
		Micrococus luteus	6–9[a]			
		Escherichia coli	6–12[a]			
	Rubia cordifolia L.	*Staphylococcus aureus*	22–32[a]	NT		Boominathan et al. (2020)
		Escherichia coli	21–32[a]			
17	*Satyrium nepalense D.Don*	NT		DPPH	0.04[e]	Kawra et al. (2020)
18	*Saussurea obvallata* (DC.) Edgew.	*Pseudomonas aeruginosa*	13.90–20.50[a]	DPPH	29.25–82.88[c]	Semwal and Painuli (2019)
		Escherichia coli	10.83–13.90[a]	H_2O_2	39.75–41.05[c]	
		Staphylococcus aureus	12.83–20.43[a]			
		Klebsiella pneumoniae	11.53–19.90[a]			
		Candida albicans	13.90–14.57[a]			
		Candida glabrata	15.43–15.90[a]			
		Candida tropicalis	8.30–13.17[a]			
19	*Tagetes minuta* L.	*Micrococus luteus*	3–8[a]	NT		Walia et al. (2020)
		Staphylococcus aureus	3–11.33[a]			
		Klebsiella pneumoniae	1.33–4.00[a]			
		Pseudomonas aeruginosa	0.50–1.00[a]			
20	*Thalictrum foliolosum* DC.	*Saccharomyces cerevisiae*	13–20[a]			Kumar et al. (2020)

(continued)

Table 6 (continued)

S.N	Plant species name	Antimicrobial profiling (ZOI)		Antioxidant profiling		References
		Candida albicans	11–18[a]			
		Candida albicans	11–19[a]			
21	*Thymus linearis* Benth.	*Staphylococcus aureus*	5–16[a]	NT		Kumar et al. (2019)
		Staphylococcus epidermidis	3–21[a]			
		Enterococcus faecalis	2–10[a]			
		Staphylococcus epidermidis	4–25[a]			
		Candida albicans	5–28[a]			
		Candida tropicalis	6–25[a]			
		Candida glabrata	8–24[a]			
22	*Urtica diocia* L.	NT		DPPH	0.42[e]	Kawra et al. (2020)
23	*Valeriana jatamansi* Jones	NT		ABTS	2.60–6.82[g]	Jugran et al. (2020)
				DPPH	2.07–6.88[g]	
				FRAP	3.64–14.75[g]	
24	*Valeriana jatamansi* Jones	*Bacillus subtilis*	6–11[a]	NT		Rawat et al. (2016)
		Staphylococcus aureus	6–8[a]			
		Micrococus luteus	6–9[a]			
		Escherichia coli	6–9[a]			
25	*Viscum album* L.	NT		DPPH	0.14[e]	Kawra et al. (2020)
26	*Zanthoxylum armatum* DC.	*Bacillus subtilis*	15.72–17.04[a]	NT		Phuyal et al. (2020)

NT not tested
[a]Zone of inhibition in mm
[b]MIC value
[c]Percent
[d]IC_{50} value in μg/mL
[e]IC_{50} value in mg/mL
[f]mg TE/g
[g]mM/100g AAE dw
[h]AAE/g dry
[i]mM ascorbic acid equivalent/100 g dry weight
[j]μg TE/g
[k]μg AE/g

AAE/g fw), 4.39 mM AAE/g fw, and 2.17 mM AAE/g fw, respectively (Kundra et al. 2020). Moreover, Painuli et al. (2018) reported antioxidant effects of *Rhododendron arboreum* and *Rhododendron campanulatum* leaves aqueous and methanol extract by DPPH, FRAP, ABTS, and total reducing power assay. *Saussurea obvallata* leaves and flowers methanol and water extracts also displayed DPPH and H_2O_2 free radical scavenging activities (Semwal and Painuli 2019). Other plant extracts, such as *Acorus calmus* (rhizome), *Habenaria intermedia* (tuber), *Hedychium spicatum* (rhizome), *Roscoea procera* (rhizome), and *Valeriana jatamansi* (root), also revealed interesting antioxidant effects through DPPH, ABTS, and FRAP assays (Rawat et al. 2017). Few other antioxidant-rich Himalayan plant species are listed in Table 6.

7 Conclusion and Upcoming Perspectives

The Himalayan region is famous worldwide for its unique, diverse, valuable, and endemic flora and fauna. Several highly valuable medicinal plants have been documented from this region, and these plants play a notable role in the human health care system. Many research groups have been increasingly devoted to the study of the therapeutic applications of a plethora of plants as well as on phytoconstituents' identification and related mechanism of action. However, despite the advance stated so far, many phytochemicals remain to be identified, and the mechanism of action of many others against various diseases is still unclear; therefore, much research is needed in this regard. On the other hand, medicinal plants in the Himalayan region face erratic harvests due to the growing demand for essential oils, herbal preparations, and drug formulation due to which many important plants have been extinct and many are on the verge of extinction. Thus, exploring more data on such plant species and their respective properties is an important issue, while protection and sustainable conservation too.

Acknowledgments N. Cruz-Martins acknowledges the Portuguese Foundation for Science and Technology under the Horizon 2020 Program (PTDC/PSI-GER/28076/2017).

Conflict of Interests The authors declare no conflict of interests.

References

Abas MF, Khatib A, Perumal V, Suppaiah V, Ismail A, Hamid M, Shaari K, Lajis NH (2016) Metabolic alteration in obese diabetes rats upon treatment with *Centella asiatica* extract. J Ethnopharmacol 180:60–69. https://doi.org/10.1016/j.jep.2016.01.001

Adeyemi MMH (2011) A review of secondary metabolites from plant materials for post-harvest storage. Int J Pure Appl Sci Technol 6(2):94–102

Aditya SJ, Naresh KL, Mokkapati A (2014) Evaluation of in vitro cytotoxicity of *Andrographis paniculata*, *Duranta serratifolia* and *Albizzia lebbeck* whole plant extracts by MTT assay against MCF-7and HT-29 cell lines. Curr Res Microbiol Biotechnol 2:351–353

Adnan M, Ali S, Sheikh K, Amber R (2019) Review on antibacterial activity of Himalayan medicinal plants traditionally used to treat pneumonia and tuberculosis. J Pharm Pharmacol 71:1599–1625. https://doi.org/10.1111/jphp.13156

Afify MRA, Fayed AS, Shalaby EA, El-Shemy AH (2011) *Syzygium cumini* (pomposia) active principles exhibit potent anticancer and antioxidant activities. Afr J Pharm Pharmaco 5:948-56. 10.5897.

Afrisham R, Aberomand M, Ghaffari MA, Siahpoosh A, Jamalan M (2015) Inhibitory effect of *Heracleum persicum* and *Ziziphus jujuba* on activity of alpha-amylase. J Bot. https://doi.org/10.1155/2015/824683

Ahmad H, Ahmad S, Shah SA, Latif A, Ali M, Khan FA, Tahir MN, Shaheen F, Wadood A, Ahmad M (2017) Antioxidant and anticholinesterase potential of diterpenoid alkaloids from *Aconitum heterophyllum*. Bioorg Med Chem 25(13):3368–3376

Ahuja J, Suresh J, Paramakrishnan N, Mruthunjaya K, Naganandhini MN (2011) An ethnomedical, phytochemical and pharmacological profile of *Artemisia parviflora* roxb. J Essent Oil Bear Plant 14:647–657. https://doi.org/10.1080/0972060X.2011.10643985

Al-Majedy YK, Kadhum AA, Al-Amiery AA, Mohamad AB (2017) Coumarins: the antimicrobial agents. Sys Rev Pharm 8(1):62

Ambu G, Chaudhary RP, Mariotti M, Cornara L (2020) Traditional uses of medicinal plants by ethnic people in the Kavrepalanchok district, Central Nepal. Plan Theory 9:759. https://doi.org/10.3390/plants9060759

Antika LD, Triana D, Ernawati T (2020) Antimicrobial activity of quinine derivatives against human pathogenic bacteria. IOP Conf Ser: Earth Environ Sci 462:012006. https://doi.org/10.1088/1755-1315/462/1/012006

Arunachalam K, Parimelazhagan T (2013) Antidiabetic activity of *Ficus amplissima* Smith. bark extract in streptozotocin induced diabetic rats. J Ethnopharmacol 147:302–310. https://doi.org/10.1016/j.jep.2013.03.004

Arvindekar A, More T, Payghan PV, Laddha K, Ghoshal N, Arvindekar A (2015) Evaluation of anti-diabetic and alpha glucosidase inhibitory action of anthraquinones from *Rheum emodi*. Food Funct 6:2693–2700. https://doi.org/10.1039/C5FO00519A

Ashraf MA (2020) Phytochemicals as potential anticancer drugs: time to ponder nature's bounty. Biomed Res Int. https://doi.org/10.1155/2020/8602879

Babykutty S, Padikkala J, Sathiadevan P, Vijayakurup V, Azis T, Srinivas P, Gopala S (2009) Apoptosis induction of *Centella asiatica* on human breast cancer cells. Afr J Trad CAM 6:9–16

Badri S, Basu VR, Chandra K, Anasuya D (2019) A review on pharmacological activities of alkaloids. World J Curr Med Pharmaceutical Res 1(6):230–234. https://doi.org/10.37022/WJCMPR.2019.01068.

Bahukhandi A, Sekar KC, Barola A, Bisht M, Mehta P (2019) Total phenolic content and antioxidant activity of *Meconopsis aculeata* Royle: a high value medicinal herb of Himalaya. Proc Natl Acad Sci India B 89(4):1327–1334

Baliga MS, Fernandes S, Thilakchand KR, D'Souza P, Rao S (2013) Scientific validation of the antidiabetic effects of *Syzygium jambolanum* DC (black plum), a traditional medicinal plant of India. J Altern Complement Med 19:191–197. https://doi.org/10.1089/acm.2011.0752

Bano A, Ahmad M, Hadda TB, Saboor A, Sultana S, Zafar M, Khan MP, Arshad M, Ashraf MA (2014) Quantitative ethnomedicinal study of plants used in the skardu valley at high altitude of Karakoram-Himalayan range, Pakistan. J Ethnobiol Ethnomed 10:43. https://doi.org/10.1186/1746-4269-10-43

Bedard PL, Hyman DM, Davids MS, Siu LL (2020) Small molecules, big impact: 20 years of targeted therapy in oncology. Lancet 395(10229):1078–1088

Belwal T, Pandey A, Bhatt ID, Rawal RS (2020) Optimized microwave assisted extraction (MAE) of alkaloids and polyphenols from *Berberis* roots using multiple-component analysis. Sci Rep 10(1):10. https://doi.org/10.1038/s41598-020-57585-8

Bhat JA, Kumar M, Pala NA, Shah S, Dayal S, Gunathilake C, Negi AK (2020) Influence of altitude on the distribution pattern of flora in a protected area of Western Himalaya. Acta Ecol Sin 40(1):30–43. https://doi.org/10.1016/j.chnaes.2018.10.006

Bhatt S, Tewari G, Pande C, Punetha D, Prakash O (2020) Antioxidative potential and compositional variation among *Origanum vulgare* L. collected from different districts of Kumaun Himalayas, Uttarakhand. J Essent Oil Res 32(2):121–131

Bhutta ZA, Sommerfeld J, Lassi ZS, Salam RA, Das JK (2014) Global burden, distribution, and interventions for infectious diseases of poverty. Infect Dis Poverty 3:21. https://doi.org/10.1186/2049-9957-3-21

Biba VS, Jeba MPW, Remani P (2013) Differential effects of *Annona squamosa* seed extracts: antioxidant, antibacterial, cytotoxic and apoptotic study. Int J Pharm Bio Sci 4:899–907

Bibi Y, Nisa S, Zia M, Waheed A, Ahmed S, Chaudhary MF (2012) In vitro cytotoxic activity of *Aesculus indica* against breast adenocarcinoma cell line (MCF-7) and phytochemical analysis. Pak J Pharm Sci 25:183–187

Boominathan S, Karthi V, Balakrishanan S (2020) Optimization of process parameters on color strength and antimicrobial activities of cotton fabric dyed with *Rubia cordifolia* extract. J Nat Fibers. https://doi.org/10.1080/15440478.2020.1818347

Bravo L (1998) Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. Nutr Rev 56(11):317–333

Bribi N (2018) Pharmacological activity of alkaloids: a review. Asian Journal of Botany 1(1):1–6

Cade WT (2008) Diabetes related microvascular and macrovascular diseases in the physical therapy setting. Phys Ther 88(11):1322–1335

Cai Y, Luo Q, Sun M (2004) Antioxidant activity and phenolic compounds of 112 traditional Chinese medicinal plants associated with anticancer. Life Sci 74:2157–2184

Calixto JB (2019) The role of natural products in modern drug discovery. An Acad Bras Ciênc. https://doi.org/10.1590/0001-3765201920190105

Chakraborty S, Roy M, Taraphdar AK, Bhattacharya RK (2004) Cytotoxic effect of root extract of *Tiliacora racemosa* and oil of *Semecarpus anacardium* nut in human tumour cells. Phytother Res 18:595–600. https://doi.org/10.1002/ptr.1501

Chan YS, Cheng LN, Wu JH, Chan E, Kwan YW, Lee SM, Leung GP, Yu PH, Chan SW (2011) A review of the pharmacological effects of *Arctium lappa* (burdock). Inflammopharmacology 19(5):245–254

Chaudhury RR, Rafei UM (2002) Traditional Medicine in Asia. World Health Organization Regional Office for South-East Asia New Delhi, India (ISBN 92 9022 2247).

Che CT, George V, Ijinu TP, Pushpangadan P, Andrae-Marobela K (2017) Traditional medicine. In: Pharmacognosy: fundamentals, applications and strategies. Academic Press, pp. 15–30. https://doi.org/10.1016/B978-0-12-802104-0.00002-0

Chen Y, Xu SS, Chen JW, Wang Y, Xu HQ, Fan NB, Li X (2012) Anti-tumor activity of *Annona squamosa* seeds extract containing annonaceous acetogenin compounds. J Ethnopharmacol 142:462–466. https://doi.org/10.1016/j.jep.2012.05.019

Cheynier V (2005) Polyphenols in foods are more complex than often thought. Am J Clin Nutr 81(1):223S–229S

Chhetri DR (2014) Medicinal plants of the Himalaya: production technology and utilization. Agrobios, India

Choedon T, Shukla SK, Kumar V (2010) Chemopreventive and anti-cancer properties of the aqueous extract of flowers of *Butea monosperma*. J Ethnopharmacol 129:208–213. https://doi.org/10.1016/j.jep.2010.03.011

Colica C, Milanovic M, Milic N, Aiello V, De Lorenzo A, Abenavoli L (2018) A systematic review on natural antioxidant properties of resveratrol. Natural Prod Commun 13:1195–1203

Cueva C, Moreno-Arribas MV, Martín-Álvarez PJ, Bills G, Vicente MF, Basilio A, Rivas CL, Requena T, Rodríguez JM, Bartolomé B (2010) Antimicrobial activity of phenolic acids against commensal, probiotic and pathogenic bacteria. Res Microbiol 161(5):372–382. https://doi.org/10.1016/j.resmic.2010.04.006

Cushnie TT, Lamb AJ (2005) Antimicrobial activity of flavonoids. Int J Antimicrob Agents 26(5):343–356

Cushnie TP, Cushnie B, Lamb AJ (2014) Alkaloids: An overview of their antibacterial, antibiotic-enhancing and antivirulence activities. Int J Antimicrob Agents 44:377–386. https://doi.org/10.1016/j.ijantimicag.2014.06.001

Dangwal LR, Chauhan AS (2015) *Dioscorea deltoidea* Wall. ex Griseb. A highly threatened Himalayan medicinal plant: an overview. Int J Pharma Bio Sci 6(1):452–460

Demasi S, Caser M, Lonati M, Cioni PL, Pistelli L, Najar B, Scariot V (2018) Latitude and altitude influence secondary metabolite production in peripheral alpine populations of the Mediterranean species *Lavandula angustifolia* Mill. Front Plant Sci 9:983. https://doi.org/10.3389/fpls.2018.00983

Detwiler RP, Hall CAS (1988) Tropical forests and the global carbon cycle. Science 239:42–47. https://doi.org/10.1126/science.239.4835.42

Dhar U (2002) Conservation implications of plant endemism in high-altitude Himalaya. Curr Sci 82(2):141–148

Ding X, Zhu FS, Li M, Gao SG (2012) Induction of apoptosis in human hepatoma SMMC-7721 cells by solamargine from *Solanum nigrum* L. J Ethnopharmacol 139:599–604. https://doi.org/10.1016/j.jep.2011.11.058

Egbuna C, Ifemeje JC, Udedi SC, Kumar S (2018) Introduction to phytochemistry. phytochemistry: volume 1: fundamentals, modern techniques, and applications. CRC Press, ISBN: 0429760337, 9780429760334

Eloff JN (1998) Which extractant should be used for the screening and isolation of antimicrobial components from plants? J Ethnopharmacol 60(1):1–8. https://doi.org/10.1016/S0378-8741(97)00123-2

Fachel FNS, Schuh RS, Veras KS, Bassani VL, Koester LS, Henriques AT, Braganhol E, Teixeira HF (2019) An overview of the neuroprotective potential of rosmarinic acid and its association with nanotechnology-based delivery systems: a novel approach to treating neurodegenerative disorders. Neurochem Int 122:47–58

Feng CY, Wang WW, Ye JF, Li SS, Wu Q, Yin DD, Li B, Xu YJ, Wang LS (2017) Polyphenol profile and antioxidant activity of the fruit and leaf of *Vaccinium glaucoalbum* from the Tibetan Himalayas. Food Chem 219:490–495

Ferrazzano G, Amato I, Ingenito A, Armando Z (2011) Pinto Gabriele and Pollio Antonino. Plant polyphenols and their anti-cariogenic properties: a review. Molecules 16:1486–1507. https://doi.org/10.3390/molecules16021486

Fowler MW (2006) Plants, medicines and man. J Sci Food Agric 86(12):1797–1804. https://doi.org/10.1002/jsfa.2598

Fu J, Wang Z, Huang L, Zheng S, Wang D, Chen S, Zhang H, Yang S (2014) Review of the botanical characteristics, phytochemistry, and pharmacology of *Astragalus membranaceus* (huangqi). Phytother Res 28:1275–1283. https://doi.org/10.1002/ptr.5188

Gao Q, Yang M, Zuo Z (2018) Overview of the anti-inflammatory effects, pharmacokinetic properties and clinical efficacies of arctigenin and arctiin from *Arctium lappa* L. Acta Pharmacol Sin 39(5):787–801

Gauchan DP, Kandel P, Tuladhar A, Acharya A, Kadel U, Baral A, Shahi AB, García-Gil MR (2020) Evaluation of antimicrobial, antioxidant and cytotoxic properties of bioactive compounds produced from endophytic fungi of Himalayan yew (*Taxus wallichiana*) in Nepal [version 2; peer review: 2 approved]. F1000Res 9:379. https://doi.org/10.12688/f1000research.23250.2

Gautam AK, Bhadauria R (2009) Homeopathic flora of Bilaspur district of Himachal Pradesh, India: a preliminary survey. Ethnobot Leaflets 1:14

Ghasemzadeh A, Ghasemzadeh N (2011) Flavonoids and phenolic acids: role and biochemical activity in plants and human. J Med Plant Res 5(31):6697–6703. https://doi.org/10.5897/JMPR11.1404

Giri A, Narasu ML (2000) Production of podophyllotoxin from *Podophyllum hexandrum*: a potential natural product for clinically useful anticancer drugs. Cytotechnology 34(1-2):17–26

Gu Y, Zhang Y, Shi X, Li X, Hong J, Chen J, Gu W, Lu X, Xu G, Ning G (2010) Effect of traditional Chinese medicine berberine on type 2 diabetes based on comprehensive metabonomics. Talanta 81:766–772. https://doi.org/10.1016/j.talanta.2010.01.015

Hajialyani M, Hosein Farzaei M, Echeverría J, Nabavi S, Uriarte E, Sobarzo-Sánchez E (2019) Hesperidin as a neuro-protective agent: a review of animal and clinical evidence. Molecules 24:648

Hajra PK, Rao RR (1990) Distribution of vegetation types in northwest Himalaya with brief remarks on phytogeography and floral resource conservation. Proc Indian Acad Sci (Plant Sci) 100:263–277. https://doi.org/10.1007/BF03053480

Han X, Shen T, Lou H (2007) Dietary polyphenols and their biological significance. Int J Mol 8(9):950–988

Hanuš LO, Hod Y (2020) Terpenes/ terpenoids in cannabis: are they important? Med Cannabis Cannabinoids 3:25–60. https://doi.org/10.1159/000509733

Harborne JB, Willians CA (2000) Advances in flavonoid research since 1992. Phytochem Oxford 55(6):481–504

Heemels MT (2016) Neurodegenerative diseases. Nature 539:179. https://doi.org/10.1038/539179a

Hong L, Guo Z, Huang K, Wei S, Liu B, Meng S, Long C (2015) Ethnobotanical study on medicinal plants used by Maonan people in China. J Ethnobiol Ethnomed 11:32. https://doi.org/10.1186/s13002-015-0019-1

Huang WY, Cai YZ, Zhang Y (2010) Natural phenolic compounds from medicinal herbs and dietary plants: potential use for cancer prevention. Nutr Cancer 62(1):1–20. https://doi.org/10.1080/01635580903191585

Hussain G, Zhang L, Rasul A, Anwar H, Sohail MU, Razzaq A, Aziz N, Shabbir A, Ali M, Sun T (2018) Role of plant-derived flavonoids and their mechanism in attenuation of Alzheimer's and Parkinson's diseases: an update of recent data. Molecules 23(4):814

Hussein RA, El-Anssary AA (2018) Plants secondary metabolites: the key drivers of the pharmacological actions of medicinal plants. Herbal Medicine. https://doi.org/10.5772/intechopen.76139

Jan S, Abbas N (2018) Himalayan phytochemicals: sustainable options for sourcing and developing bioactive compounds. Elsevier, ISBN: 0081022360, 9780081022368

Jawla S, Kumar Y, Khan MSY (2011) Antimicrobial and antihyperglycemic activities of *Acacia modesta* leaves. Pharmacologyonline 2:331–347

Jayashree G, Muraleedhara GK, Sudarslal S, Jacob VB (2003) Anti-oxidant activity of *Centella asiatica* on lymphoma-bearing mice. Fitoterapia 74:431–434. https://doi.org/10.1016/S0367-326X(03)00121-7

Jonah SA (2013) Pharmacology of free radicals and the impact of reactive oxygen species on the testis. J Reprod Infertil 14(4):158–172

Jonathan G, Rivka R, Avinoam S, Lumír H, Nirit B (2015) Hypoglycemic activity of withanolides and elicitated *Withania somnifera*. Phytochemistry 116:283–289

Joshi K (2011) Ethnobotanical study of plants used for the treatment of *Diabetes mellitus* in the mountainous regions of Nepal. J Non-timber For Prod 18:19–26

Joshi V, Joshi RP (2013) Some plants used in ayurvedic and homoeopathic medicine. J Pharmacogn Phytochem 2(1):269–275

Joshi RK, Satyal P, Setzer WN (2016) Himalayan aromatic medicinal plants: a review of their ethnopharmacology, volatile phytochemistry, and biological activities. Medicines 3(1):6. https://doi.org/10.3390/medicines3010006

Jugran AK, Rawat S, Bhatt ID, Rawal RS (2020) Essential oil composition, phenolics and antioxidant activities of *Valeriana jatamansi* at different phenological stages. Plant Biosystems 28:1–8

Jurić S, Stracenski KS, Król-Kilińska Ż, Žutić I, Uher SF, Đermić E, Topolovec-Pintarić S, Vinceković M (2020) The enhancement of plant secondary metabolites content in *Lactuca* *sativa* L. by encapsulated bioactive agents. Sci Rep 10:3737. https://doi.org/10.1038/s41598-020-60690-3

Juyal D, Thawani V, Thaledi S, Joshi M (2014) Ethnomedical properties of *Taxus wallichiana* zucc. (Himalayan yew). J Tradit Complement Med 4(3):159–161

Kar A, Choudhary BK, Bandyopadhyay NG (2003) Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in alloxan diabetic rats. J Ethnopharmacol 84:105–108. https://doi.org/10.1016/S0378-8741(02)00144-7

Katiyar C, Gupta A, Kanjilal S, Katiyar S (2012) Drug discovery from plant sources: an integrated approach. Ayu 33(1):10–19. https://doi.org/10.4103/0974-8520.100295

Kaur P, Walia A, Kumar S, Kaur S (2009) Antigenotoxic activity of polyphenolic rich extracts from *Aegle marmelos* (L.) Correa in human blood lymphocytes and *E. coli* PQ 37. Rec Nat Prod 3(1):68–75

Kawra M, Saklani S, Parcha V (2020) Preliminary phytochemical screening and antioxidant activity of five medicinal plants of Garhwal Himalaya: a comparative study. Vegetos 33(3):610-3.

Kazi S (2014) Use of traditional plants in *Diabetes mellitus*. Int J Pharm 4(4):283–289

Khan I, Najeebullah S, Ali M, Shinwari ZK (2016) Phytopharmacological and ethnomedicinal uses of the genus *Berberis* (berberidaceae): a review. Trop J Pharm Res 15:2047–2057. https://doi.org/10.4314/tjpr.v15i9.33

Khan S, Richa, Jhamta R, Kaur H (2020) Antidiabetic and antioxidant potential of *Zanthoxylum armatum* DC. leaves (Rutaceae): an endangered medicinal plant. Plant Sci Today 7:93–100. https://doi.org/10.14719/pst.2020.7.1.665

Khare CP (2008) Indian medicinal plants: an illustrated dictionary Springer Science & Business Media, Cham

Khazdair MR, Anaeigoudari A, Hashemzehi M, Mohebbati R (2019) Neuroprotective potency of some spice herbs, a literature review. J Tradit Complement Med 9:98–105

Kittakoop P, Mahidol C, Ruchirawat S (2014) Alkaloids as important scaffolds in therapeutic drugs for the treatments of cancer, tuberculosis, and smoking cessation. Curr Top Med Chem 14(2):239–252

Kooti W, Moradi M, Ali-Akbari S, Sharafi-Ahvazi N, Asadi-Samani M, Ashtary-Larky D (2015) Therapeutic and pharmacological potential of *Foeniculum vulgare* Mill: a review. J Herbmed Pharmacol 4(1):1–9

Kooti W, Farokhipour M, Asadzadeh Z, Ashtary-Larky D, Asadi-Samani M (2016) The role of medicinal plants in the treatment of diabetes: a systematic review. Electron Physician 8(1):1832

Kumar M, Malik J (2012) Pharmacognostical studies and evaluation of quality parameters of *Butea frondosa* leaves. Int J Pharmcy Pharm Sci 4:610–614

Kumar P, Sati SC (2020) Chemical composition, antioxidant and antimicrobial activities of Himalayan *Fraxinus micrantha* Lingelsh leaf extract. Nat Prod Res. https://doi.org/10.1080/14786419.2019.1710706

Kumar V, Van Staden J (2016) A Review of *Swertia chirayita* (Gentianaceae) as a Traditional Medicinal Plant. Front Pharmacol 6:308. https://doi.org/10.3389/fphar.2015.00308

Kumar A, Kamal A, Singh S, Padalia RC, Tandon S, Chauhan A, Saikia D, Verma RS (2019) Chemical composition, antimicrobial activity, kinetics and mechanism of action of Himalayan-thyme (*Thymus linearis* Benth.). J Essent Oil Res 32(1):59–68. https://doi.org/10.1080/10412905.2019.1662337

Kumar R, Sharma N, Rolta R, Lal UR, Sourirajan A, Dev K, Kumar V (2020) *Thalictrum foliolosum* DC: An unexplored medicinal herb from north western Himalayas with potential against fungal pathogens and scavenger of reactive oxygen species. Biocatal Agric Biotechnol. https://doi.org/10.1016/j.bcab.2020.101621

Kundra R, Samant SS, Sharma RK (2020) Assessment of antioxidant potential of *Trillium govanianum* Wall. ex. D. Don, a critically endangered medicinal plant of northwestern Indian Himalaya. Proc Natl Acad Sci India Sect B Biol Sci 90:95–101. https://doi.org/10.1007/s40011-018-01062-w

Kundu A, Ghosh A, Singh NK, Singh GK, Seth A, Maurya SK, Hemalatha S, Laloo D (2016) Wound healing activity of the ethanol root extract and polyphenolic rich fraction from *Potentilla fulgens*. Pharm Biol 54(11):2383–2393

Kunyanga CN, Imungi JK, Okoth MW, Biesalski HK, Vadivel V (2012) Total phenolic content, antioxidant and antidiabetic properties of methanolic extract of raw and traditionally processed Kenyan indigenous food ingredients. LWT Food Sci Technol 45:269–276. https://doi.org/10.1016/j.lwt.2011.08.006

Kurhekar JV (2016) Tannins-antimicrobial chemical components. Int J Technol Sci 9:5–9

Kurup PNV (2002) "Ayurveda". Traditional Medicine in Asia edited by Chaudhury Ranjit Roy, Rafei Uton Muchatar., WHO-Regional Office for South East Asia, New Delhi, India, pp 3–16

Lee HG, Yu KA, Oh WK, Baeg TW, Oh HC, Ahn JS, Jang WC, Kim JW, Lim JS, Choe YK, Yoon DY (2005) Inhibitory effect of jaceosidin isolated from *Artemisia argyi* on the function of E6 and E7 oncoproteins of HPV 16. J Ethnopharmacol 98:339–343. https://doi.org/10.1016/j.jep.2005.01.054

Li J, Li QW, Gao DW, Han ZS, Lu WZ (2009) Antitumor and immunomodulating effects of polysaccharides isolated from *Solanum nigrum* Linne. Phytother Res 23:1524–1530. https://doi.org/10.1002/ptr.2769

Libro R, Giacoppo S, Soundara Rajan T, Bramanti P, Mazzon E (2016) Natural phytochemicals in the treatment and prevention of dementia: an overview. Molecules 21:518

Lindahl JF, Grace D (2015) The consequences of human actions on risks for infectious diseases: a review. Infect Ecol Epidemiol 5:30048. https://doi.org/10.3402/iee.v5.30048

Manish K, Pandit MK (2018) Geophysical upheavals and evolutionary diversification of plant species in the Himalaya. Peer J 6:e5919. https://doi.org/10.7717/peerj.5919

Manzinea PR, Ettcheto M, Cano A, Busquets O, Marcello E, Pelucchi S, Di Luca M, Endres K, Olloquequi J, Camin A, Cominettia MR (2019) ADAM10 in Alzheimer's disease: pharmacological modulation by natural compounds and its role as a peripheral marker. Biomed Pharmacother 113:108661

Masood M, Arshad M, Qureshi R, Sabir S, Amjad MS, Qureshi H, Tahir Z (2015) *Picrorhiza kurroa*: An ethnopharmacologically important plant species of Himalayan region. Pure Appl Biol 4(3):407

Maurya N, Velmurugan BK (2018) Therapeutic applications of cannabinoids. Chem Biol Interact 293:77–88

Maurya R, Akanksha J, Singh AB, Srivastava AK (2008) Coagulanolide, a withanolide from *Withania coagulans* fruits and antihyperglycemic activity. Bioorg Med Chem Lett 18:6534–6537. https://doi.org/10.1016/j.bmcl.2008.10.050

Meenakshi P, Bhuvaneshwari R, Rathi MA, Thirumoorthi L, Guravaiah DC, Jiji MJ, Gopalakrishnan VK (2010) Antidiabetic activity of ethanolic extract of *Zaleya decandra* in alloxan-induced diabetic rats. Appl Biochem Biotechnol 162:1153–1159. https://doi.org/10.1007/s12010-009-8871-x

Milton JD, Jose MA, Beaulah SN, Ruskin RS, Kumaran J (2013) In vitro and in vivo anticancer evaluation of *Xanthium strumarium* root extracts. Int J Adv Pharm Biol Sci 3:10–16

Mishra AP, Saklani S, Salehi B, Parcha V, Sharifi-Rad M, Milella L, Iriti M, Sharifi-Rad J, Srivastava M (2018) *Satyrium nepalense*, a high altitude medicinal orchid of Indian Himalayan region: chemical profile and biological activities of tuber extracts. Cell Mol Bio 64(8):35–43

Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA (2007) Indian herbs and herbal drugs used for the treatment of diabetes. J Clin Biochem Nutr 40(3):163–173. https://doi.org/10.3164/jcbn.40.163

Mohd T, Belwal T, Bhatt ID, Pande V, Nandi SK (2018) Polyphenolics in leaves of *Paris polyphylla*: an important high value Himalayan medicinal herb. Ind Crop Prod 117:66–74

Morroni F, Sita G, Graziosi A, Turrini E, Fimognari C, Tarozzi A, Hrelia P (2018) Protective Effects of 6-(Methylsulfinyl)hexyl Isothiocyanate on Aβ1-42-Induced Cognitive Deficit, Oxidative Stress, Inflammation, and Apoptosis in Mice. Int J Mol Sci 19(7):2083. https://doi.org/10.3390/ijms19072083

Mueller-Harvey I, McAllan AB (1992) Tannins: their biochemistry and nutritional properties. Advances in plant cell biochemistry and biotechnology. JAI Press Inc, USA
Mukesh R, Namita P (2013) Medicinal plants with antidiabetic potential-A review. American-Eurasian J Agric Environ Sci 13(1):81–94
Mushtaq S, Hassan QP, Sharma R, Majeed R, Dar AH, Sultan P, Khan IA, Ali SA, Ali MN (2017) Evaluation of anticancer and antimicrobial activities of selected medicinal plants of Kashmir Himalayas, India. Indian J Tradit Knowl 16:141–145
Myers SS, Patz JA (2009) Emerging threats to human health from global environmental change. Annu Rev Environ Resour 34:223–252
Nair PKR, Melnick SJ, Wnuk SF, Rapp M, Escalon E, Ramachandran C (2009) Isolation and characterization of an anticancer catechol compound from *Semecarpus anacardium*. J Ethnopharmacol 122:450–456. https://doi.org/10.1016/j.jep.2009.02.001
Neupane P, Lamichhane J (2020) Overview of Himalayan medicinal plants and phytomedicine. Int J Innov Sci Res Technol 5(2):857–866
Nisa S, Bibi Y, Waheed A, Zia M, Sarwar S, Ahmed S, Chaudhary MF (2011) Evaluation of anticancer activity of *Debregeasia salicifolia* extract against estrogen receptor positive cell line. Afr J Biotechnol 10:990–995
Nisa S, Bibi Y, Zia M, Waheed A, Chaudhary MF (2013) Anticancer investigations on *Carissa opaca* and *Toona ciliata* extracts against human breast carcinoma cell line. Pak J Pharm Sci 26:1009–1012
Ojha SN, Tiwari D, Anand A, Sundriyal RC (2020) Ethnomedicinal knowledge of a marginal hill community of Central Himalaya: diversity, usage pattern, and conservation concerns. J Ethnobiol Ethnomed 16:1–21. https://doi.org/10.1186/s13002-020-00381-5
Omar SH, Scott CJ, Hamlin AS, Obied HK (2017) The protective role of plant biophenols in mechanisms of Alzheimer's disease. J Nutr Biochem 47:1–20
Osadebe PO, Odoh EU, Uzor PF (2014) The search for new hypoglycemic agents from plants. Afr J Pharm Pharmaco 8(11):292–303
Painuli S, Kumar N (2016) Prospects in the development of natural radioprotective therapeutics with anti-cancer properties from the plants of Uttarakhand region of India. J Ayurveda Integr Med 7(1):62–68. https://doi.org/10.1016/j.jaim.2015.09.001
Painuli S, Rai N, Kumar N (2015) GC-MS analysis of methanolic extract of leaves of *Rhododendron campanulatum*. Int J Pharm Pharm Sci 7:299–303
Painuli S, Rai N, Kumar N (2016) Gas chromatography and mass spectrometry analysis of methanolic extract of leaves of *Rhododendron arboreum*. Asian J Pharm Clin Res 9:101–104
Painuli S, Joshi S, Bhardwaj A, Meena RC, Misra K, Rai N, Kumar N (2018) In vitro antioxidant and anticancer activities of leaf extracts of Rhododendron arboreum and Rhododendron campanulatum from Uttarakhand region of India. Phcog Mag 14(57):294–303.
Pamhidzai D, Isaac G (2013) TLC separation, antibacterial and anti-inflammatory activity of extracts derived from *Zanthoxylum humile* roots. Intern J Res Ayurveda Pharm 4:482–486
Pandey PK (2007) Rare medicinal herbs of the Himalayas: an ardent need for preservation. Chem Biodivers 4(7):1605–1607. https://doi.org/10.1002/cbdv.200790141
Pandey G, Khatoon S, Pandey MM, Rawat AK (2018) Altitudinal variation of berberine, total phenolics and flavonoid content in *Thalictrum foliolosum* and their correlation with antimicrobial and antioxidant activities. J Ayurveda Integr Med 9(3):169–176. https://doi.org/10.1016/j.jaim.2017.02.010
Paramanick D, Panday R, Shukla SS, Sharma V (2017) Primary pharmacological and other important findings on the medicinal plant "*Aconitum heterophyllum*" (aruna). J Pharmacopunct 20(2):89–92. https://doi.org/10.3831/KPI.2017.20.011
Patel S, Gheewala N, Suthar A, Shah A (2009) In-vitro cytotoxicity activity of *Solanum nigrum* extract against Hela cell line and Vero cell line. Int J Pharm Pharm Sci 1:38–46
Paul SM, Mytelka DS, Dunwiddie CT, Persinger CC, Munos BH, Lindborg SR, Schacht AL (2010) How to improve R&D productivity: the pharmaceutical industry's grand challenge. Nat Rev Drug Discov 9(3):203–214
Paul R, Prasad M, Sah NK (2011) Anticancer biology of *Azadirachta indica* L (neem): a mini review. Cancer Biol Ther 12:467–476. https://doi.org/10.4161/cbt.12.6.16850

Perveen S, Al-Taweel A (2018) Terpenes and Terpenoids. BoD – Books on Demand. ISBN: 1789847761, 9781789847765

Petsko GA (2010) When failure should be the option. BMC Biol 8:61. https://doi.org/10.1186/1741-7007-8-61

Phuyal N, Jha PK, Raturi PP, Rajbhandary S (2020) In vitro antibacterial activities of methanolic extracts of fruits, seeds, and bark of *Zanthoxylum armatum* DC. J Trop Med. https://doi.org/10.1155/2020/2803063

Pohl F, Lin PKT (2018) The potential use of plant natural products and plant extracts with antioxidant properties for the prevention/treatment of neurodegenerative diseases: in vitro, in vivo and clinical trials. Molecules 23:3283

Popescu R, Kopp B (2013) The genus *Rhododendron*: an ethnopharmacological and toxicological review. J Ethnopharmacol 147(1):42–62

Potdar D, Hirwani RR, Dhulap S (2012) Phyto-chemical and pharmacological applications of *Berberis aristata*. Fitoterapia 83(5):817–830

Prakash D, Upadhyay G, Singh BN, Dhakarey R, Kumar S, Singh KK (2007) Free-radical scavenging activities of Himalayan *rhododendrons*. Curr Sci 25:526–532

Prior RL (2003) Fruit and vegetables in the prevention of cellular oxidative damage. Am J Clin Nutr 78:570–578

Purnima BM, Kothiyal P (2015) A review article on phytochemistry and pharmacological profiles of *Nardostachys jatamansi* DC-medicinal herb. J Pharmacogn Phytochem 3(5):102–106

Qian HF, Li Y, Wang L (2017) *Vaccinium bracteatum* thunb. leaves' polysaccharide alleviates hepatic gluconeogenesis via the downregulation of miR-137. Biomed Pharmacother 95:1397–1403

Rafe MR (2017) A review of five traditionally used anti-diabetic plants of Bangladesh and their pharmacological activities. Asian Pac J Trop Med 10:933–939

Rahimi-Madiseh M, Lorigoini Z, Zamani-Gharaghoshi H, Rafieian-Kopaei M (2017) *Berberis vulgaris*: specifications and traditional uses. Iran J Basic Med Sci 20:569–587. https://doi.org/10.22038/IJBMS.2017.8690.

Rahman K, Khan SU, Fahad S, Shinwari ZK, Khan D, Kamal S, Ullah I, Anjum SI, Man S, Khan AJ, Khan WU (2018) In vitro biological screening of a critically endangered medicinal plant, *Atropa acuminata* Royle Ex Lindl of north western Himalaya. Sci Rep 8:11028. https://doi.org/10.1038/s41598-018-29231-x

Rajeshkumar NV, Kuttan R (2001) Protective effect of Picroliv, the active constituent of *Picrorhiza kurroa*, against chemical carcinogenesis in mice. Teratog Carcinog Mutagen 21:303–313. https://doi.org/10.1002/tcm.1018

Rao RK, Ali N, Reddy MN (1978) Occurrence of both sapogenins and alkaloid lycorine in *Curculigo orchioides*. Indian J Pharm Sci 40:104–105

Rao PK, Hasan SS, Bhellum BL, Manhas RK (2015) Ethnomedicinal plants of Kathua district, J&K, India. J Ethnopharmacol 171:12–27. https://doi.org/10.1016/j.jep.2015.05.028

Rashidi AA, Mirhashemi SM, Taghizadeh M, Sarkhail P (2013) Iranian medicinal plants for diabetes mellitus: a systematic review. Pak J Biol Sci 16:401–411

Ratan P, Kothiyal P (2011) *Fagopyrum esculentum* Moench (common buckwheat) edible plant of Himalayas: a review. Asian J Pharmacy Life Sci 1:427–442

Ratnasooriya WD, Somarathna KIWK, Premakumara GAS, Ediriweera ERHSS (2011) Lack of antiglycation activity of fresh juice of whole plant of *Enicostema axillare* (lam.) raynal. J Pharm Negat Results 2:55–57

Ravishankar B, Shukla VJ (2007) Indian systems of medicine: a brief profile. Afr J Trad CAM 4:319–337

Rawat S, Jugran AK, Bahukhandi A, Bahuguna A, Bhatt ID, Rawal RS, Dhar U (2016) Antioxidant and anti-microbial properties of some ethno-therapeutically important medicinal plants of Indian Himalayan Region. 3 Biotech 6(2):154.

Rawat S, Bhatt ID, Rawal RS, Nandi SK (2017) Geographical and environmental variation in chemical constituents and antioxidant properties in *Roscoea procera* Wall. J Food Biochem 41(2):e12302

Rawat S, Jugran AK, Bhatt ID, Rawal RS (2018) *Hedychium spicatum*: a systematic review on traditional uses, phytochemistry, pharmacology and future prospectus. J Pharm Pharmacol 70(6):687–712

Rawat V, Ghildiyal A, Singh L, Jugran AK, Bhatt ID, Nandi SK, Pande V (2019) Methyl jasmonate induced polyphenols and antioxidant production in callus suspension culture of *Nardostachys jatamansi*. Plant Biosyst 1–9. https://doi.org/10.1080/11263504.2019.1701124

Raymond SS, Jonathan SJ, Michael WP (2010) The Essence of Analgesia and Analgesics. Cambridge University Press: 82–90.

Reddy KP, Bid HK, Nayak VL, Chaudhary P, Chaturvedi JP, Arya KR, Konwar R, Narender T (2009) In vitro and in vivo anticancer activity of 2-deacetoxytaxinine J and synthesis of novel taxoids and their in vitro anticancer activity. Eur J Med Chem 44:3947–3953. https://doi.org/10.1016/j.ejmech.2009.04.022

Roberts MF, Wink M (1998) Alkaloids: biochemistry, ecology, and medicinal applications. Plenum Press, New York, London. https://doi.org/10.1007/978-1-4757-2905-4

Rosenberg M (2012) The European Academy of Ayurveda: 20 years of Ayurvedic education in Germany. Anc Sci Life 32(1):63–65. https://doi.org/10.4103/0257-7941.113797

Roy AB, Purohit R (2018) Indian shield: Precambrian evolution and Phanerozoic reconstitution. Elsevier. ISBN 0128098406:9780128098400

Russo P, Frustaci A, Del Bufalo A, Fini M, Cesario A (2013) Multitarget drugs of plants origin acting on Alzheimer's disease. Curr Med Chem 20(13):1686–1693

Sahreen S, Khan MR, Khan RA, Shah NA (2013) Estimation of flavonoids, antimicrobial, antitumor and anticancer activity of *Carissa opaca* fruits. BMC Complement Altern Med 13:372. https://doi.org/10.1186/1472-6882-13-372

Saito T, Nishida M, Mm S, Tanabe A, Eitsuka T, Yuan SH, Ikekawa N, Nishida H (2016) The fruit of *Acanthopanax senticosus* (Rupr. et Maxim.) Harms improves insulin resistance and hepatic lipid accumulation by modulation of liver adenosine monophosphate–activated protein kinase activity and lipogenic gene expression in high-fat diet–fed obese mice. Nutr Res 36:1090–1097. https://doi.org/10.1016/j.nutres.2016.09.004

Salminen A, Lehtonen M, Suuronen T, Kaarniranta K, Huuskonen J (2008) Terpenoids: natural inhibitors of NF-κB signaling with anti-inflammatory and anticancer potential. Cell Mol Life Sci 65:2979–2999. https://doi.org/10.1007/s00018-008-8103-5

Samal J, Dehury RK (2016) An evaluation on medical education, research and development of AYUSH systems of medicine through five year plans of India. J Clin Diagn Res 10(5):IE01–IE05. https://doi.org/10.7860/JCDR/2016/18194.7793

Saxena M, Saxena J, Nema R, Singh D, Gupta A (2013) Phytochemistry of medicinal plants. J Phramacogn Phytochem 1(6):168–182

Scalbert A (1991) Antimicrobial properties of tannins. Phytochemistry 30(12):3875–3883

Semwal P (2017) Investigations on reproductive biology genetic variation and medicinal properties of *Saussurea obvallata* (DC.) Edgew in Uttarakhand. PhD Thesis submitted to Graphic Era University, Dehradun, Uttarakhand, India. http://hdl.handle.net/10603/212319

Semwal P, Painuli S (2019) Antioxidant, antimicrobial, and GC-MS profiling of *Saussurea obvallata* (Brahma Kamal) from Uttarakhand Himalaya. Clin Phytosci 5:12. https://doi.org/10.1186/s40816-019-0105-3

Semwal P, Painuli S, Joshi P, Chaukiyal SP (2017) Socioeconomic status of *Eclipta prostrata* Linn. (Bhringraj) in the life of locals of Kedarnath Shrine, Uttarakhand, India. Indian Forester 143:1325–1327

Semwal P, Painuli S, Badoni H, Bacheti R (2018) Screening of phytoconstituents and antibacterial activity of leaves and bark of *Quercus leucotrichophora* A. Camus from Uttarakhand Himalaya. Clin Phytosci 4:30. https://doi.org/10.1186/s40816-018-0090-y

Semwal P, Painuli S, Tewari D, Bussmann RW, Palni LMS, Thapliyal A (2020) Assessment of non-timber Brahma Kamal (*Saussurea obvallata* (DC.) Edgew.), an important Himalayan. Ethnobot Res Appl 19:40. https://doi.org/10.32859/era.19.40.1-15

Semwal P, Painuli S, Cruz-Martins N (2021) Dioscorea deltoidea Wall. Ex Griseb: A review of traditional uses, bioactive compounds and biological activities. Food Biosci 41:100969. https://doi.org/10.1016/j.fbio.2021.100969

Shakthi Deve A, Sathish Kumar T, Kumaresan K, Rapheal VS (2014) Extraction process optimization of polyphenols from Indian *Citrus sinensis*—As novel antiglycative agents in the management of diabetes mellitus. J Diabetes Metab Disord 13:11. https://doi.org/10.1186/2251-6581-13-11

Sharma E, Gaur AK (2012) *Aconitum balfourii* Stapf: a rare medicinal herb from Himalayan Alpine. J Med Plants Res 6(22):3810–3817

Sharma A, Sharma L, Goyal R (2020) GC/MS Characterization, in-vitro antioxidant, anti-inflammatory and antimicrobial activity of essential oils from *Pinus* plant species from Himachal Pradesh, India. J Essent Oil-Bear Plants 23:522–531. https://doi.org/10.1080/0972060X.2020.1803147

Shen XL, Liu H, Xiang H, Qin XM, Du GH, Tian JS (2016) Combining biochemical with 1H NMR-based metabolomics approach unravels the antidiabetic activity of genipin and its possible mechanism. J Pharm Biomed 129:80–89. https://doi.org/10.1016/j.jpba.2016.06.041

Shengji P, Huyin H, Lixin Y (2009) Medicinal plants and their conservation in China with reference to the Chinese Himalayan Region. Asian Medicine 5(2):273–290. https://doi.org/10.1163/157342109X568810

Shibue T, Weinberg RA (2017) EMT, CSCs, and drug resistance: the mechanistic link and clinical implications. Nat Rev Clin Oncol 14(10):611

Sinatra RS, Jahr JS, Watkins-Pitchford JM (2010) The essence of analgesia and analgesics. Cambridge University Press. ISBN: 1139491989, 9781139491983

Singh S, Farswan M, Ali S, Afzal M, Al-Abbasi F, Kazmi I, Anwar F (2014) Antidiabetic potential of triterpenoidsaponin isolated from *Primula denticulate*. Pharm Biol 52:750–755. https://doi.org/10.3109/13880209.2013.869759

Singh H, Lily MK, Dangwal K (2015) Evaluation and comparison of polyphenols and bioactivities of wild edible fruits of North-West Himalaya, India. Asian Pac J Trop Dis 5(11):888–893

Singh L, Dixit P, Srivastava RP, Pandey S, Verma PC, Saxena G (2019) Ethnobotany and pharmacology of *Pinus* species growing naturally in Indian Himalayas: A plant review. Curr Pharm Biotenol 20(15):1281–1287

Singla RK, Dubey AK, Garg A, Sharma RK, Fiorino M, Ameen SM, Haddad MA, Al-Hiary M (2019) Natural polyphenols: Chemical classification, definition of classes, subcategories, and structures. J AOAC Int 102(5):1397–1400

Sofowora A, Ogunbodede E, Onayade A (2013) The role and place of medicinal plants in the strategies for disease prevention. Afr J Tradit Complement Altern Med 10:210–229. https://doi.org/10.4314/ajtcam.v10i5.2

Sohrabipour S, Kharazmi F, Soltani N, Kamalinejad M (2014) Biphasic effect of *Solanum nigrum* fruit aqueous extract on vascular mesenteric beds in non-diabetic and streptozotocin-induced diabetic rats. Pharm Res 6:148–152

Son YO, Kim J, Lim JC, Chung Y, Chung GH, Lee JC (2003) Ripe fruits of *Solanum nigrum* L. inhibits cell growth and induces apoptosis in MCF-7 cells. Food Chem Toxicol 41:1421–1428. https://doi.org/10.1016/S0278-6915(03)00161-3

Soni D, Grover A (2019) Picrosides from *Picrorhiza kurroa* as potential anti-carcinogenic agents. Biomed Pharmacother 109:1680–1687. https://doi.org/10.1016/j.biopha.2018.11.048

Soto-Hernández M, Tenango MP, García-Mateos R (2017) BoD-Books on Demand (ISBN: 9535129597, 9789535129592).

Sparreboom A, Cox MC, Acharya MR, Figg WD (2004) Herbal remedies in the United States: potential adverse interactions with anticancer agents. J Clin Oncol 22(12):2489–2503

Srivastava P, Agnihotri R, Sharma D, Meena N, Sundriyal YP, Saxena A, Bhushan R, Sawlani R, Banerji US, Sharma C, Bisht P (2017) 8000-year monsoonal record from Himalaya revealing reinforcement of tropical and global climate systems since mid-Holocene. Sci Rep 7:14515. https://doi.org/10.1038/s41598-017-15143-9

Subramani R, Narayanasamy M, Feussner KD (2017) Plant-derived antimicrobials to fight against multi-drug-resistant human pathogens. 3 Biotech 7(3):172

Sudha P, Zinjarde SS, Bhargava SY, Kumar AR (2011) Potent _-amylase inhibitory activity of Indian Ayurvedic medicinal plants. BMC Complement Altern Med 11:5. https://doi.org/10.1186/1472-6882-11-5

Sukandar EY, Adnyana IK, Nurfitria RS (2015) Antioxidant potential of garlic and turmeric mixture—A traditional Indonesian formulation. Indian J Trad Knowl 14:632–636

Tewari D, Zengin G, Ak G, Sinan KI, Cziáky Z, Mishra ST, Jekő J (2020) Phenolic profiling, antioxidants, multivariate, and enzyme inhibitory properties of wild Himalayan Fig (*Ficus palmata* Forssk.): a potential candidate for designing innovative nutraceuticals and related products. Anal Lett 1–8. https://doi.org/10.1080/00032719.2020.1804395

Thakur M, Asrani RK, Thakur S, Sharma PK, Patil RD, Lal B, Parkash O (2016) Observations on traditional usage of ethnomedicinal plants in humans and animals of Kangra and Chamba districts of Himachal Pradesh in north-western Himalaya, India. J Ethnopharmacol 191:280–300

Tiwari R, Rana CS (2015) Plant secondary metabolites: a review. Int J Eng Res Gen Sci 3(5):661–670

Tranchida F, Shintu L, Rakotoniaina Z, Tchiakpe L, Deyris V, Hiol A, Caldarelli S (2015) Metabolomic and lipidomic analysis of serum samples following C*urcuma longa* extract supplementation in high-fructose and saturated fat fed rats. PLoS One 10:e0135948. https://doi.org/10.1371/journal.pone.0135948

Trinh BTD, Staerk D, Jäger AK (2016) Screening for potential α-glucosidase and α-amylase inhibitory constituents from selected Vietnamese plants used to treat type 2 diabetes. J Ethnopharmacol 186:189–195. https://doi.org/10.1016/j.jep.2016.03.060

Trombetta D, Castelli F, Sarpietro GM, Venuti V, Cristani M, Daniele C, Saija A, Mazzanti G, Bisignano G (2005) Mechanisms of antibacterial action of three monoterpenes. Antimicrob Agents Chemother 49(6):2474–2478. https://doi.org/10.1128/AAC.49.6.2474-2478.2005

Tsao R (2010) Chemistry and biochemistry of dietary polyphenols. Nutrients 2(12):1231–1246

Uniyal SK, Singh KN, Jamwal LB (2006) Traditional use of medicinal plants among the tribal communities of Chhota Bhangal, Western Himalaya. J Ethnobiol Ethnomed 2:14. https://doi.org/10.1186/1746-4269-2-14

Upadhyay RK (2017) Tulsi: A holy plant with high medicinal and therapeutic value. Int J Green Pharm 11:S1–S12

Vella F (1990) Biochemistry: By CK Mathews and KE van Holde. pp 1299. Benjamin/Cummings Publishing Co, Redwood City, CA, USA. ISBN 0-8053-5015-2. Biochem Educ 18(3):154–154. https://doi.org/10.1016/0307-4412(90)90236-H

Velmurugan BK, Rathinasamy B, Lohanathan BP, Thiyagarajan V, Weng C-F (2018) Neuroprotective role of phytochemicals. Molecules 23:2485

Verma R, Kumar D, Nagraik R, Sharma A, Tapwal A, Puri S, Kumar H, Kumari A, Nepovimova E, Kuca K (2021). Mycorrhizal inoculation impact on *Acorus calamus* L.-An ethnomedicinal plant of western Himalaya and its in silico studies for anti-inflammatory potential. J Ethnopharmacol 265:113353

Vitousek PM, Mooney HA, Lubchenco J, Melillo JM (1997) Human domination of Earth's ecosystems. Science 277(5325):494–499

Walia S, Mukhia S, Bhatt V, Kumar R, Kumar R (2020) Variability in chemical composition and antimicrobial activity of *Tagetes minuta* L. essential oil collected from different locations of Himalaya. Ind Crop Prod 150:112449

Wan W, Jiang B, Sun L, Xu L, Xiao P (2017) Metabolomics reveals that vine tea (*Ampelopsis grossedentata*) prevents high-fat-diet-induced metabolism disorder by improving glucose homeostasis in rats. PLoS One 12:e0182830. https://doi.org/10.1371/journal.pone.0182830

Wang R, Tang XC, Neuroprotective effects of huperzine A (2005) A natural cholinesterase inhibitor for the treatment of Alzheimer's disease. Neurosignals 14(1-2):71–82

Wang J, Song Y, Chen Z, Leng SX (2018) Connection between systemic inflammation and neuro-inflammation underlies neuroprotective mechanism of several phytochemicals in neurodegen-erative diseases. Oxid Med Cell Longev (Article ID 1972714). https://doi.org/10.1155/2018/1972714

Watt G, Karl T (2017) In vivo evidence for therapeutic properties of cannabidiol (CBD) for Alzheimer's disease. Front Pharmacol 8:20

Xie W, Du L (2011) Diabetes is an inflammatory disease: Evidence from traditional Chinese medicines. Diabetes Obes Metab 13:289–301. https://doi.org/10.1111/j.1463-1326.2010.01336.x

Xiong W, Luo G, Zhou L, Zeng Y, Yang W (2009) *In-vitro* and *in-vivo* antitumor effects of acetylshikonin isolated from *Arnebia euchroma* (Royle) Johnst (Ruanzicao) cell suspension cultures. Chin Med 4:14. https://doi.org/10.1186/1749-8546-4-14

Yamamoto N, Kanemoto Y, Ueda M, Kawasaki K, Fukuda I, Ashida H (2011) Anti-obesity and anti-diabetic effects of ethanol extract of *Artemisia princeps* in c57bl/6 mice fed a high-fat diet. Food Funct 2:45–52. https://doi.org/10.1039/C0FO00129E

Yang L, Wen KS, Ruan X, Zhao YX, Wei F, Wang Q (2018) Response of plant secondary metabolites to environmental factors. Molecules 23(4):762. https://doi.org/10.3390/molecules23040762

Yoon IS, Jung Y, Kim HJ, Lim HJ, Cho SS, Shim JH, Kang BY, Cheon SH, Kim SN, Yoon G (2014) Hypoglycemic effect of *Paeonia lactiflora* in high fat diet-induced type 2 diabetic mouse model. Korean J Pharmacogn 45:194–199

Yu JO, Liao ZX, Lei JC, Hu XM (2007) Antioxidant and cytotoxic activities of various fractions of ethanol extract of *Dianthus superbus*. Food Chem 104:1215–1219. https://doi.org/10.1016/j.foodchem.2007.01.039

Yuan HD, Yuan HY, Chung SH, Jin GZ, Piao GC (2010) An active part of Artemisia sacrorum ledeb. Attenuates hepatic lipid accumulation through activating amp-activated protein kinase in human hepg2 cells. Biosci Biotechnol Biochem 74:322–328. https://doi.org/10.1271/bbb.90651

Yuan H, Ma Q, Ye L, Piao G (2016) The traditional medicine and modern medicine from natural products. Molecules 21(5):559. https://doi.org/10.3390/molecules21050559

Yuan N-N, Cai C-Z, Wu M-Y, Su H-X, Li M, Lu J-H (2019) Neuroprotective effects of berberine in animal models of Alzheimer's disease: a systematic review of pre-clinical studies. BMC Complement Altern Med 19:109

Zeb A, Sadiq A, Ullah F, Ahmad S, Ayaz M (2014) Phytochemical and toxicological investigations of crude methanolic extracts, subsequent fractions and crude saponins of Isodon rugosus. Biol Res 47:57. https://doi.org/10.1186/0717-6287-47-57

Zhang Z, Zhou L, Xie N, Nice EC, Zhang T, Cui Y, Huang C (2020) Overcoming cancer therapeutic bottleneck by drug repurposing. Sig Transduct Target Ther 5:113. https://doi.org/10.1038/s41392-020-00213-8

Zhi XY (2009) Traditional Chinese medicine diagnosis and treatment of type 2 diabetes in Tianjin urban population. J Chin Integr Med 7:823–826. https://doi.org/10.3736/jcim20090905

Zhu BC, Henderson G, Yu Y, Laine RA (2003) Toxicity and repellency of patchouli oil and patchouli alcohol against Formosan subterranean termites *Coptotermes formosanus* Shiraki (Isoptera: Rhinotermitidae). J Agric Food Chem 51(16):4585–4588. https://doi.org/10.1021/jf0301495