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Pharmacophylogeny of Genus *Allium* L.

Abstract

The genus *Allium* is well known for its ethnomedicinal significances. It comprises over 1,100 species with diverse therapeutic potentials. This study explores the pharmacophylogeny of *Allium*, integrating traditional knowledge with modern scientific methods. The investigation compass 139 distinct medicinal categories, including 610 utilization records from 168 published sources, offering a comprehensive understanding of *Allium* species for diverse therapeutic applications especially antidiabetic and antioxidant properties. Phylogenetic analysis reveals distinct clades with significant antidiabetic and antioxidant activities, in 42 out of 185 species of genus *Allium*. This is supported by the presence of bioactive compounds such as allicin, flavonoids, phenolics etc. A heat map systematically depicts the ethnomedicinal relevance of various *Allium* species within clades, illuminating their potential contributions to human health. These findings emphasize the evolutionary convergence of pharmacological traits within specific lineages. By integrating traditional medicinal knowledge with modern scientific methodologies, this study pioneers a holistic approach to harnessing the therapeutic potential of natural plant resources, particularly within the diverse genus *Allium*. This interdisciplinary approach offers promising avenues for drug discovery and healthcare enhancement, emphasizing the importance of integrating traditional wisdom with scientific inquiry in harnessing the therapeutic potential of *Allium* species.

Keywords: *Allium*, Pharmacophylogeny, Therapeutic uses, Antidiabetic, Antioxidant, Ethnomedicinal

1. Introduction

The genus *Allium* L. (Amaryllidaceae) commonly known as onion is a diverse and economically significant group of flowering plants. The genus comprises over 1,100 recognized species, making it one of the largest genera in the plant kingdom (Pandey et al., 2022). Since ancient times, people have turned to nature for natural solutions to health issues, particularly to reduce pain and discomfort, and to expand their overall well-being. Until the eighteenth century, plant-based medicines were the main medical aid available to all members of the human race (Ijnu et al., 2022). Use of the *Allium* species in India is important from the perspective of ethnopharmacology. Due to its distinctive flavour and ethnomedicinal significance, the pharmacological properties of the genus *Allium* have been studied in therapeutic aspects for a long time (Borborah et al., 2014). In India, the roots of traditional

medicine and healthcare can be traced back to 5000 years BCE. The recognition of the need for healthcare and the understanding of ailments date back to ancient literature such as the "Rigveda" (1700-1100 BCE), "Yajurveda" (1400-1000 BCE), and "Atharva Veda" (1200 BCE). Subsequently, the emphasis on the use of plants and multi-herbal formulations became prominent and found widespread application in manuscripts such as the "Charaka Samhita" (990 BCE), "Sushruta Samhita" (660 BCE), and "Dhanwantari Nidhantu" (1800 CE) (Adhikari et al., 2018).

The term "pharmacophylogeny" was introduced by Chinese researcher Peigen Xiao in the 1980s, emphasizing the examination of the phylogenetic relationship among medicinal plants. It is nurtured by molecular phylogeny, chemotaxonomy, ethnopharmacology, and bioactivity studies. Pharmacophylogeny, a comprehensive discipline emphasizes that genetically close plants contain similar chemical or bioactive composition and thus exert similar therapeutic effects. This might be due to close genetic relation (Xiao et al., 2006). On the other hand, not all plants with genetic relation have the same active constituents, concentration, and bioactivities. This may be due to different ecological factors e.g. habitat, soil composition, and climate (Gong et al., 2020). Pharmacophylogeny suggests that healing plants of the related taxonomic groups are more likely to possess the analogous chemical profiles/efficacies (Hao et al., 2022). Pharmacophylogeny is an interdisciplinary topic that studies the correlation between plant phylogeny, chemical composition, and curative effects (Gong et al., 2020). Ethnobotanical investigations play an important role in enhancing our understanding of the pharmacophylogeny of plants. Since ancient times, the indigenous plants of every region have been utilized by human being to obtain medicines and foods. The relationships between human groups and plants including different kinds of uses, practices & beliefs constitute ethnobotany (Ram et al., 2004). Ethnobotanical convergence refers to the similar uses for plants included in the same node of a phylogeny (Garnatje et al., 2017). In the recent years several reviews & research paper on pharmacophylogeny have been published viz. Peng et al., (2006) Berberidaceae; Xiao et al., (2006) *Aconitum*; Xiao et al., (2007) *Frittilaria*; Pei-Gen et al., (2007), Gao et al., (2008) Cimicifugeae: Ranunculaceae; Xu et al., (2008) Schisandraceae; Kumar et al., (2012) *Micromeria biflora* and *Citrus reticulata*; Li et al., (2013) *Salvia*; Hao & Xiao, (2020), Zaman et al., (2021), Shen et al., (2022) *Scutellaria baicalensis*; and Cui et al., (2022) *Artemisia*. Most of the studies on pharmacophylogeny have been carried out in China. In India, a notable absence of research on pharmacophylogeny in any group prompted our initiative to conduct a comprehensive study on genus *Allium*. Addressing this gap, our research

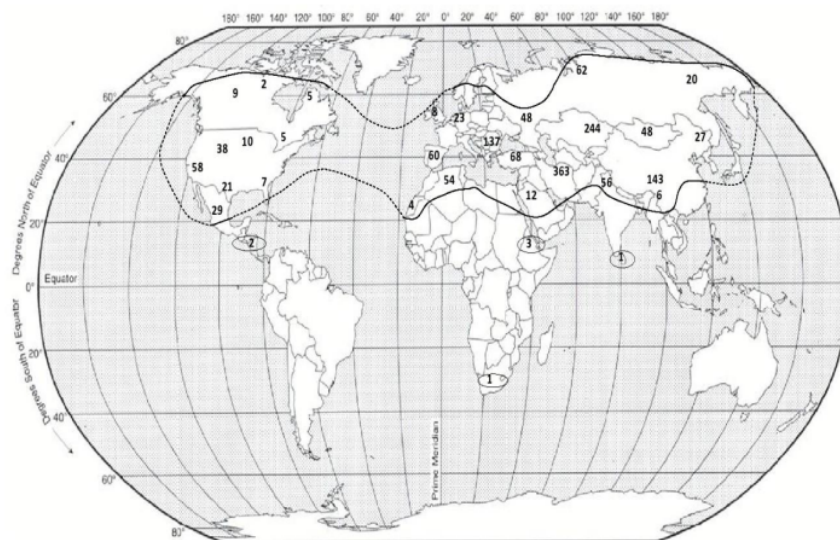
explores the intricate relationships between pharmacology and phylogeny of genus *Allium*, shedding light on unique perspectives that can contribute significantly to the field of pharmaceutical sciences in the Indian context.

Phylogenetic tools provide explanatory power & shapes ethnobotanical uses. Phylogeny provides strong predictive perspectives for the usage of medicinal plants that are not available in traditional plant classifications (Saslis et al., 2012). In countries like India & China which has huge diversity but the phylogenetic information of ethnomedicinal and therapeutic use of several taxa are scarce. The primary aim of this study was to explore how the integration of traditional medicinal knowledge with phylogenetic analysis could facilitate the identification of *Allium* species with potential antidiabetic and antioxidant bioactivities. With this objective in mind, the study has been conducted, focusing on the following key goals.

- i) compilation of data from ethnobotanical sources to create a comprehensive ethnomedicinal and therapeutic uses of the genus *Allium*
- ii) study of Pharmacophylogeny of the genus *Allium* on the basis of DNA sequence.
- iii) highlight taxa that could have antidiabetic and antioxidant properties supported by evidence from traditional medicine and phylogenetic considerations.

2. Global Distribution of Genus *Allium*

Amaryllidaceae spread all over the world and consists of 79 genera including *Allium* (Sabiou et al., 2019). Genus *Allium* consists of about 1,100 taxa out of which 1,063 names of the species are now accepted (POWO, 2022). The genus *Allium* exhibits a broad distribution (map 1) including the Holarctic region, and ranging from the dry subtropics to the boreal zone (Fritsch & Friesen, 2002). The taxa are extensively dispersed throughout the sub-temperate and temperate zones of the northern hemisphere (Pandey et al., 2022). The Irano-Turanian biogeographical area is the primary centre of evolution for the genus *Allium*, with secondary centres of diversity located in the Mediterranean Basin, south-western and central Asia, and western North America (Fritsch and Friesen, 2002).



Map 1: Global distribution of wild species genus *Allium*. The numbers indicate the species richness in different regions (WCSP 2015, as referenced in Pandey et al., 2022).

3. Material and Method

3.1. Literature Survey

The information on medicinal uses of the genus *Allium* was compiled by broad literature study of published sources from 1920-2023. We searched thorough online database by using the keyword “*Allium*” including reviews of the ethnobotanical uses, pharmacological activities and medicinal uses of the genus *Allium*. A list of the plant was prepared from the published literature. The nomenclature of all the taxa were studied with the help of Plant of the World Online (<https://powo.science.kew.org/>), International Plant Naming Index (<https://www.ipni.org/>), The Plant list (<http://www.theplantlist.org/>), Biodiversity Heritage Library (<https://www.biodiversitylibrary.org/>), world flora online (<https://www.worldfloraonline.org/>), Tropicos (<https://www.tropicos.org/home>) and World Checklist of Selected Plant Families (<http://apps.kew.org/wcsp/retrievedon17.12.2014>). Protologues of all the name and type specimen for the same were also studied and examined. A table of accepted name was prepared for species within genus *Allium* with the help of published literature and aforementioned databases (supplementary file S1). The literature search components and related review type were documented and illustrated using PRISMA

2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) available at <http://www.prisma-statement.org/PRISMAStatement/FlowDiagram>.

3.2. Phylogenetic Tree Construction

3.2.1. Data Retrieval

A comprehensive examination of 185 *Allium* species representing all as documented in the genus was conducted for the purpose of pharmacophylogenetic analysis (Friesen et al., 2002). In this study, the Internal Transcribed Spacer (ITS-1 and ITS-2) regions of the taxa in question and out group (Friesen et al., 2006) (fig.3) were obtained from the National Center for Biotechnology Information (NCBI)/GenBank. This dataset was employed for the construction of a phylogenetic tree (supplementary file S3).

3.2.2. Phylogenetic Tree Construction and Cluster Analysis

Sequences retrieved from the NCBI database were subjected to alignment using the default settings in the MUSCLE multiple sequence alignment tool. Manual adjustments were made to correct base gaps and any identified inaccuracies. The construction of the phylogenetic tree was carried out utilizing the MEGA11 software, employing the Maximum Likelihood Phylogenetic Test with 100 bootstrap replicates. Model Test v.0.1 was used to determine optimal models for nucleotide substitution, and a Bayesian phylogenetic hypothesis was generated utilizing the GTR+I+G model for the Internal Transcribed Spacer (ITS) region (Pellicer et al., 2018). Interactive visualization of the phylogenetic tree was accomplished using the Interactive Tree of Life (ITOL <https://itol.embl.de/about.cgi>).

4. Phylogenetic Distribution of *Allium* species

The application of phylogenetic tools contributes significant explanatory power and shapes the ethnobotanical utilization of the species. Phylogeny offers robust predictive perspectives for medicinal plant usage, surpassing the information available in conventional plant classifications (Saslis et al., 2012). This investigation explores the phylogenetic distribution of species in genus *Allium* and their medicinal applications, utilizing two endorsed primary approaches as recommended by Pellicer et al. (2018). First primary approach is to evaluate the extent of phylogenetic clustering pertaining to diverse reported applications of *Allium* spp. within the phylogenetic tree. Second primary approach endeavours to pinpoint specific lineages within the phylogeny of genus *Allium* that exhibit antioxidant and antidiabetic properties.

5. Result and Discussion

5.1. Research in Electronic Databases

Initially, a comprehensive search using the keyword 'Allium' yielded a total of 598 articles in the electronic database. Google Scholar contained the highest number of articles (78), followed by Science Direct (42) and PubMed Central (6). Contributions from Springer, CABI, MDPI, Wiley, HindaWi, and Taylor & Francis were 8, 2, 7, 8, 2, and 6, respectively. Additionally, 25 records were identified through the Online Database PFAF.org, comprising information on 20 species, while Dr. Duke's Phytochemical & Ethnobotanical Database included records of 5 distinct species. During the selection process, 455 duplicate articles were excluded after reviewing abstracts and keywords. A total of 168 articles were considered suitable for inclusion in the manuscript, consisting of 126 experimental articles and 27 literature reviews.

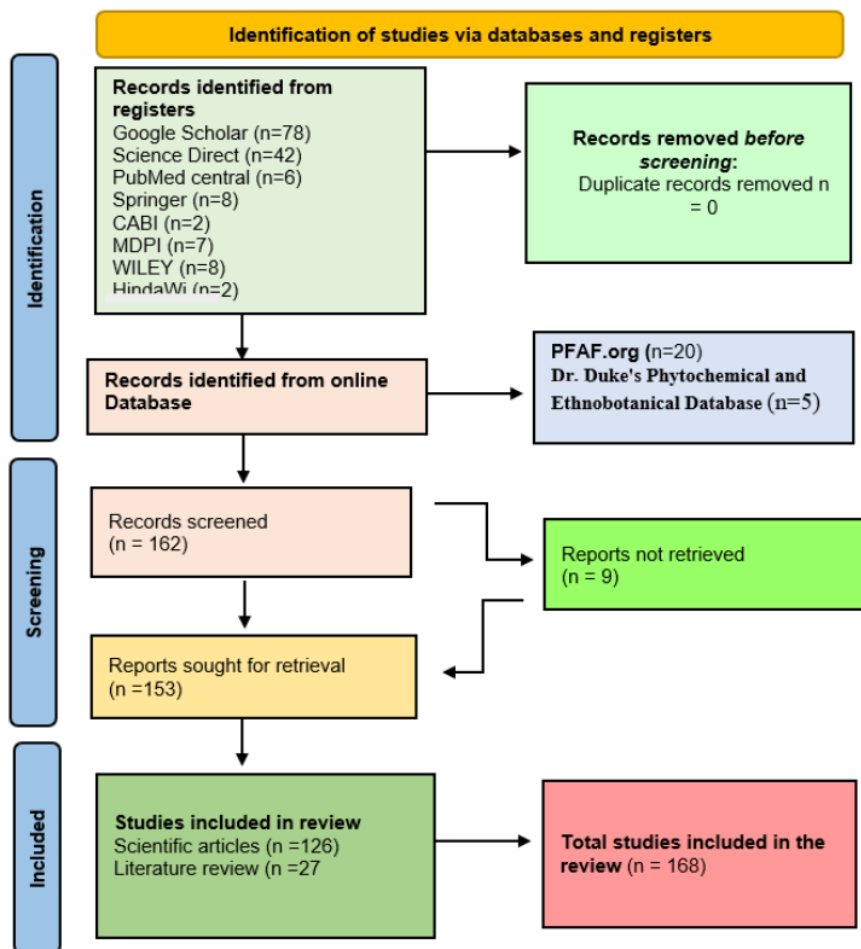


Figure 1. PRISMA flow diagram showing studies included in the review literature of Pharmacophylogeny of Genus *Allium* L.

5.2. Phytochemical Significance and Therapeutic Potential of *Allium* species

A dataset comprising 42 records was meticulously curated for pharmacophylogeny, including 39 accepted species names and 3 synonyms (POWO, 2022). These entries were categorized into 139 usage categories. Notably, 29 out of the 42 species were localized within the hot node of the phylogenetic tree (fig. 3), with data gleaned from 168 published sources. The relevant data pertaining to these categories is delineated in supplementary file S1 and S2. The

predominant therapeutic categories included 17 species for digestive system disorders, 15 for cardiovascular diseases, and 15 exhibiting anticancer properties. Notably, 12 of the identified species were specifically utilized in the treatment of diabetes, while 21 were acknowledged for their antioxidant activities, attributed to the presence of bioactive compounds such as allicin, alliin, flavonoids, phenolics, tannins, and glycosides (supplementary file S1).

Allicin, a prominent phytochemical within genus *Allium*, is well-studied and renowned for conferring the characteristic pungent aroma and taste upon crushing or chopping. This compound is enzymatically synthesized through the interaction of the Alliinase enzyme with the precursor compound alliin (Najeebullah et al., 2021). Wild *Alliums* additionally serve as rich sources of naturally occurring folic acid, fiber, flavonoids, vitamins, and minerals, including thiamine, riboflavin, carotenes, niacin, pyridoxine, lutein, zeaxanthin etc (Mahajan et al., 2019). Cavallito and Bailey (1940) successfully isolated and characterized allicin. When plant tissues incur damage, the release of the alliinase enzyme catalyzes the conversion of S-alk(en)yl cysteine sulfoxide into chemically unstable OSCs (Organosulphur compounds), spontaneously yielding compounds that confer the medicinal properties and flavor associated with *Allium* plants (Deka et al., 2022). The exploitation of wild *Allium* spp. is prevalent among local residents, with all parts of the *Allium* plant being consumed, excluding perhaps the seeds. Noteworthy phytochemicals such as Kaempferol, Isorhamnetin, Morin, Fisetin, Galangin, (Emir et al., 2022); Ajoene, (Singh et al., 2020); Dillapiole, coniferol, (Mahanashi et al., 2022); Lectin, S-methyl-L-cysteine, Limonene, (Selim & Sakeran 2014); Quercetin, Alliin, and Allicin (Kim et al., 2018) play a key role in the therapeutic attributes of *Allium* spp. exhibiting antidiabetic, antioxidant, or dual activities (fig. 2).

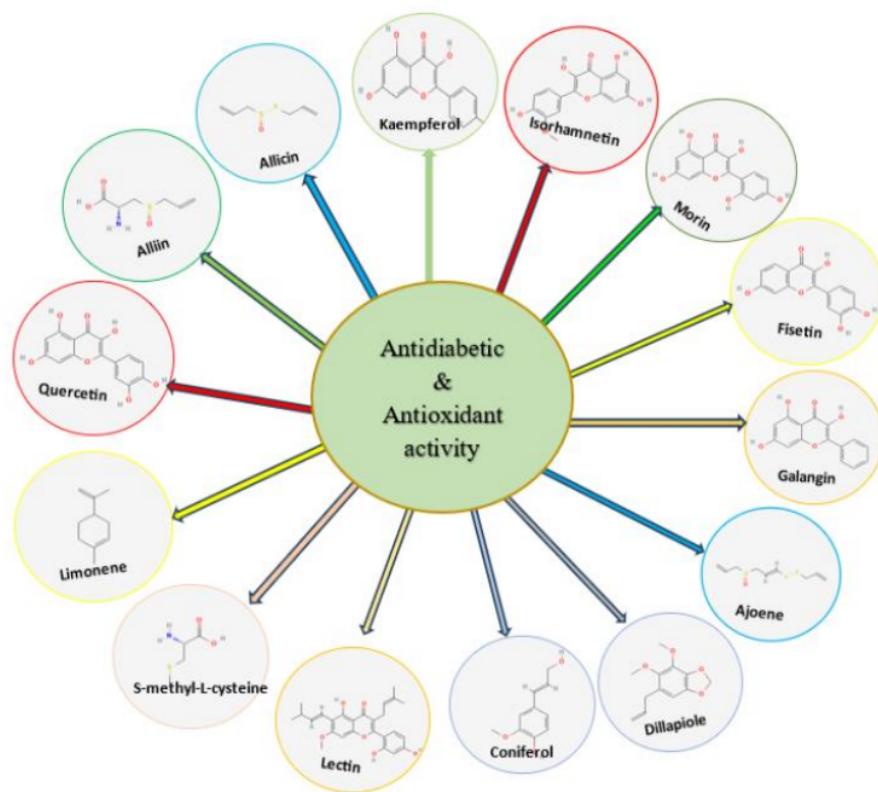


Figure 2. Selected Phytochemical from *Allium* species responsible for Antioxidant and Antidiabetic activity

5.3. Phylogenetic Distribution of species with Therapeutic Uses

Phylogenetic trees serve as instrumental tools in unraveling the evolutionary dynamics within genus *Allium*, providing key insights into the evolutionary relationships among distinct medicinally important species. This information is paramount in comprehending the evolution and divergence of pharmacological traits inherent within the genus *Allium*. Utilizing hot nodes on the phylogenetic tree (fig. 3), we recognized species associated with type II diabetes and antioxidant-related symptoms. A total of 29 species within prominent nodes were identified as likely candidates exhibiting antidiabetic, antioxidant, or dual activities. This determination was relied entirely on the investigation of traditional medicinal uses through phylogenetic analysis. Notably, these lineages include documented antidiabetic and antioxidant activities in species such as *A. akaka*, *A. ampeloprasum*, *A. ascolanicum*, *A. angulosum*, *A. barsczewskii*, *A.*

canadense, *A. carinatum*, *A. carolinianum*, *A. cepa*, *A. chinense*, *A. fistulosum*, *A. consanguineum*, *A. flavum*, *A. hookeri*, *A. humile*, *A. mongolium*, *A. nutans*, *A. paradoxum*, *A. ramosum*, *A. roseum*, *A. rubellum*, *A. sativum*, *A. scabriscapum*, *A. schoenoprasum*, *A. tuberosum*, *A. victorialis*, *A. vineale*, *A. ursinum*, and *A. wallichii*. The species identified within these hot nodes represent novel lines of inquiry, as they lack any corresponding use reports in the existing literature. Bootstrap values observed in the phylogenetic tree indicate the robustness of branches, with a 100 Bootstrap value suggesting strong support for a particular lineage. *Allium* species within these high-confidence nodes exhibit potential in the realms of diabetes treatment and free radical scavenging activity.

In the context of reported ethnobotanical uses, 29 out of 42 species were identified within the hot nodes of the phylogenetic tree, from a total of 185 species included in the analysis. The application of the hot nodes approach facilitated the mapping of reported medicinal uses, particularly those related to type II diabetes and antioxidant activity, demonstrating an overabundance of these traits across the phylogeny.

The antidiabetic effects observed in *Allium* species are attributed to bioactive compounds that enhance insulin sensitivity, inhibit key enzymes in glucose metabolism, and regulate glucose homeostasis. Notably, allicin, previously underestimated in its prevalence within the genus, exhibits potential for both diabetes treatment and free radical scavenging activity (Deka et al., 2021). Additionally, the antioxidant properties observed in these species can be attributed to secondary metabolites that scavenge free radicals, mitigating oxidative stress and averting cellular damage (Hwang et al., 2015).

The pharmacophylogenetic analysis lays the foundation for understanding the distribution of these beneficial traits across related species. This knowledge informs the exploration of *Allium* species for pharmaceutical purposes, aiding in the identification of potential candidates for drug development. Furthermore, it highlights the potential of natural resources in traditional medicine and nutraceuticals for managing diabetes and promoting overall health.

The study unveils several distinct clades within the genus *Allium* characterized by notable antidiabetic and antioxidant properties. The correlation between evolutionary relationships and secondary metabolites provides insights into the molecular underpinnings of these pharmacological activities, emphasizing the potential of *Allium* species in developing novel therapeutics for diabetes and oxidative stress-related conditions. We identified medicinal applications for 42 *Allium* spp, including 3 synonyms viz; *A. nutans*, *A. porrum*, & *A. bodeanum* (POWO, 2022) with 29 of these species integrated into a phylogenetic tree. Primarily, 29 species were specifically employed in the treatment of Diabetes and Free radical

scavenging activity, categorized as Antidiabetic (12 species), Antihyperglycemia (2 species), Antioxidant (21 species), and Hepatoprotective activity (5 species). It is noteworthy that among the 42 species with documented ethnobotanical use, 29 were included in the phylogeny, with a focus on Antioxidant and Diabetes-related symptoms (fig 3, supplementary file S2).

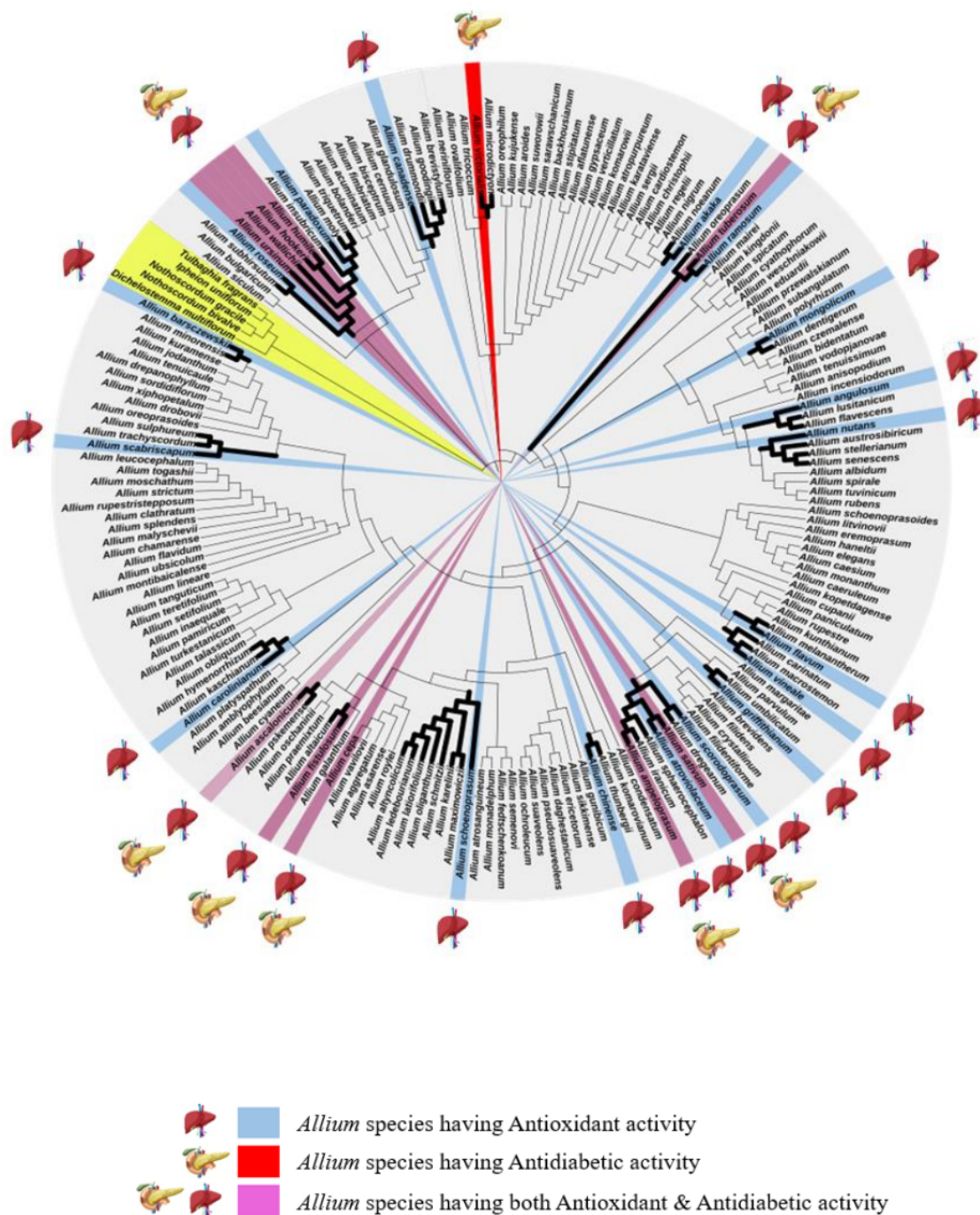


Figure 3. Hot nodes of *Allium* species having Antidiabetic & Antioxidant properties due to presence of secondary metabolites.

5.4. Medicinal use of the taxa studied

This comprehensive analysis involved the classification of 613 utilization records, derived from 168 published sources (supplementary file S1). These records were systematically organized into 139 distinct use categories (supplementary file, S2), adhering to the Economic Botany Data Collection Standard established and previously employed in studies by (Ernst et al., 2016 & Pellicer et al., 2018). The study is based on the medicinal uses of plant species, including a total of 139 categories, however we focussed on specific therapeutic uses either antidiabetic or antioxidant or both activities in 39 species of genus *Allium*. Furthermore, the investigation included the extraction of usage records specifically related to diabetes and free radical scavenging activity, denoted by codes such as Antidiabetic (med_19), Antihyperglycemia (med_27), Antioxidant (med_39), and Hepatoprotective (med_95) (supplementary file S1).

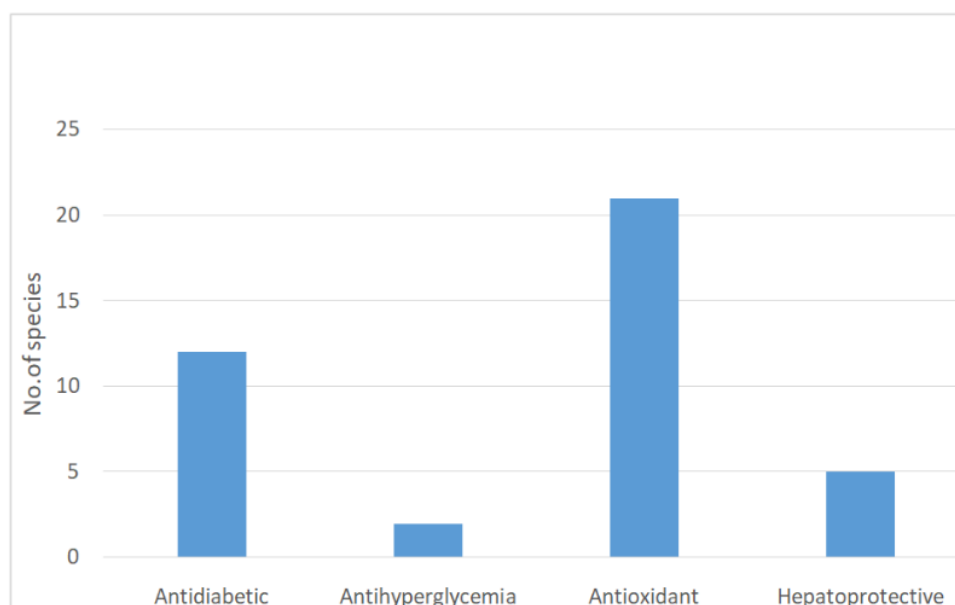


Figure 4. Number of *Allium* species cited in the literature used for the treatment of Antidiabetic and Antioxidant activity present in the phylogeny.

5.5. Phytochemical and Ethno-medicinal relationship of *Allium*

The manifestation of antidiabetic and antioxidant properties within a subset of *Allium* species is attributed to the presence of Allicin, as reported in a specific cohort of taxa (Lu et al., 2011). Especially, Allicin has been identified in seven species, namely *A. ampeloprasum*, *A. ascalonicum*, *A. cepa*, *A. chinense*, *A. fistulosum*, *A. hookeri*, and *A. sativum*, out of a total of 29 species incorporated within the hot nodes of the phylogenetic tree (fig. 3). The instances where Allicin presence is confirmed are denoted in bold within the dataset. Additionally, Allicin has been reported in 11 other distinct species, exhibiting involvement in various biological activities (table 1) & supplementary file S1).

It is noteworthy that among the diverse species identified to contain Allicin, only a selected few were previously acknowledged as primary sources of this compound, probably scarce of detailed investigation in the species of Genus in Question (supplementary file S1). The phylogenetic analysis postulates that the Allicin biosynthesis pathway may be a plesiomorphic character within the genus. Consequently, the widespread distribution of species in genus *Allium* suggests the potential for utilizing alternative species at the local level for the treatment of diabetes and other related conditions. This highlights the versatility of Allicin-producing species and their applicability in diverse medicinal contexts within the genus.

Table 1. Allicin content in seven investigated *Allium* species out of 29 on hot node of phylogenetic tree (supplementary file S1).

Species	Antidiabetic activity, Allicin (+/-)	Antioxidant activity, Allicin (+/-)
<i>Allium ampeloprasum</i>	Yes, -	Yes, +
<i>Allium akaka</i>	No	Yes, -
<i>Allium angulosum</i>	No	Yes, -
<i>Allium ascalonicum</i>	Yes, -	Yes, +
<i>Allium atroviolaceum</i>	No	Yes, -
<i>Allium barszczewskii</i>	No	Yes,

		-
<i>Allium canadense</i>	No	Yes, -
<i>Allium carinatum</i>	No	Yes, -
<i>Allium carolinianum</i>	No	Yes, -
<i>Allium cepa</i>	Yes, -	Yes, +
<i>Allium chinense</i>	No	Yes, +
<i>Allium fistulosum</i>	Yes, -	Yes, +
<i>Allium flavum</i>	No	Yes, -
<i>Allium griffithianum</i>	No	Yes, -
<i>Allium hookeri</i>	Yes, +	Yes, +
<i>Allium humile</i>	Yes, -	Yes, -
<i>Allium mongolicum</i>	No	Yes, -
<i>Allium nutans</i>	No	Yes, -
<i>Allium paradoxum</i>	No	Yes, -
<i>Allium ramosum</i>	No	Yes, -
<i>Allium roseum</i>	No	Yes, -
<i>Allium rubellum</i>	No	Yes, -

<i>Allium sativum</i>	Yes, +	Yes, +
<i>Allium scabriscapum</i>	No	Yes, -
<i>Allium schoenoprasum</i>	No	Yes, -
<i>Allium tuberosum</i>	Yes, -	Yes, -
<i>Allium victorialis</i>	Yes, -	No
<i>Allium vineale</i>	No	Yes, -
<i>Allium ursinum</i>	Yes, -	Yes, -
<i>Allium wallichii</i>	Yes, -	Yes, -

5.6. Ethno-medicinal uses of *Allium*

The majority of *Allium* species are esteemed for their gustatory qualities, finding extensive utilization as culinary flavors (Sabiu et al., 2019). These botanical entities constitute a prolific reservoir of phytonutrients and bioactive compounds, including flavonoids, glucosides, steroids, phenolics, alkaloids, and an array of organosulfur compounds such as Allicin, Allin, DATS (diallyl trisulfide), DADS (diallyl disulfide), crucial for sustaining daily physiological functions (Kim et al., 2018).

Scientific investigations have substantiated the medicinal properties inherent in the genus *Allium*. Notably, empirical evidence indicates that highest consumption of *Allium* vegetables correlates with a diminished likelihood of developing various afflictions, including diabetes, cardiovascular disease, cancer etc (supplementary file S1). The heatmap depicts the presence other biological activities apart from Antidiabetic and Antioxidant activity due to the presence of phytoconstituents in the species on hot node of phylogenetic tree (supplementary file S1). The ethnomedicinal applications of *Allium* species identified within the hot node of the phylogenetic tree, along with their predominant bioactive constituents and corresponding biological activities, are systematically delineated through the construction of a heatmap (fig.

5). This comprehensive representation illuminates the multifaceted therapeutic attributes associated with these *Allium* species, providing a nuanced understanding of their ethno medicinal relevance and potential contributions to human health.

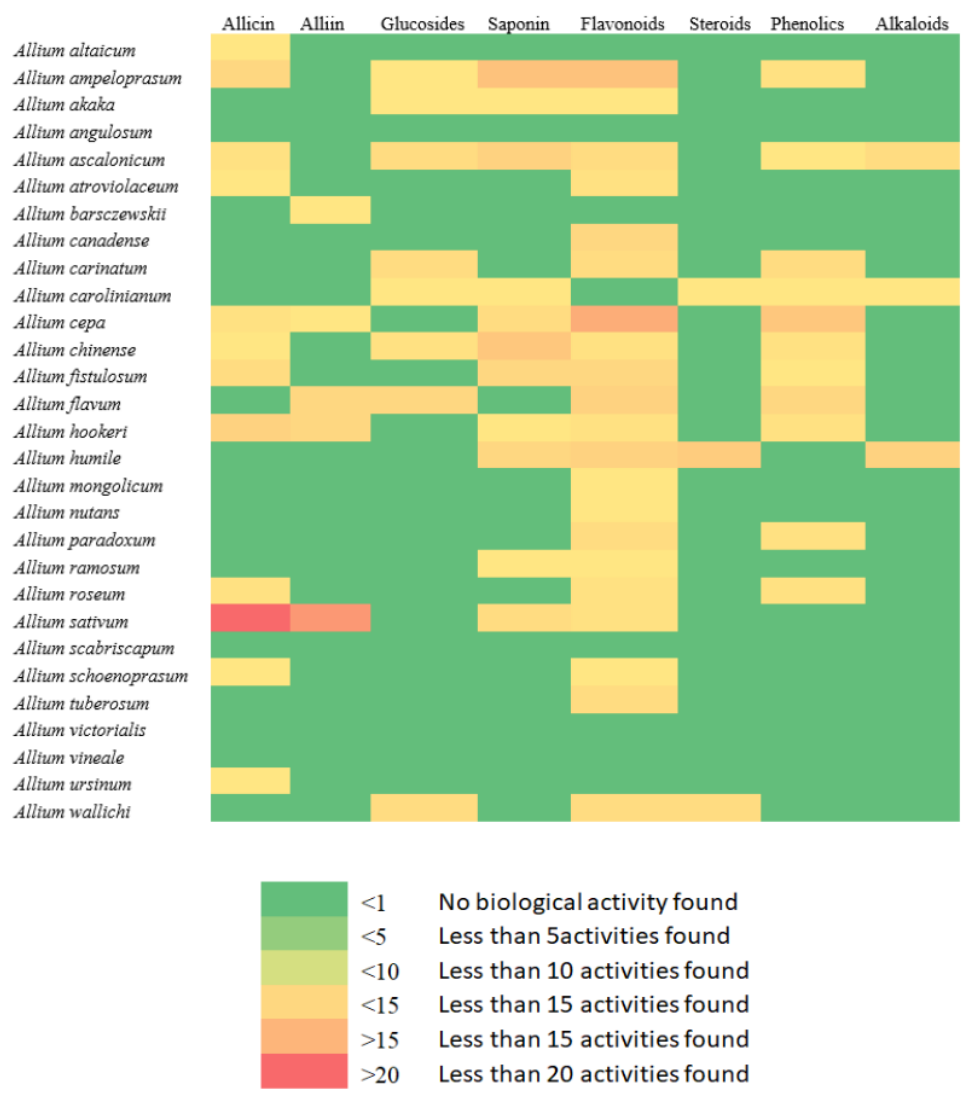


Figure 5. Number of Biological activities found in different species on hot node of phylogenetic tree due to presence of frequently found secondary metabolites.

6. Discussion

6.1. Phylogenetic Prediction of Antidiabetic and Antioxidant Activity of Genus *Allium*

The genus *Allium* has long been recognized for its ethnopharmacological significance, owing to its diverse medicinal properties and widespread traditional use across different cultures (Borborah et al., 2014). This study builds upon this rich tradition by investigating into the intricate relationships between phylogeny, pharmacology, and traditional medicinal knowledge within the genus *Allium*. Pharmacophylogeny, as elucidated by Xiao et al., (2006) and Hao et al., (2022) provides a theoretical framework for understanding how phylogenetic relationships among plants can inform their chemical composition and therapeutic effects. The phylogenetic analysis of 185 species of *Allium* has unveiled a distinctive clades or lineages within the taxonomic genus *Allium*, comprising species acknowledged for their pronounced antidiabetic and antioxidant activities. Specifically, the examination of phylogenetic relationships has delineated several clades including species like *A. wallichii*, *A. tuberosum*, *A. ursinum*, *A. hookeri*, and *A. humile*, exhibiting concurrent antioxidant and antidiabetic properties. Comparable attributes are detected in another lineage that contain species such as *A. cepa*, *A. fistulosum*, *A. ascalonicum*, and a subclade housing species like *A. ampeloprasum* and *A. sativum*. The antioxidant properties are further evident in lineages with species such as *A. schoenoprasum*, *A. chinense*, *A. carolianum*, *A. akaka*, *A. ramosum*, *A. nutans*, *A. angulosum*, *A. mongolicum*, *A. griffithianum*, *A. scorodoprasum*, *A. flavum*, *A. vineale*, *A. barsczewskii*, *A. paradoxum*, *A. roseum*, *A. canadense*, and *A. atrovioleaceum*. Conversely, the antidiabetic properties are notable in a lineage housing *A. victoralis*, forming a clade with *A. christophii*, suggesting a possible extension of the antidiabetic trait to the latter, necessitating empirical validation.

The presence of secondary metabolites, including flavonoids, alkaloids, and phenolic compounds, in these species is postulated to play a pivotal role in conferring these therapeutic properties (Mahajan et al., 2019). These findings corroborate with previous studies highlighting the potential of phylogenetic approaches in predicting medicinal properties of plants (Pellicer et al., 2018). Besides, these findings allude to a potential evolutionary convergence within specific lineages, indicating a concerted development of these pharmacological traits. Our study also emphasizes the significance of phytochemical analysis in elucidating the therapeutic potential of *Allium* species. Compounds such as allicin, flavonoids, and phenolics have been identified as key bioactive constituents responsible for the observed antidiabetic and antioxidant activities (Najeebullah et al., 2021).

7. Conclusion

In conclusion, our study elucidates the pharmacophylogeny of genus *Allium*, highlighting their potential as sources of antidiabetic and antioxidant activities due to the presence of bioactive compounds. Through integration of traditional knowledge and phylogenetic analysis, we identify distinct clades within the genus exhibiting significant therapeutic properties. This interdisciplinary approach emphasizes the importance of exploring natural plant resources for drug discovery and healthcare enhancement. By bridging traditional medicinal practices with modern scientific methodologies, our findings offer valuable insights into the evolutionary and pharmacological dynamics of genus *Allium*, paving the way for future research and the development of drugs and novel therapeutics.

8. Future Prospective

In the future, further exploration of *Allium* species could focus on in-depth phytochemical analysis to identify novel bioactive compounds with potential therapeutic applications. Additionally, studies examining the mechanisms of action underlying the antidiabetic and antioxidant effects of *Allium* constituents could provide valuable insights into their pharmacological properties. Furthermore, collaborative efforts between traditional medicine practitioners and modern researchers may facilitate the integration of ethnobotanical knowledge with scientific evidence, leading to the development of evidence-based herbal medicines.

9. Acknowledgment & Funding

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10. Supplementary Files: S1, S2 & S3.

11. References

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