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REVIEW

Phytochemical and Medical Perspective of an Endangered Plant *Angelica glauca*: Review on its Current Status and Future Research

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Angelica glauca is an important medicinal plant commonly distributed in Himalayan region of Jammu & Kashmir, Himachal Pradesh and Uttarakhand region of India. Plant possesses immense medicinal potential and is utilized in traditional and modern medicine systems for the treatment of several aliments. The plant has become endangered due to unrestricted harvesting from natural resources, poor germination rate and lack of adequate commercial cultivation. Inspite of inherent medicinal potential there exist a wide research gap to analyze and validate biochemical activities along with isolation, purification and structural elucidation of secondary metabolites. Considering the present endangered status micropropagation studies are required not only with an objective of conservation of *A. glauca*, but also to felicitate mass propagation of the plant. Micropropagation as well as vegetative propagation processes are required to be optimized to develop protocol which are easily reproducible, efficient and can be simultaneously employed for commercial cultivation. Their also exits potential of analytical studies such as HPLC, FTIR, NMR, LC-MS (plant oil as well as plant extract) to provide complete biochemical profiling of the plant, as at present comparatively insufficient literature is available pertaining to biochemical and metabolic characteristics features and properties of the plant. The present review provides an insight into scientific studies conducted so far and research potential pertaining to biochemistry and medicinal properties of *A. glauca.*

Keywords: ***Angelica glauca,*** **Biological activity, Micropropagation, Phytochemistry.**

INTRODUCTION

Medicinal and aromatic plants have been an indispensable component of traditional and modern system of medicine. Inherent medicinal potential of such plant species has laid the foundation of traditional medicinal literature (such as Ayurveda) practiced since ages for treatment of numerous diseases, disorders and ailments. The medicinal plants are also backbone of pharmaceutical and cosmetic products. Invention and development of modern tools and technique for assessment and validation of biological and pharmacological activities of medicinal plants have provided technical support to scientific studies conducted on medicinal and aromatic plants. Various bioanalytical techniques make it feasible to isolate, purify various biologically active phytocompounds from plants and respective validation of medicinal properties of plant extract, essential oil to compounds. Technique such as HPLC, GC-MS, suspension culture, quantitate estimation, spectrometry, XRD, to name a few have provided valuable insight pertaining to plant metabolites, their respective production, mode of action and other characteristics features responsible for their medicinal properties. Potential of medicinal plant not fully exposed yet *Angelica glauca* is one such plants. *A. glauca* Edgew. is a rhizomatous herb with immense medicinal and aromatic potential. The shrub is distributed in high altitude regions of the Himalayas in Jammu & Kashmir, Himachal Pradesh and Uttarakhand states of India [1]. The plant is native to 1500-3700 m altitude. *A. glauca* belongs to family Apiaceae and is known by local (common) names choru, gandhrayan, *etc*. Unrestricted harvesting from natural stands for medicinal, domestic (traditional) and pharmaceutical purposes, poor germination rate, destruction of habitat and lack of adequate

cultivation practices (especially at commercial scale) have made the herb endangered [2-5].

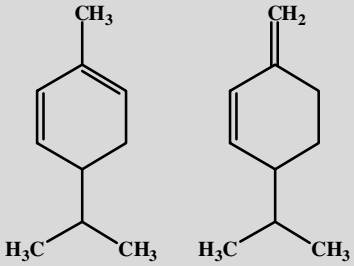
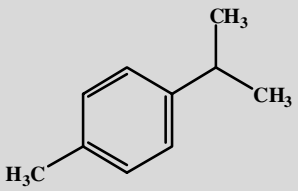
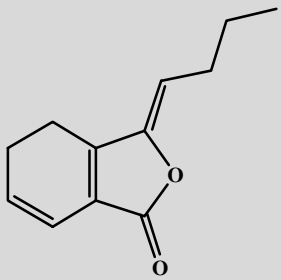
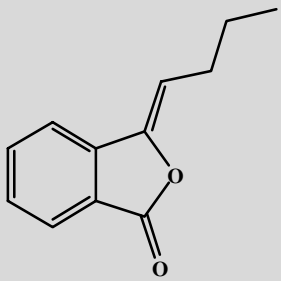
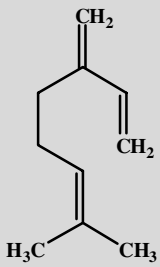
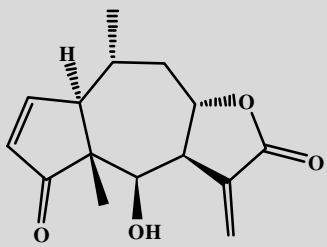
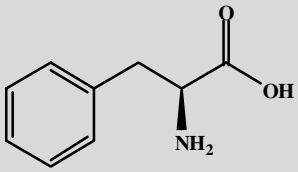
Propagation: Propagation through seeds can be regarded as a challenge since seeds of *A. gluaca* are reported to exhibit late maturity in the season. Nautiyal *et al.* [6] has reported 8% germination rate in *A. glauca.* Khandari *et al.* [7] analyzed the effect of gibberellic acid (GA_3), temperature and light on germination and reported a low seed viability of 55.5% after 1 month of storage, which further decreased to 33-35% and 12% after a storage period of 6 and 12 months, respectively. Treatment of gibberellic acid (GA_3) and presence of light was reported to enhance germination. Vashistha *et al.* [8] reported vegetative propagation to be appropriate means of cultivation of *A. gluaca* owing to poor germination rate. Rhizomes were utilized for vegetative propagation with application of auxin to promote sprouting percentage as well as rooting. Exogenous fortification of indole butyric acid (IBA, 100-200 ppm); indole acetic acid (IAA, 100 ppm) and gibberellic acid (GA_3, 100 ppm) resulted in better response compared to control treatment. Butola *et al.* [9] analyzed seed germination under different temperatures (5, 15, 25, 30 ºC) and photoperoids (light 24 h, dark 24 h & alternative photoperoids 16 h & 8 h light) and sowing depth (0.5, 1.0, 1.5 & 2.0 cm), which revealed that alternative photoperoids 16 h & 8 h light, temperature 25 ºC and soil depth 1.0 cm are most appropriate treatment for germination of *A. glauca* seeds.

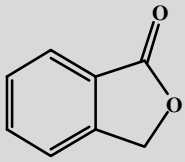
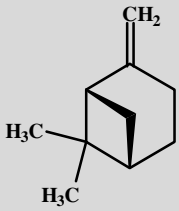
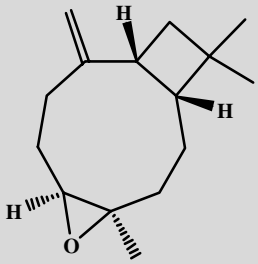
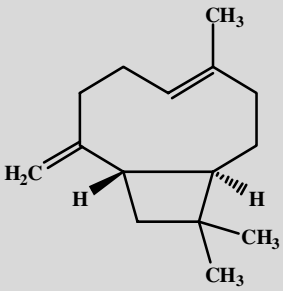
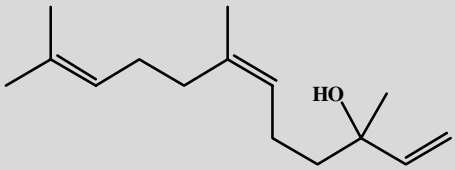
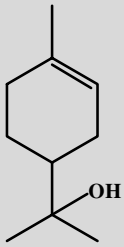
Micropropagation studies: Tissue culture plays an key role in conservation and mass propagation of endangered species, which reduces the danger of extinction. Bisht *et al.* [10] reported an efficient micro propagation protocol to *in vitro* propagate *A. gluaca* through somatic embryogenesis. Callus development from leaves was achieved on to 2,4-D fortified medium. Regeneration of somatic embryos from callus was achieved onto indole-3-acetic acid (NAA) and 6-benzylaminopurine (BAP) fertilized medium. The study reported 75% survival rate of regenerated plants and also reported the production of synthetic seeds. In a similar study [11], epicotyl, hypocotyl and cotyledonary nodes were utilized as explant and regeneration of callus from all three explants was reported with maximum callus regeneration from epicotyl explant. Regeneration of plant lets from somatic embryo was reported on to one-half strength Murashige & Skoog (MS) medium containing no plant growth hormones secondary somatic embryo formation was reported on MS medium fortified with 2 µM NAA and 2 µM IBA. A maximum survival rate of 85% was reported when *in vitro* raised plants were acclimatized and transplanted under natural condition. A study conducted by Rawat *et al.* [12] appears to be a complete micro propagation study reporting multiple shoot regeneration from rhizomes on to MS medium supplemented with BAP and IAA. A maximum survival rate of 72% of regenerated plants was reported. The study also provided a comparative phytochemical analysis of *in vitro* regenerated and mother plant. Higher tannin, flavonoid and total phenol were found in tissue culture raised plants. The GC-MS analysis revealed the similar chemicals composition of essential oil extracted from tissue culture and mother plant.

Phytochemistry: Numerous medicinal properties and biological activities of *A. glauca* are attributed to presence of wide range of phytocompounds (Table-1). Available literature reports oil of the plant to be highly rich in different classes of organic compounds. Agnihotri *et al.* [4] conducted the GC-MS and NMR analysis of oil extracted from aerial parts of *A. glauca* at the flowering stage and reported presence of 34 phytocompounds with phellandrene (13.5%), *trans*-carveol (12.0%), β-pinene (11.7%), thujene (7.5%), β-caryophyllene oxide (7.2%), β-caryophyllene (7.0%), γ-terpinene (6.7%), nerolidol (6.5%), β-bisabolene (5.2%) and germacrene D (4.5%) to comprise major constituents of the oil. In another study, the *A. glauca* plant material was subjected to hydrodistillation for the essential oil extraction [11]. The GC-MS analysis of the extracted oil revealed presence of about 45 compounds out of which 30 were identified. The essential oil exhibited antibacterial activity against *E. coli*, *S. aureus*, *P. multocida* and *B. subtilis* and antifungal activity against *Microsporum canis* (maximum inhibition), *Fusarium solani*, *Candida albicans*, *Aspergillus flavus* (minimum inhibition). Along with the antimicrobial activity, the oil was also reported to possess phytotoxic and antioxidant activities. Purohit *et al.* [13] reported presence of 26 phytocompounds in oil of *A. glauca* with major compounds (*Z*)-ligustilide, (*Z*)-butylidene phthalide, (*E*)-butylidene phthalide and (*E*)-ligustilide. Kaul *et al.* [3] reported presence of 68 phytocompounds in essential oil of *A. glauca* as depicted by GC-MS with major compounds 3-phellandrene (15.29%), (*Z*)-ligustilide and 3-valeryl phthalide (31.55%). The study also reported that oil to be rich in monoterpenes, oxygenated monoterpenes, sesquiterpenes, phenylpropanoids and phthalides. Irshad *et al.* [14] conducted the GC-MS analysis of three plant materials *viz*. *A. glauca*, *Plectranthus rugosus* and *Valeriana wallichii*, collected from the different locations of Jammu & Kashmir state and depicted that the obtained essential oil contain major phytocompounds e.g. β-pinene, α-phellandrene, β-caryophyllene.

Thappa *et al.* [15] extracted the essential oil from the root of *A. glauca* Edgew. (Family Apiaceae) collected from the different Himalayan regions at different stages of the plant. The major phytocompounds detected through GC-MS analysis were terpene hydrocarbons (methyl octene, limonene, β-pinene, α-pinene, β-phellendrene), phthalides [(*Z*)-3-butylidene phthalide (*Z*)- and (*E*)-ligustilide] and citronellyl acetate. Which indicates that (*Z*)-ligustilide and (*Z*)-butylidene phthalide found at high concentration in Himachal Pradesh state than Jammu & Kashmir states of India, where as citronellyl acetate, α-pinene, limonene and β-phellandrene was recorded at high concentration in Jammu & Kashmir state than Himachal Pradesh state. At different stages, the concentration of methyl octene & α-pinene was high at flowering stage and low at maturity stage except limonene and β-pinene which is found to be increased at the maturity stage. Rawat *et al.* [12] reported presence of 31 phytocompounds to be present in essential oil of *A. glauca* root in control and *in vitro* raised plants by GC-MS analysis. Out of total 31 phytocompounds identified to be present in micropropagated as well as wild plant, concentration of 28 compounds was reported to be high in tissue culture raised plants than control plants. A major portion of fatty acid composition of petroleum ether seed extract of *A. glauca* was reported [16] to comprise of

TABLE-1
SUMMARY OF MAJOR BIOLOGICAL ACTIVE METABOLITES OF *A. glauca*

Compound name	Structure	Biological activity	Ref
α-Phellandrene		Antifungal activity Anti-inflammatory activity	[35,36]
p-Cymene		Antioxidant, anti-inflammatory, antinociceptive, anxiolytic, anticancer and antimicrobial effects	[37,38]
Z-ligustilide		Anticancer, anti-inflammatory, antioxidant as well as neuroprotective activities	[39,40]
(*Z*)-3-Butylidenephthalide		Antihyperglycemic activity	[41]
Monoterpenes		Analgesic, anti-inflammatory, anticonvulsant, antidepressant, anti-Alzheimer, anti-Parkinsonian, antiviral and antibacterial (antituberculosis) effects	[42]
Sesquiterpene		Antitumor, cytotoxic, antimicrobial and phytotoxic activity, antifungal, antibacterial.	[43,44]
Phenylpropanoids		Antimicrobial, antioxidant, anti-inflammatory, hepatoprotective, phytopreparations, antidiabetic, anticancer activities	[45,46]

Phthalides		Actions on the central nervous system, anti-platelet aggregation and anti-thrombosis, cardiac function modulation and anti-angina, inhibition of smooth muscle cell proliferation, Insecticidal Effect.	[47,48]
β-Pinene		Antimicrobial, anticancer, anti-inflammatory and antiallergic properties.	[49,50]
β-Caryophyllene oxide (BCPO)		Anticancer activities, affecting growth and proliferation of numerous cancer cells.	[51]
β-Caryophyllene		Inflammatory pathologies, such as nervous system diseases (Parkinson's disease, Alzheimer's disease, sclerosis, stroke) and tumours (colon, breast, pancreas, lymphoma, melanoma and glioma cancer).	[52,53]
Nerolidol		Antimicrobial, antibiofilm, antioxidant, anti-parasitic, skin-penetration enhancer, skin-repellent, anti-nociceptive, anti-inflammatory and anticancer, antifungal	[54,55]
α-Terpineol		Cardiovascular and antihypertensive effects, Antioxidant activity, Anticancer activity, Antinociceptive activity, Anticonvulsant and sedative activity	[56]

unsaturated fatty acids like petroselinic acid and oleic acid. GC-MS technique has also been employed for comparative analysis of essential oil of *A. glauca* collected from two different geographical locations Sissu (Himachal Pradesh state) and Panwali Kantha (Uttarakhand state) and revealed that the presence of *Z*-ligustilide was higher among the plants collected from Uttarakhand state compared to the plants collected from Himachal Pradesh state [17]. Table-2 summarizes the major phytocompounds reports to be present in different *Angelica* species.

Biological activities: Several medicinal properties of *A. glauca* include antimicrobial activity, antioxidant activity, anti-inflammatory, insecticidal activity, immunotoxin activity are summarized in Table-3. The plant is also reported to be effective for the treatment of bronchitis, rheumatism, stomach disorders, urinary problems, metrorrhagia, dysmenorrhea, *etc*. The plant is utilized in treatment or as a remedy for vomiting, headache, stomach disorders, dysentery, asthma, malaria, urinary disorders, bronchitis, arthritis, fever, *etc*. [18-20]. Irshad *et al.* [20] studied the antioxidant activity of essential oil of fresh plant material of *A. glauca* collected from Jammu and Kashmir state. The study revealed plant has good DPPH radical scavenging activity 93.4% of inhibition and inhibition of peroxidation 45.05%. Rawat & Gupta [21] also studied the antioxidant activity of methanolic and acetonic seed extract of *A. glauca* from 17 different locations of Uttarakhand (India). The study suggested

TABLE-2
GC-MS ANALYSIS OF OIL EXTRACTED FROM DIFFERENT SPECIES OF GENUS *Angelica*

Species	Source for oil extraction	Major phytocompounds	Ref.
Angelica archangelica L	Seeds (fruit)	β-Phellandrene (33.6-63.4%), α-phellandrene (7.4%) and α-pinene (4.2-12.8%)	[57]
Angelica archangelica L	Roots	GC-MS analysis of oil from roots depicted presence of α-phellandrene, β-phellandrene and α-pinene, β-pinenes as major phytocompounds	[58]
Angelica viridiflora	Aerial plant	Caryophyllene oxide (61.7%); 3,4-dimethyl-3-cyclohexan1-carboxaldehdye (5.8); and isobutyl-2-methylpent-3-yl ester of phthalic acid (~5.5)	[59]
Angelica cincta	Aerial plant	α-Pinene (67.2%), sabinene (5.8) and β-pinene (4.9)	[59]
Angelica urumiensis	Leaf	Palmitic acid (14.14%), hexahydrofarnesyl acetone (10.03%), 1-dodecanol (7.55%), linoleic acid (6.37%) and oleic acid (5.34%)	[60]
Angelica urumiensis	Stem	Palmitic acid (13.37), -cadinol (9.24%), (epi)- -cadinol (5.76%) and -cadenine (6.11%)	[60]
Angelica dahurica	Roots	α-Pinene (46.3%), sabinene (9.3%), myrcene (5.5%) and 1-dodecanol (5.2%)	[61]
Angelica pubescentis	Roots	α-Pinene (37.6%), *p*-cymene (11.6%), limonene (8.7%), cryptone (6.7%) and β-phellandrene (3.8%)	[61]
Angelica gigas Nakai	Roots	A total of 116 compounds, in which 40 hydrocarbons, 37 alcohols, 15 esters, 12 aldehydes, 7 ketones and 5 miscellaneous were identified. Major hydrocarbons were α-pinene (30.89%), 2,4,6-trimethyl heptane (13.39%), α-limonene (4.29%), camphene (4.10%) and 2-methyl octane (3.27%)	[62]
Angelica koreana	Roots	Sabinene (31.85%) was the main component of oil, alongwith other phytocompounds including *m*-cresol (4.46%) and α-pinene (4.00%), α-bisabolol (3.63%) and α-bornyl acetate (2.30%)	[63]
Angelica acutiloba	Roots	Roots exhibited highest proportion of monoterpenes compared to stems and leaves such as γ-terpinene, *p*-cymene and *cis*-β-ocimene and the lowest content of 3*n*-butyl phthalide	[64]
Angelica acutiloba	Stem	Higher percentage of 3*n*-butyl phthalide in stem was reported as compared to roots and leaves	[64]
Angelica acutiloba	Leaves	Leaves shows highest content of *trans*-2-hexenal and *cis*-3-hexenol	[64]

that the methanolic seed extract from Bageshwar city exhibited maximum β-carotene (77.7%) and DPPH activity (37.4%). Devi *et al.* [22] analyzed the antioxidant activity and radical scavenging activity of plant extract of *A. glauca*. The study revealed that the plant extract showed total phenolic content (TPC) 486 ± 1.29 GAE µg/10 mL and total flavonoid content (TFC) 486 ± 1.29 GAE µg/10 mL. Similarly, Arya *et al.* [23] reported the antioxidant activity of methanol, petroleum ether, chloroform and water extracts of *A. glauca* stem and roots collected from Tung Nath area of Uttarakhand state. The study reported that the methanolic extract of *A. glauca* shows highest antioxidant activity compared to other solvents.

Nautiyal *et al.* [6] also conducted the antioxidant activity of petroleum ether seed extract of *Angelica glauca* by 2,2-diphenyl-1-picrylhydrazyl (DPPH), nitroblue tetrazolium (NBT), hydrogen peroxide (H_2O_2) and 2,2′-azino-*bis*(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) radical scavenging assay. The study revealed that all assays show the high radical scavenging activity. Arya *et al.* [24] studied antioxidant activity of hydroalcoholic and aqueous root powder extract of *A. gluaca* by using standard method. The study revealed that the hydroalcoholic extract exhibits the highest (IC_{50} = 68.1 ± 0.34 µg/mL) antioxidant activity. There are several other medicinal plants such as *Withania somnifera*, *Raulfia sespentina*, *Picrorihza kurroa* whose roots/rhizomes have been identified to possess the several medicinal properties. Similar studies are required to identify and validate bioactive phytocompounds presents in aerial parts of *A. glauca* along with their associated biological activities.

A. glauca, a medicinal and aromatic herb has been reported to possess immense medicinal potential attributed to several bioactive metabolites synthesized in the plant. Inspite of the reported biological activities, the optimum utilization of herb is challenged due to its limited availability of plant material. Numerous medicinal and aromatic plants are presently identified as endangered species mainly due to utilization of roots/rhizomes for traditional, medicinal and industrial purposes. *A. glauca* is one such plant whose present endangered status is attributed to extensive harvesting of roots of plants along with poor germination rate. Hence, optimization of *in vitro* as well as *in vivo* cultivation practices for conservation and mass propagation is crucially important. Micropropagation has been successfully utilized for conservation of wide range of plants species including medicinal and aromatic plants, crops, forest trees and others. Tissue culture technique not only provides an effective and efficient method for plant propagation but also can be simultaneously utilized for genetic modification and establishment of suspension culture. Establishment of suspension cultures have been successfully utilized for the production of important secondary metabolites and other phytocompounds in several plant species *Withania somnifera* [25], *Valariana wallichi* [26]. Synthesis of secondary metabolites through suspension culture not only provide a reliable source to full fill their respective requirement by medicinal and pharmaceutical, cosmetic and food processing industries [27] but simultaneously reduces excessive harvesting of plants for industrial purposes. A common traditional application of roots of *A. glauca* is fortification to food recipes as flavouring agent especially in regions of Kumaun and Gharwal, India. Antioxidant and antimicrobial activities also indicate likelihood of the plant/essential oil to be utilized in preservation of food [28]. However, scientific studies are required to evaluate and

TABLE-3
SUMMARY OF MAJOR BIOCHEMICAL AND MICROPROPAGATION STUDIES CONDUCTED w.r.t *A. glauca*

Micropropagation studies				
Explant	Media, PGR	Morphological responses	% Survival of regenerated plant	Ref.
Leaf	MS, 2,4-D	Callus		
	MS, NAA, BAP	Somatic embryogenesis	75	[5]
	Sodium alginate $CaNO_3$	Synthetic seeds		
Epicotyl	MS, 2,4-D	Callus (95.8%)		
	MS, BA + NAA	Callus (100%)		
		Somatic embryo		
Hypocotyl	2,4-D	Callus (70.8%)	85	[29]
Cotyledonary node	2,4-D	Callus (58.3%)		
Somatic embryo	1/2MS + NO PGR	Plantlet regeneration		
	MS + NAA + BA	Secondary embryo formation		
Rhizomes	MS + BAP + IAA	Multiple shoot	72	[32]
	MS + IAA + NAA	*In vitro* rooting		

Biological/pharmacological studies			
Biological/Pharmacological activity	Plant part/Extract/ Oil utilized	Critical finding of the study	Ref.
Antioxidant activity Antimicrobial activity	Whole plant (Essential oil)	Essential oil exhibited good antioxidant activity as well as antimicrobial activity.	[20]
Antioxidant activity	Roots	Hydroalcoholic extract shows higher radical scavenging activity compared to aqueous extract & essential oil.	[42]
Broncho dilating and Immuno suppressant activity	Essential oil	Oil of *A. glauca* analyzed for efficient to reduce anxiety	[30]
Anxiolytic effect	Roots	Potential role of *A. glauca* to reduce anxiety	[10]
Irritant and cytotoxic activity	Roots	Six different coumarins isolated from root exhibited the cytotoxic activity	[36]
Antimicrobial activity	Methanolic extract (root and stem)	Antimicrobial activity against *S. aureous, S. pneumonia, S. pyogenus, P. aeruginosa & K. pneumonia.*	[33]
Green synthesis of silver nanoparticles	Aqueous extract of roots	Rich flavonoid and phenolic content, antioxidant potential, antibacterial potential.	[34]
Antioxidant activity	Petroleum ether extract of seeds	High radical scavenging activity	[28]
Antioxidant activity	Root extract	Free radical scavenging ability	[12]
Antioxidant activity	Plant extract	Inhibition up to 95.81% was reported	[2]
Phytochemical screening	Oil	GC-MS revealed presence of diverse and medicinally important phytocompounds.	[31]
Germination Potential Index	Seeds	Under photopheroids 16 h & 8 h light, temperature 25^0C and soil depth 1.0cm shows maximum germination.	[8]
GC-MS and antifungal activity	Essential oil	Antifungal activity against *Microsporum canis.* GC-MS revealed presence of diverse and medicinally important phytocompounds.	[19]
GC-MS and NMR analysis	Essential oil from aerial parts	Presence of diverse and medicinally important phytocompounds.	[1]
GC-MS	Oil	Extracted oil rich in monoterpenes, oxygenated monoterpenes, sesquiterpenes, phenylpropanoids and phthalides	[22]

authentic utilization of plant as food flavouring and preservative agent.

Metabolic studies have been identified as to be an effective approach for the analysis of biologically active metabolites present in plant extract and has become an integral part of drug research [29]. There exists a scope for isolation, purification and structural elucidation of secondary metabolites along with assessment of their inherent biological and pharmacological activities (Fig. 1). Metabolomics have been successfully utilized in elucidating metabolic pathways in several plant species. In a significant molecular study conducted by Butola *et al.* [9] on a related species *Angelica gigas* Nakai genome wide SSR markers were developed through next generation sequencing. Similar studies are required to be conducted for *A. glauca* so as to design and develop molecular markers which can serve as an effective tool in molecular breeding studying relationships between different genus, genetic mappings and related molecular aspects.

Conclusion

Angelica glauca is an important medicinal plant with potential to be utilized as herb in pharmaceuticals and other value-added products. However, interdisciplinary research combining biological and chemical science studies are required to achieve mass propagation, production of improved varieties, structural validation of the phytocompounds alongwith the chemistry involved in synthesis of bioactive metabolites and their inherent potential in drug designing, therapeutic agent

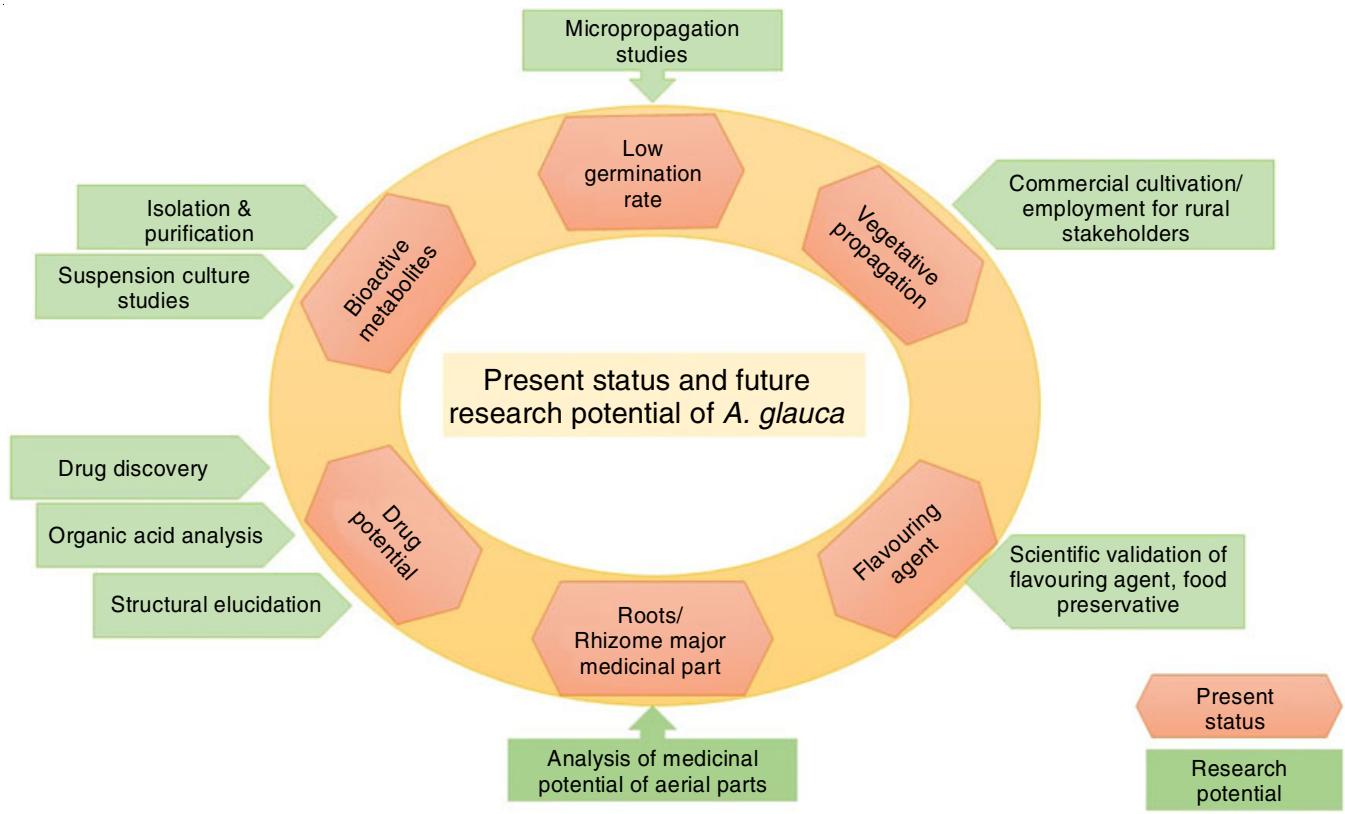


Fig. 1. Summary of research potential of *A. glauca* pertaining to biochemical studies of phytoconstituents

and other biological activities. The plant possesses inherent potential to be utilized in treatment of various ailments. Beside scientific studies, commercial cultivation of plant is also needed to be encouraged which will not only make available sufficient raw material but will simultaneously serve to be financial asset for regional stakeholders.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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