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Computational network pharmacology and virtual screening analysis of chemical constituents of plants used in the Traditional Drink "Al-Jur" against COVID-19 and Seasonal Respiratory Diseases

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Dedication

إلى من كلّل العرق جبينه، ومن علّمني أن النجاح لا يأتي إلا بالصبر والإصرار

إلى النور الذي أنار دربي، والسراج الذي لا ينطفئ نوره أبدًا

من بذل الغالي والنفيس، ومن استمددت منه قوة واعتزازًا بذاتي

أبي الغالي

إلى من جعلت الجنة تحت أقدامها، وتصدّت للشدائد بدعائها

إلى الإنسانة العظيمة التي لطالما تمنيت أن تقرّ عينها في يومي هذا

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إخوتي الأعزاء

إلى الجوهرة النادرة، منبع الحنان والعطاء

أم مهدي

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وآخر دعوانا أن الحمد لله رب العالمين

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Dedication

بسم الله الرحمن الرحيم

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Abstract

This study combines computational network pharmacology and virtual screening to evaluate the therapeutic potential of the traditional multi-herb beverage "Al-Jur" against COVID-19 and other respiratory infections. Traditionally used to treat respiratory and digestive disorders, "Al-Jur" is analyzed here for its key bioactive compounds and their pharmacological interactions.

Using systems-level pharmacology tools, interactions between phytochemicals and disease-related protein targets were mapped, with particular focus on COVID-19 and other respiratory pathogens. In parallel, bioactive compounds were virtually screened against these targets to assess binding affinities and potential inhibitory effects.

Results suggest that the compounds from "Al-Jur" act on a network of functionally related proteins, influencing entire biological pathways rather than single molecular targets. These findings support the potential of this traditional remedy as a multi-target therapeutic candidate for managing respiratory infections, including COVID-19.

Key words: Al-Jur tea, medicinal plants, bioactive compounds, computational network pharmacology, respiratory diseases, COVID-19

Résumé

Cette étude combine la pharmacologie réseau computationnelle et le criblage virtuel pour évaluer le potentiel thérapeutique de la boisson traditionnelle multi-plantes « Al-Jur » contre la COVID-19 et d'autres infections respiratoires. Traditionnellement utilisée pour traiter les troubles respiratoires et digestifs, « Al-Jur » est ici analysée pour ses composés bioactifs clés et leurs interactions pharmacologiques.

À l'aide d'outils de pharmacologie à l'échelle des systèmes, les interactions entre les phytocomposés et les cibles protéiques liées aux maladies ont été cartographiées, avec un accent particulier sur le COVID-19 et d'autres agents pathogènes respiratoires. Parallèlement, les composés bioactifs ont été soumis à un criblage virtuel contre ces cibles afin d'évaluer leurs affinités de liaison et leurs effets inhibiteurs potentiels.

Les résultats suggèrent que les composés de « Al-Jur » agissent sur un réseau de protéines fonctionnellement liées, influençant des voies biologiques entières plutôt que des cibles moléculaires uniques. Ces découvertes soutiennent le potentiel de ce remède traditionnel comme candidat thérapeutique multi-cibles pour la prise en charge des infections respiratoires, y compris la COVID-19.

Mots clés : Thé Al-Jur, plantes médicinales, composés bioactifs, pharmacologie des réseaux informatiques, maladies respiratoires, and COVID-19.

الملخص

تستند هذه الدراسة إلى دمج تقنيات الصيدلة الشبكية الحاسوبية والفحص الافتراضي من أجل تقييم الإمكانات العلاجية للمشروب التقليدي "الجور" في مكافحة فيروس كوفيد-19 وأمراض الجهاز التنفسي الأخرى. يُعرف "الجور" بأنه منقوع عشبي يتكون من مجموعة متنوعة من النباتات المستخرجة من الغابات، وقد استُخدم تقليديًا لعلاج اضطرابات الجهاز التنفسي والهضمي على مدى فترة طويلة.

في هذا البحث، تم تحليل المركبات النشطة بيولوجيًا الموجودة في "الجور" بشكل منهجي، مع التركيز على تفاعلاتها مع البروتينات المستهدفة المرتبطة بأمراض الجهاز التنفسي، لا سيما فيروس SARS-CoV-2 والفيروسات التنفسية الموسمية الأخرى. وقد تم استخدام بيانات مستمدة من قواعد بيانات صيدلانية معتمدة لبناء شبكات تفاعلية بين المركبات الكيميائية والنقاط البيولوجية المستهدفة، مما أتاح تحديد الأهداف العلاجية الرئيسية ذات الصلة بالعدوى الفيروسية.

إلى جانب ذلك، أُجري فحص افتراضي للمركبات النشطة في "الجور" لتقييم قدرتها على الارتباط بالبروتينات المرتبطة بأمراض الجهاز التنفسي وكوفيد-19، وذلك بهدف تحديد مدى قوة التثبيط المحتمل لهذه المركبات. أظهرت نتائج الدراسة أن هذه المركبات لا تستهدف بروتينًا واحدًا فقط، بل تعمل على شبكة من الأهداف الوظيفية المرتبطة ببعضها البعض، مما يؤثر على مسارات بيولوجية كاملة داخل الخلية. وعندما يتم استهداف بروتين رئيسي في هذه الشبكة، يؤدي ذلك إلى تأثيرات متسلسلة عبر البروتينات المتفاعلة معه، مما يعزز التأثير العلاجي للمركبات.

الكلمات المفتاحية: مشروب الجور، النباتات الطبية، المركبات النشطة بيولوجيًا، علم الأدوية الشبكي، أمراض الجهاز التنفسي، كوفيد-19

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Abbreviations

ORDs: Occupational Respiratory Diseases

HRCT: High-Resolution Computed Tomography

COPD: Chronic Obstructive Pulmonary Diseases

CLRDs: Chronic Lower Respiratory Diseases

HRT: Upper Respiratory Tract

LRTs: Lower Respiratory Tracts

RTIs: Respiratory Tract Infections

ARDS: Acute Respiratory Distress Syndrome

LRIs: Lower Respiratory Tract Infections

WHO: World Health Organization

SARS-COV-2: The Severe Acute Respiratory Syndrome Coronavirus 2

ACE2: The Angiotensin -Converting Enzyme 2

NP: Network Pharmacology

HTS: High-Throughput Screening

NMR: Nuclear Magnetic Resonance

CADD: Computer -aided Drug Design

EGFR: Epidermal Growth Factor Receptor

MAPK1: Mitogen-Activated Protein Kinase 1

PI3K: Phosphoinositide 3-kinases

AKT1: Protein Kinase B

INSR: Insulin Receptor

CACNA1C: Calcium channel subunit alpha-1C

TRPV1: Transient Receptor Potential Vanilloid 1

STAT3: Signal Transducer and Activator of Transcription 3

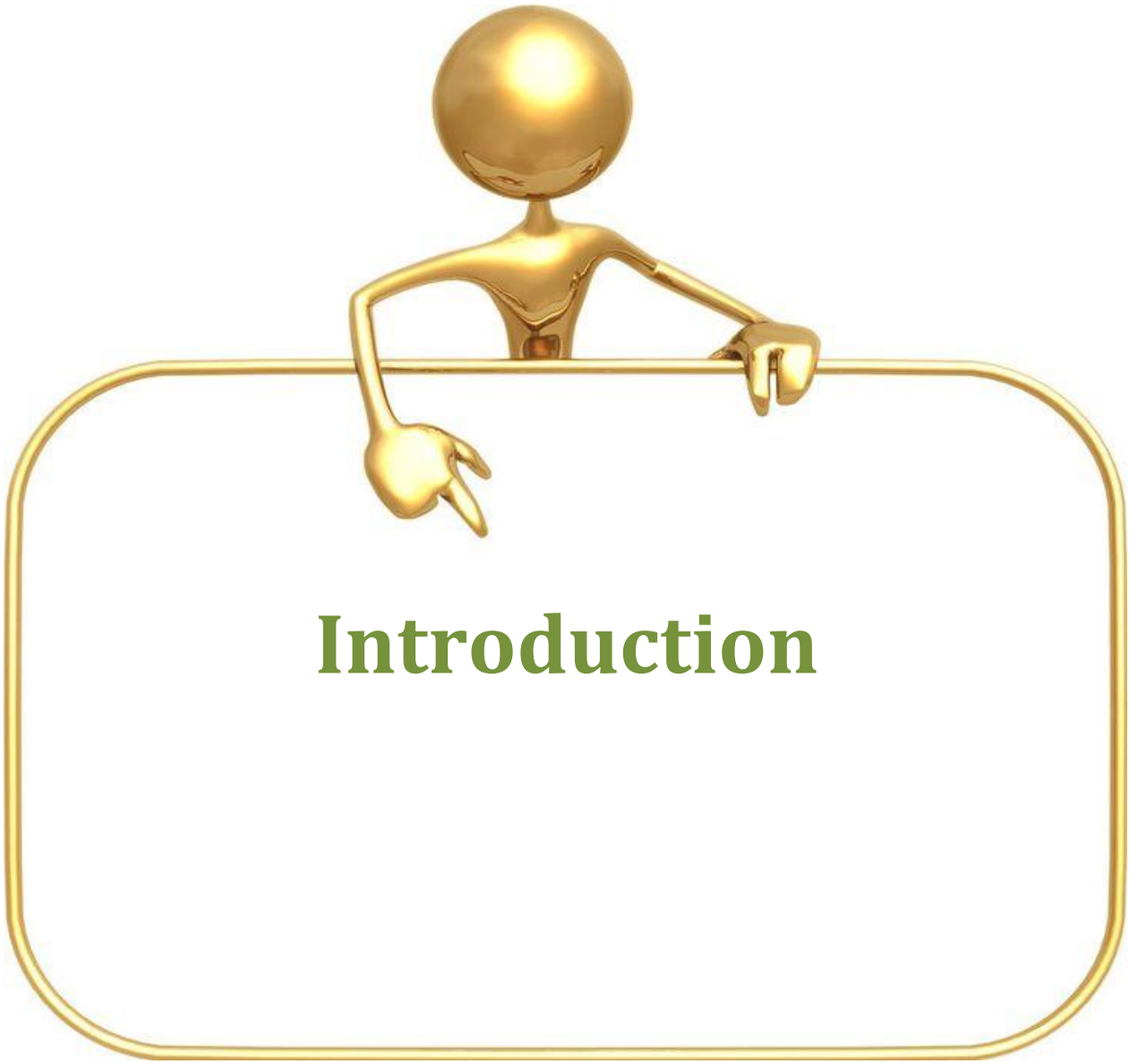
BDKRB2: Bradykinin Receptor B2

HTR2A :5-HT2A serotonin receptor

ERK1/2: Extracellular signal-regulated kinases

AR: Androgen Receptor

NO: Nitric Oxide



Introduction

At the beginning of the 18th century, medical practice in Algeria was primarily based on traditional methods, due to the absence of formal medical institutions and codified legal frameworks. Algerian traditional medicine, rooted in a millennia-old heritage, seamlessly integrated ancient knowledge from Islamic civilization with the practical use of natural substances, particularly medicinal plants.

Plant-based remedies formed the central pillar of this therapeutic system. Healers possessed in-depth knowledge of local flora and its therapeutic applications, passing down their expertise orally from generation to generation. These traditional practitioners were vital members of their communities, with their healing methods often intertwined with spiritual beliefs to address ailments attributed to supernatural causes. This holistic approach reflects the foundational importance of traditional medicine in the daily lives of Algerians at the time, drawing from the intellectual legacy of Islamic medical scholars (Belhouala & Benarba, 2021; Clark, 2021; Tahri et al., 2020).

Within this traditional medical context, the herbal drink "Al-Jur" holds a special place as one of the oldest and most renowned plant-based remedies. Originating from the regions of Bousaada and Djelfa, this multi-herb preparation gained popularity during the French colonial period. Primarily consumed during the winter months, it has traditionally been used to relieve respiratory ailments.

Today, the rise of network pharmacology offers a unique opportunity to revisit this ancestral knowledge through the lens of modern science. This interdisciplinary approach, combining systems biology, bioinformatics, and pharmacology, enables the study of complex interactions between drugs, biological targets, and entire systems. Unlike classical approaches that focus on a single molecular target, network pharmacology models the full spectrum of interactions among genes, proteins, and metabolic pathways, providing a scientific framework particularly well-suited to the multi-target nature of traditional medicines (Wang et al., 2022; Miao et al., 2022).

In the face of current public health challenges, including seasonal respiratory diseases and the COVID-19 pandemic, the scientific investigation of traditional remedies such as "Al-Jur" is of particular relevance. This study aims to elucidate the chemical constituents (essential oils and

phenolic compounds) of the plants used in this traditional beverage and to assess their potential effectiveness against COVID-19 and seasonal respiratory illnesses using advanced computational approaches in network pharmacology.

Network pharmacology methodology will be applied to map the interactions between the chemical constituents of "Al-Jur" and the biological targets associated with respiratory diseases and COVID-19. Data extracted from established pharmacological databases will be used to build interaction networks and identify key therapeutic targets.

This manuscript is organized into two main parts: a comprehensive literature review presenting the fundamental concepts of the study, followed by a section detailing the methodology, results, and discussion. The work concludes with a general synthesis summarizing the main findings of the study.

Bibliographic part

Chapter 01 :
« Al-Jur »

1-Al Jur:

Al-Jur is a traditional beverage with deep historical roots, renowned for its unique blend of natural ingredients and cultural significance.

Figure 1: The popular Naseem or Jazwa cafe in Bou Saada, where coffee and Al-Jur are prepared.

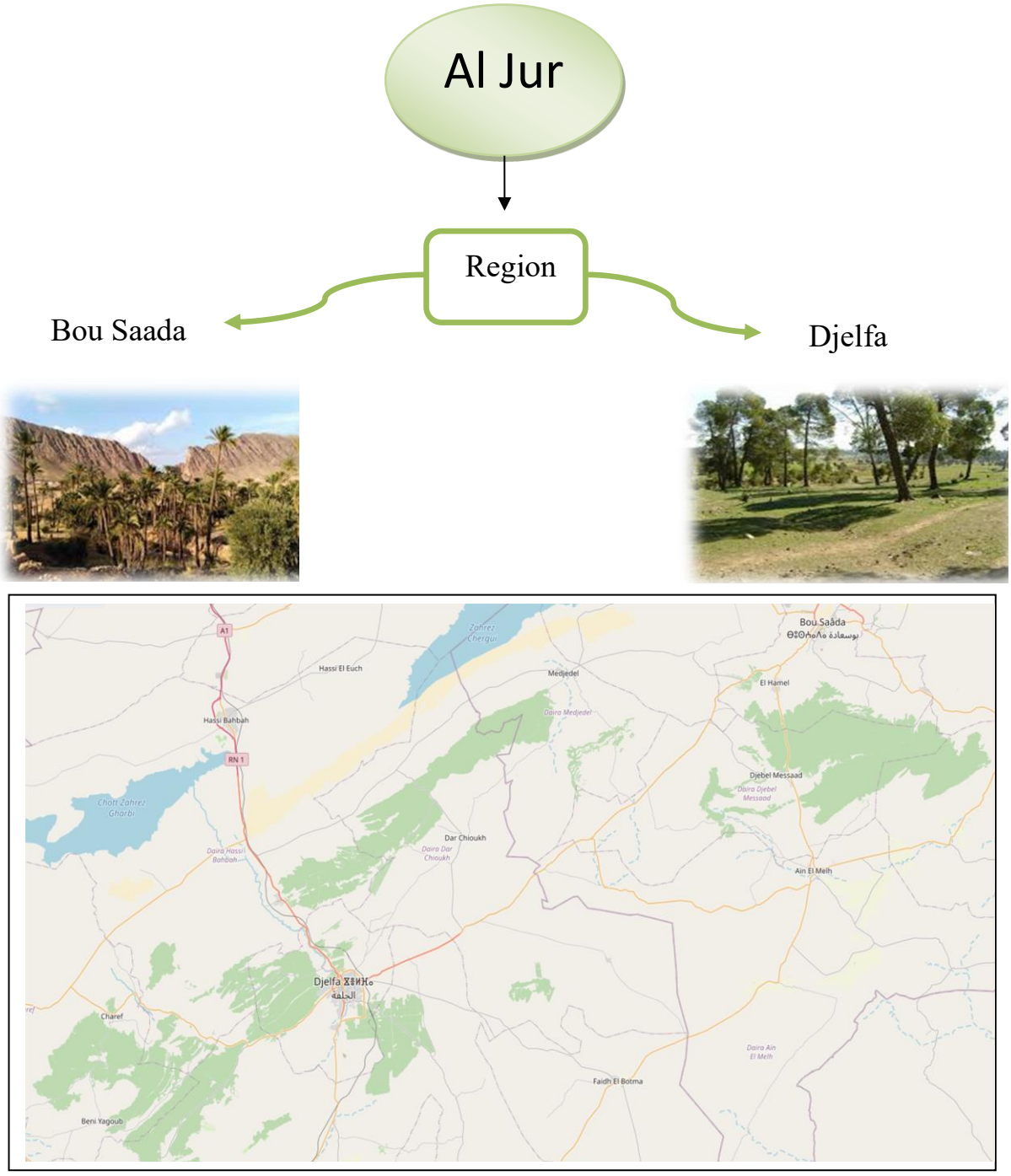


Figure 2: Harvesting areas of medicinal plants used in Al-Jur.

2-Plants contained in "Al Jur":

Drawing its essence from diverse botanicals, the traditional drink **"Al Jur":** is created using 10 different plants, representing a rich variety of families.

Table1: List of Plants medicinal.

Family	Scientific Name	Franch Name		Vernacular Name
Anacardiaceae	*Pistacia Lentiscus L*	Lentisque	Dhrou	ضرو
Asteraceae	*Artemisia herba alba Asso*	Armoise blanche	Chih	شيح
	Artemisia campestris L	Armoise champêtre	Degoufet	دقفت
Cistaceae	*Cistus salvifolius L*	Ciste à feuilles de sauge	Alkassa	القاصة
Cupressaceae	*Juniperus phoenicea L*	Genévrier de phoenecie	Aârâar	عرعار
Fagaceae	*Quercus Ilex L*	Chêne vert	Bellout	بلوط
Lamiaceae	*Thymus algériensis, boiss et reut*	Thym d'Algérie	Djertil	جرتيل
	Rosmarinus officinalis L	Romarin	Aklil el-djabel	اكليل الجبل
Pinaceae	*Pinus halepensis Mill*	Pin d'Alep	Senouber	صنوبر
Oleaceae	*Phillyrea angustifolia L*	Filaire a feuillées étroit	ktem	قتم

3-Identification of family members:

These trees and shrubs primarily thrive in tropical and subtropical regions, though they also extend into temperate zones, particularly the Mediterranean, where many are notable for their aromatic qualities or distinctive botanical characteristics. Each of these plant families is further categorized into species, which are then subdivided into genera.

Table2: Identification of family members (species- genera).

the family	species	genera	References
Anacardiaceae	600 - 700	70 -77	(Hoff, M. (1997))
Asteraceae	902	90	(Shen F, et al.,2023)
Cistaceae	200	8	(Zerrougui-Bekrar 2019)
Cupressaceae	160	29	(Poncet et al., 2021)
Lamiaceae	258	690	(CHERIET & DIFALLAH, 2024)
Pinaceae	230 -240	11	(Thibeault & Chimie, 2023)
Oleaceae	600	30	(Adjim & Djezzar, 2023)
Fagaceae	18000	640	(Sato, S., et al., (2010).)

4-Identification of the plants:

Figure 3: *Pistacia Lentiscus* L.

4.1 *Pistacia Lentiscus* L:

a. Botanical description:

Bushy shrub generally not exceeding 1.5 to 2 m although it can sometimes reach 5 to 6 m in height. Evergreen paripinnate leaves, with 4-10 pairs of oblong-lanceolate or elliptical, obtuse, mucronate, blabrous leaflets measuring 15-45mm long and 5-10mm wide, dark green and shiny above, paler, and dull below, they take on a purplish tint in winter. The flowers are in small racemes, in the axils of the leaves, with a five-lobed calyx, with 5 stamens, reddish in color. The fruit, in October-November, is a globular drupe, not very fleshy, the size of a pea, initially red, then black when ripe, 4 to 5mm in diameter (MAHMOUD, 1988).

b. Habitat: Mastic tree is dioicous, found in Mediterranean Europe, Mediterranean region, and Iberian Peninsula in the west, through southern France.

c. Harvest period: Spring-summer (MAHMOUD, 1988).

d. Part used: Leaves, fruit, mastic.

e. Chemical principles: α- pinene, β- pinene, limonene, terpene-4-ol and terpeneol7, contain β- caryophylline, germaerene and γ-cadinene.

f. Therapeutic properties: Antiatherogenic activity, antimicrobial activity, Antioxidant activity, Hepatoprotective activity, Antiarthritic and Antigout activity, Anticancer activity, Wound healing activity, Lipid lowering effect **(**Milia E,et al., 2021 **).**

g. Traditional use: Treatment of stomachaches, Hypertension, Sore throats, Coughs, Eczema, Kidney stones, Jaundice, possess stimulant properties, Possess diuretic properties, Treatment of respiratory problems, Treatment of disorders of the digestive system(Zitouni et al.,2023).

Figure 4: *Artemisia herba alba Asso.*

4.2. *Artemisia herba alba Asso*:

a. Botanical description:

The plant is characterized by capitula that are pauciflorous or multiflorous but heterogamous, with female ray florets and hermaphrodite disc florets. The corolla can be glabrous or pilose, and the receptacle can be glabrous or hairy. Leaves are described as whitish or green, large, or small, silvery-silky, or punctate and pubescent, with varying arrangements (pinnatisect or ternatisect). The plant is classified as a perennial herbaceous plant, 40-70 cm tall, with herbaceous stems, found in clear mountain forests (Younsi, F.et al 2016).

b. Habitat: growing in mountain habitats of North Africa (Algeria, Morocco, Tunisia) (Matsabisa et al., 2022).

c. Harvest period: Spring-Summer.

d. Part used: The whole plant.

e. Chemical principles: The main class was that of oxygenated monoterpenes. The compound present in the highest quantity was camphor, the other main components being α- and β-thujone, 1,8-cineole, piperitenone and camphene (Baranová et al., 2025).

f. Therapeutic properties: Antioxidant activity**,**Antibacterial activity(Mahboub et al., n.d.) to treat bronchitis, diarrheas, hypertension and diabetes (Matsabisa et al., 2022)

g. Traditional use: the treatment of digestive and neurological disorders. It is also used to treat genitourinary, metabolic diseases, osteo-articular, dermatological and respiratory diseases (Benkhaira et al., 2021).

Figure 5: *Artemisia campestris* L.

4.3. *Artemisia campestris L*:

a. Botanical description:

This species often presents as a perennial herbaceous plant, reaching heights of approximately 30 to 100 cm. Its stems are typically erect and may exhibit branching, depending on specific environmental conditions and genetic factors. The leaves of *Artemisia campestris* L campestris are alternate, deeply lobed, and exhibit a finely dissected appearance, allowing for effective photosynthesis while minimizing water loss, a critical adaptation in various

ecosystems. The leaf arrangement and morphology contribute to the plant's overall aesthetic, often yielding a silvery-green color due to a covering of fine hairs, which serves both protective and photosynthetic functions(Ekiert et al.,2020).

b. Habitat: Very widespread on the high plateaus and the Sahara (it is a steppe plant) (MAHMOUD, 1988).

c. Harvest period: Spring-Summer.

d. Part used: The aerial part.

e. Chemical principles: sesquiterpenoid lactones, flavonoids, coumarins, phenolic acids, sterols, polyacetylenes, carotenoids, vitamins, and cyanogenic glycosides(Ekiert et al.,2020).

f. Therapeutic properties: Antioxidant activity**,** Antibacterial activity**,** diarrheas.(Ekiert et al).

g. Traditional use: used for alleviating gastrointestinal discomfort and treating gynecological diseases**,** curing ulcers and diarrhea**…**(Ekiert et al.,2020).

Figure 6: *Cistus salvifolius* L.

4.4. *Cistus salvifolius* L:

a-Botanical description:

this perennial shrub typically reaches a height of 1 to 1.5 meters. The plant is distinguished by its slender, erect stems and dense foliage, which consists of small, ovate to lanceolate leaves measuring approximately 2 to 5 cm in length. These leaves are notably grayish green, covered with fine hairs that serve to reduce water loss by reflecting sunlight and minimizing transpiration, an essential adaptation in the arid condition's characteristic of Mediterranean climates (Puglielli Tutor & Gratani, 2018).

b. Habitat: Rocky slopes, dry grasslands, prefers sunny locations, nutrient-poor, calcareous soils (Boubekeur, S., Messaoudi, M.et al (2022)

c. Harvest period: Spring.

d. Part used: The leaves.

e. Chemical principles: flavonoids, condensed tannins, and hydrolysable tannins.

f. Therapeutic properties: Antioxidant Activity, Antibacterial activity, Anti-inflammatory activity, antifungal (Sayah et al., 2017).

g. Traditional use: mainly against peptic ailments and skin disorders, such as burns, wounds, and infections(Tomou et al., 2022).

Figure7 : *Juniperus phoenicea* L.

4.5. *Juniperus phoenicea* L:

a-Botanical description:

is a shrub or small evergreen tree which can grow 5-8m with a trunk up to 1-2m in diameter1. The shrub form develops several stems close to the ground, while its upright form is monopodial2. The crown is dense, first conical then broadening and irregular in age, with ascending and often curved branches2, 3. The bark is dark greyish brown, peeling in narrow strips3. On young plants the leaves are needle-like, about 1mm wide and 5-14mm long, with 2 stomatal bands above and beneath (Caudullo, G., & de Rigo, D. 2016).

b. Habitat: The distribution of Phoenician juniper covers the whole Mediterranean basin (Caudullo, G., & de Rigo, D. 2016).

c. Harvest period: Berries: Sept – Nov. Wood: Feb–Mar.

d. Part used: Leaves, cones, tar.

e. Chemical Principles : Polyphenols, Flavonoids..(Nasri et al., 2011).

f. Therapeutic properties: antibacterial, anti-inflammatory, antiviral, expectorant, sedative, herbicidal, insect-repellent, and aromatic properties.(Khalil et al., 2025).

g. Traditional use: It has been employed to address various ailments, including diarrhea, rheumatism, diabetes, and respiratory issues.Abu-Darwish, M.,2014)

Figure 8 :*Quercus Ilex* L.

4.6. *Quercus Ilex* L:

a. Botanical description:

is a broadleaved evergreen tree or shrub, which can grow up to 25m and exceptionally 30m with over 2m of trunk diameter1, 2. Its lifespan may reach more than 1000 years2-4. The crown is broad, domed, with ascending branches and often with low stems. The bark is brownish-black and shallowly cracked into small, square, thin plates5. The twigs and the buds are grey-tomentose1. Very variable in the shape, the leaf is generally lanceolate to oval, 3-7cm long, thick but not rigid, cuneate, or rounded at the base, with 1-2cm woolly petioles. The margins are waved or sinuate, but they can be dentate or in some case spinose on young trees or sprouts1, 5. They unfold in spring silvery-white then pale yellow, covered with dense hairs. Soon leaves become rough and shiny blackish green on the upper side, grey and densely pubescent on the lower (De Rigo, D., & Caudullo, G. 2016).

b. Habitat is native to and predominantly distributed across the central-western Mediterranean basin, including countries such as Portugal, Spain, France, Italy, Greece, Morocco, Algeria, and parts of Turkey and the Balkans (De Rigo, D., & Caudullo, G. 2016).

c. Harvest period: Spring.

d. Part used: The leaves, fruits, cupules, and bark of young branches.

e. Chemical principles: phenolic and flavonoid….(Barkat et al., 2019).

f. Therapeutic properties: Antioxidant activity**,** Antibacterial activity, diabetes**,** anti-inflammatory(Taib et al., 2020).

g. Traditional use: them as antiseptics and to treat gastrointestinal tract disorders such as diarrhea and hemorrhoids It is widely used to treat gonorrhea, gastritis, asthma, (Taib et al., 2020).

Figure 9: Thymus algeriensis.

4.7.*Thymus algeriensis*:

a. Botanical description:

typically measuring between 10 to 40 cm in height. Its structure includes slender, erect, and hairy twigs, adorned with opposite grayish-green foliage consisting of ovate-oblong to linear leaves, which measure approximately 4-10 mm in length (El Midaoui et al., 2023).

b. Habitat found in regions such as Morocco, Algeria, Tunisia, and Libya, is primarily recognized for its resilient growth in diverse bioclimatic zones, ranging from subhumid to lower arid environments (Jaouadi et al., 2019).

c. Harvest period: Summer.

d. Part used: the flowering herbaceous branches.

f. Chemical Principles: flavonoids, phenolic acids (Jaouadi et al., 2019).

g. Therapeutic properties: Antioxidant activity**,** Antibacterial activity, antifungal, antitumor effect (Jaouadi et al., 2019).

h. Traditional use: Its traditional uses are diverse, encompassing treatments for infections, digestive issues, and respiratory disorders, all attributed to its healing and stimulating properties (Righi et al., 2020).

Figure 10: *Rosmarinus officinalis* L.

4.8 *Rosmarinus officinalis* L*:*

a. Botanical Description:

Rosemary is a dense bush, branched, evergreen and blue–white flower, reaching a height of about 1 m. It is characterized by leaves with 1 – 4 cm long and 2 – 4 mm wide, sessile, leathery, linear to linear-lanceolate, with curved edges, dark green upper side and granulosa and page bottom tormentors, with prominent midrib, and very characteristic smell (Andrade et al., 2018).

b. Habitat: perennial shrub native to the Mediterranean area and is widely distributed in many parts of the world (Tuttolomondo et al., 2017).

c. Harvest period: Spring-Summer.

d. Part used: Leaves, flowers.

f. Chemical principles: contains a variety of chemical compounds, including essential oils, phenolic compounds, and triterpenes. The essential oil is rich in monoterpenes like α-pinene, 1,8-cineole (also known as eucalyptol), and camphor. Other notable components include rosmarinic acid, carnosic acid, and carnosol, which are phenolic compounds with antioxidant properties (Atti-Santos et al., 2005).

g. Therapeutic properties: Anticancer, Antinociceptive, Antithrombotic, Antiulcerogenic, Antidiabetic Anti-inflammatory, Antioxidant, Antibacterial (Habtemariam, 2016).

h. Traditional use: Rosemary has been widely used not only in cooking, especially to modify and enhance flavors, but also in traditional medicine, being a highly appreciated medicinal plant to prevent and cure colds, rheumatism, pain of muscles and joints (Andrade et al., 2018).

Figure 11: *Pinus halepensis Mill.*

4.9 *Pinus halepensis Mill*:

a. Botanical description:

It is an evergreen perennial tree reaching heights up to 20 m. It is characterized by very narrow dark green leaves that grow in pairs. It has a tortuous trunk with a diameter that ranges from 80 to 100 cm covered with thick, cracked bark, and pedunculate cone. It possesses fine, flexible, and light green needles. The seeds have a long of 5–6 mm(El Omari et al., 2021).

b. Habitat: Common in Algeria, especially in mountainous regions, in large colonies, it prefers hot and dry places, it can be cultivated(Guit et al., 2015).

c. Harvest period: The buds are harvested immediately before they open (April). Drying in the shade.

d. Part used: Bark, small twigs, buds, resin.

f. Chemical principles: contains various chemical compounds, including essential oils rich in terpenes like α-pinene and β-caryophyllene. The oil also contains other compounds such as limonene, α-humulene, and aromadendrene(Fekih et al., 2014).

g. Therapeutic properties: Anticancer, Antidiabetic, Anti-inflammatory, Antioxidant Antibacterial (El Omari et al., 2021).

h. Traditional use: particularly for its resin. It's been employed for its antiseptic, anti-inflammatory, and analgesic properties, often used to treat respiratory issues, wounds, and skin conditions. Additionally, the seeds are used in traditional Algerian medicine for treating infections and inflammations(El Omari et al., 2021).

Figure12 : Phillyrea angustifolia L.

4.10 *Phillyrea angustifolia* L:

a. Botanical description:

is an evergreen shrub that can grow up to 5 meters tall, characterized by its dense, bushy appearance and slender, flexible branches that emerge from the base. The bark is smooth and grayish brown, gradually darkening with age. The leaves are simple, arranged oppositely along the branches, and typically elongated, displaying linear to lanceolate shapes. Their texture is tough, with entire or subtly toothed margins, dark green on the upper surface and pale underneath. The small, fragrant flowers are greenish-white and appear in compact clusters near the leaf axils. The plant produces drupe-like fruits, blue-black in color when ripe, which begin as rounded but develop a slightly pointed apex as they mature—resembling small olives in structure.

b. Habitat: Common in Algeria, especially in mountainous regions, in large colonies (Boufissiou et al., 2022).

c. Harvest period: The fruit of Phillyrea angustifolia is typically ready for harvest in the fall. The flowers bloom in spring and summer, and the purplish-black berries (fruit) appear afterward in the fall season.

d. Part used: The fruit**,** Leaves, flowers.

f. Chemical principles: Secoiridoids, Flavonoids, Phenolic Acids (Nediani et al., 2019).

g. Therapeutic properties: Anti-inflammatory, Antimicrobial, Antibacterial, Potential Antiviral: In-silico studies suggest some phenolic compounds from *P. angustifolia* leaves, like Demethyloleuropein and Oleuropein aglycone, could potentially inhibit the SARS-CoV-2 main protease.

h. Traditional use: in the Bou Saada region of Algeria. This local plant has been used to treat a variety of ailments, including intermittent fevers, headaches, and menstrual problems. In addition, the flowers have been used to make poultices for headaches, the leaves have been used as a gargle and to stimulate menstruation, and the leaves and fruits have both been used to reduce fever. In addition, the plant has astringent and antiseptic properties (Boufissiou et al., 2022).

Chapter02:
Seasonal Respiratory Diseases And COVID-19

1-Respiratory Diseases:

Respiratory diseases are a broad category of illnesses that directly affect the airways and lungs**,** critically impairing a person's ability to breathe and perform vital gas exchange. Their spectrum is wide, encompassing everything from rapid-onset acute infections to persistent, chronic conditions. This group of diseases represents a substantial burden on global health: in 2019, they were tragically the third highest cause of death globally**,** responsible for 4.0 million fatalities and impacting more than 454.6 million individuals worldwide (Momtazmanesh et al.,2023).

2-Occupational respiratory diseases (ORD):

encompass a broad spectrum of lung conditions that arise primarily from exposure to harmful substances encountered in various work environments. These diseases are frequently associated with inhalation of *noxious agents*, including both organic and inorganic dust particles, as well as chemical fumes, which can lead to significant lung damage over time(Satija et al., 2013)**.**

The classification of ORD includes a variety of disorders such as pneumoconiosis**,** asbestos-related conditions**,** and hypersensitivity pneumonitis, among others. Public health efforts have aimed to enhance awareness of these diseases as they represent one of the most common work-related health issues, second only to workplace injuries (Matyga et al., 2023a).

The accurate and early diagnosis of Occupational Respiratory Diseases (ORDs) is paramount, not only for the timely intervention and improved prognosis of affected workers but also for implementing crucial preventive measures that protect their colleagues from similar exposures. Advances in medical imaging, particularly High-Resolution Computed Tomography (HRCT), have significantly enhanced the ability to visualize intricate lung architecture and identify pathologies characteristic of ORDs. Detailed interpretation of HRCT scans is therefore indispensable for an early and precise diagnosis, facilitating prompt medical and preventive interventions.

The persistent evolution of industrial work environments necessitates continuous vigilance regarding potential respiratory hazards. Despite advancements in occupational health and safety, a substantial workforce remains at risk. For instance, in the United States, an estimated 30 million workers are still susceptible to ORDs, with thousands of annual fatalities attributed to these preventable conditions (OSHA; NIOSH). This underscores the critical importance of robust workplace safety regulations, consistent exposure monitoring, and ongoing medical surveillance programs to mitigate the incidence and severity of ORDs. Ultimately, a

comprehensive and multidisciplinary approach encompassing prevention, accurate diagnosis, and effective management is essential to reduce the casting burden of ORDs on individuals, healthcare systems, and society.

Occupational respiratory diseases (ORD) encompass a diverse array of conditions primarily arising from the inhalation of harmful substances in the workplace. These diseases can be broadly categorized into fibrotic and non-fibrotic forms. Fibrotic diseases, such as pneumoconiosis, arise from long-term exposure to inhaled dusts, typically mineral-based, leading to scarring of the lung tissue. Common forms of pneumoconiosis include asbestosis, silicosis, and coal workers' pneumoconiosis, each associated with specific occupational exposures. On the other hand, non-fibrotic disorders, which include asthma and chronic obstructive pulmonary disease (COPD), are characterized by inflammation and narrowing of the airways without extensive fibrosis Ma (Tyga et al., 2023b).

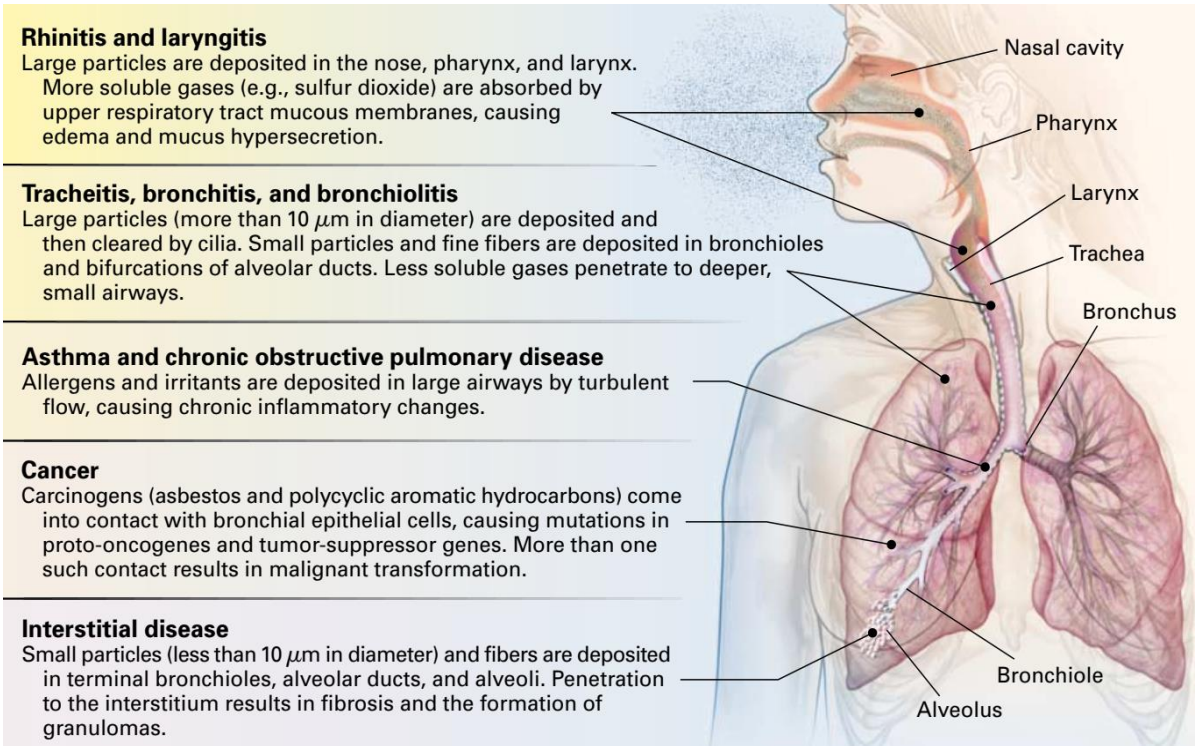


Figure 13: Occupational Respiratory Diseases.

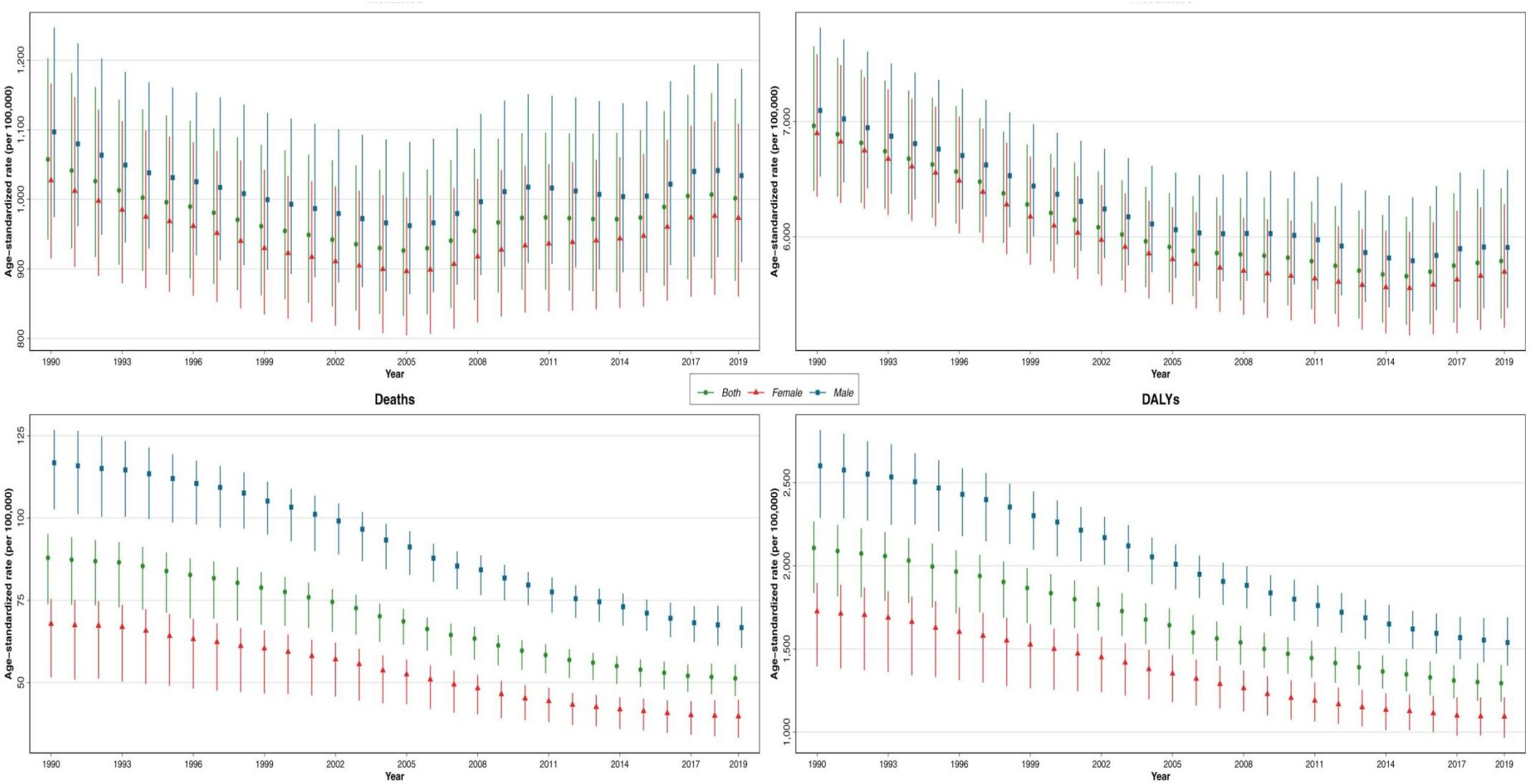


Figure 14: Global age-standardised rates of incidence, prevalence, deaths, and DALYs of chronic respiratory diseases in men, women, and in both sexes combined, 1990–2019. DALYs = Disability-Adjusted Life Years.

3-Types of Respiratory Diseases:

A-Chronic Lower Respiratory Diseases:

Chronic Lower Respiratory Diseases (CLRDs) represent a broad spectrum of conditions primarily impacting the airways and vital lung structures. This diverse group includes prominent illnesses such as chronic obstructive pulmonary disease (COPD), asthma, lung cancer, bronchiectasis, interstitial lung diseases, occupational lung diseases, and pulmonary hypertension. Each of these disorders uniquely compromises lung function, frequently resulting in substantial morbidity and mortality. As highlighted by(Gould et al., 2023), a shared characteristic among these diseases is the presence of common pathophysiological traits like inflammation and the detrimental remodeling of lung tissue, which collectively severely impede gas exchange and overall respiratory function.

B- Respiratory Tract Diseases:

Represent a broad spectrum of infections affecting either the upper or lower divisions of the respiratory system. The upper respiratory tract (URT) encompasses structures superior to the vocal cords, whereas the lower respiratory tract (LRT) includes the trachea, bronchi, bronchioles, and lungs(Journal & 2014)**.** Respiratory tract infections (RTIs) are globally recognized as a leading public health concern, with individuals typically experiencing two to five episodes annually. The clinical manifestations of these infections vary widely from mild conditions like the common cold, predominantly caused by rhinoviruses and coronaviruses, to severe threats such as bronchiolitis and pneumonia, which result from more virulent pathogens, including adenoviruses and influenza viruses(William Potter, C., 2007). The annual burden of influenza alone is substantial, contributing to significant mortality rates ranging from 1,000 to 25,000 deaths per 50 million population, thereby highlighting the critical need for continuous surveillance and robust public health interventions.

C- Respiratory Insufficiency:

Respiratory insufficiency, defined as the inability of the respiratory system to maintain adequate gas exchange, presents a significant clinical challenge, particularly in critically ill patients. It occurs when there is a failure in ventilation, pulmonary gas exchange, or pulmonary perfusion, leading to alterations in arterial blood gases, such as hypoxemia and hypercapnia (Oronsky et al., 2023). Melville Arnott (1960) stated that respiratory insufficiency represents a precursor to respiratory failure, where the respiratory system cannot effectively meet the metabolic demands of internal respiration. This condition becomes increasingly critical as it progresses, underscoring the need for prompt diagnosis and intervention. Clinically, respiratory insufficiency can be categorized into distinct types based

on underlying pathophysiological mechanisms. These include hypoventilation due to respiratory muscle weakness, ventilation-perfusion mismatches that disrupt efficient gas exchange, and diffusion impairments that hinder gas transfer across the alveolar-capillary membrane (Hope, 1962)**.**

D- Respiratory Failure:

Respiratory failure is a life-threatening medical condition defined by the respiratory system's inability to maintain adequate arterial oxygenation or effectively eliminate carbon dioxide. This dysfunction can result in respiratory acidosis, hypoxemia, or both, requiring prompt and often intensive medical intervention. Respiratory failure is broadly categorized into two main types: hypoxemic and hypercapnic. Hypoxemic respiratory failure is characterized by a marked decrease in arterial oxygen levels, typically due to impaired gas exchange or insufficient alveolar ventilation. It is commonly associated with conditions such as pneumonia, acute respiratory distress syndrome (ARDS), and pulmonary edema. In contrast, hypercapnic respiratory failure arises primarily from alveolar hypoventilation, leading to elevated levels of carbon dioxide in the blood. Contributing factors may include chronic obstructive pulmonary disease (COPD), respiratory muscle fatigue, or central nervous system depression that impairs the drive to breathe (Summers et al., 2021).

E-Respiratory Distress Syndrome Acute:

Acute Respiratory Distress Syndrome (ARDS) is a life-threatening pulmonary condition marked by extensive inflammation of the alveolar-capillary membrane, which severely impairs gas exchange. This leads to hypoxemia and, in many cases, progresses to respiratory failure. ARDS may arise as a complication of various clinical insults, such as pneumonia, sepsis, traumatic injury, or aspiration of gastric contents. Following these initial lung insults, a cascade of pathological processes is triggered, disrupting normal respiratory function(Kaufman & Kaufman, 2016). A defining feature of ARDS is the accumulation of protein-rich fluid within the alveoli, caused by damage to the alveolar epithelium and a robust inflammatory response. This fluid infiltration hinders the production of surfactant, a vital substance that maintains alveolar stability, resulting in alveolar collapse (atelectasis), decreased lung compliance, and considerable difficulty in effective breathing.

F- Respiratory Distress:

Respiratory distress is a critical clinical condition resulting from impaired gas exchange and inadequate oxygenation within the lungs, severely compromising a patient’s ability to breathe effectively. It is commonly manifested by rapid, shallow breathing, increased respiratory effort, and, in severe cases, the inability to sustain sufficient oxygen saturation levels. A

comprehensive understanding of respiratory distress requires examining its underlying causes, the associated physiological disruptions, and the diverse diagnostic and therapeutic strategies employed. One prominent example of respiratory distress is acute respiratory distress syndrome (ARDS), which illustrates the complexity and multifactorial nature of this condition. In ARDS, increased permeability of the alveolar-capillary barrier leads to the accumulation of pulmonary edema, significantly impeding gas exchange. This pathophysiology is often aggravated by fluid overload, further compromising respiratory function (Rawal et al., 2018).

G-Multiple Respiratory Infection:

Respiratory infections encompass a wide spectrum of illnesses caused by a variety of pathogens that affect both the upper and lower respiratory tracts. Anatomically, the respiratory system consists of distinct regions, including the nasal passages, pharynx (throat), trachea, bronchi, bronchioles, and alveoli, each of which is susceptible to specific viral and bacterial agents (William Potter, C., 2007). Among these pathogens, viruses are particularly significant in the context of respiratory tract infections (RTIs), with common examples including rhinoviruses, coronaviruses, adenoviruses, and influenza viruses. These viruses can produce a range of clinical manifestations, from mild symptoms such as the common cold to more severe conditions like pneumonia.

In addition to viral agents, a complex interplay exists within the respiratory microbiome, particularly involving bacterial communities residing in the upper respiratory tract. These include commensal organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*, which typically contribute to the maintenance of a healthy microbial balance (Bosch et al., 2013). However, under certain conditions, these bacteria can transition to pathogenic forms, especially in vulnerable populations such as young children. Disruption of this microbial ecosystem can significantly increase the risk of severe respiratory illnesses.

The colonization and behavior of these bacterial populations are influenced by multiple factors, including microbial interactions and the host's immune responses. This highlights the crucial role of the respiratory microbiome in the development and progression of disease. The dynamic and often synergistic relationship between viral and bacterial pathogens underscores the importance of integrated research approaches to fully understand the mechanisms underlying respiratory infections.

H- Respiratory Tract Infection:

Respiratory tract infections (RTIs) encompass a wide spectrum of diseases that affect the respiratory system and are generally categorized into upper respiratory tract infections (URIs)

and lower respiratory tract infections (LRIs)**.** URIs include conditions such as pharyngitis, laryngitis, tonsillitis, sinusitis, and otitis media, while LRIs primarily involve bronchitis and pneumonia. These infections pose a significant public health burden, accounting for a considerable proportion of medical consultations, hospital admissions, and, regrettably, mortality, particularly in the United States (Medicine & 1988) (Journal & 2014, 2014).

Pharyngitis alone contributes to nearly 40 million physician visits annually, with a variety of causative pathogens implicated, among which group A Streptococcus is notably prevalent. Acute bronchitis, in most cases, is caused by viral agents and does not require antibiotic therapy unless a secondary bacterial infection is suspected. In contrast, chronic bronchitis is often associated with recurrent exacerbations that frequently necessitate antibiotic treatment, underscoring the importance of accurate diagnosis and tailored clinical management (Journal & 2014, 2014).

4- COVID-19:

Officially declared a pandemic by the World Health Organization (WHO) on March 11, 2020, COVID-19 quickly emerged as a significant global health crisis. The disease itself is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), initially identified in Wuhan, China, in late 2019 (Lai et al2020)**.** SARS-CoV-2, a positive-sense, single-stranded RNA virus, primarily spreads through respiratory droplets and fomites. This transmission can lead to a broad spectrum of illness, from asymptomatic cases to severe acute respiratory distress syndrome (ARDS), which can ultimately be fatal. By February 25, 2021, the pandemic had already resulted in over 113 million confirmed infections and more than two million fatalities worldwide, undeniably highlighting its profound impact on global health and mortality.

The intrinsic structural characteristics of SARS-CoV-2, the causative agent of COVID-19, are pivotal to its transmission dynamics and pathogenic mechanisms. This enveloped RNA virus, belonging to the *Coronaviridae* family, is defined by its single-stranded RNA genome. Central to its infectivity is the spike (S) glycoprotein, which critically mediates viral entry into host cells by binding to the angiotensin-converting enzyme 2 (ACE2) receptor on human cell surfaces (Al Heialy et al., 2020).This specific receptor-ligand interaction initiates conformational changes and subsequent membrane fusion, facilitating the viral genome's entry into the host cell's cytoplasm and enabling subsequent replication. Given their potential to alter transmissibility and vaccine efficacy, emerging variants of SARS-CoV-2, particularly those harboring mutations within the spike protein, are a primary focus of ongoing scientific investigation.

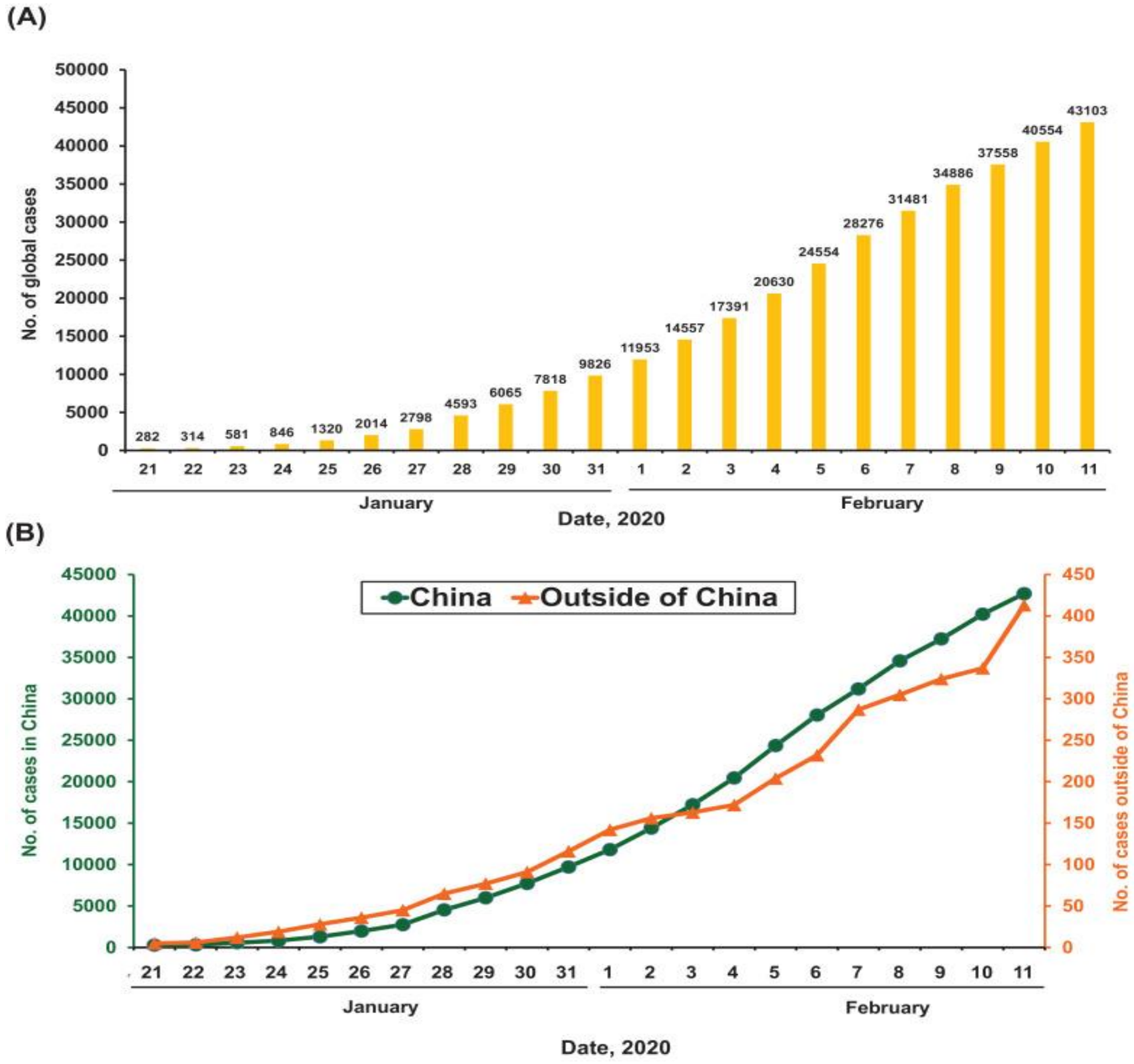


Figure 15: Daily accumulative cases of laboratory-confirmed cases of 2019 coronavirus disease (COVID-19) as of 11 February 2020: (A) daily numbers of global cases; and (B) daily numbers of cases from China [including Hong Kong Special Administrative Region (SAR).

Chapter03:
Network pharmacology

1-Network pharmacology:

Network pharmacology (NP) represents a paradigm shift in drug discovery by integrating systems biology with pharmacology, ultimately enhancing our understanding of drug actions and interactions at multiple levels. The essence of NP lies in the utilization of networks to model the complexity of biological systems, where nodes represent biological entities, such as genes, proteins, and metabolites, and edges signify the functional or regulatory relationships between them(Iorio et al., 2013). This framework allows researchers to visualize and analyze the intricate web of interactions that characterize cellular networks, laying the groundwork for innovative approaches to drug development. The increasing abundance of large-scale genomic, transcriptomic, and proteomic data facilitates the identification of thousands of molecular interactions, providing a rich resource for uncovering both on-target and off-target effects of pharmacological agents.

One of the most significant advancements in NP is its ability to address the limitations of traditional drug discovery, particularly related to side effects and the treatment of multifactorial diseases (Chandran et al., 2016). Classical pharmacology often focuses on single, highly specific targets, leading to limited therapeutic efficacy and unintended adverse effects. In contrast, NP embraces a holistic approach, recognizing that most diseases arise from the dysfunction of multiple proteins within interconnected pathways. By examining how compounds derived from natural products can modulate these diverse targets, NP proposes a more comprehensive strategy for drug design that improves both safety and effectiveness. This multidisciplinary approach not only broadens our understanding of drug mechanisms but also opens new avenues for therapeutic innovation, especially for complex diseases where a multifaceted treatment strategy is critical. Consequently, the integration of network biology principles into pharmacological research is essential for fostering the next generation of medicines that effectively target the dynamic nature of biological systems.

2. Historical Background:

The evolution of drug discovery has been significantly marked by the recognition of the complexities inherent in human diseases, which are often driven by multifactorial processes rather than isolated molecular dysfunctions. Historically, the traditional pharmacological approach focused predominantly on single, specific targets in the disease pathway. However, this strategy has encountered considerable limitations, particularly evident in the frequent side effects of treatments and the challenges posed by complex diseases (Chandran et al., 2016)An essential turning point in addressing these challenges arose from the realization that many active compounds derived from traditional medicinal practices might offer viable leads. These compounds tend to modulate multiple biological targets, aligning closely with the multifactorial nature of most diseases.

The advent of network pharmacology (NP) signifies a paradigm shift in this landscape. Taking root in the early 2000s, NP emerged as a contemporary approach that marries the principles of systems biology with pharmacology. It allows for the exploration of drug actions through the lens of complex interactions within biological networks. With the rapid development of computational technologies, researchers began to document the intricate molecular interactions that drugs maintain within living cells. This new discipline posits that rather than targeting a single entity, effective drug therapies must consider the broader systemic context and the interrelated networks governing biological functions. Consequently, NP not only facilitates the identification of new therapeutic avenues but also enhances the safety and efficacy of existing medications by revealing how drugs function across multiple targets and pathways.

The postgenomic era, marked by advancements in molecular biology and bioinformatics, catalyzed the growth of network biology, which underscores the principles guiding cellular interactions. The systemic analysis of molecular interactions within living organisms is therefore becoming a cornerstone of modern biomedical research, bridging empirical knowledge with computational advances. By systematically cataloging these interactions, scientists are now equipped to address the challenges that plagued traditional pharmacological methods, positioning network pharmacology as a crucial discipline for the future of drug discovery and development.

3-Integrating Network Pharmacology and Traditional Medicine:

Network pharmacology significantly enhances our understanding of traditional medicine by providing a scientific framework to analyze complex herbal formulations and their mechanisms of action. This approach bridges ancient healing practices with modern scientific methodologies in several important ways: Network pharmacology systematically illustrates drug mechanisms by analyzing molecular associations between traditional remedies and their treatment targets. This is particularly valuable because traditional medicine systems are characterized by holistic, multi-component, multi-target, and multi-pathway therapies, which align perfectly with network pharmacology's analytical framework**.** (Wang et al., 2022)

The approach transforms our understanding from the traditional "single-target" paradigm to a more comprehensive multi-target mechanism perspective (Miao et al., 2022).By expressing the relationship between drug components and their action targets in network form, researchers can identify key active components and primary drug targets through analysis of network nodes(Miao et al., 2022) (Zhou et al., 2020).For identifying bioactive compounds, network pharmacology combines computational and experimental approaches to analyze the biological basis of herbs and their compounds(Wang et al., 2022). This helps scientists screen active ingredients through parameters like oral bioavailability and drug-likeness, revealing which components can be effectively absorbed and utilized by the human body (Miao et al., 2022).

Network pharmacology proves especially valuable for traditional Chinese medicine (TCM) and other traditional systems like Ayurveda, where complex compositions make it difficult to explain treatment mechanisms through conventional methods (Miao et al., 2022) **(**Biology & 2023).The approach enables researchers to directly identify drugs and disease targets from large datasets and understand the mechanisms and pathways between them(Zhou et al., 2020). The integration creates a bridge between ancient knowledge and modern science, enhancing the credibility of both approaches. This synergy allows for deeper understanding of therapeutic effects and potential mechanisms of action at a systems level, providing scientific validation for traditional claims while potentially unlocking novel therapeutic insights**.** (Wang et al., 2022) (Biology & 2023).

4-Phenolic compounds and Essential oils a promised source for discovery drug:

4.1-Phenolic compounds:

Phenolic compounds, also known as polyphenols, constitute a significant class of secondary metabolites. They are characterized by the presence of one or more phenolic rings in their chemical structure and are vital in the plant kingdom, primarily functioning in growth regulation, defense mechanisms, and signaling pathways (Gugleva et al.,2021) **.**

These compounds are synthesized through the shikimic and acetic acid biosynthetic pathways and are ubiquitous in various plant species, thus contributing significantly to the therapeutic potential of many herbal remedies. Their diverse structures and functional groups confer upon them a range of bioactive properties that extend beyond their well-known antioxidant capabilities**,** anti-inflammatory, and anticancer effects**.**

4.2-Essential oils:

Essential oils, complex aromatic extracts from plants, are primarily composed of hydrocarbons and their oxygenated derivatives. These compounds originate from two distinct isoprenoid biosynthetic pathways and are synthesized in specialized plant structures like glandular trichomes**,** typically found on the surfaces of flowers and leaves (Sharifi-Rad et al., 2017).

These oils are characteristically aromatic, volatile, and hydrophobic. Each essential oil is a unique blend, typically containing 20 to 70 different chemical components, with lower molecular weight compounds being the most prevalent (Russo et al., 2015). The functional properties of essential oils are most often attributed to their primary constituents, which include monoterpenes, terpenoids, and phenylpropanoids**.**

Specific compounds within these categories are known to exhibit significant biological activities, such as antimicrobial, antioxidant, anti-inflammatory, and anticancer effects.

Table3: Software tools and server sites used in network pharmacology.

	Name	Software or server	License to use	Link
network pharmacology	Cytoscape	software	Academic	https://cytoscape.org/
	SwissADME	Server	Academic	http://www.swissadme.ch/index.php
	String	Server	Academic	https://string-db.org
	Shiny	Server	Academic	http://bioinformatics.sdstate.edu/go
	Venny	Server	Academic	https://bioinfogp.cnb.csic.es/tools/venny/
	PubChem	Server	Academic	https://pubchem.ncbi.nlm.nih.gov/
	SwissTarget Prediction	Server	Academic	http://www.swisstargetprediction.ch
	Genes Cards	Server	Academic	https://www.genecards.org
	DisgenEt	Server	Academic	https://www.disgenet.org/search

Experimental Part

1. Plant Selection and Disease Targeting:

The first step is selecting a plant for your study. You'll want to choose a plant that has shown effectiveness against a particular disease. Once you've selected your plant and disease, you'll need resources to gather the necessary data.

2. Download and Organize the Data:

Once you have the plant data, download it in Excel format. It's crucial to stay organized create a dedicated folder for this data. Open the Excel file and filter it based on your interests (Phenolic compounds and Essential oils). Highlight the key compounds, and you're ready to proceed (the annex01).

3. Collecting SMILES Data:

Next, you'll need to gather the SMILES (Simplified Molecular Input Line Entry System) codes for each compound. You can do this by searching the compound's name on a database like **PubChem** to obtain the SMILES. If a compound doesn't have a SMILES structure, you can use the IUPAC name and tools like Marvin Sketch to draw the structure and generate the SMILES code.

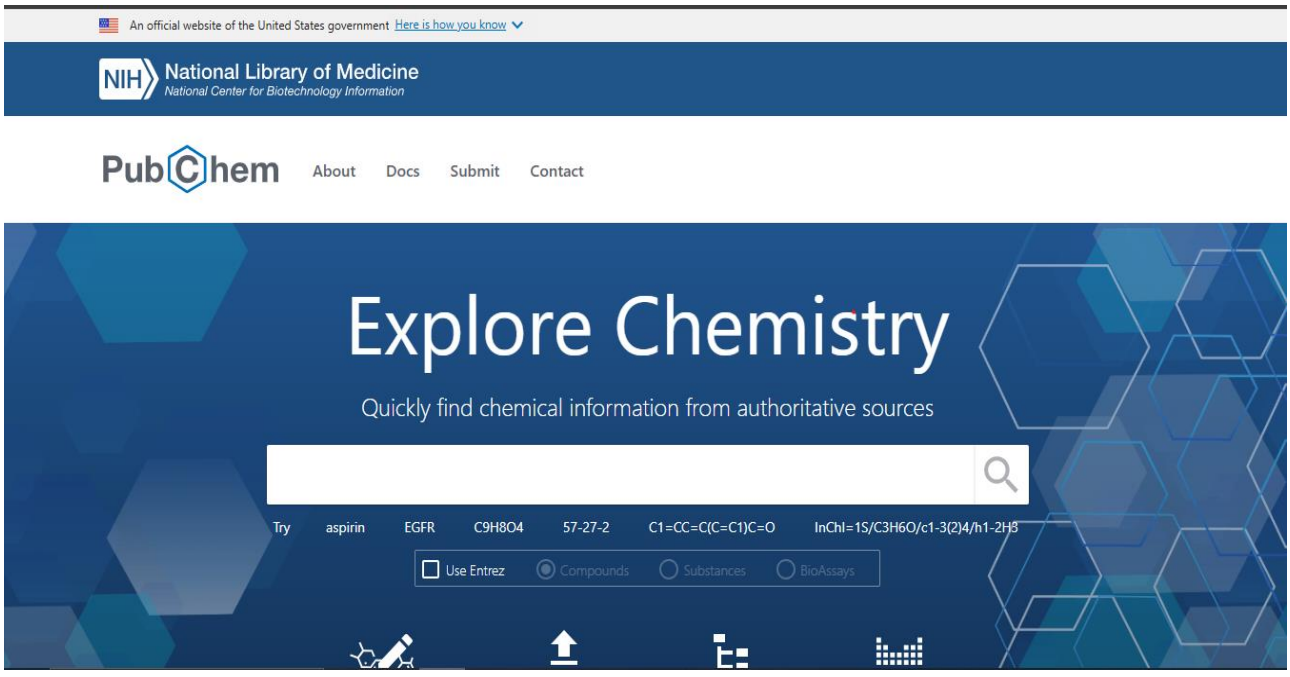


Figure 16: PubChem server.

PubChem is a public chemical information resource, developed and maintained by the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM), an institute within the U.S. National institutes of Health (NIH). It collects chemical substance descriptions and their biological activities from more than 500 data sources and disseminates these data to the public free of charge. Since the launch in 2004 as a component of the NIH Molecular Libraries Roadmap Initiatives,

PubChem has been a key information resource for biomedical research communities in many areas such as cheminformatics, chemical biology, medicinal chemistry, and drug discovery(Kim, 2019).

4. Analyzing Compound Properties:

After collecting the SMILES codes, organize them into a new sheet. From here, you'll need to analyze the compounds' properties. You can use tools like SwissADME to (the annex02).

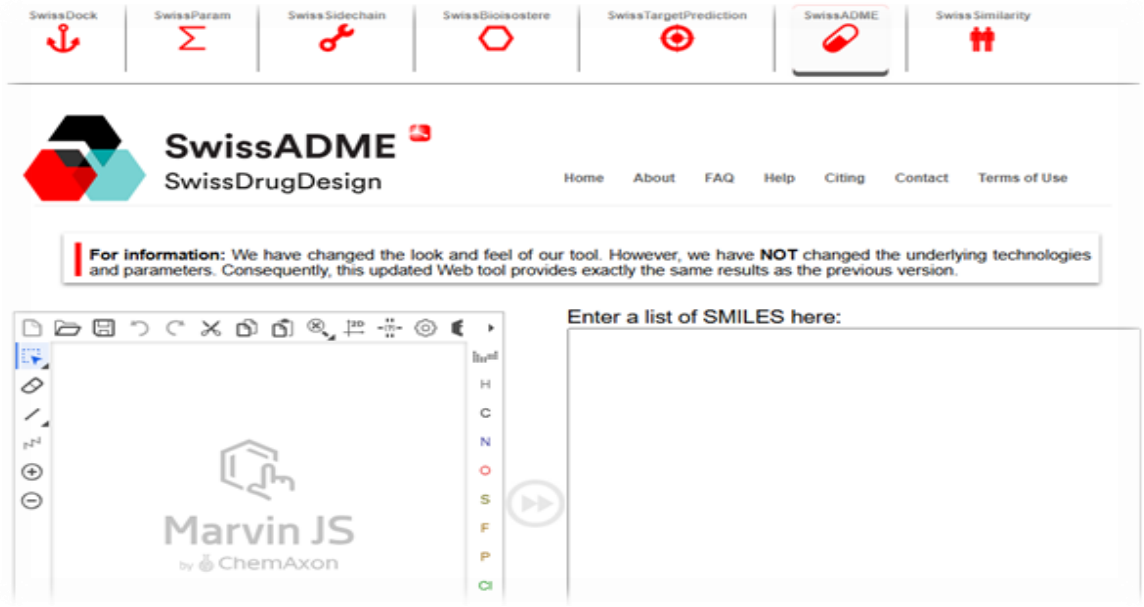


Figure 17: SwissADME server.

The SwissADME web tool is a pivotal resource in the field of drug discovery, facilitating the evaluation of critical physicochemical, pharmacokinetic, and drug-likeness parameters for small molecules. Developed to cater to both novice and experienced researchers, SwissADME provides a straightforward, user-friendly interface that does not require any prior knowledge of computer-aided drug design (CADD). This accessibility is a significant advantage, as it democratizes key drug design processes and allows broader participation in drug discovery endeavors (Daina et al.,2017).

The components are filtered according to the following data:

1) logarithm of partition coefficient (log P) between −0.4 and 5.6,
2) molecular weight 160–480 g/mol and has 20–70 atoms.
3) molar refractivity of 40–130, which is related to the volume.
4) The Bioavailability <0.3.
5) The Toxicity <0.5.

As implemented in the Pfizer registration systems, the rule-of-five generates an alert for compounds when any two or more of the following conditions are not satisfied:

1. Molecular weight (MW) <500 Da
2. Number of hydrogen bond acceptors <10

3. Number of hydrogen bond donors <5
4. Calculated n-octanol-water partition coefficient (Clog P) <5(Ghose et al., 1999; Pillai et al., 2001)

5. Target Prediction for Compounds:

Once you've completed these steps, it's time to conduct target prediction. You can upload your compounds into a tool like SuperPred, which will generate two files for you. From these files, copy the UniProt IDs and organize them into a string, collecting the unique gene names by server **SwissTarget Prediction**.

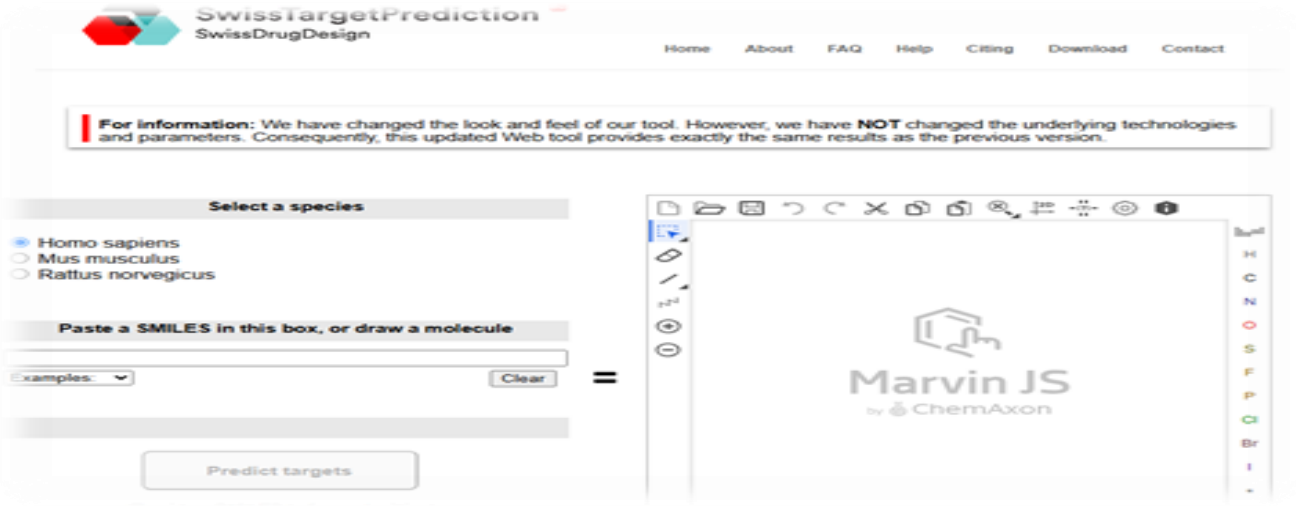


Figure 18: SwissTarget Prediction server.

SwissTarget is an important resource in the realm of computational drug discovery and target identification. It functions as a platform utilizing established methods for ligand-based virtual screening, enabling users to identify potential drug targets based on compound similarity. The underlying technology borrows from the Swiss Similarity toolkit, which categorizes compounds into four main classes: (1) "Drugs" encompassing a variety of approved and experimental agents; (2) "Bioactive" compounds, derived from databases such as ChEMBL and the Human Metabolome Database; (3) "Commercial" compounds offered by various vendors; and (4) "Synthesizable" compounds isolated from vendor listings (Bragina et al., 2022). This classification not only streamlines the identification process but also allows researchers to screen through extensive libraries, including those focusing on biological activity across different molecular targets such as G-Protein Coupled Receptors (GPCRs) and kinases.

6-Disease Target Collection:

Now, we need to get targets for the disease (DC). One excellent resource for this is **GeneCards and DisgenEt**. After logging in, search for your disease, and you'll find detailed information, including the

GIFT score, which indicates the relevance of the gene to the disease. A score above 30 is generally considered significant, with higher scores indicating more extensive research.

Figure 19: GeneCards server.

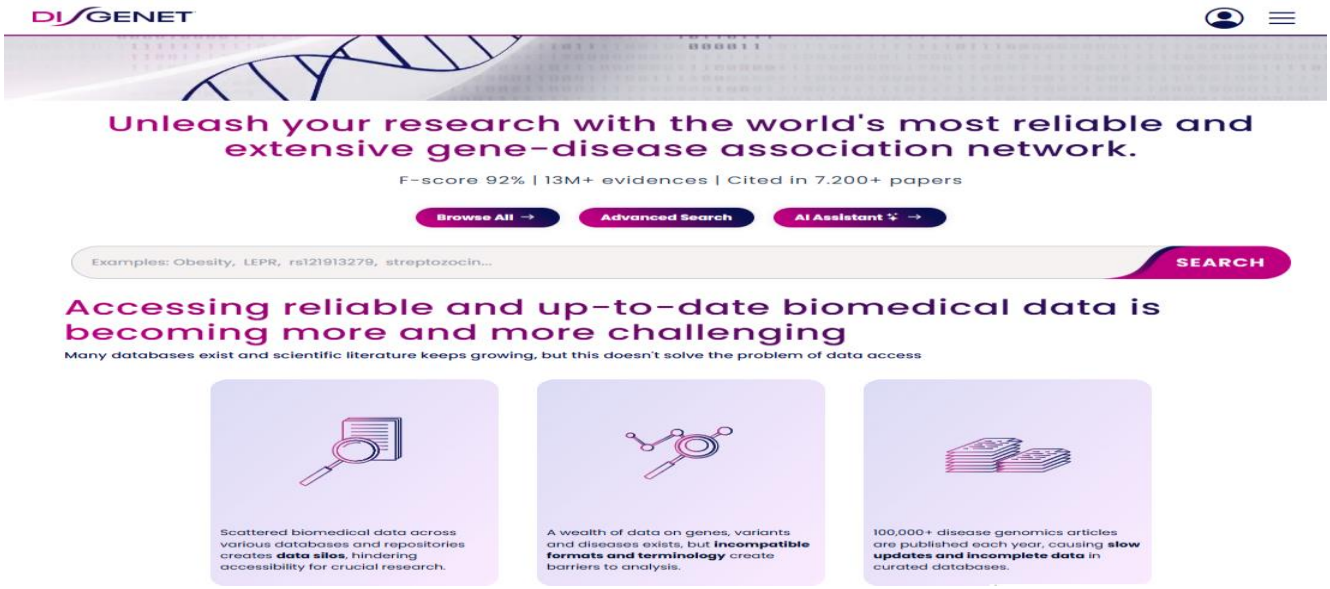


Figure 20: DisgenEt server.

GeneCards is a comprehensive database designed to serve as a vital resource for genomic research, particularly in the context of human diseases. Initially developed to provide information about all known human genes, GeneCards includes details about gene function, expression, and potential associations with diseases. This database aggregates data from numerous genomic sources, providing a one-stop resource for researchers seeking to explore gene-related information. Key features of GeneCards include access to gene summaries, protein structure, gene ontology, and relevant publications, which collectively

assist researchers in understanding the multifaceted roles of genes in health and disease (Piñero et al., 2016).

DisGeNET is a crucial platform for researchers engaged in the identification and analysis of gene-disease associations. Developed to aggregate information about human disease-associated genes and variants, DisGeNET exemplifies an integrative approach that combines expert-curated databases and automated text-mining techniques to maximize data availability. As of its latest release, version 4.0 in June 2016, DisGeNET provides an extensive repository of 429,036 gene-disease associations (GDAs), linking 17,381 genes to 15,093 distinct diseases, disorders, and clinical phenotypes(Piñero et al., 2016) .

7-Comparing Bioactive Compounds with Disease Targets:

To identify target matches, you can use a tool called **Venny** to map your bioactive compound genes against disease genes. After entering the data, Venny will show you the overlapping genes. If there's no overlap or a very minimal overlap, it might indicate that you need to adjust your target prediction settings. Repeat this process for all your compounds and save the overlapping genes in separate files. These overlapping genes are crucial for your next steps.

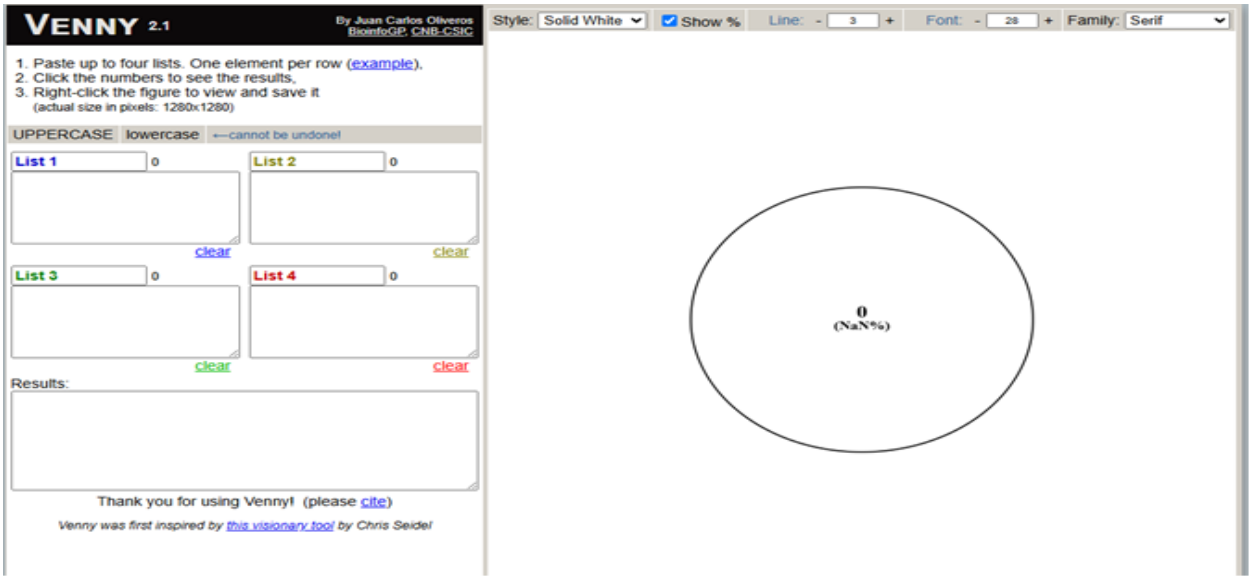


Figure 21: Venny server.

Server venny an online bioinformatics tool used for drawing Venn diagrams to compare up to four lists of elements. It is a web-based application developed by Juan Carlos Oliveros that allows users to input multiple datasets and visually analyze their intersections and unique elements through interactive Venn diagrams. Venny can also be used offline as a single HTML file opened in a browser, making it a versatile tool for comparing gene lists, protein sets, or other biological data(Eberhardt et al., 2021).

8-Network Construction:

This process merges databases of target compounds and target diseases directly into Cytoscape. Within Cytoscape, nodes represent biological entities, and edges depict their interactions. Users can import and consolidate multiple datasets into a single, unified network, then apply various layouts and visual styles to improve interpretability.

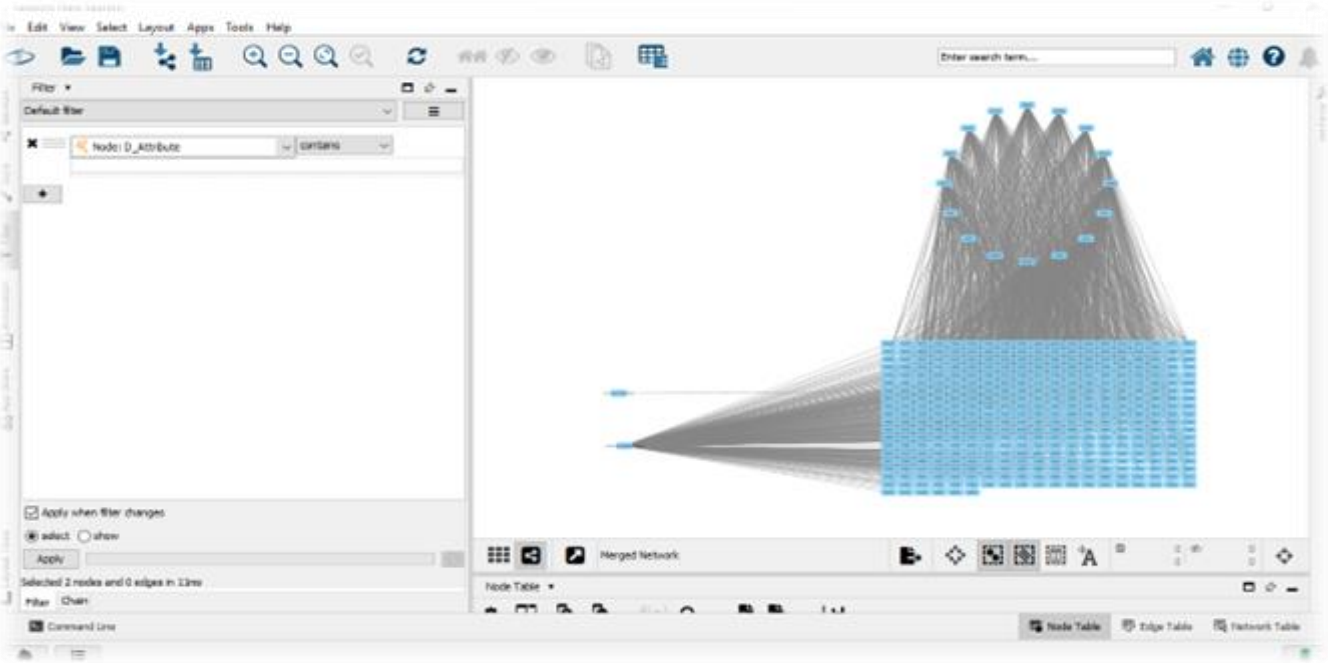


Figure22: Cytoscape software.

Cytoscape is a powerful open-source software platform designed to facilitate the visualization and analysis of complex networks such as biological pathways and protein-protein interaction networks. Initially developed for biological research, Cytoscape has broadened its scope to incorporate network visualization in various fields, including social sciences, computer science, and systems biology. It enables researchers to depict networks with customizable visual properties, allowing them to convey intricate relationships among nodes (representing entities) and edges (representing connections) effectively. With the advent of web-based services, such as Cytoscape Web, researchers can now visualize and interact with their networks through dynamic browser interfaces (Lopes et al., 2010).

9-Protein Interaction and Gene Ontology:

Next, you'll return to a tool like **STRING** and **SHINY** to analyze protein interactions and gene ontology. This step will help you explore the molecular functions, biological processes, and pathways associated with your compounds. Understanding these interactions will help refine your predictions and give your insight into the biological relevance of your study.

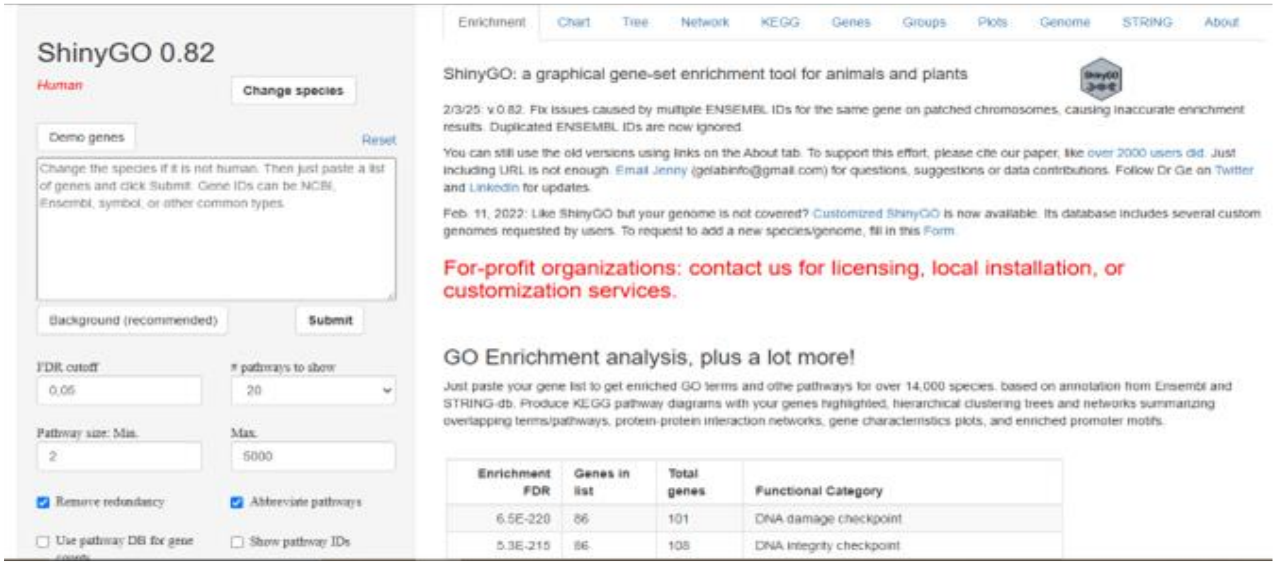


Figure 23: Shiny server .

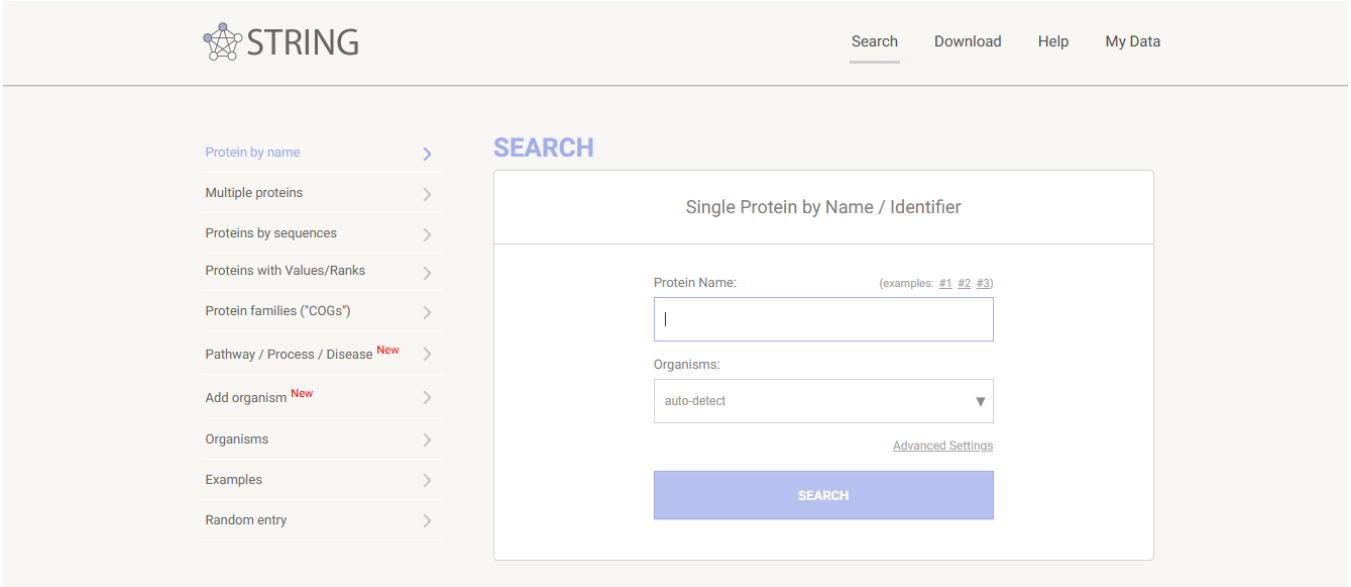


Figure 24: String server.

The STRING and SHINY database compiles, scores and integrates protein-protein association information drawn from experimental assays, computational predictions, and prior knowledge. Its goal is to create comprehensive and objective global networks that encompass both physical and functional interactions. Additionally, provides supplementary tools such as network clustering and pathway enrichment analysis.(*Venny 2.1.0.*)

Results and Discussion

1-*Thymus algeriensis*:

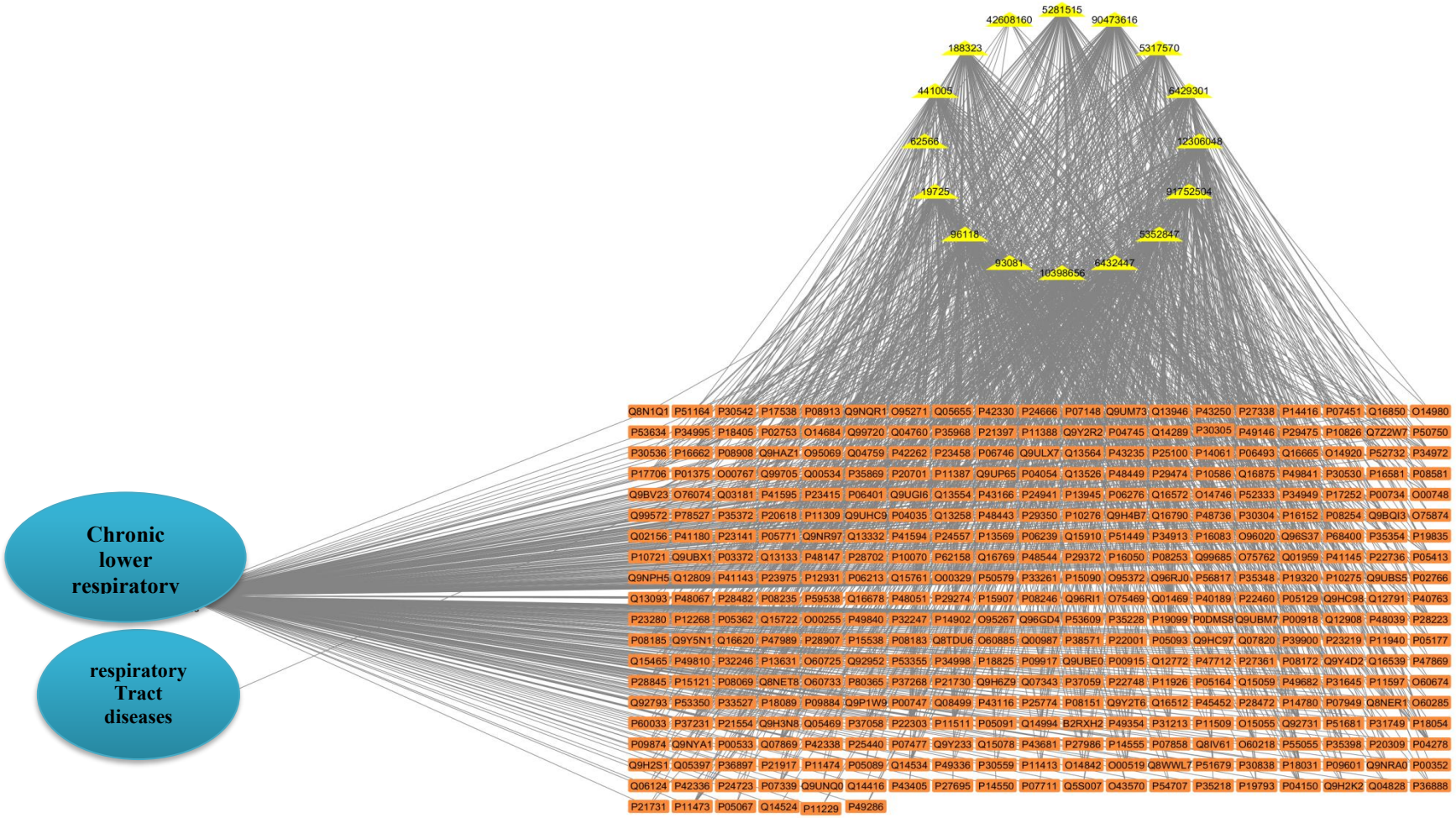


Figure 25: Compound-Target-Disease Network of plant *Thymus algeriensis* .

Table4: Node table of compound-target-disease network of plant *Thymus algeriensis*.

C_attribute	Betweenness Centrality	Degree
188323	0.04202239	100
90473616	0.04080212	100
96118	0.03768286	100
10398656	0.02491732	100
19725	0.02102417	100
6432447	0.04267294	99
91752504	0.03750731	97
12306048	0.01632525	97
5352847	0.0272206	95
5317570	0.01220029	83
441005	0.01108551	82
6429301	0.00911705	80
5281515	0.00911705	80
93081	0.00151597	30
62566	1.15E-04	11
42608160	9.25E-05	10

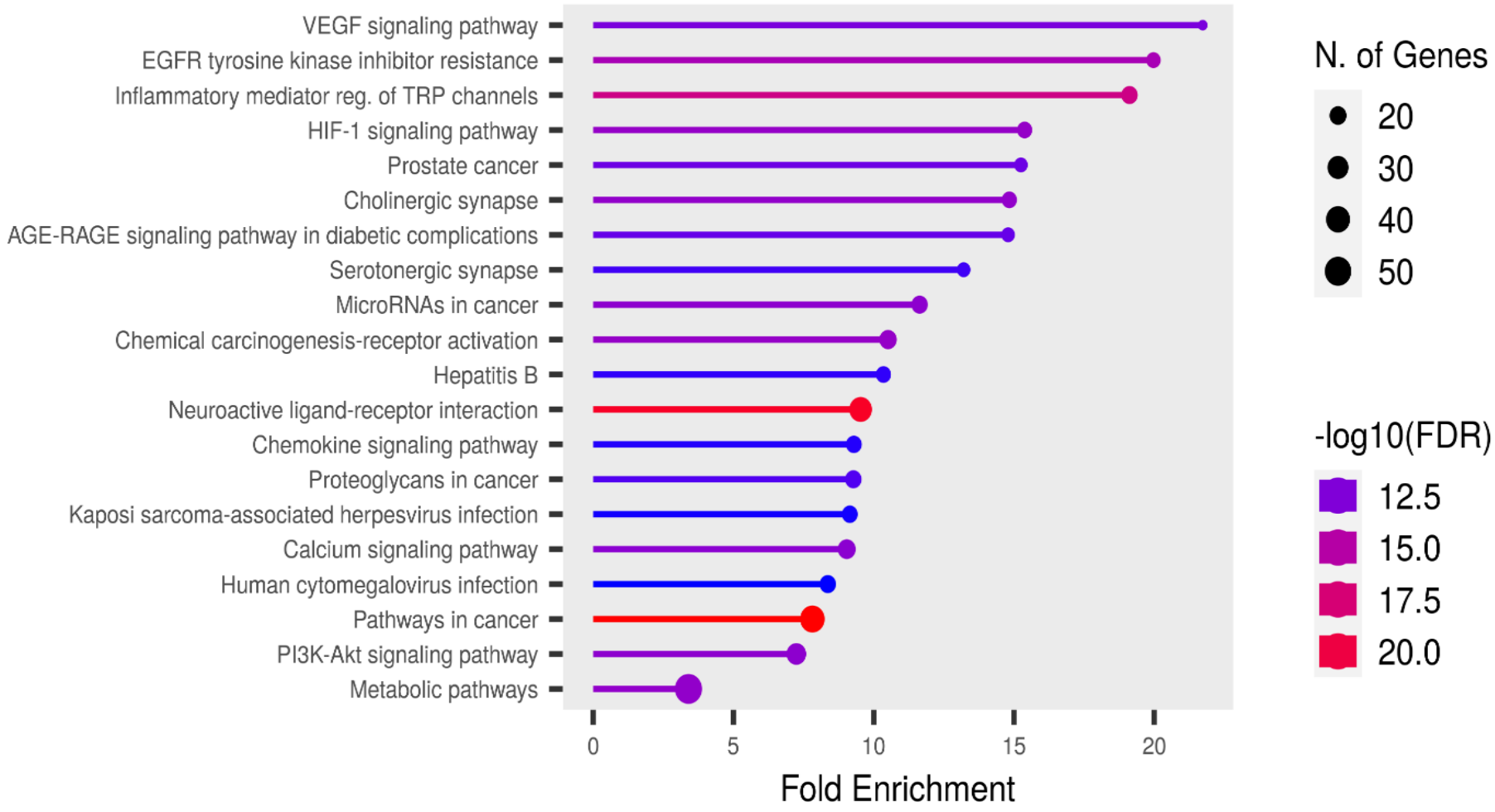


Figure 26: KEGG Pathway Enrichment Analysis of *Thymus algeriensis* with Associated Gene Counts and Significance.

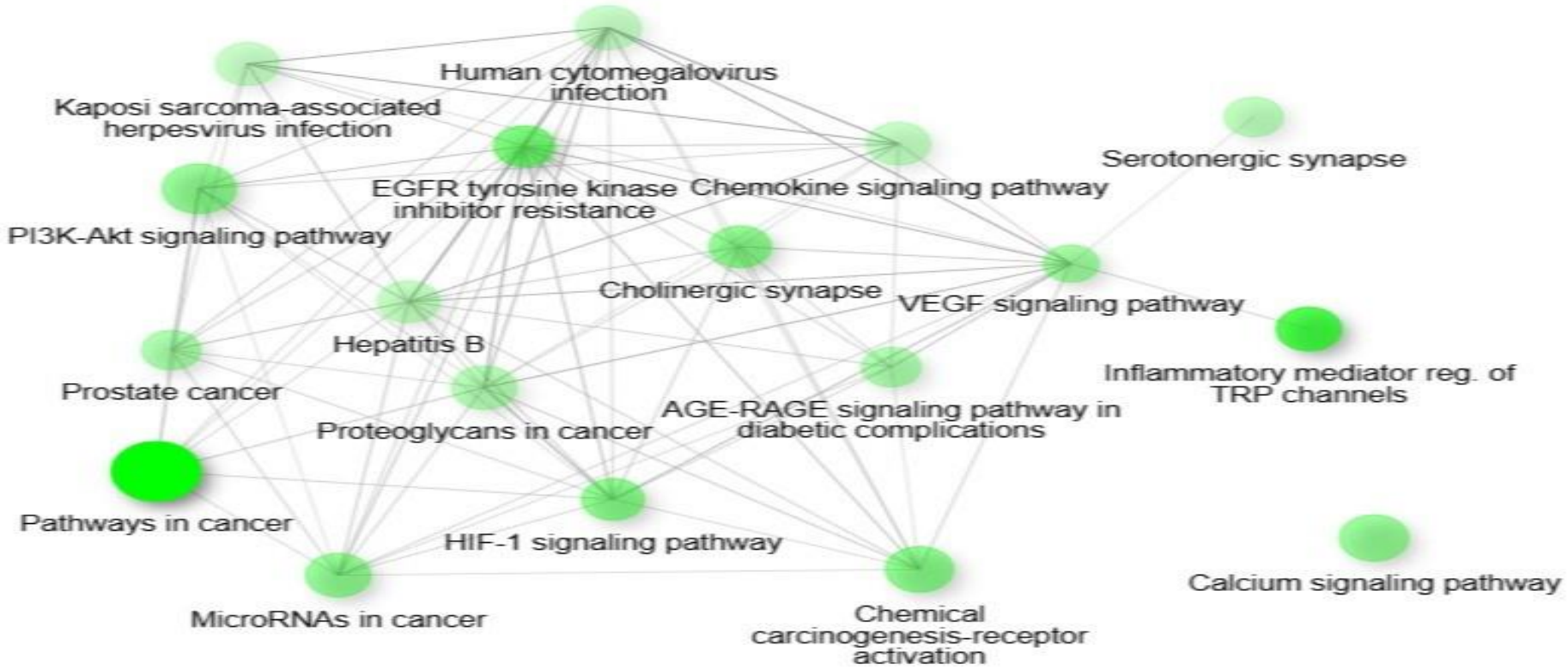


Figure 27: KEGG Pathway Interaction Network in plant *Thymus algeriensis*

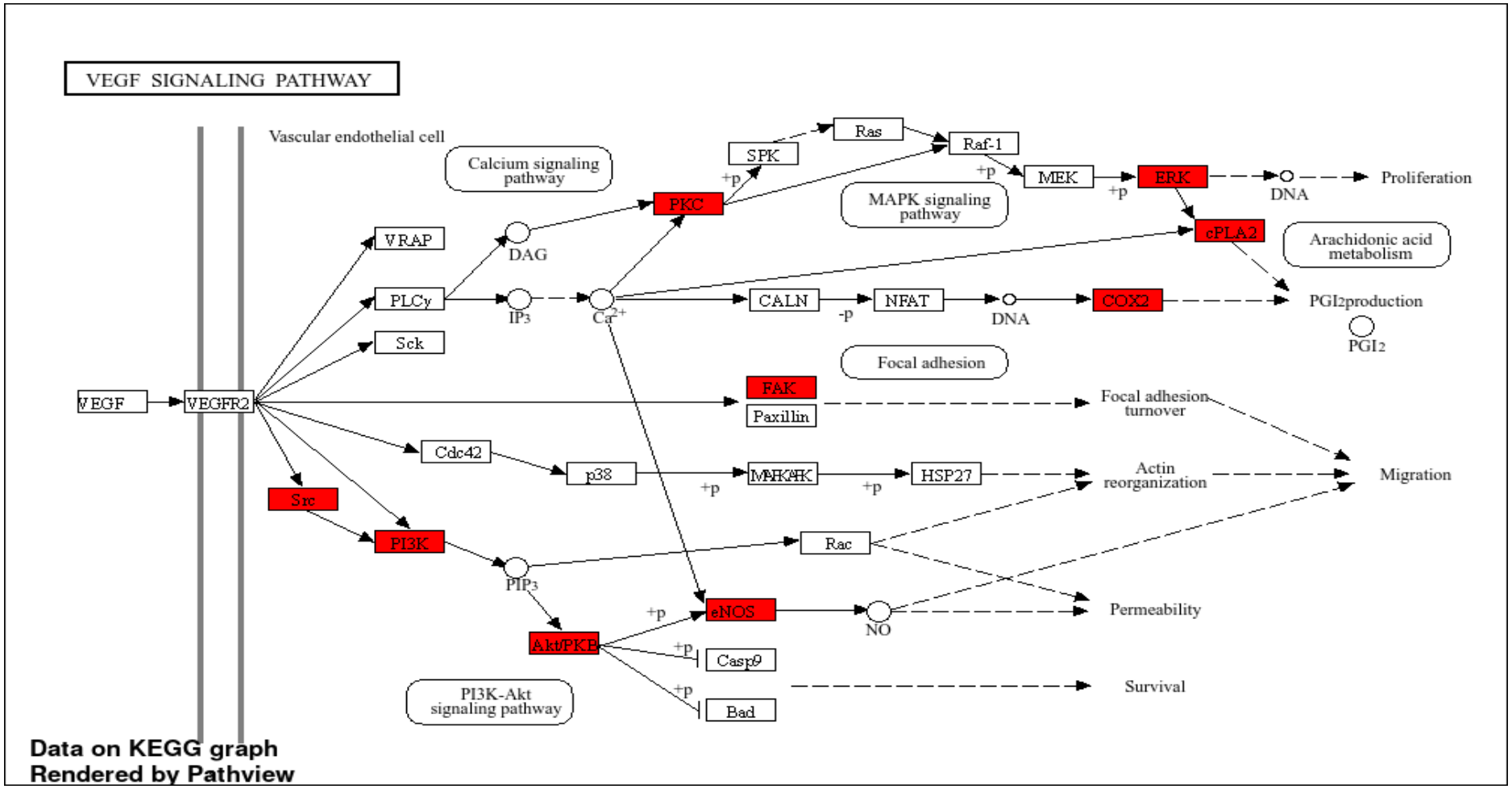


Figure 28: VEGF Signaling Pathway in *Thymus algeriensis* with Enriched/Highlighted Components.

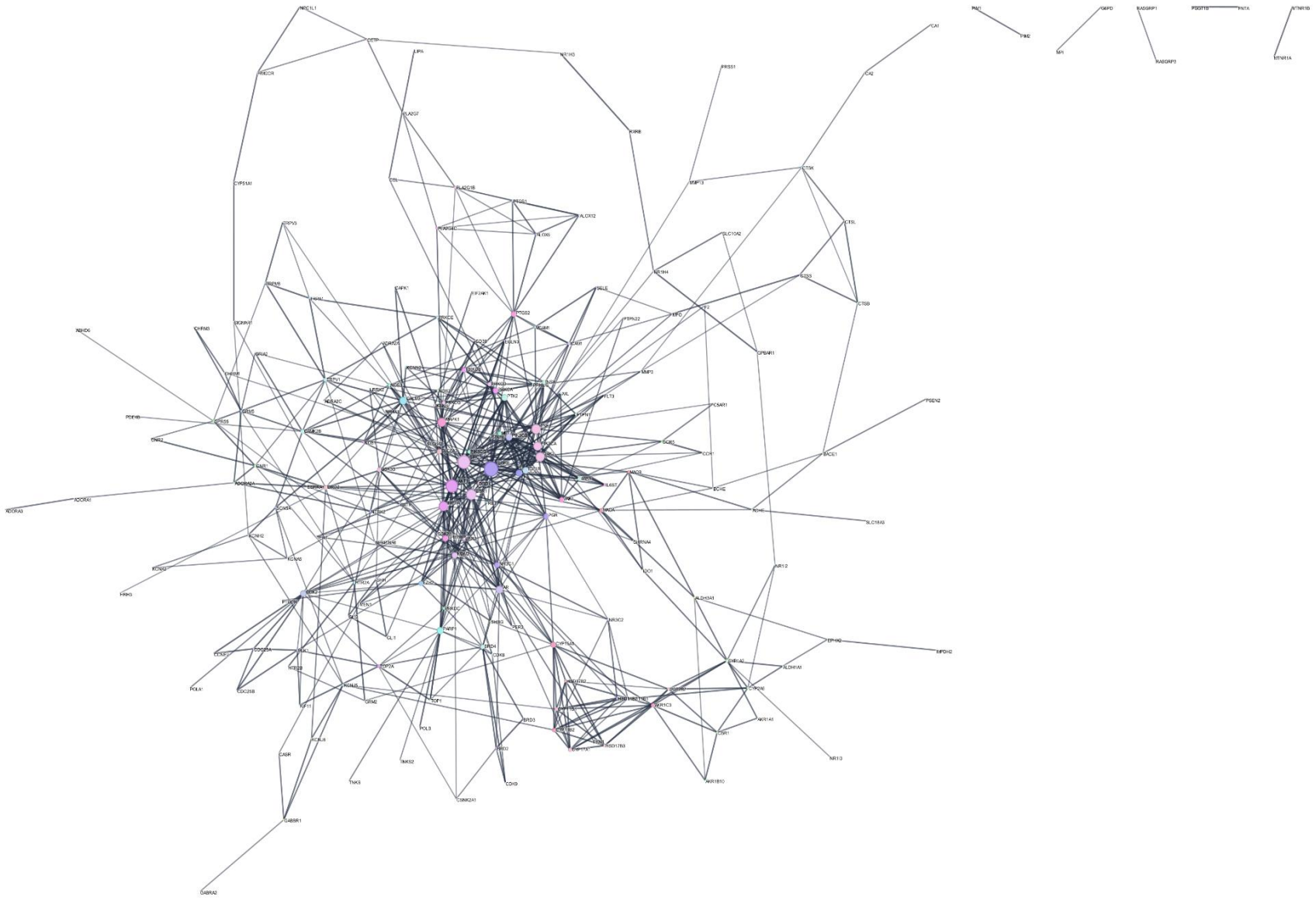


Figure 29: Protein-Protein Interaction Network (Interactome) of *Thymus algeriensis*

Table5: Protein-Protein Interaction (PPI)String degree.

display name	Betweenness Centrality	Degree
EGFR	0.120563179	37
SRC	0.094679407	33
AKT1	0.094899831	32
ESR1	0.118203368	26
TNF	0.153149615	24
HIF1A	0.046056809	24
JAK2	0.030654748	23
MAPK1	0.065883577	22
PIK3CA	0.014041725	21
AR	0.058256948	19
CALM3	0.097197053	19
PIK3CB	0.006138921	17
PIK3CD	0.006138921	17
PARP1	0.050620344	17
IGF1R	0.003738517	16
PTK2	0.008865257	16
CREBBP	0.028279326	15
MDM2	0.022533692	15
CDK2	0.054445778	15

1-Identification of Core Compounds and Their Network Significance:

The initial analysis of the compound-target-disease network (Figure25) and its corresponding node metrics (table4) shows that there are several highly influential compounds in the network. The compounds with the identification numbers 188323, caryophyllene acetate (90473616), tetramethyl-scutellarein (96118), and alpha-cadinol (10398656) all exhibit the maximum degree (100), indicating they interact with a broad range of protein targets. This poly pharmacological nature suggests they can modulate multiple biological processes simultaneously. Compound longiborneol (6432447) stands out with the highest Betweenness Centrality (0.0427), despite a slightly lower degree (99). High betweenness centrality marks it as a critical "bridge" in the network, connecting distant clusters of proteins. Its influence may be more strategic than that of other high-degree compounds, controlling key communication points within the biological system.

These compounds (which would be mapped to their chemical names, e.g., quercetin, luteolin, etc.) The primary drivers of the observed biological effect are a combination of several other factors. Their importance is defined not only by the number of targets (Degree) but also by their strategic position within the target network (Betweenness Centrality).

2. Key Protein Targets as Mediators of Compound Action:

The high-degree compounds all converge on a set of protein targets. Cross-referencing the edge table .csv with the top compounds reveals frequently targeted proteins. For example, proteins like P00533 (EGFR), P49841 (MAPK1), the PI3K/Akt family proteins, and P06213 (INSR) are central. The PPI network (Figure29) visualizes the functional significance of this targeting strategy. The network is not a random collection of proteins but a densely interconnected functional module. These compounds target interacting proteins within the human interactome and thus achieve their broad effects by targeting hub proteins within the human interactome. Hitting one key protein can trigger a cascade of downstream effects through its many interacting partners.

3. Linking Targets to Disease via Enriched Pathways:

The pathway enrichment analysis (Figure26) reveals the biological *consequences* of modulating these core targets. The most significant pathways provide a direct mechanistic link to the pathophysiology of respiratory diseases.

VEGF Signaling Pathway:

Relevance: This is the top hit by fold enrichment and has a highly significant FDR. VEGF is critical for angiogenesis (new blood vessel formation), which is a key process in airway remodeling in chronic diseases like asthma and COPD, as well as in tumor growth in lung cancer. It is also a pro-inflammatory mediator.

Connection: The KEGG map (Figure28) provides a clear illustration. The highlighted red boxes, PI3K, Akt, Src, PKC, ERK (MAPK), cPLA2, are the very proteins targeted by the key compounds. This provides a direct, traceable line: Compound → PI3K/Akt → VEGF Pathway Activation/Modulation → Airway Remodeling/Inflammation.

PI3K-Akt Signaling Pathway:

Relevance: This is a master regulatory pathway controlling cell survival, proliferation, and inflammation. Its dysregulation is a hallmark of pulmonary fibrosis (driving fibroblast proliferation), airway smooth muscle hypertrophy in asthma, and the survival of cancer cells.

Connection: As shown in the pathway-pathway network (Figure27), "PI3K-Akt signaling" is a central node connecting to "Pathways in cancer," "EGFR tyrosine kinase inhibitor resistance," and other crucial pathways. This confirms its role as a central hub through which the compounds exert widespread effects.

Inflammatory and Immune Pathways:

Relevance: The significant enrichment of the "Inflammatory mediator reg. of TRP channels" and "Chemokine signaling pathway" directly addresses the chronic inflammation characteristic of most respiratory diseases.

Connection: Chemokines are responsible for recruiting immune cells (like neutrophils and eosinophils) to the lung, perpetuating the inflammatory cycle. TRP channels are involved in sensory nerve activation, cough, and neurogenic inflammation. The compounds' ability to target proteins in these pathways suggests a strong anti-inflammatory or immunomodulatory potential. The analysis reveals a coherent and biologically plausible mechanism of action underlying the therapeutic effects of the identified phytochemicals. A limited group of key compounds, distinguished by their high Degree and Betweenness Centrality values within the pharmacological network, emerge as the principal active ingredients. These molecules exert their therapeutic influence by interacting with a core set of hub proteins, including EGFR, PI3K, Akt, and MAPK1, which occupy central positions within the human protein-protein interaction network.

Targeting these hubs leads to the modulation of several crucial signaling pathways, with the VEGF and PI3K-Akt pathways standing out as primary routes affected. These pathways are essential regulators of cellular proliferation, survival, angiogenesis, and tissue maintenance. Moreover, the simultaneous modulation of inflammatory and chemokine signaling pathways contributes to the suppression of chronic inflammation and aberrant immune responses. Collectively, this pharmacological activity addresses the fundamental pathological mechanisms involved in respiratory diseases, including persistent inflammation, abnormal tissue remodeling and fibrosis, and dysregulated cell growth associated with cancer-like processes. This integrated network perspective underscores the therapeutic relevance of the studied compounds, supporting their potential as multi-target agents in the treatment of complex respiratory disorders.

2- *Juniperus phoenicea* :

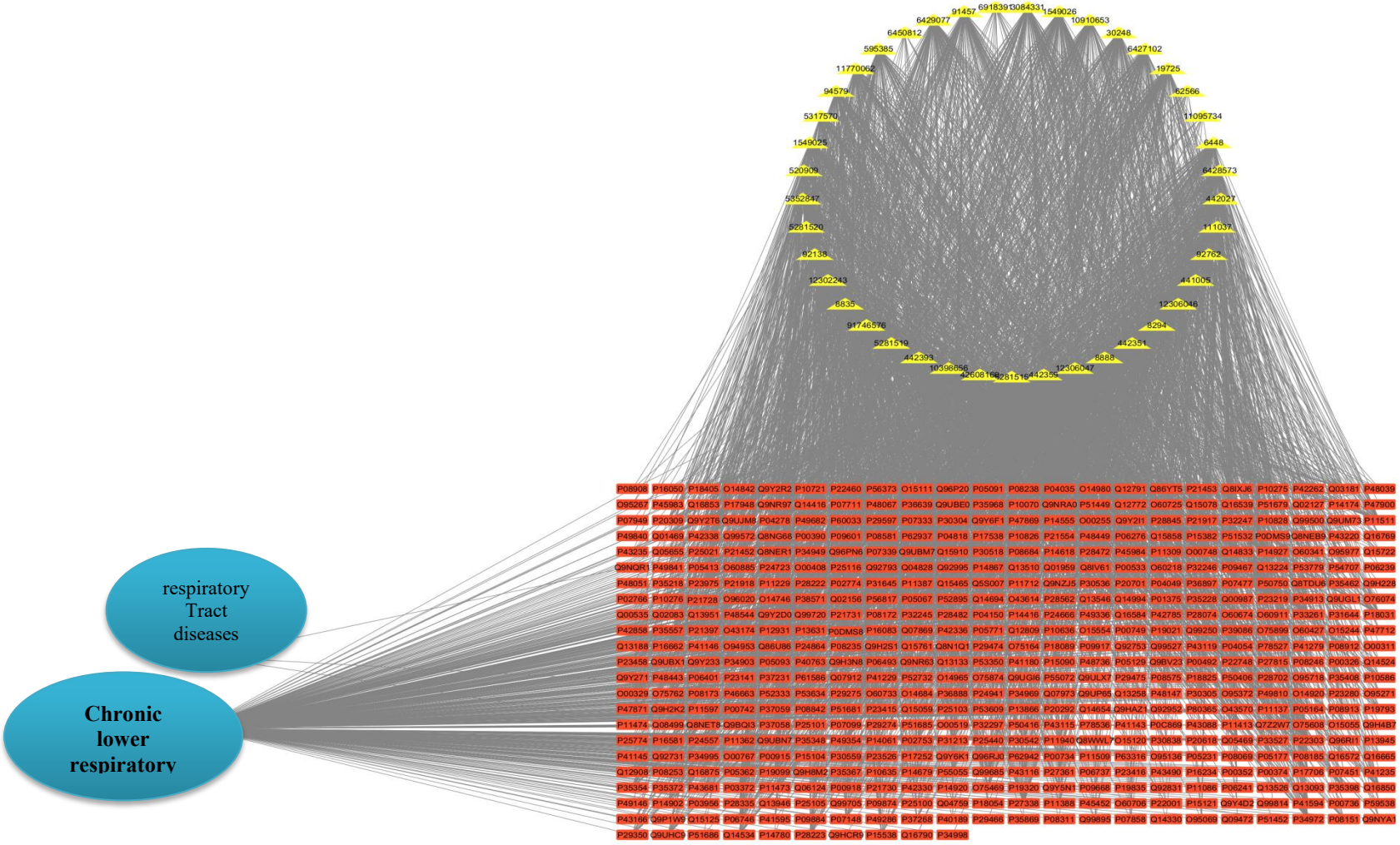


Figure 30: Compound-Target-Disease Network of plant *Juniperus phoenicea*

Table6: Node table of compound-target-disease network of plant *Juniperus phoenicea*.

C_attribute	BetweennessCentrality	Degree
12302243	0.01552551	100
11770062	0.01082985	100
10398656	0.00747608	100
3084331	0.00780359	100
94579	0.01494713	100
92762	0.00820527	100
92138	0.01714767	100
91457	0.01270483	100
19725	0.00604721	100
6429077	0.02126722	99
5352847	0.01342552	99
442027	0.01776116	99
6428573	0.01698873	98
1549026	0.01465513	98
1549025	0.01465513	98
111037	0.01355043	98
8888	0.01811377	98
8835	0.01836788	98
6427102	0.01451811	97
30248	0.01175835	97
6448	0.01415385	97
12306046	0.0044069	96
12306047	0.00418373	95
8294	0.01501359	95
442351	0.00397536	93
91746576	0.00624208	89
595385	0.00730931	89
442359	0.00357267	88
520909	0.00313942	87
5317570	0.00579856	84
441005	0.0045743	83
5281515	0.00288416	80
10910653	0.00282683	79
5281519	0.00413501	77
5281520	0.00141687	42
442393	2.27E-04	23
6918391	2.80E-04	17
6450812	3.38E-05	11
62566	3.38E-05	11
42608160	2.66E-05	10
11095734	2.82E-05	10

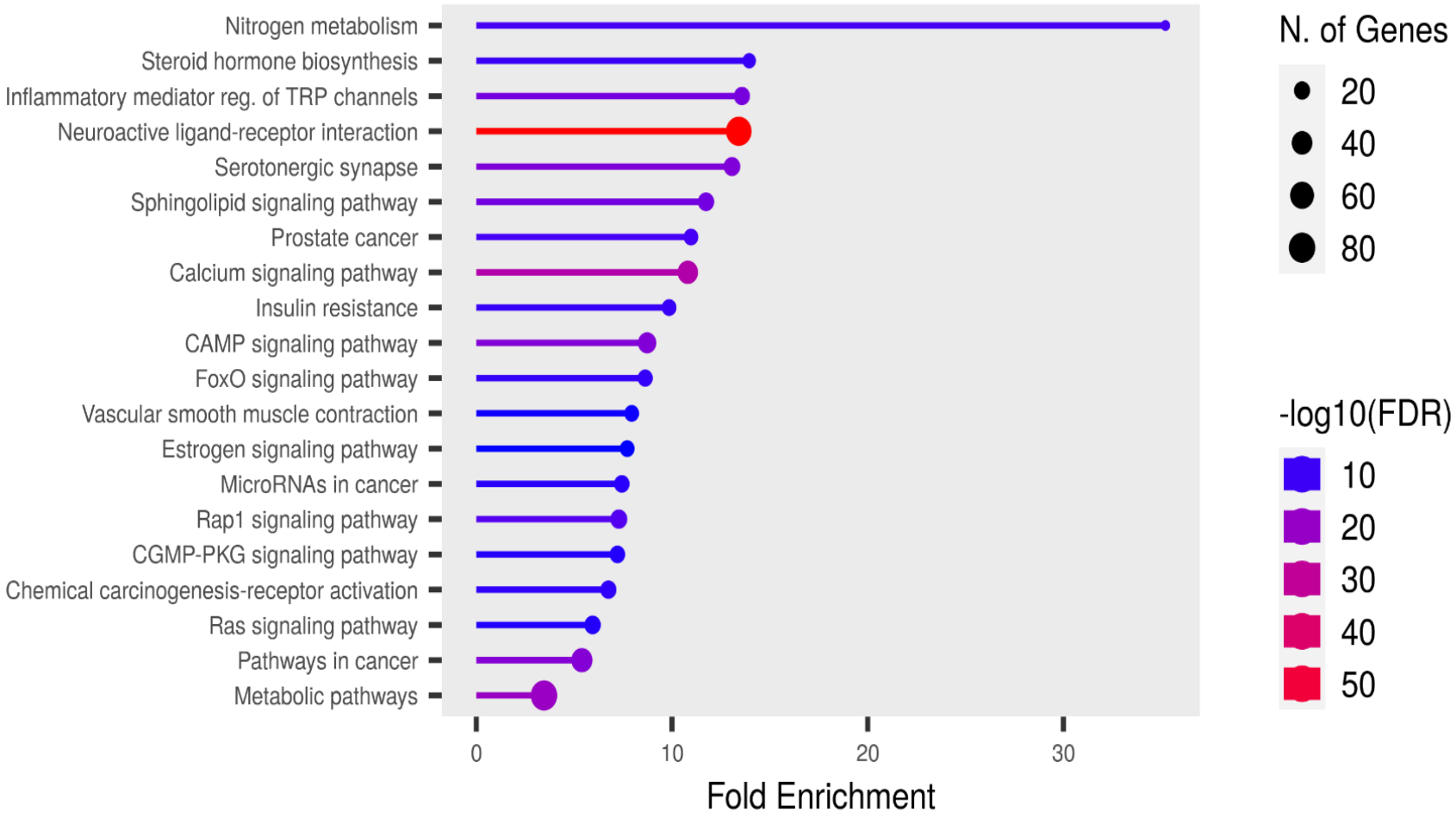


Figure 31: KEGG Pathway Enrichment Analysis of *Juniperus phoenicea* with Associated Gene Counts and Significance.

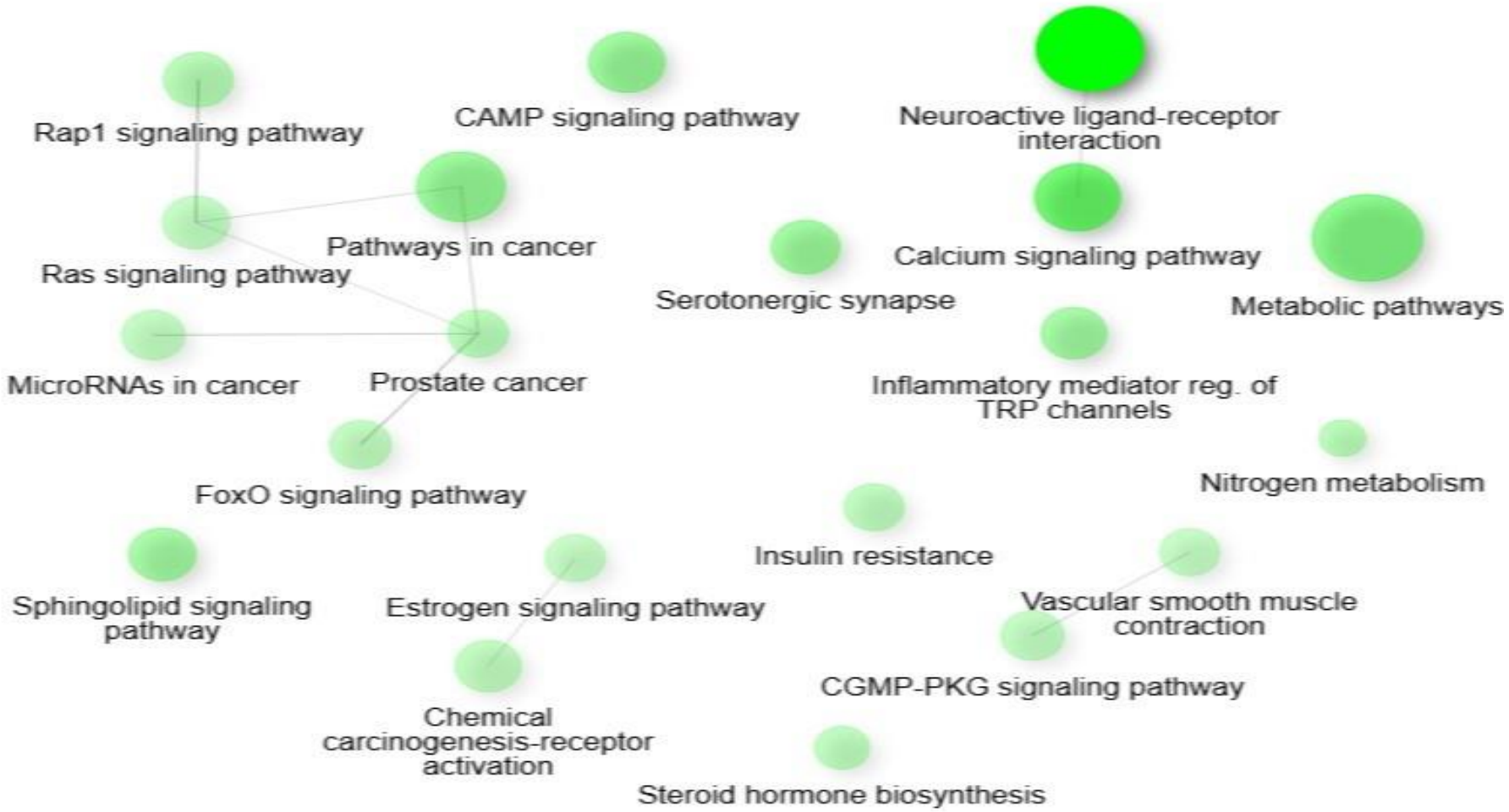


Figure 32: KEGG Pathway Interaction Network in plant *Juniperus phoenicea*.

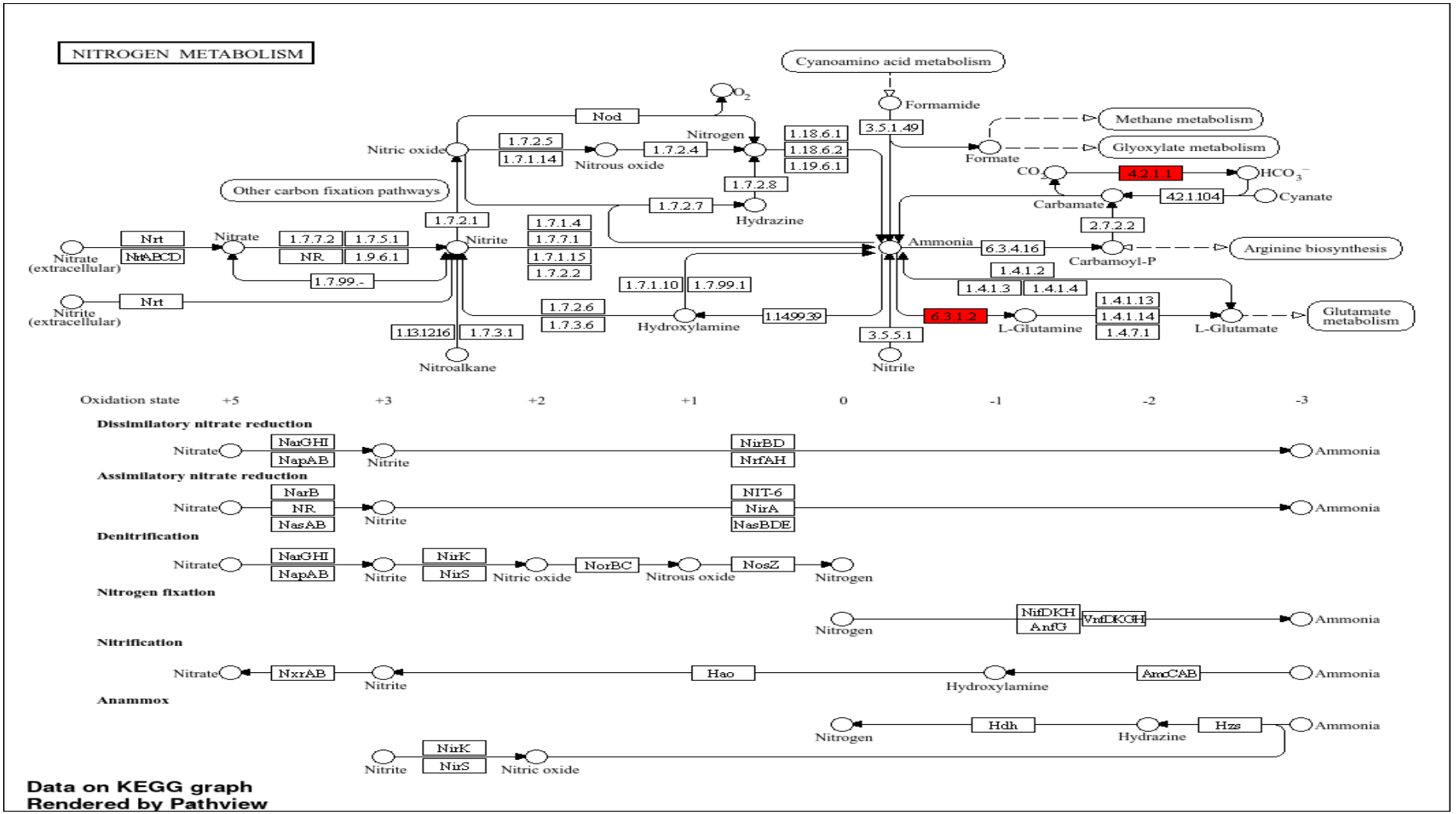


Figure 33: Nitrogen Metabolism Pathway in Juniperus phoenicea with Enriched/Highlighted Components (KEGG Analysis).

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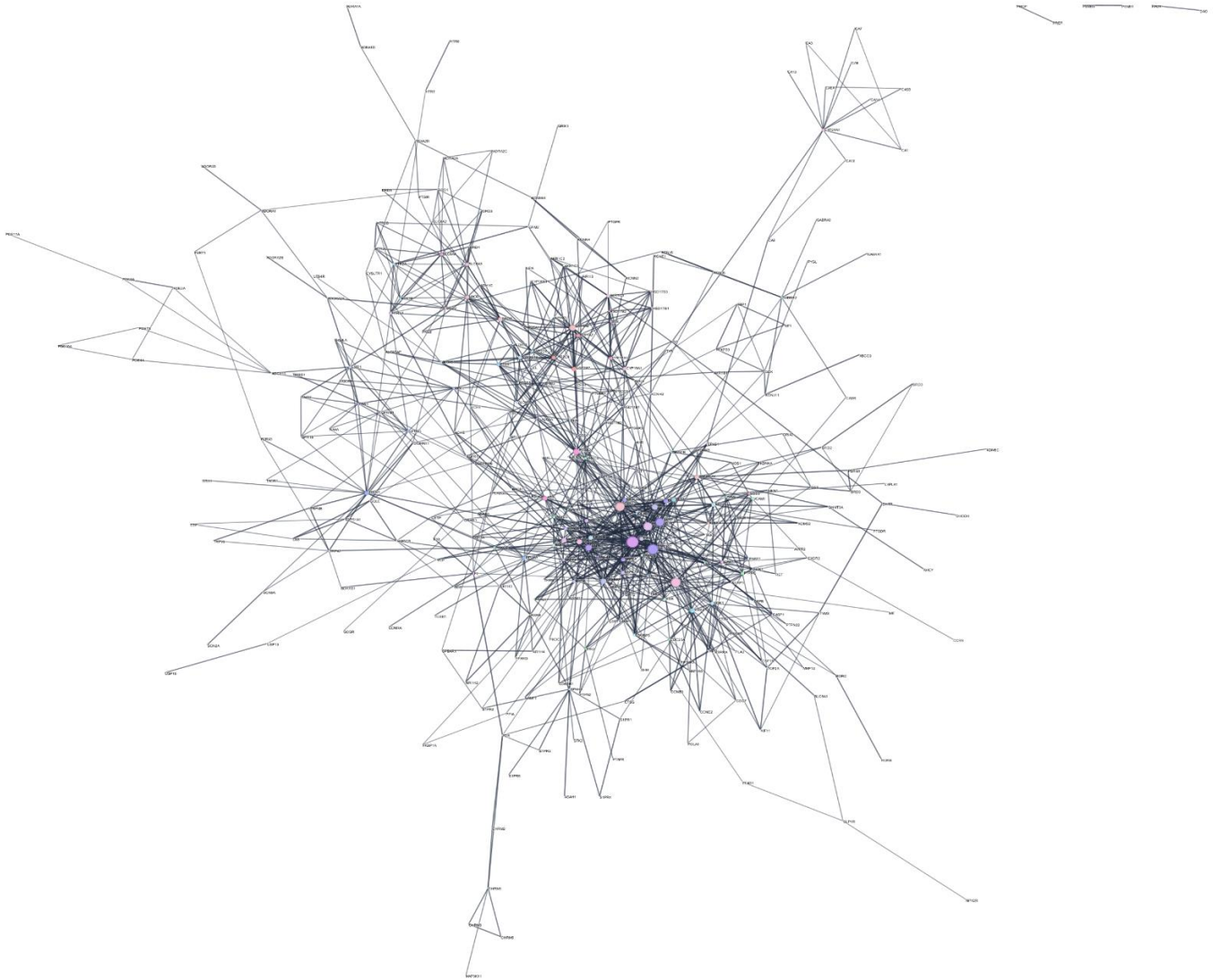

Figure34: Protein-Protein Interaction Network (Interactome) of *Juniperus phoenicea* .

Table7: Protein-Protein Interaction (PPI)String degree of plant Juniperus phoenicea.

display name	Betweenness Centrality	Degree
SRC	0.154919248	45
EGFR	0.092658933	40
IL6	0.116820747	36
ESR1	0.087908124	35
HSP90AB1	0.073300478	33
EP300	0.068477646	32
CYP3A4	0.038571098	24
PTGS2	0.074880759	24
MAPK3	0.051898201	24
AR	0.044846213	22
CREBBP	0.029542684	21
PPARG	0.058329044	20
MAPT	0.033273542	19
APP	0.033983784	18
CDK2	0.022142816	18
UGT2B7	0.009991405	17
SMARCA4	0.033534807	17
MAOA	0.0378595	17
PGR	0.009532638	17
TRPV1	0.084865918	17
PIK3CB	0.017513765	17
MAPK8	0.007779964	16
FYN	0.007570207	16
MDM2	0.014519582	16
EZH2	0.018516806	16
CYP2C9	0.014126939	15
MAOB	0.026864019	15
MAPK14	0.008116282	15
NR3C1	0.018452113	15
PPARA	0.04982132	15

1. Identification of Core Bioactive Compounds:

The compound-target-disease network (Figure30) and its associated node metrics (table6) reveal a group of highly influential compounds. A significant number of compounds, including alpha-calacorene (12302243), Cubenol (11770062), alpha-cadinol (10398656), t-muurolol (30844331), isopulegul acetate (94579), beta-cudesmol (92138), and elemol (914557), exhibit the maximum degree of 100. This indicates a profound polypharmacological profile, where each compound interacts with a wide array of protein targets. Such broad-spectrum activity is characteristic of compounds capable of modulating complex disease states involving multiple biological dysfunctions. It is the most important node in the topologically important class of compounds, possessing the highest Betweenness Centrality (0.0213). While its degree (99) is marginally lower than the top-degree compounds, its high centrality marks it as

a critical link between different protein clusters. Its role is likely strategic, controlling key signal transduction bottlenecks within the cellular network. Similarly, compounds citronellyl butanoate (8835) (0.0184) and beta-cudesmol (92138) (0.0171) also show high centrality, reinforcing their importance.The therapeutic potential is driven by a core set of compounds defined by both the breadth of their interactions (Degree) and their strategic control over information flow within the target network (Betweenness Centrality).

2. Convergence on a Densely Interconnected Protein Sub-network:

The identified compounds do not target random proteins but converge on a specific, functionally related set of targets. The PPI network (Figure34) visualizes this as a dense, highly interconnected "functional module" rather than a sparse collection of unrelated proteins. The Merged Network default table (the annex) shows some of these key target interactions. The top edge by betweenness (1295.15) connects cis-calamenene to protein P51452 (CACNA1C), a calcium channel subunit critical for vascular smooth muscle contraction and cardiac function. Other frequently targeted proteins are involved in signaling cascades, such as those related to G-protein coupled receptors and kinases. The compounds work by modulating a network of proteins. A cascade of downstream effects is triggered by targeting key nodes within this module, amplifying the initial compound-protein interaction across multiple biological systems.

3. Linking Protein Targets to Respiratory Disease via Key Biological Pathways:

The pathway enrichment analysis (Figure31) identifies the biological processes most significantly perturbed by the compounds' targeting activity, providing a direct link to the pathophysiology of respiratory diseases.

Neuroactive Ligand-Receptor Interaction:

Relevance: This is the most significant pathway, as indicated by its high -log10(FDR), gene count, and central position in the pathway network (Figure32). In the respiratory system, this pathway governs neurogenic inflammation. Airway nerves release neuropeptides (like substance P and CGRP) that bind to receptors on smooth muscle, glands, and immune cells, driving bronchoconstriction, mucus hypersecretion, and inflammatory cell infiltration, hallmarks of asthma and COPD.

Connection: The compounds' strong enrichment in this pathway suggests they modulate these neuro-immune interactions, potentially reducing airway hyperresponsiveness and inflammation.

Nitrogen Metabolism:

Relevance: This pathway shows the highest Fold Enrichment. While seemingly unrelated, the KEGG map (Figure33) reveals its direct relevance through the production of Nitric Oxide (NO). NO is a master regulator in the lungs; it acts as a potent bronchodilator and vasodilator but can also contribute to

oxidative stress and inflammation (as peroxynitrite) when produced in excess by inducible NO synthase (iNOS) during inflammation.

Connection: The highlighted enzymes on the map (e.g., 6.3.1.2 - carbamoyl-phosphate synthase) indicate that the compounds directly interfere with the metabolic precursors to NO synthesis. This suggests a mechanism for normalizing the NO balance, which is often dysregulated in asthma and other inflammatory lung diseases.

Calcium and Vascular Signaling:

Relevance: The "Calcium signaling pathway" and "Vascular smooth muscle contraction" pathways are highly significant. Calcium is the final trigger for smooth muscle contraction, and its dysregulation leads to airway narrowing (bronchoconstriction) in asthma and COPD. It is also central to inflammatory cell activation and degranulation.

Connection: By targeting proteins within these pathways (like the CACNA1C), the compounds can directly interfere with the mechanisms of bronchoconstriction and potentially reduce the hypertensive remodeling of pulmonary arteries seen in severe respiratory conditions. The data together support a coherent and integrated mechanistic framework for understanding the therapeutic activity of the principal phytochemicals in the Al-Jur formulation. A core group of major bioactive compounds, recognized through high Degree and Betweenness Centrality within the pharmacological network, emerges as central to the observed biological activity. These compounds interact with a densely interconnected network of protein targets that play pivotal roles in fundamental cellular signaling processes.

This network-based interaction leads to the modulation of three critical physiological systems particularly relevant to chronic respiratory diseases: neuro-receptor signaling, nitric oxide bioavailability, and calcium-mediated smooth muscle contraction. These compounds have the potential to alleviate neurogenic inflammation and airway hyperresponsiveness, restore the balance between bronchodilation and inflammation via nitric oxide regulation, and alleviate bronchoconstriction by affecting calcium-dependent muscle contraction mechanisms. The therapeutic promise of these compounds in treating the complex and multifactorial pathology of respiratory illnesses is based on this multi-target, multi-pathway mechanism of action. The findings strongly recommend that these phytochemicals should be continued as part of integrated strategies in respiratory disease treatment.

3- *Artemisia herba-alba Asso*:

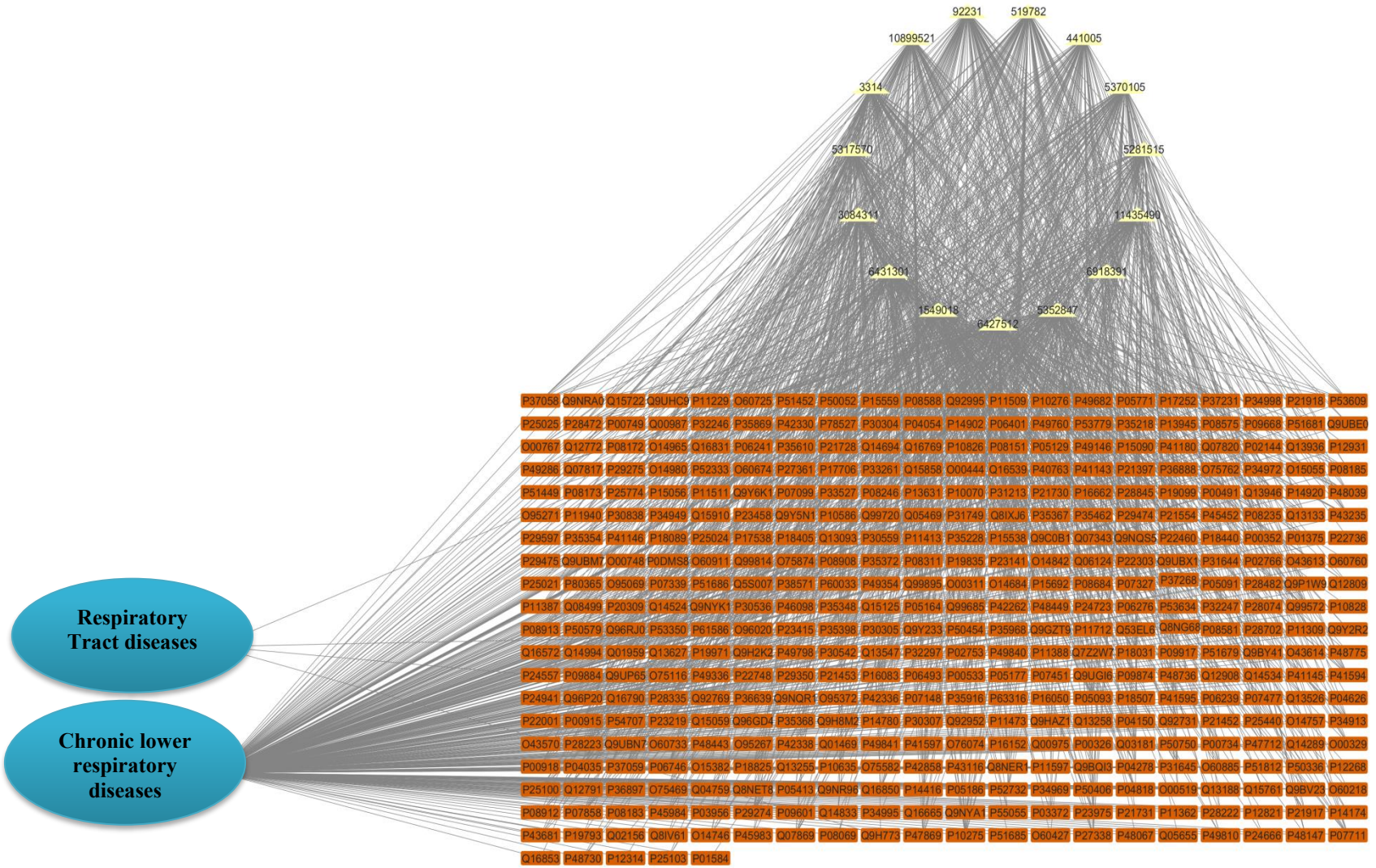

Figure 35: Compound-Target-Disease Network of plant *Artemisia herba-alba Asso*.

Table8: Node table of compound-target-disease network of plant *Artemisia herba-alba Asso*.

C_attribute	Betweenness Centrality	Degree
3084311	0.02382152	100
92231	0.02796708	99
11435490	0.02813419	98
10899521	0.02373771	98
6427512	0.01860797	98
5370105	0.02390165	98
1549018	0.02893061	98
519782	0.02020064	98
5352847	0.02373163	97
6431301	0.02289487	96
3314	0.03817471	95
5317570	0.01269026	83
441005	0.01225606	82
5281515	0.01237026	80
6918391	5.42E-04	17

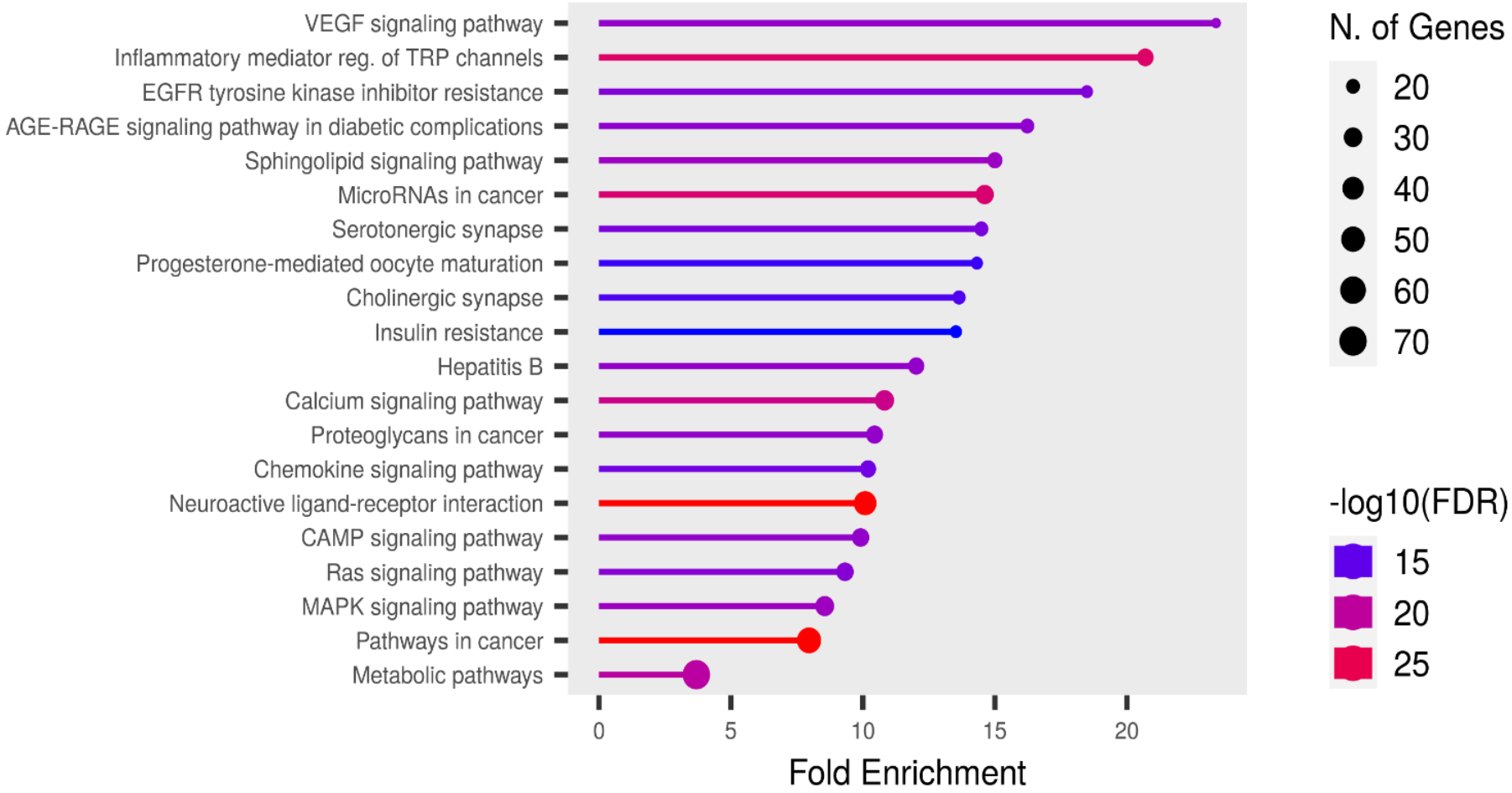

Figure 36: KEGG Pathway Enrichment Analysis of *Artemisia herba-alba Asso* with Associated Gene Counts and Significance.

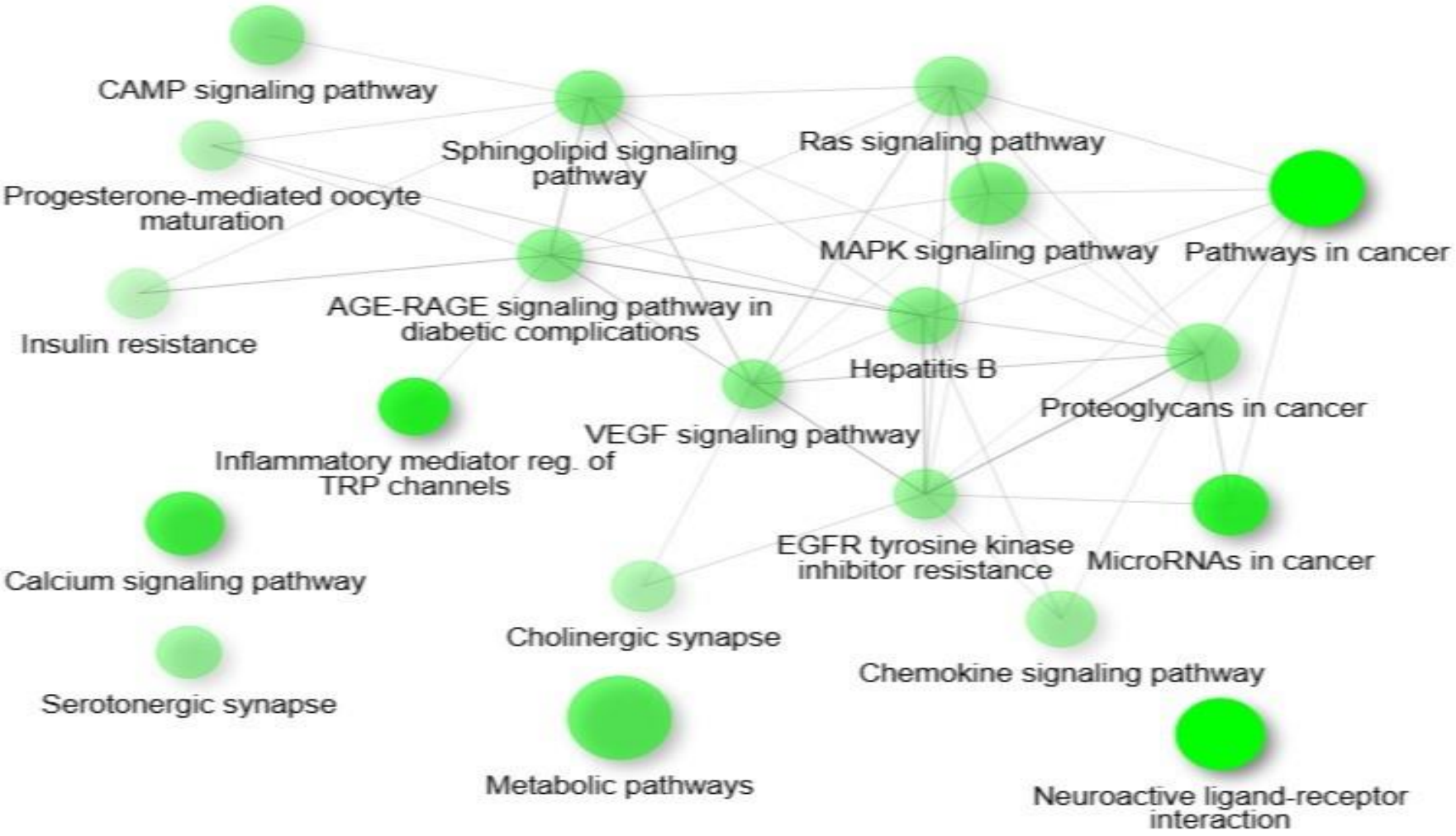

Figure 37: KEGG Pathway Interaction Network in plant Artemisia herba-alba Asso.

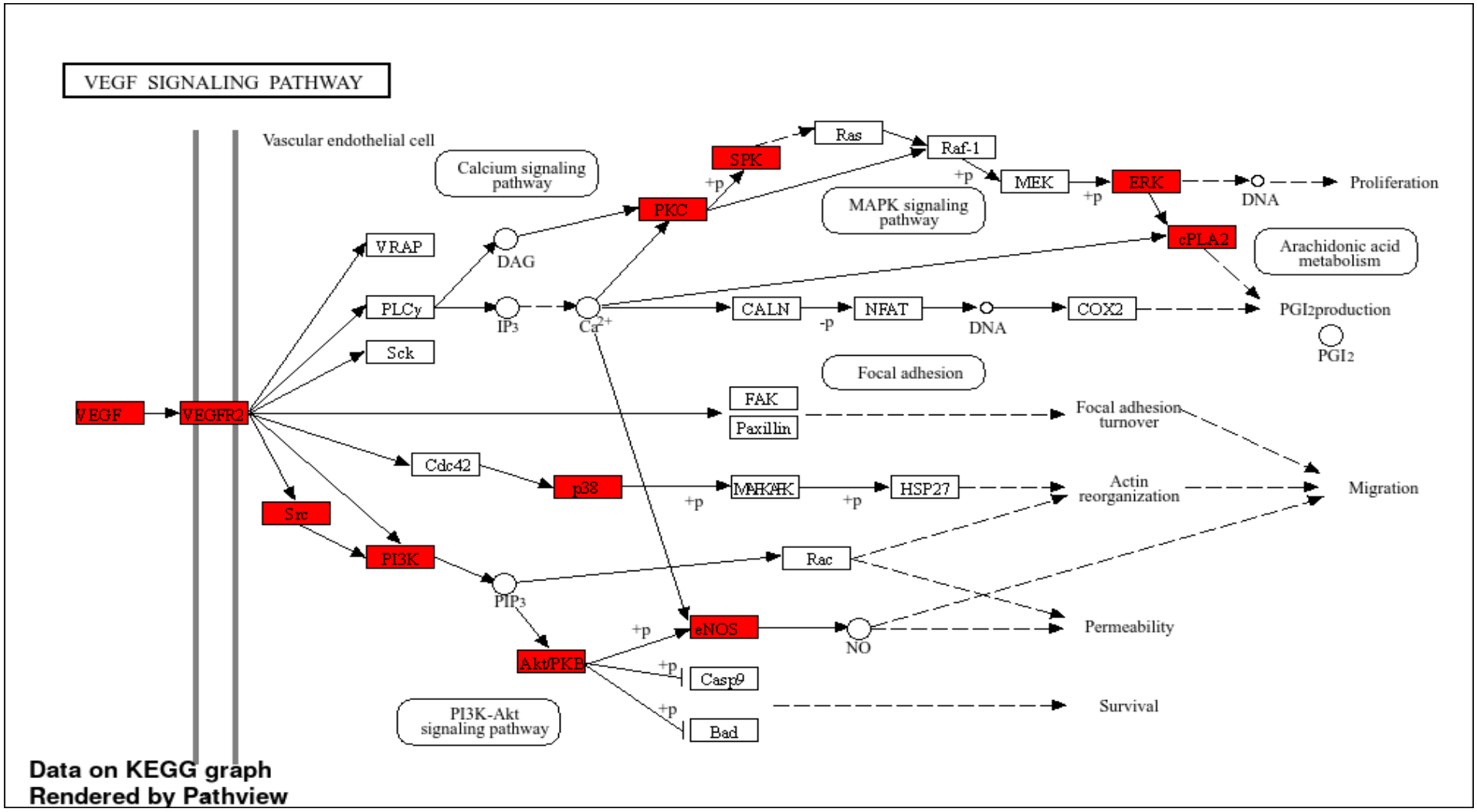

Figure 38: VEGF Signaling Pathway in Artemisia herba-alba Asso. with Enriched/Highlighted Components (KEGG Analysis).

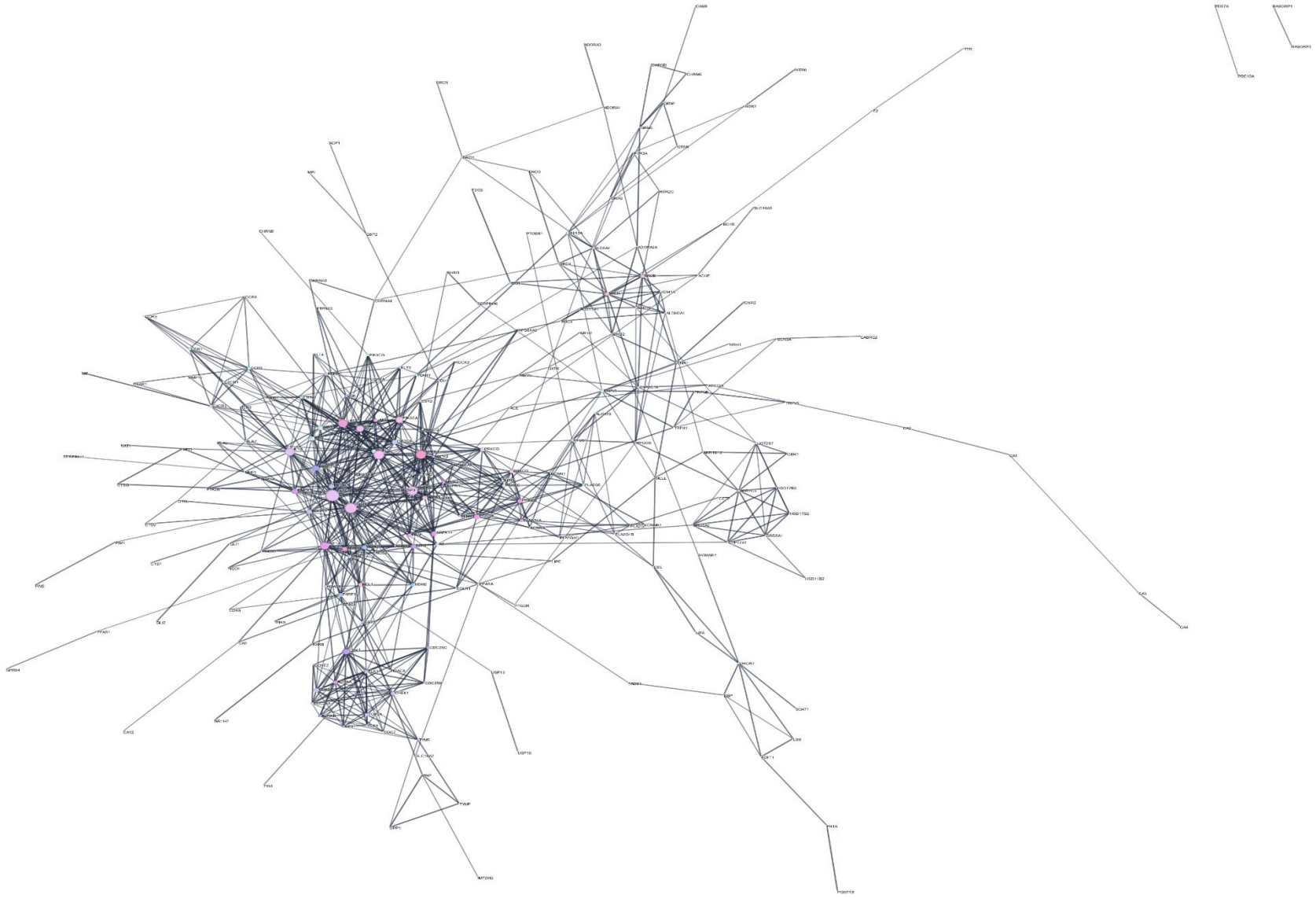

Figure 39: Protein-Protein Interaction Network (Interactome) of *Artemisia herba-alba Asso*.

Table9: Protein-Protein Interaction (PPI)String degree of plant *Artemisia herba-alba Asso*.

display name	betweenness Centrality	Degree
STAT3	0.119576173	42
AKT1	0.088652148	37
SRC	0.092877805	32
MAPK3	0.066426778	32
MAPK1	0.057292799	31
JAK2	0.06794511	29
IL1B	0.10609783	28
HIF1A	0.088372037	27
PIK3CA	0.027662481	23
PTPN11	0.01990523	23
CDK1	0.047866584	20
ERBB2	0.026763276	20
MMP9	0.056395214	19
PRKCA	0.019324699	17
MAPK14	0.029951021	17
RHOA	0.012029992	17
BCL2L1	0.038276478	17
PIK3CB	0.008338776	17
EZH2	0.040836897	16
JAK3	0.005034958	16
PPARG	0.04026371	15
MAPK8	0.010500645	15
PRKCB	0.014595348	15
CDK2	0.014566553	15
PARP1	0.022097659	15
HDAC1	0.015122574	15
KDR	0.005063608	15

1. Identification of Core Bioactive Compounds by Network Topology:

The compound-target network (Figure35) and its topological metrics (table 8) identify a set of highly influential compounds based on their connectivity. It has the maximum degree of interaction (100), meaning it interacts with the broadest range of protein targets. Several other compounds, including spathulenol (92231), myrteny acetate (11435490), trans-chrysanthenly acetate (10899521) , and jasmone(1549018) , also exhibit exceptionally high degrees (98-99), indicating a strong Poly pharmacological profile. Compound eugenol (3314) has the highest Betweenness Centrality (0.038), marking it as the most critical "bottleneck" in the network. Despite a slightly lower degree (95), its strategic position suggests it controls vital communication points between different protein clusters

Compounds myrteny acetate (11435490) (0.028) and jasmone (1549018) (0.029) also have high centrality scores, reinforcing their importance in mediating the network's effects. A key group of compounds is likely to drive therapeutic potential. Their importance is defined by their broad target engagement (High Degree) and their strategic control over biological information flow (High Betweenness Centrality).

2. Convergence on a Functionally Cohesive Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a densely interconnected module, as visualized in the PPI network (Figure39). This suggests that the compounds modulate a coordinated biological system rather than isolated targets. The edge table (annex) shows the main interactions. The edge with the highest betweenness (919.63) connects the top centrality compound eugenol (3314) to proteins P51452 (CACNA1C) and Q9H773 (CACNA1E), which are subunits of voltage-gated calcium channels. Other crucial targets identified through their connections to multiple top compounds include proteins central to kinase signaling pathways. The compounds work by targeting a specific protein group in the body. Modulating one or more hub proteins within this complex (like signaling kinases or ion channels) can trigger a cascade of downstream events, amplifying the therapeutic signal throughout the relevant biological systems.

3. Linking Targets to Respiratory Disease via Enriched Signaling Pathways:

The pathway enrichment analysis (Figure36) reveals the biological consequences of this multi-target activity, providing a direct mechanistic link to the pathophysiology of chronic respiratory diseases.

VEGF Signaling Pathway:

Relevance: This is the most significant pathway by Fold Enrichment (>20) and has an exceptionally low FDR. In respiratory diseases like asthma, COPD, and pulmonary fibrosis, Vascular Endothelial Growth Factor (VEGF) drives angiogenesis and airway remodeling, leading to thickened, dysfunctional airways. It is also a potent mediator of vascular permeability, contributing to airway edema and inflammation.

Connection: The KEGG map (Figure38) provides a clear, traceable mechanism. The compounds directly target numerous key nodes in this pathway, including VEGF itself, and critical downstream effectors like Src , PI3K, Akt, PKC, and ERK (a MAPK). This demonstrates a direct line of influence: Compound → PI3K/Akt/MAPK → VEGF Pathway Modulation → Attenuation of Airway Remodeling and Inflammation.

-Inflammatory and Immune Pathways:

Relevance: The significant enrichment of the "Inflammatory mediator reg. of TRP channels" and "Chemokine signaling pathway" directly points to a potent anti-inflammatory mechanism. TRP channels on sensory nerves are critical for initiating cough and neurogenic inflammation. Chemokines orchestrate the recruitment of damaging inflammatory cells (like neutrophils and eosinophils) to the lungs.

Connection: As seen in the pathway network (Figure37), these inflammatory pathways are connected to other core pathways like MAPK and Calcium signaling, suggesting a coordinated immunomodulatory effect. By targeting these pathways, the compounds can likely suppress the chronic inflammatory cycle that drives disease progression.

-Cancer and Proliferation Pathways:

Relevance: "Pathways in cancer," "MAPK signaling," and "Ras signaling" are highly enriched and central in the pathway network (Figure37). While overtly related to cancer, these pathways are master regulators of cell proliferation, survival, and differentiation. These same processes are pathologically activated in non-cancerous respiratory diseases, such as the proliferation of fibroblasts in pulmonary fibrosis and the hypertrophy of airway smooth muscle in asthma.

Connection: The compounds' ability to modulate these pathways suggests they can interfere with the abnormal tissue repair and cellular proliferation that are the cause of chronic airway and interstitial lung diseases. The evidence agrees that the traditional Al-Jur formulation contains several phytochemicals which have therapeutic potential. These compounds emerged as principal agents based on their high centrality measures within the compound-target-disease network. These compounds exert their effects by modulating a closely interconnected set of protein targets, particularly pivotal kinases like PI3K, Akt, and ERK, as well as ion channels such as CACNA1C. This strategic engagement across multiple targets results in the perturbation of fundamental biological pathways, including VEGF signaling, MAPK/Ras signaling, and several inflammatory cascades. Crucially, these pathways align with the major pathological hallmarks of chronic respiratory diseases. For example, inhibition of the VEGF pathway can reduce airway remodeling and vascular permeability; downregulation of chemokine signaling and TRP channels may attenuate chronic inflammation and immune cell infiltration; and MAPK and cancer-associated pathways could normalize aberrant cell proliferation. Finally, the integrated network pharmacology approach shows that the therapeutic action of the Al-Jur drink's phytoconstituents is not mediated through isolated molecular interactions, but rather through a coordinated, multi-target strategy. This systemic modulation reflects the complex, multifactorial nature of respiratory diseases and supports the rationale for utilizing plant-based formulations in managing such conditions.

4- *Pistacia Lentiscus*:

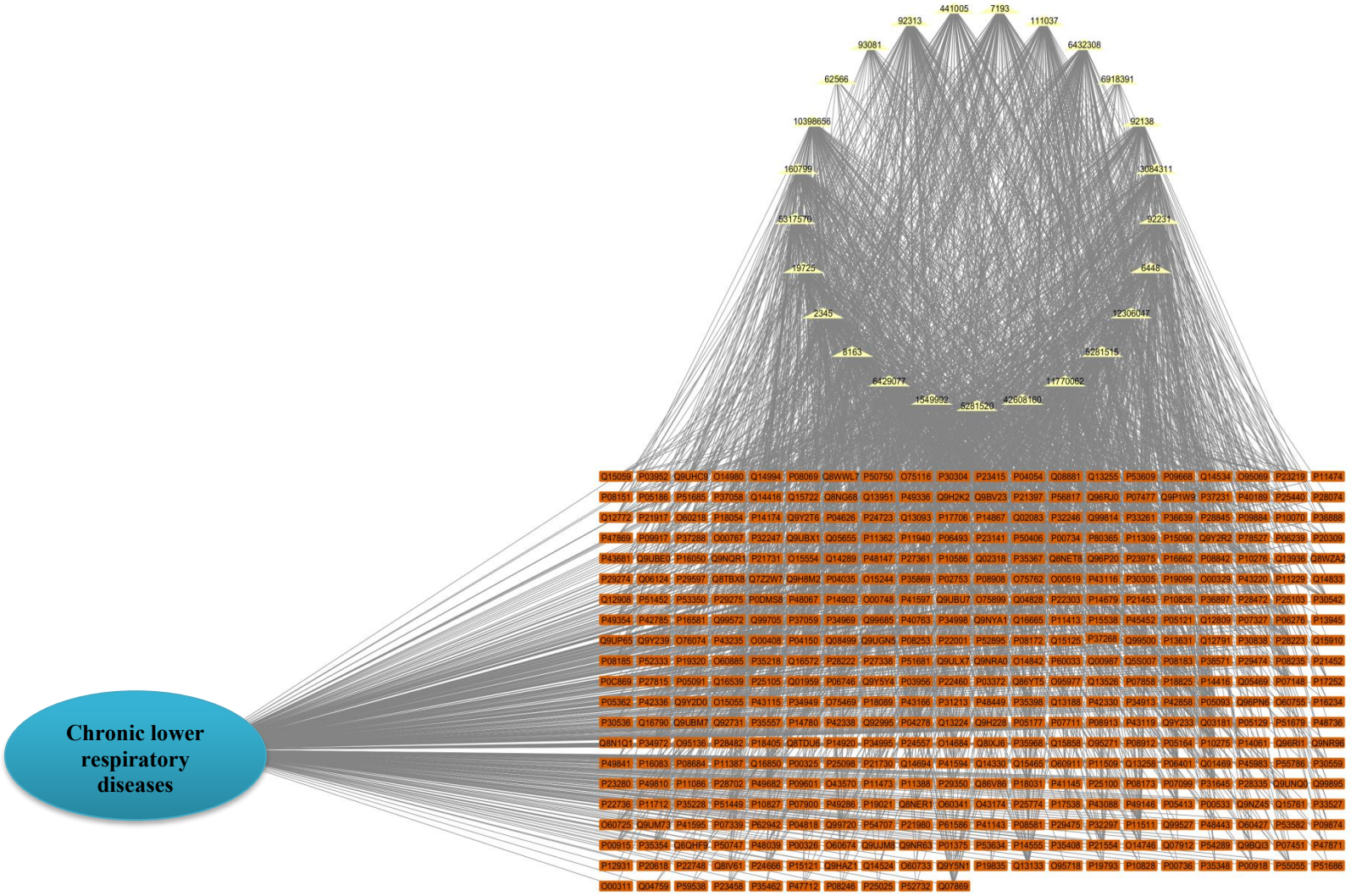

Figure 40: Compound-Target-Disease Network of plant *Pistacia Lentiscus*.

Table10: Node table of compound-target-disease network of plant *Pistacia Lentiscus*.

C_attribute	Betweenness Centrality	Degree
11770062	0.0161628	100
10398656	0.01268042	100
6432308	0.00896843	100
3084311	0.01216838	100
1549992	0.02086636	100
160799	0.01789491	100
92313	0.00907423	100
92231	0.02186033	100
92138	0.02534105	100
19725	0.01111863	100
8163	0.02782181	100
6429077	0.02904509	99
2345	0.02754832	99
111037	0.02543089	98
6448	0.02752745	98
7193	0.02758358	97
12306047	0.00806906	95
5317570	0.00756872	83
441005	0.01019256	83
5281515	0.00580467	80
5281520	0.00318523	42
93081	9.43E-04	30
6918391	3.99E-04	17
62566	6.10E-05	11
42608160	4.78E-05	10

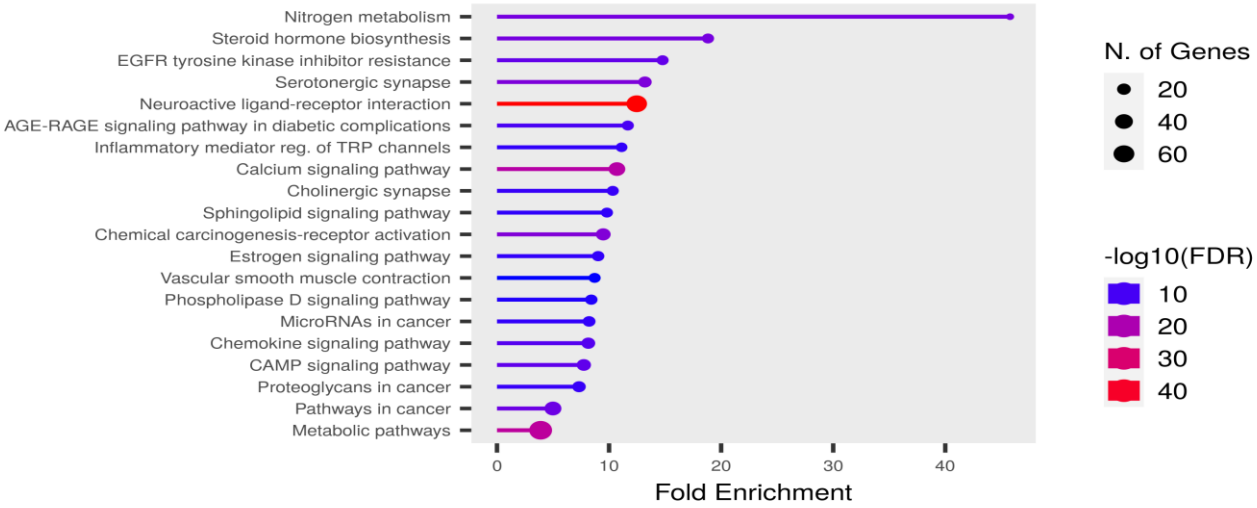

Figure 41: KEGG Pathway Enrichment Analysis of *Pistacia Lentiscus* with Associated Gene Counts and Significance.

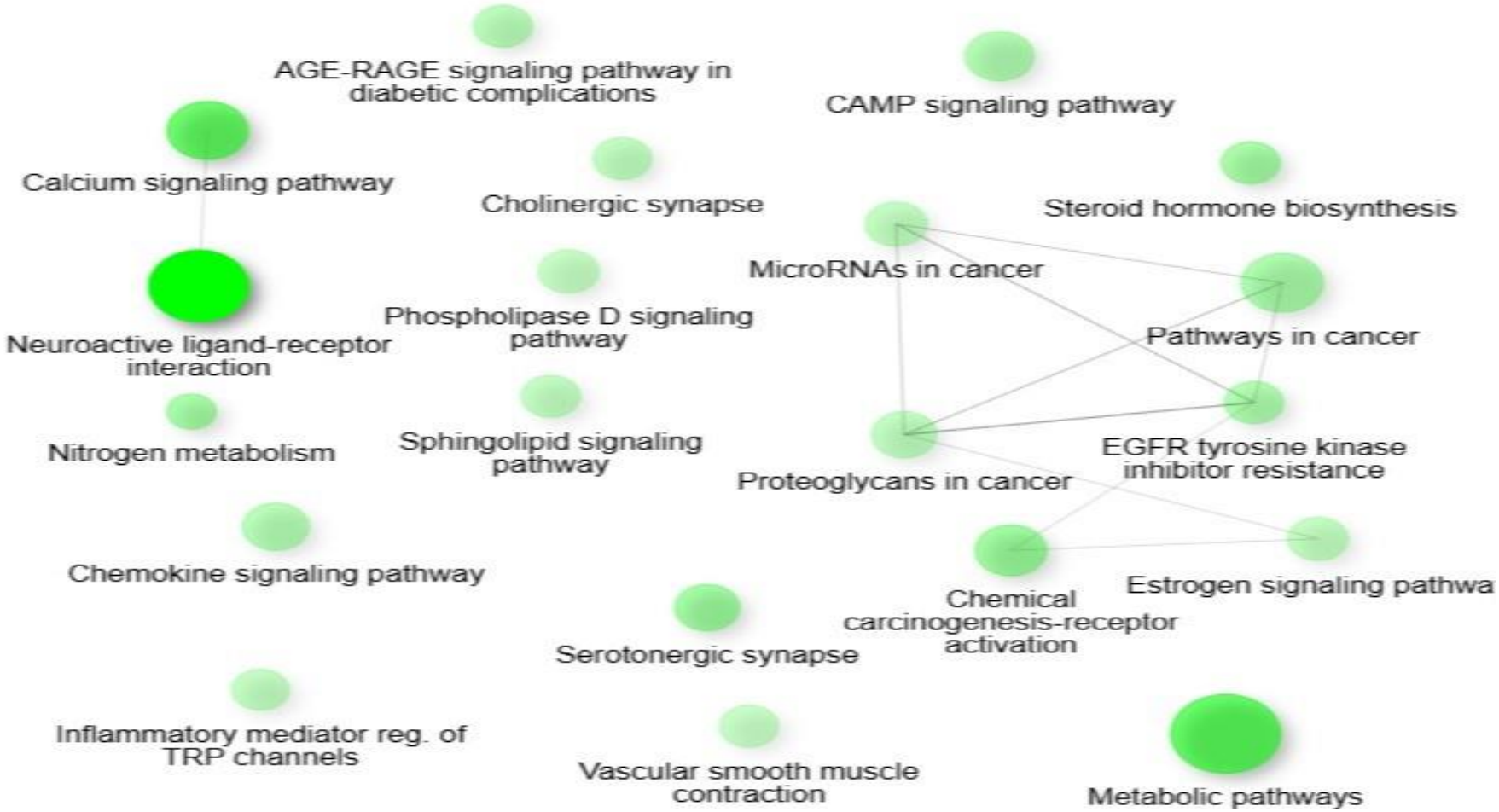

Figure 42: KEGG Pathway Interaction Network in plant *Pistacia Lentiscus*.

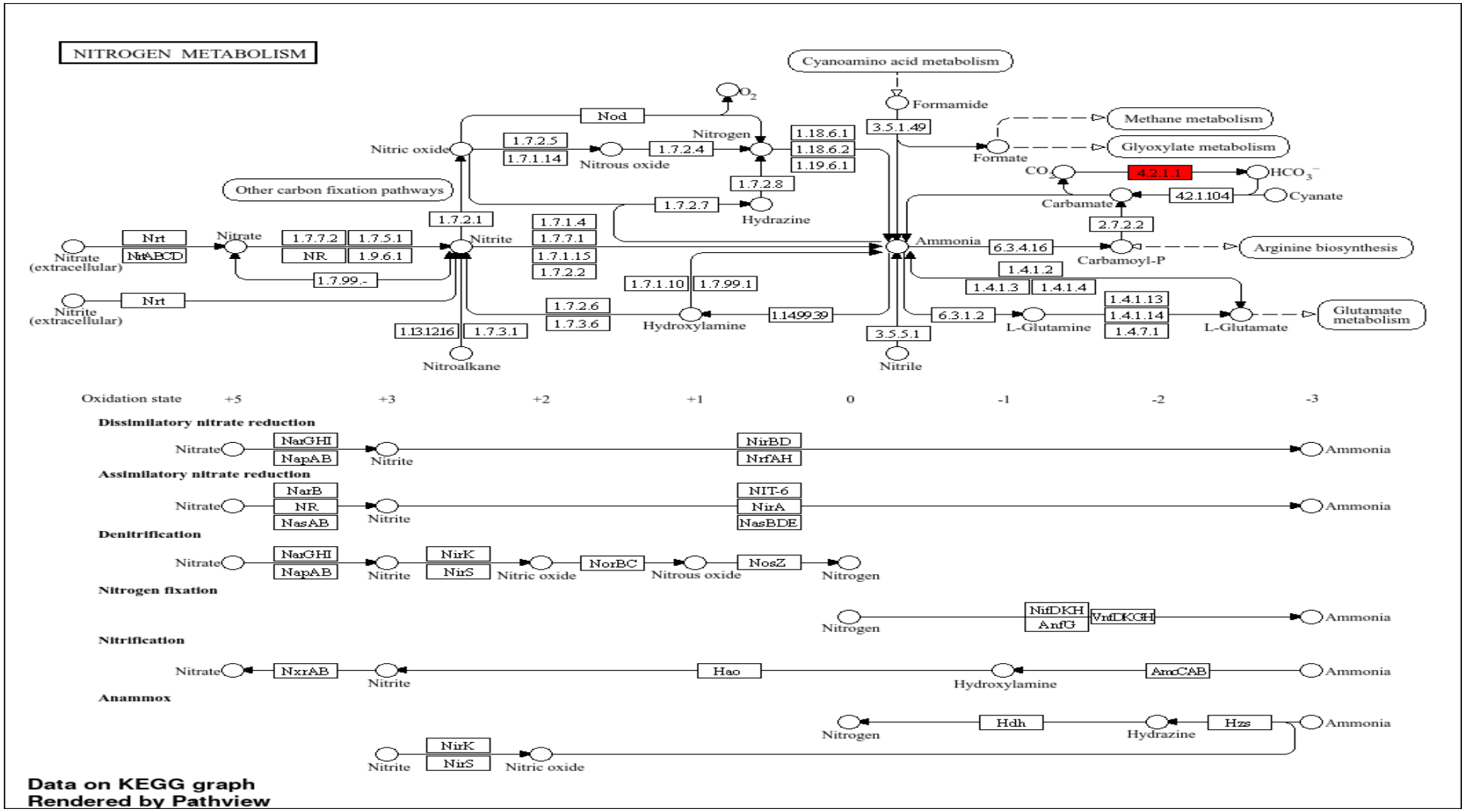

Figure 43: Nitrogen Metabolism Pathway in Pistacia Lentiscus with Enriched/Highlighted Components (KEGG Analysis).

Figure 44: Protein-Protein Interaction Network (Interactome) of *Pistacia Lentiscus*.

Table11: Protein-Protein Interaction (PPI)String degree of plant *Pistacia Lentiscus*.

display name	Betweenness Centrality	Degree
STAT3	0.107848308	38
EGFR	0.12675313	38
SRC	0.069683142	34
HSP90AA1	0.175969333	32
JAK2	0.044123605	29
PTGS2	0.152343437	26
CYP3A4	0.067208213	24
ERBB2	0.063159207	24
ESR1	0.062694549	22
PIK3CD	0.01628905	22
PIK3CB	0.01628905	22
JAK3	0.00612329	19
CYP19A1	0.072879382	18
MAPK1	0.048534629	18
MMP9	0.08935849	18
MAOA	0.041914313	17
JAK1	0.002401811	17
UGT2B7	0.018119082	16
AKR1C3	0.034214365	16
CYP2C9	0.021908515	15
MAOB	0.031666206	15
ICAM1	0.019670506	15
AR	0.043345836	15

1. Identification of Core Compounds via Network Centrality:

The compound-target-disease network (Figure40) and its corresponding node metrics (table10) identify a set of highly influential compounds through their topological properties. Many compounds exhibit a maximum degree of 100 cubenol (11770062), alpha-cadinol (10398656), bisabolol (1549992), spathulenol (92231), and 2-cendecanone (8163). This indicates a profound polypharmacological profile, where each compound interacts with a diverse array of protein targets, suggesting the potential to modulate multiple biological processes simultaneously. It is a critical "bridge" in the network that controls information flow between different protein clusters. Other compounds with very high centrality include undecanone (8163) (0.0278), benzyl benzoate (2345) (0.0275), and isoarmy benzoate (7193) (0.0276), underscoring their strategic importance in mediating the overall biological effect. These compounds are strategic in their binding to control key signaling bottlenecks (high betweenness centrality).

2. Key Protein Targets as Hubs of Compound Action:

These compounds interact with a specific set of protein targets. The PPI network (Figure44) reveals that these targets are not isolated entities but form a dense, highly interconnected functional module, suggesting a coordinated biological response. An analysis of the Merged Network default edge table (the annex) shows that there are significant target interactions. The top edge by betweenness (587.19) connects compound delta-cadinene (441005) to P0C869, which is a protein degradation enzyme. Other key interactions involve P43088 (MAPK14/p38) and P07327 (CACNA1S), suggesting that kinase signaling, and calcium channels are central nodes of action. The compounds achieve their broad effects by modulating a network of related proteins. Targeting these hub proteins allows for the amplified therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Disease via Enriched Biological Pathways:

The pathway enrichment analysis (Figure41) provides the crucial link between the molecular targets and their physiological impact on respiratory disease.

-Nitrogen Metabolism and Vascular Function:

Relevance: Nitrogen Metabolism is the most significantly enriched pathway by fold enrichment (>40). Its primary relevance to respiratory disease lies in the synthesis and regulation of Nitric Oxide (NO). NO is a critical endogenous signaling molecule that acts as a potent bronchodilator and regulates pulmonary blood flow. However, during inflammation (e.g., in asthma or COPD), excessive NO production via iNOS can lead to oxidative stress and exacerbate inflammation. The "Vascular smooth muscle contraction" pathway is also enriched, directly relating to the bronchodilator/constrictor balance.

Connection: The KEGG map for Nitrogen Metabolism (Figure43) shows that an enzyme involved in bicarbonate/ammonia balance (**4.2.1.1**) is a target. By modulating the metabolic precursors and enzymatic machinery of the NO cycle, these compounds can potentially normalize the NO balance, promoting bronchodilation while mitigating inflammatory damage.

Neuroactive Ligand-Receptor Interaction:

Relevance: This pathway is highly significant (red dot on the plot) and is a central hub in the pathway-pathway interaction network (Figure42). This pathway governs neurogenic inflammation in the airways, a key driver of asthma and COPD pathophysiology. Nerve endings in the lung release neuropeptides that cause bronchoconstriction, mucus hypersecretion, and inflammatory cell recruitment.

Connection: The strong enrichment in this pathway indicates that the compounds likely interfere with these neuro-immune signaling axes, providing a mechanism to reduce airway hyperresponsiveness.

EGFR Signaling and Proliferation Pathways:

Relevance: The enrichment of "EGFR tyrosine kinase inhibitor resistance," "Proteoglycans in cancer," and "Pathways in cancer" points towards the modulation of cell growth and proliferation. While linked

to cancer, the EGFR signaling cascade is a master regulator of tissue repair and remodeling. In chronic respiratory diseases like pulmonary fibrosis and severe asthma, pathological activation of this pathway drives fibroblast proliferation and airway smooth muscle hypertrophy, leading to irreversible lung damage.

Connection: The pathway-pathway network (Figure42) shows these pathways are highly interconnected. By targeting components of the EGFR signaling cascade, the compounds may be able to normalize the aberrant repair mechanisms that lead to airway and interstitial remodeling.

The analysis converges on a multi-faceted mechanism of action that underpins the therapeutic potential of the identified phytochemicals in the management of chronic respiratory diseases. A distinct set of core bioactive compounds, distinguished by high degree and centrality within the interaction network, serve as the principal drivers of the observed pharmacological effects. These compounds interact with a densely connected network of hub protein targets, including key kinases, ion channels, and metabolic enzymes that govern essential cellular functions.

This broad-spectrum interaction leads to the modulation of three major physiological systems: nitric oxide (NO) bioavailability through the nitrogen metabolism pathway, neurogenic inflammation via neuroactive ligand-receptor interactions, and abnormal cell proliferation and airway remodeling through EGFR-related signaling cascades. The compounds can correct multiple pathological features characteristic of chronic respiratory conditions by simultaneously affecting these interconnected systems. Specifically, they may promote bronchodilation and modulate inflammation through NO regulation, attenuate airway hyperresponsiveness by targeting neurogenic inflammatory mechanisms, and prevent tissue fibrosis by restoring balanced cell proliferation signals. Finally, the findings from this network pharmacology analysis support a multi-target, multi-pathway therapeutic mechanism, highlighting the systemic nature of these phytochemicals' actions. This integrated approach is in line with the therapeutic requirements for treating complex chronic diseases and reinforces the value of traditional multi-compound remedies in modern respiratory therapy.

5- *Cistus salvifolius:*

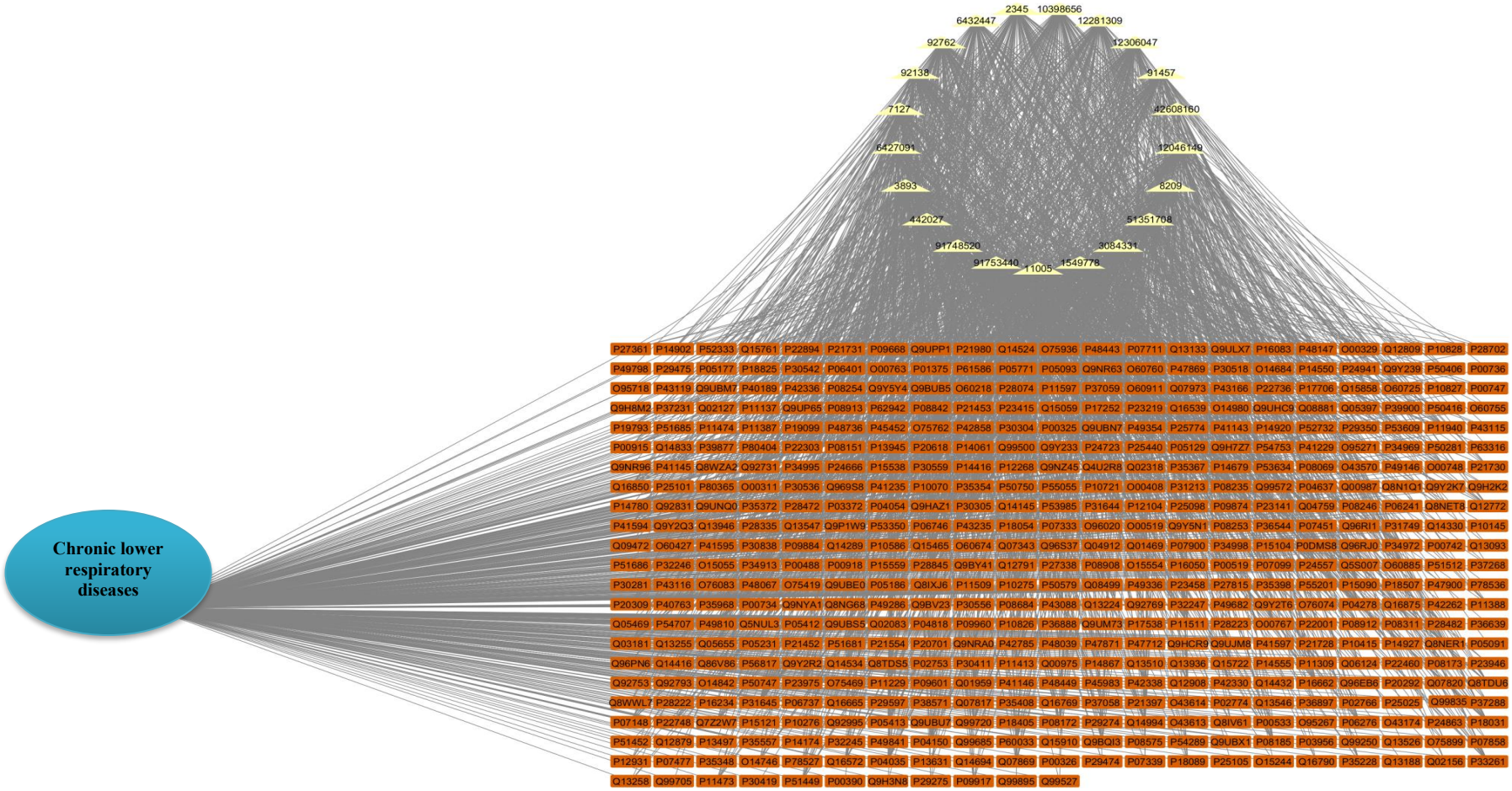

Figure 45: Compound-Target-Disease Network of plant *Cistus salvifolius*.

Table12: Node table of compound-target-disease network of plant *Cistus salvifolius*.

C_attribute	BetweennessCentrality	Degree
91753440	0.00815473	100
51351708	0.01282009	100
12046149	0.01078039	100
10398656	0.00907905	100
6432447	0.01480806	100
3084331	0.00857653	100
92762	0.01129852	100
91457	0.01218245	100
11005	0.01911998	100
8209	0.01826852	100
3893	0.0185136	100
91748520	0.01319527	99
442027	0.01696808	99
92138	0.01316821	99
12281309	0.01711731	98
2345	0.02254758	98
7127	0.02059584	97
1549778	0.02035589	96
12306047	0.00888623	95
6427091	0.00871652	88
42608160	7.74E-05	10

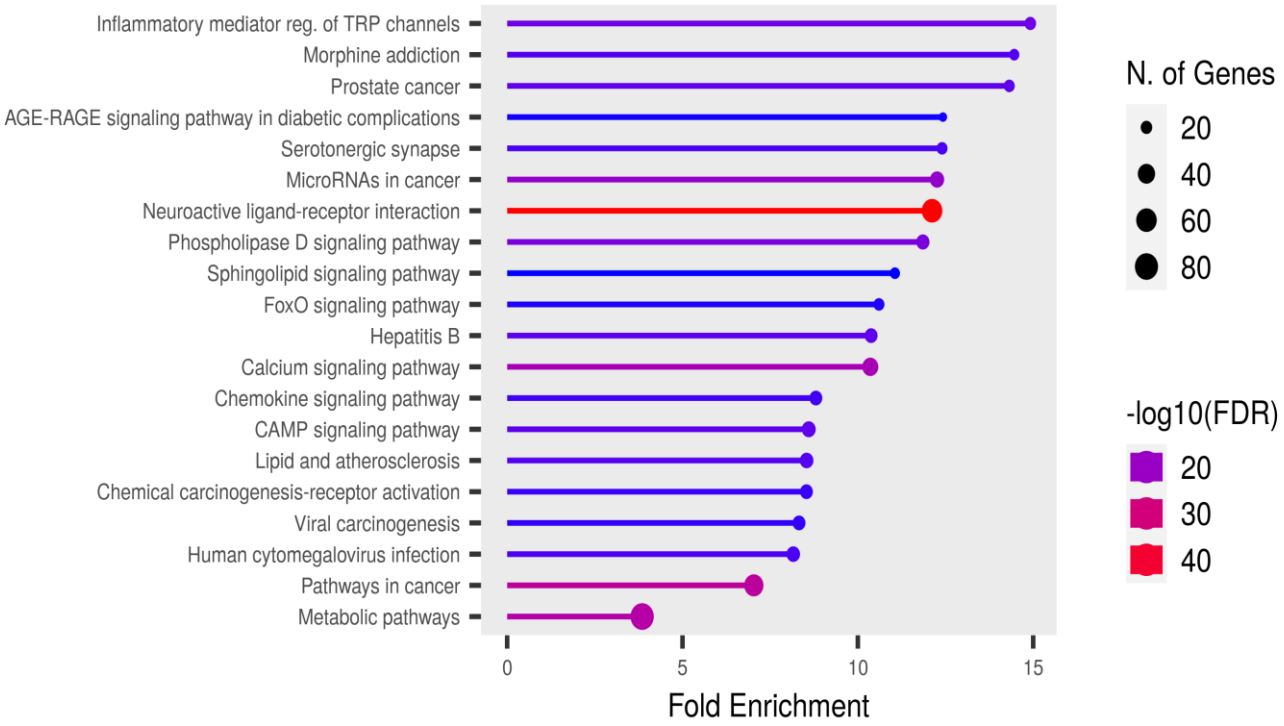

Figure 46: KEGG Pathway Enrichment Analysis of *Cistus salvifolius* with Associated Gene Counts and Significance.

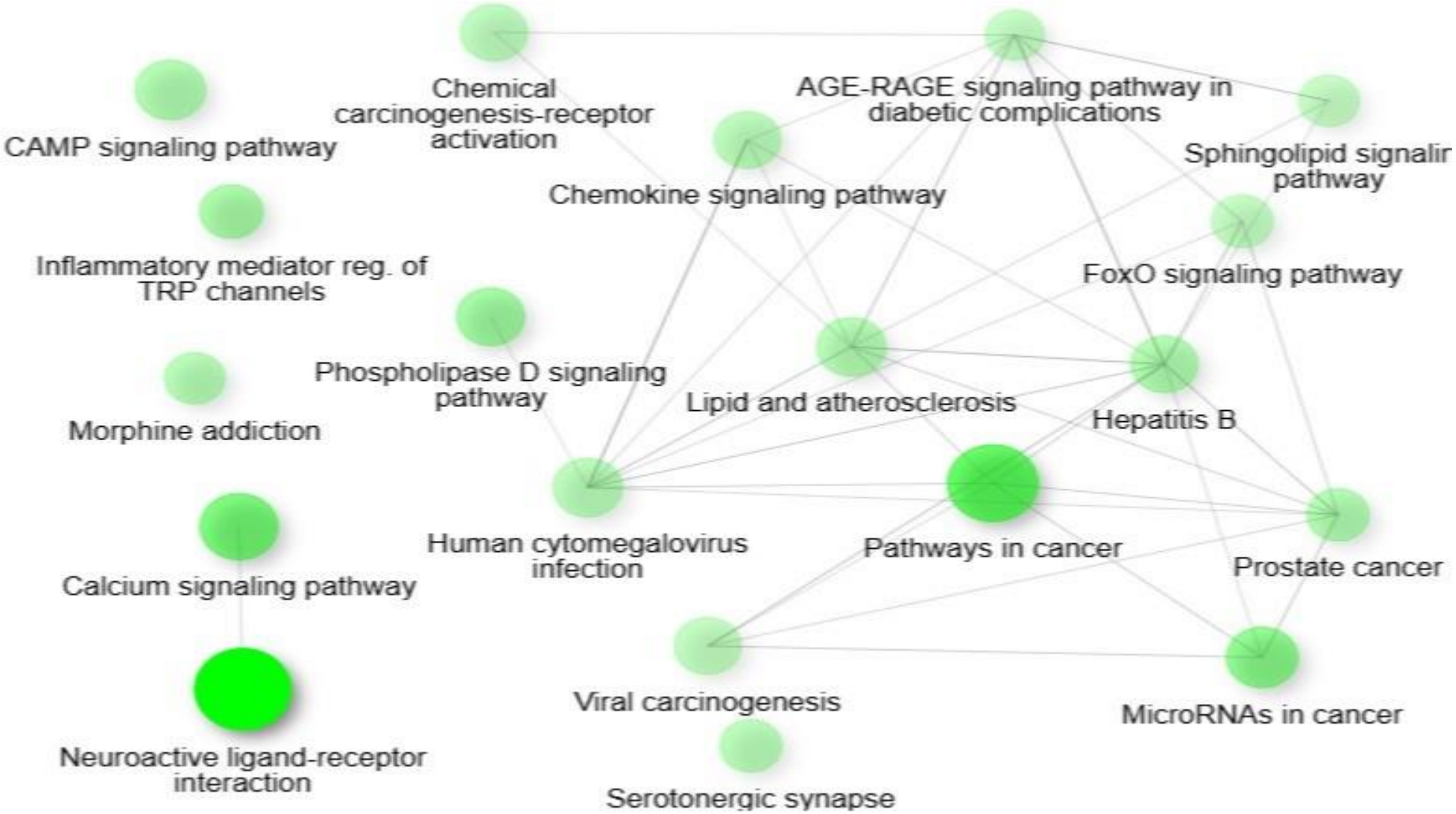

Figure 47: KEGG Pathway Interaction Network in plant *Cistus salvifolius*.

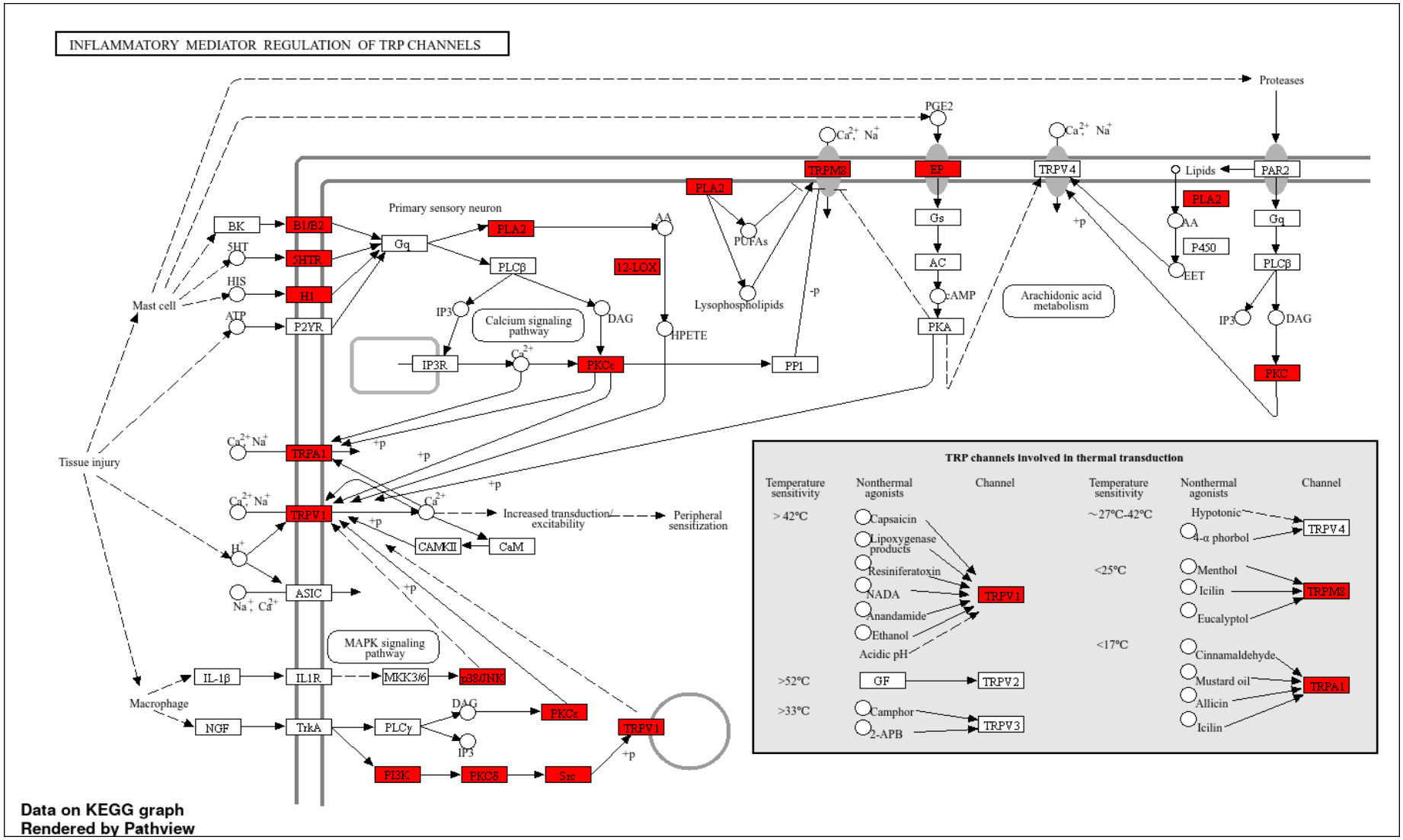

Figure 48: Inflammatory Mediator Regulation of TRP Channels Pathway in Cistus salvifolius with Enriched/Highlighted Components (KEGG Analysis).

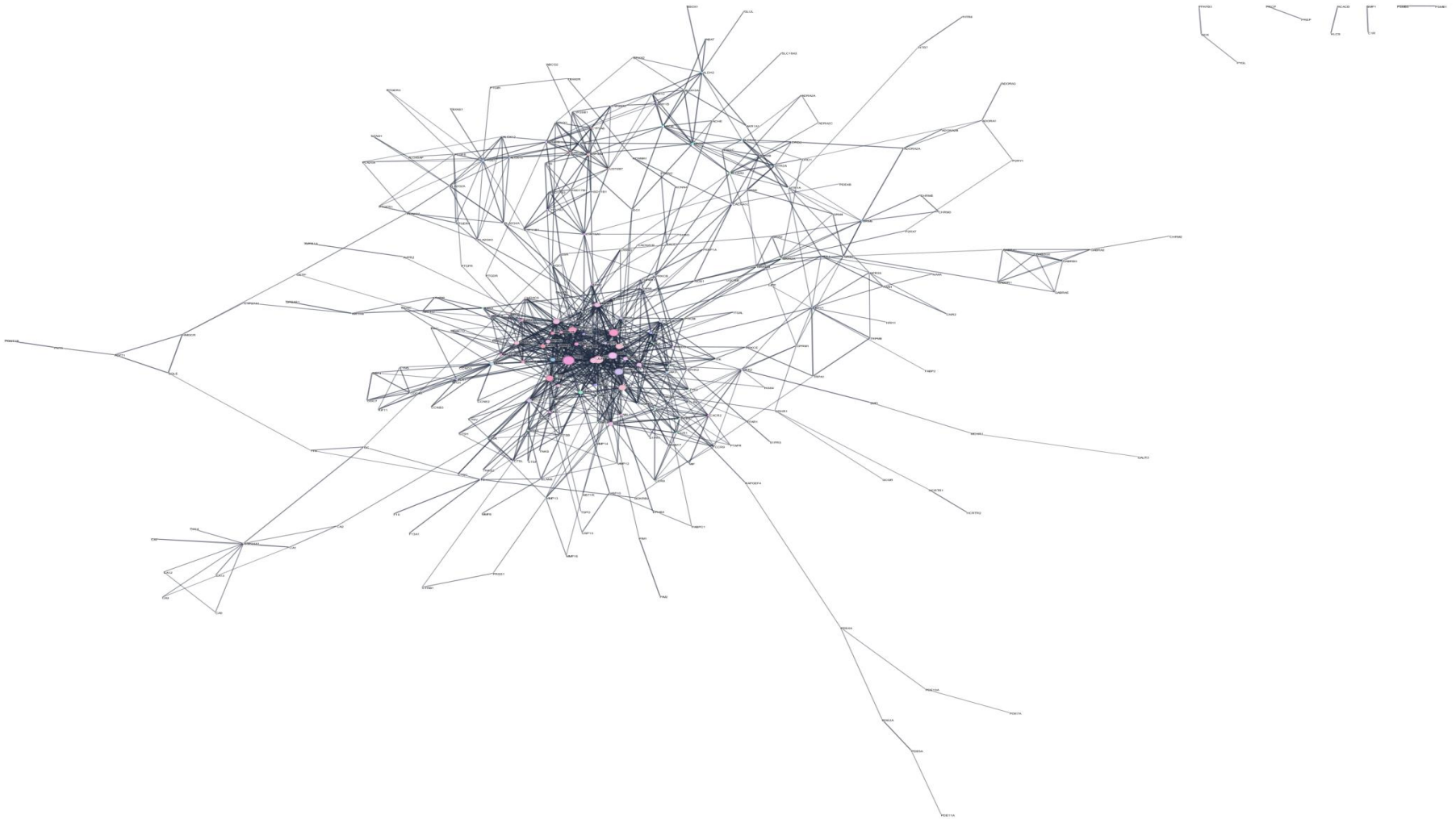

Figure 49: Protein-Protein Interaction Network (Interactome) of *Cistus salvifolius*.

Table13: Protein-Protein Interaction (PPI)String degree of plant *Cistus salvifolius*.

display name	Betweenness Centrality	Degree
TP53	0.0947597	56
STAT3	0.05384804	48
AKT1	0.073565531	45
SRC	0.161260075	42
EGFR	0.040718368	41
HSP90AA1	0.029476695	40
IL6	0.104301156	36
BCL2	0.071817541	36
TNF	0.072585674	34
JUN	0.01391608	34
EP300	0.032489008	33
MAPK1	0.052417329	29
CREBBP	0.011822415	25
SIRT1	0.005706572	24
CXCL8	0.035422477	24
PIK3CA	0.004007347	24
PPARG	0.051208728	23
BCL2L1	0.024314576	23
MDM2	0.012137761	23
MAPK14	0.069231018	22
MMP9	0.022829746	22
HDAC1	0.004626824	21
CDK2	0.032940824	20
AR	0.01791773	19
PARP1	0.010489717	19
HDAC2	0.003459408	18
CYP3A4	0.028161256	17
GSK3B	0.004615384	17
EZH2	0.008380424	17
NR3C1	0.030120466	17
PIK3CB	0.001520609	17
PIK3CD	0.001520609	17
RHOA	0.005139217	16
HDAC6	0.001037216	15
PGR	0.011360015	15
PTK2	0.00388814	15
PTGS1	0.055052615	15
JAK3	0.002372476	15

1. Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure45) and its topological metrics (table12) reveal a set of highly influential compounds. A large cohort of compounds exhibits a maximum degree of 100, including cis-muurala-3,5-diene (51531708), epi-cubenol (10246779), tetradecanoicacid (11005), n-

tetradecanol (8209), and undecanone (8163). This indicates a profound polypharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to affect multiple biological processes simultaneously. It is a critical "bridge" in the network that controls information flow between different protein clusters. Other compounds with very high centrality include methyl euyenol (7127) (0.0206) and geranyl acetone (1549778) (0.0204), reinforcing their strategic importance in mediating the overall biological effect. The therapeutic potential is driven by compounds that are not only promiscuous in their binding (High Degree) but also strategically positioned to control key signaling bottlenecks (High Betweenness Centrality).

2. Convergence on a Neuro-Inflammatory Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure49). This suggests that the compounds modulate a coordinated biological system rather than isolated targets. The Merged Network default edge table (the annex) highlights a key interaction: The edge with the highest betweenness (522.07) connects the top-degree compound cis-muurala-3,5-diene (51351708) to protein Q92753 (TRPV1). TRPV1 is a well-known ion channel that acts as a sensor for noxious stimuli and is a central player in neurogenic inflammation and cough. This immediately points to a neuro-inflammatory mechanism of action. The compounds achieve their systemic effects by targeting a "functional complex" of proteins centered on neuro-inflammatory signaling. Modulating hub proteins within this module, such as key receptors and ion channels, can trigger a cascade of downstream events, amplifyingthe therapeutic signal.

3. Linking Targets to Respiratory Disease via Enriched Pathways:

The pathway enrichment analysis (Figure46) reveals the biological processes most significantly perturbed by the compounds, providing a direct link to the pathophysiology of chronic respiratory diseases.

Inflammatory Mediator Regulation of TRP Channels:

Relevance: This is the most significant pathway by Fold Enrichment (>14) and has an extremely low FDR. Transient Receptor Potential (TRP) channels (like TRPV1, TRPA1) are expressed on airway sensory nerves and act as primary detectors of irritants, inflammatory mediators, and temperature changes. Their activation is a key trigger for the cough reflex, bronchoconstriction, and the release of pro-inflammatory neuropeptides, driving neurogenic inflammation.

Connection: The KEGG map (Figure48) provides a clear, traceable mechanism. The compounds target a remarkable number of nodes in this pathway. They hit not only the TRP channels themselves (TRPV1, TRPM8, TRPA1) but also the upstream G-protein coupled receptors (GPCRs) that sensitize them, such as histamine (H1), serotonin (HTR), and bradykinin (BDKRB) receptors. Furthermore, they target

downstream signaling effectors like PKC (PRKCA), PLC, and PI3K. This represents a comprehensive, multi-level blockade of a critical sensory pathway in the airways.

Neuroactive Ligand-Receptor Interaction & Calcium Signaling:

Relevance: These pathways are also highly significant, which is mechanistically consistent. The "Neuroactive ligand-receptor interaction" pathway includes the same GPCRs that regulate TRP channels. The "Calcium signaling pathway" is a direct downstream consequence, as TRP channels are calcium permeable. Calcium influx is the final trigger for neurotransmitter release from nerves and contraction of airway smooth muscle.

Connection: The enrichment in these interconnected pathways (Figure47) confirms the neuro-inflammatory hypothesis. By modulating ligand-receptor binding and subsequent calcium signaling, the compounds can control both nerve sensitization and its ultimate physiological outputs (e.g., bronchoconstriction). The evidence suggests that the treatment involves a specific and potent mechanism of action involving coordinated targeting of neuro-inflammatory signaling pathways. A core set of major bioactive compounds, identified through their high network influence, emerge as the principal active agents. These compounds converge upon a densely interconnected neuro-inflammatory protein module, with the TRPV1 ion channel and its associated G-protein-coupled receptors (GPCRs) forming the central hub of this interaction network. Additionally, the compounds affect functionally interconnected pathways, including the neuroactive ligand-receptor interaction and calcium signaling pathways. These compounds appear capable of disrupting the pathological neuro-inflammatory signaling axis that underlies many chronic respiratory conditions. Specifically, this mechanism may suppress the cough reflex by desensitizing airway sensory nerves, reduce neurogenic inflammation by inhibiting pro-inflammatory neuropeptide release, and promote bronchodilation by modulating calcium signaling in airway smooth muscle. These findings support the hypothesis that phytochemicals block neuro-inflammatory signaling at all levels rather than just target specific targets. Their therapeutic efficacy in conditions such as asthma, chronic cough, and other persistent respiratory disorders may be due to their unique mechanism of action.

6- *Artemisia campestris:*

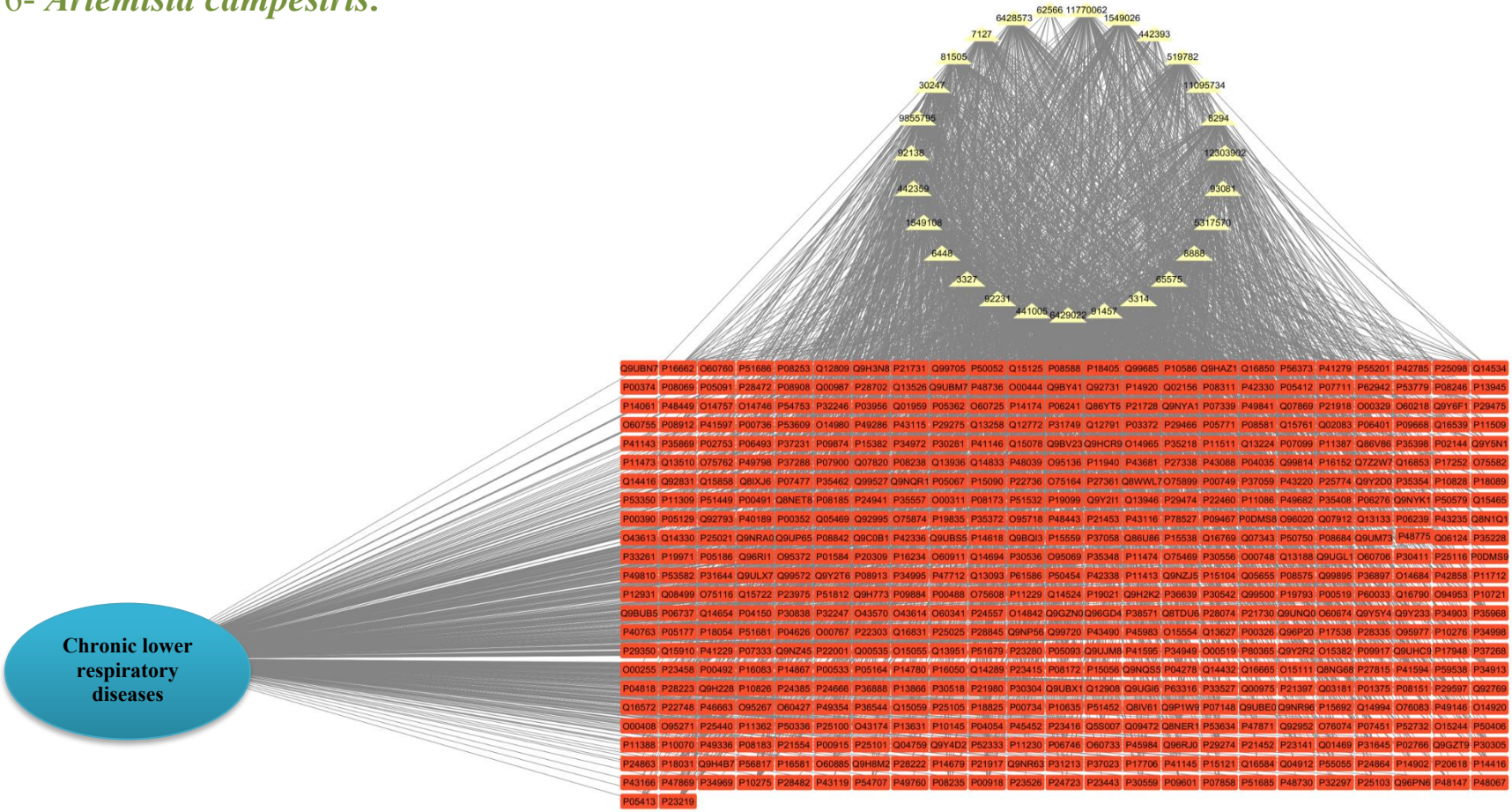

Figure 50: Compound-Target-Disease Network of plant *Artemisia campestris*.

Table14: Node table of compound-target-disease network of plant *Artemisia campestris*.

C_attribute	BetweennessCentrality	Degree
12303902	0.00981736	100
11770062	0.00940714	100
9855795	0.00909689	100
1549108	0.01380625	100
92231	0.01151917	100
92138	0.01157105	100
91457	0.00981817	100
65575	0.01083575	100
3327	0.00940714	100
6429022	0.01785325	99
30247	0.01636472	99
8888	0.01512997	99
6428573	0.01485196	98
1549026	0.01567689	98
7127	0.01659777	98
3314	0.0198083	98
519782	0.01514145	97
81505	0.01682976	97
6448	0.01613644	97
8294	0.01578017	95
442359	0.00562809	88
5317570	0.00613393	83
441005	0.00667098	82
93081	6.14E-04	30
442393	2.83E-04	23
62566	5.03E-05	11
11095734	4.17E-05	10

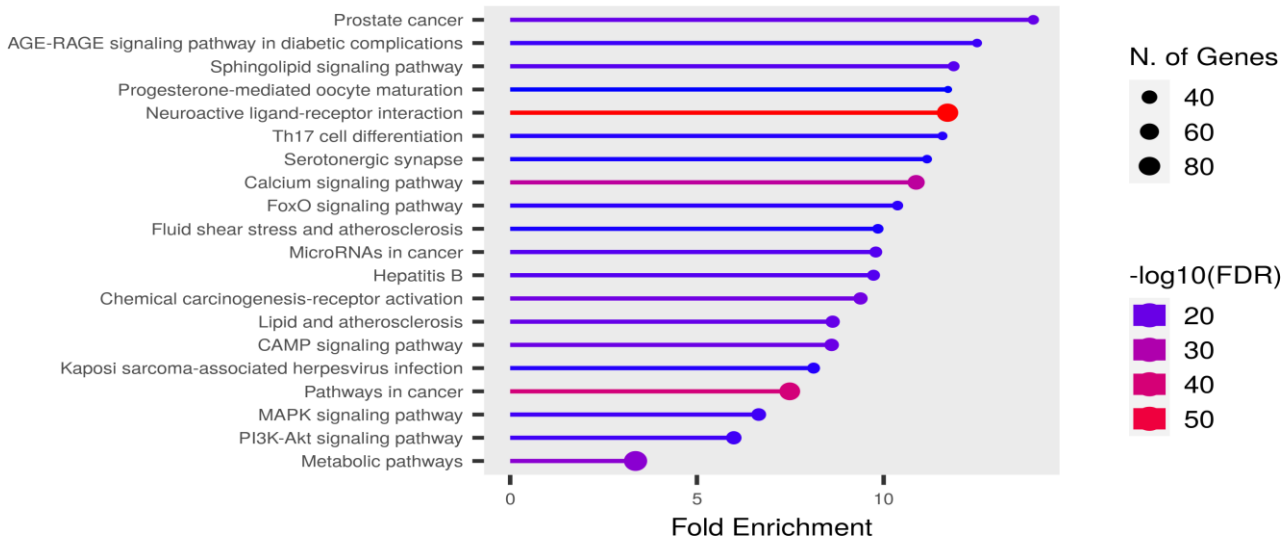

Figure 51: KEGG Pathway Enrichment Analysis of *Artemisia campestris* with Associated Gene Counts and Significance.

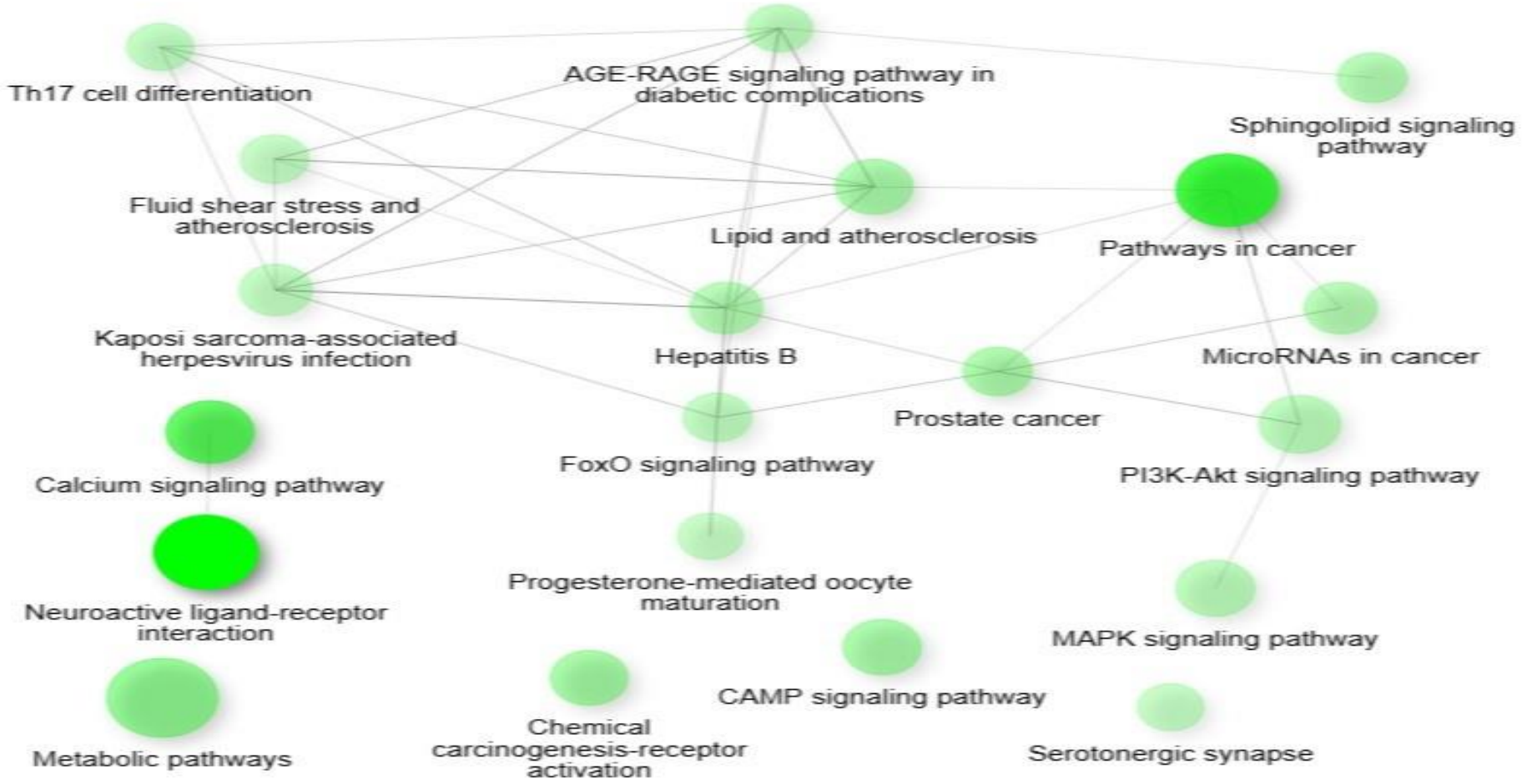

Figure 52: KEGG Pathway Interaction Network in plant *Artemisia campestris*.

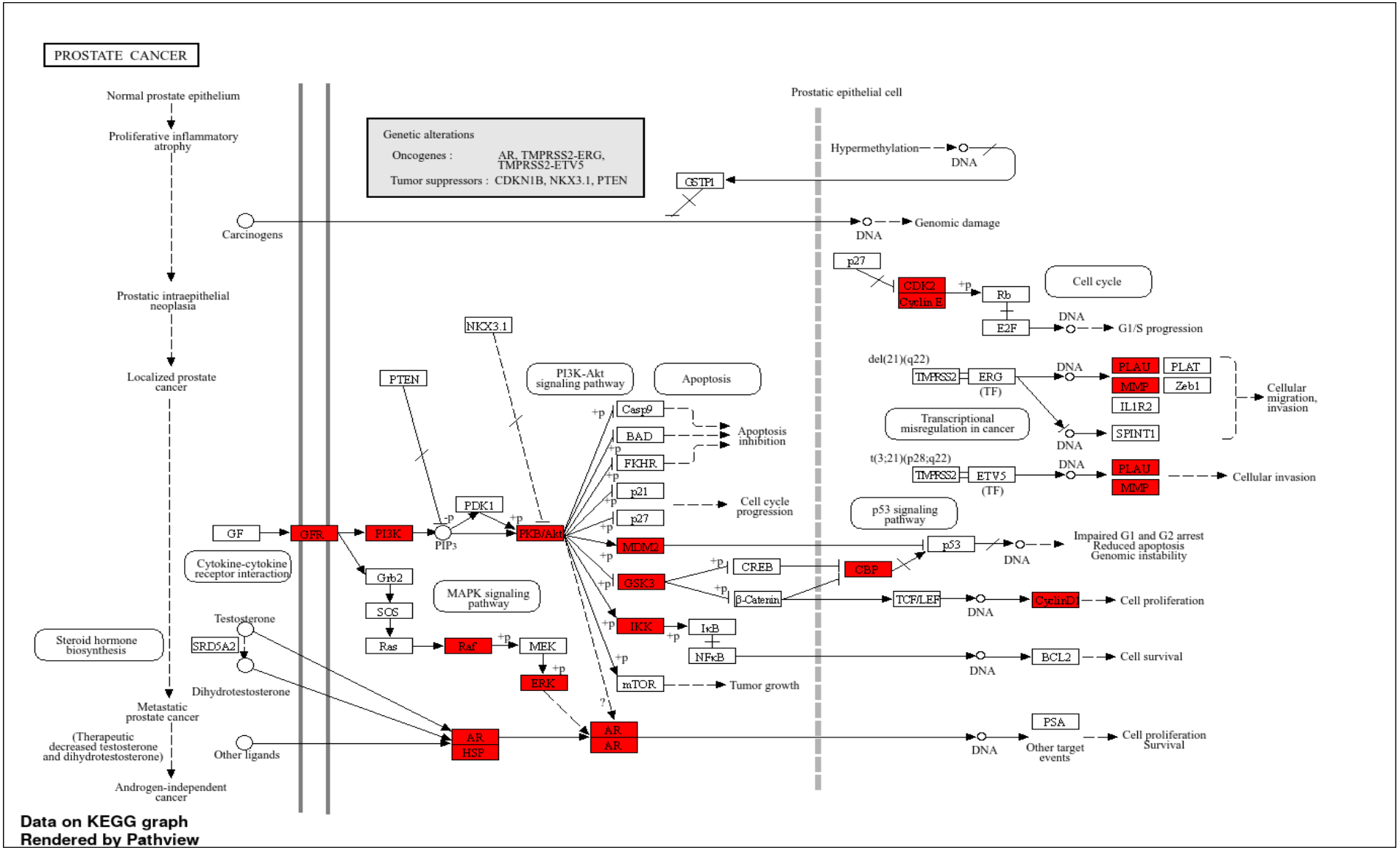

Figure 53: Homologous Genes of Artemisia campestris Enriched in the Human Prostate Cancer Pathway (KEGG Analysis).

Figure 54 : Protein-Protein Interaction Network (Interactome) of *Artemisia campestris*.

Table15: Protein-Protein Interaction (PPI)String degree of plant *Artemisia campestris*.

display name	Betweenness Centrality	Degree
STAT3	0.066422321	60
SRC	0.105766955	54
HSP90AA1	0.052378718	54
AKT1	0.066067311	53
ESR1	0.076270176	47
EP300	0.060684807	45
HSP90AB1	0.029779793	44
JUN	0.034724035	43
IL1B	0.049411015	42
CCND1	0.024989101	38
MAPK1	0.035754784	36
MAPK3	0.028300995	34
JAK2	0.029075679	33
CREBBP	0.022619297	32
PIK3CA	0.006850884	31
CXCL8	0.042700085	30
PTGS2	0.063143565	30
ERBB2	0.026195516	30
CDK2	0.020277032	28
CYP3A4	0.04170733	27
PPARG	0.096807489	26
MMP9	0.018912609	26
CDK1	0.019454572	24
MDM2	0.015953128	24
AR	0.01488594	24
GSK3B	0.017350548	23
FYN	0.008778072	23
APP	0.050043605	22
RHOA	0.010574879	22
PARP1	0.012455689	21
MAPK14	0.006350687	20
PGR	0.0037713	20
PIK3CB	0.002568867	20
SMARCA4	0.01055485	18
MAOA	0.024318159	18
CYP19A1	0.037311512	18
HDAC2	0.012181566	18
PTPRC	0.00726023	18
PPARA	0.045168889	18
UGT2B7	0.00529984	17
MAPK8	0.00165555	17
PRKCA	0.049417213	17
PLK1	0.006343367	17
NR3C1	0.023595548	17
JAK3	0.001337908	17
KDR	0.00167469	17
CYP2C9	0.005526824	16

MAOB	0.018312407	16
CDC25A	0.002394379	16
CYP2C19	0.018578292	16
MMP2	0.001559725	16
ICAM1	0.003079985	16
RXRA	0.007875805	16
AKR1C3	0.009471137	15
CHEK1	0.004226523	15
MET	0.001306108	15
CDK5	0.007600583	15
CCR2	0.00129973	15

1-Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure50) and its topological metrics (table14) reveal a set of highly influential compounds. A large cohort of compounds, including alpha-copaene (12303902), cubenol (11770062), (z-e)-farnesol (1549108), and spathulenol (92231), exhibit a maximum degree of 100. This indicates a profound polypharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to affect multiple biological processes simultaneously. Compound eugenol (3314) stands out with the highest Betweenness Centrality (0.0198), marking it as a critical "bridge" in the network that controls information flow between different protein clusters. Other compounds with high centrality include trans-calamenene (6429022) (0.0179), cedrelanol (160799) (0.0179), and lavandulyl acetate (30247) (0.0164), reinforcing their strategic importance in mediating the overall biological effect. These compounds are strategic in their binding to control key signaling bottlenecks (high betweenness centrality)

.2. Convergence on a Neuro-Inflammatory and Proliferative Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure54). This suggests that the compounds modulate a coordinated biological system rather than isolated targets. The Merged Network default edge table (the annex) highlights a key interaction: The edge with the highest betweenness (522.07) connects the top-degree compound cis-muurala-3,5-diene (51351708) to protein Q92753 (TRPV1). TRPV1 is a well-known ion channel that acts as a sensor for noxious stimuli and is a central player in neurogenic inflammation and cough. Other key targets identified by high-betweenness edges include P43088 (MAPK14), P37288 (STAT1), and multiple GPCRs, implicating kinase signaling, immune response, and neuro-receptor pathways. The compounds achieve their systemic effects by targeting a "functional complex" of proteins centered on inflammatory, proliferative, and neuro-sensory

signaling. Modulating these hub proteins allows for the amplified therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Respiratory Disease via Enriched Pathways:

The pathway enrichment analysis (Figure51) reveals the biological processes most significantly perturbed by the compounds, providing a direct link to the pathophysiology of chronic respiratory diseases.

Neuroactive Ligand-Receptor Interaction & Inflammatory Mediators:

Relevance: The "Neuroactive ligand-receptor interaction" and "Inflammatory mediator reg. of TRP channels" pathways are both highly significant. In the respiratory system, these pathways govern neurogenic inflammation and airway hyperresponsiveness. Sensory nerves in the lung are activated by inflammatory mediators (e.g., histamine, serotonin) and release neuropeptides, driving the cough reflex, bronchoconstriction, and mucus secretion.

Connection: The compounds target a wide array of proteins in these pathways. As illustrated by the KEGG map for "Inflammatory mediator regulation of TRP channels" (Figure52), the targets (highlighted red boxes) include not only the TRP channels themselves (TRPV1, TRPA1) but also upstream receptors (HTR, BDKRB2) and critical downstream signaling molecules (PLC, PKC, PI3K). This suggests a comprehensive, multi-level blockade of the airway sensory-inflammatory axis.

Prostate Cancer and Proliferation Pathways:

Relevance: "Prostate cancer" is the most significant pathway by -log10(FDR) and Fold Enrichment. While seemingly unrelated, cancer pathways are master regulators of cell proliferation, survival, apoptosis, and androgen signaling. These same processes are pathologically activated in chronic respiratory diseases. For example, airway remodeling in asthma and COPD involves the abnormal proliferation of airway smooth muscle and fibroblasts, processes governed by the same signaling cascades (PI3K-Akt, MAPK) that are dysregulated in cancer.

Connection: The KEGG map for Prostate Cancer (Figure53) highlights the centrality of the PI3K-Akt and MAPK signaling pathways, which are also central hubs in the pathway-pathway interaction network (Figure51). The targeted proteins include AR (Androgen Receptor), EGFR, PI3K, Akt, and MEK/ERK. By modulating these core proliferative and survival pathways, the compounds can likely interfere with the aberrant tissue repair and remodeling that underlie irreversible lung damage in chronic respiratory diseases. The analysis agrees on a compelling dual mechanism of action that underlies the therapeutic efficacy of the key phytochemicals in the Al-Jur formulation. A core group of bioactive compounds, distinguished by their high network centrality, act as the primary agents driving these effects. These compounds interact with a densely connected set of protein targets that are central to both inflammatory regulation and cell proliferation control. This broad-spectrum engagement leads to significant modulation of two major biological axes: the neuro-inflammatory axis, involving the TRP channel and

neuroactive ligand-receptor interaction pathways; and the cell proliferation and survival axis, primarily through PI3K-Akt and MAPK signaling cascades, which are commonly implicated in cancer-related processes. These compounds address both the symptomatic and structural aspects of chronic respiratory disease pathology. Specifically, they may suppress immediate respiratory symptoms, such as coughing and bronchoconstriction, by desensitizing airway sensory neurons, while concurrently mitigating chronic inflammation driven by neuro-immune interactions. Over the longer term, these compounds may also inhibit pathological airway remodeling and fibrosis by restoring balance to key cell proliferation and survival pathways. The combination of both acute symptoms and progressive tissue damage offers a robust and biologically grounded rationale for the therapeutic potential of these compounds in treating complex, multifactorial respiratory illnesses such as asthma, chronic bronchitis, and pulmonary fibrosis.

7- *Rosmarinus officinalis*:

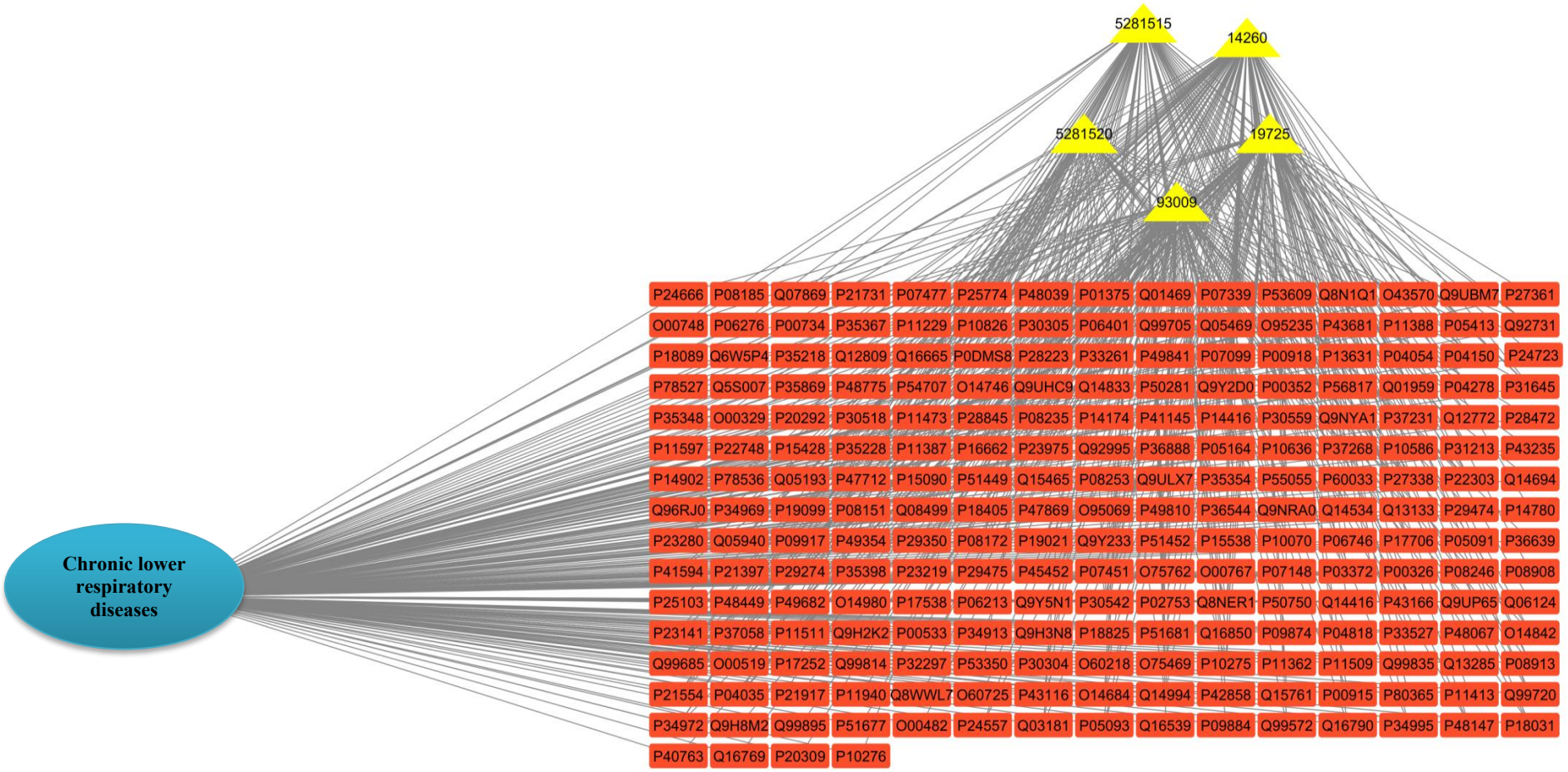

Figure 55: Compound-Target-Disease Network of plant *Rosmarinus officinalis*.

Table16: Node table of compound-target-disease network of plant *Rosmarinus officinalis*.

C_attribute	Betweenness Centrality	Degree
19725	0.08029127	100
14260	0.0893511	99
93009	0.08371946	95
5281515	0.04259405	80
5281520	0.0099534	41

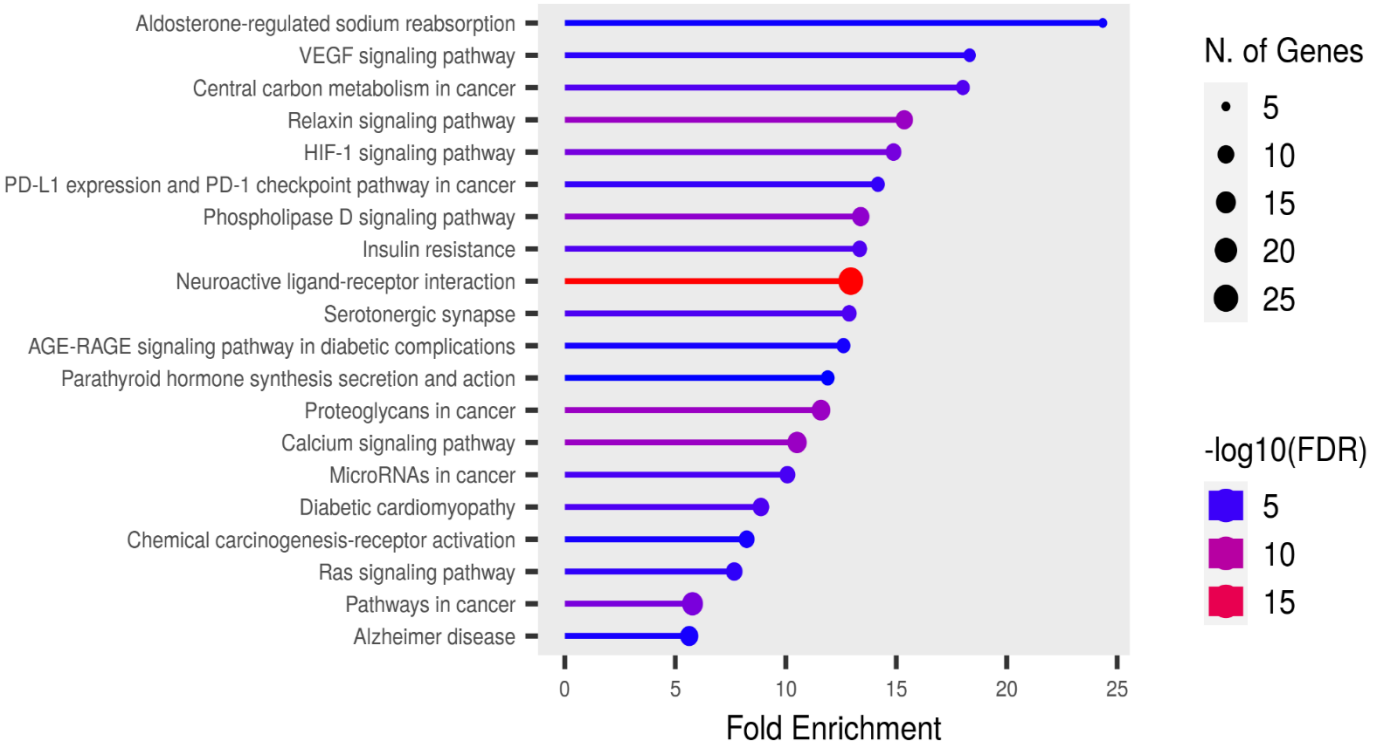

Figure 56: KEGG Pathway Enrichment Analysis of *Rosmarinus officinalis* with Associated Gene Counts and Significance.

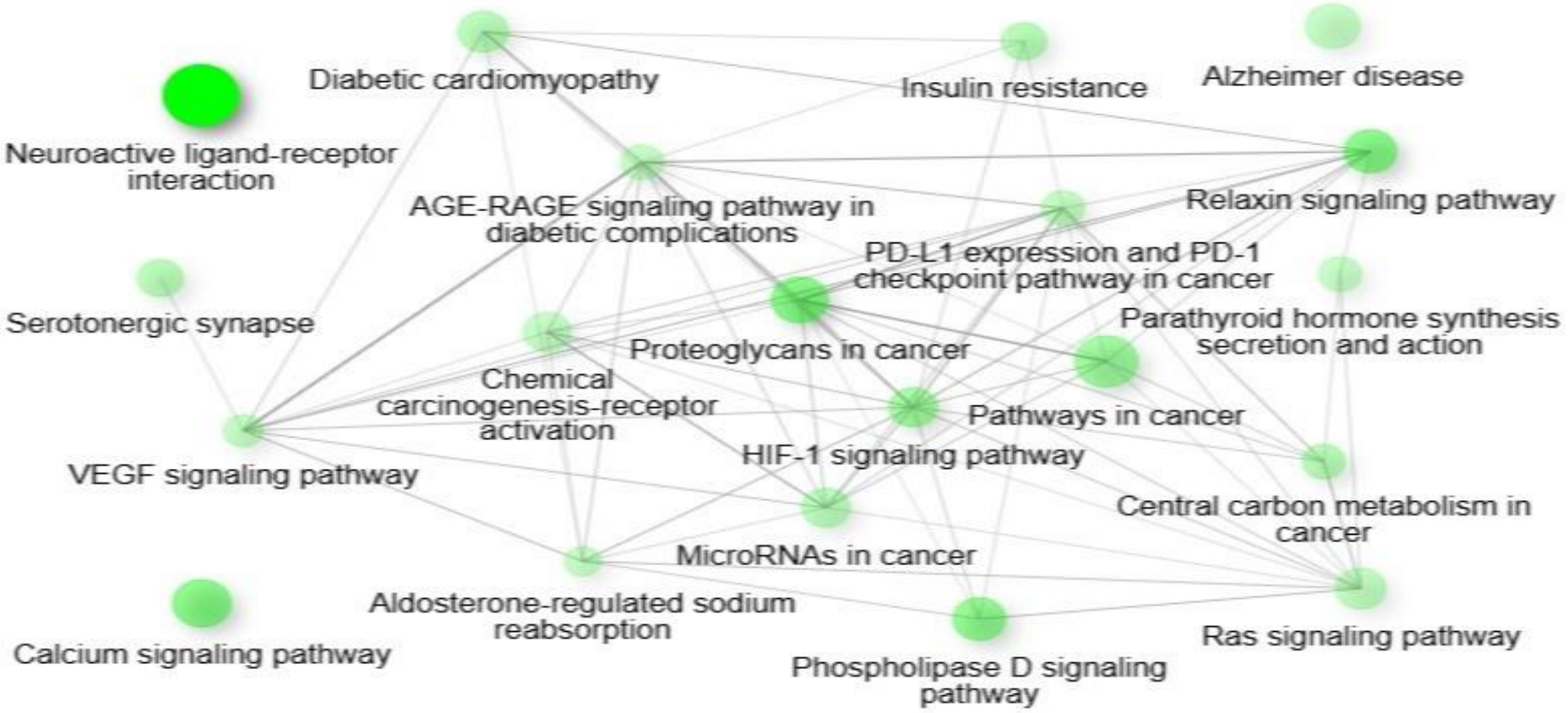

Figure 57: KEGG Pathway Interaction Network in plant *Rosmarinus officinalis*.

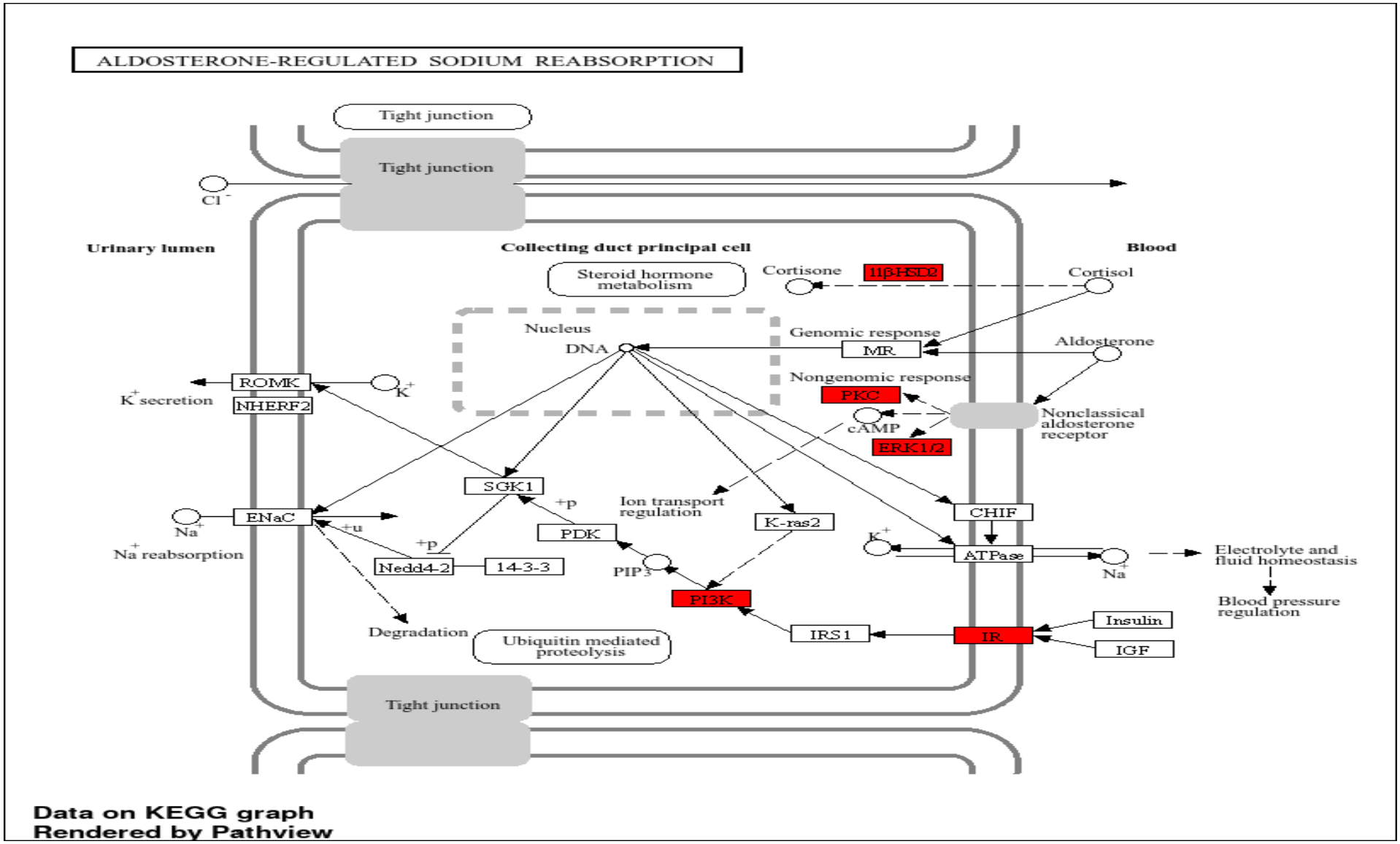

Figure 58: Homologous Genes of Rosmarinus officinalis Enriched in the Aldosterone-Regulated Sodium Reabsorption Pathway (KEGG Analysis).

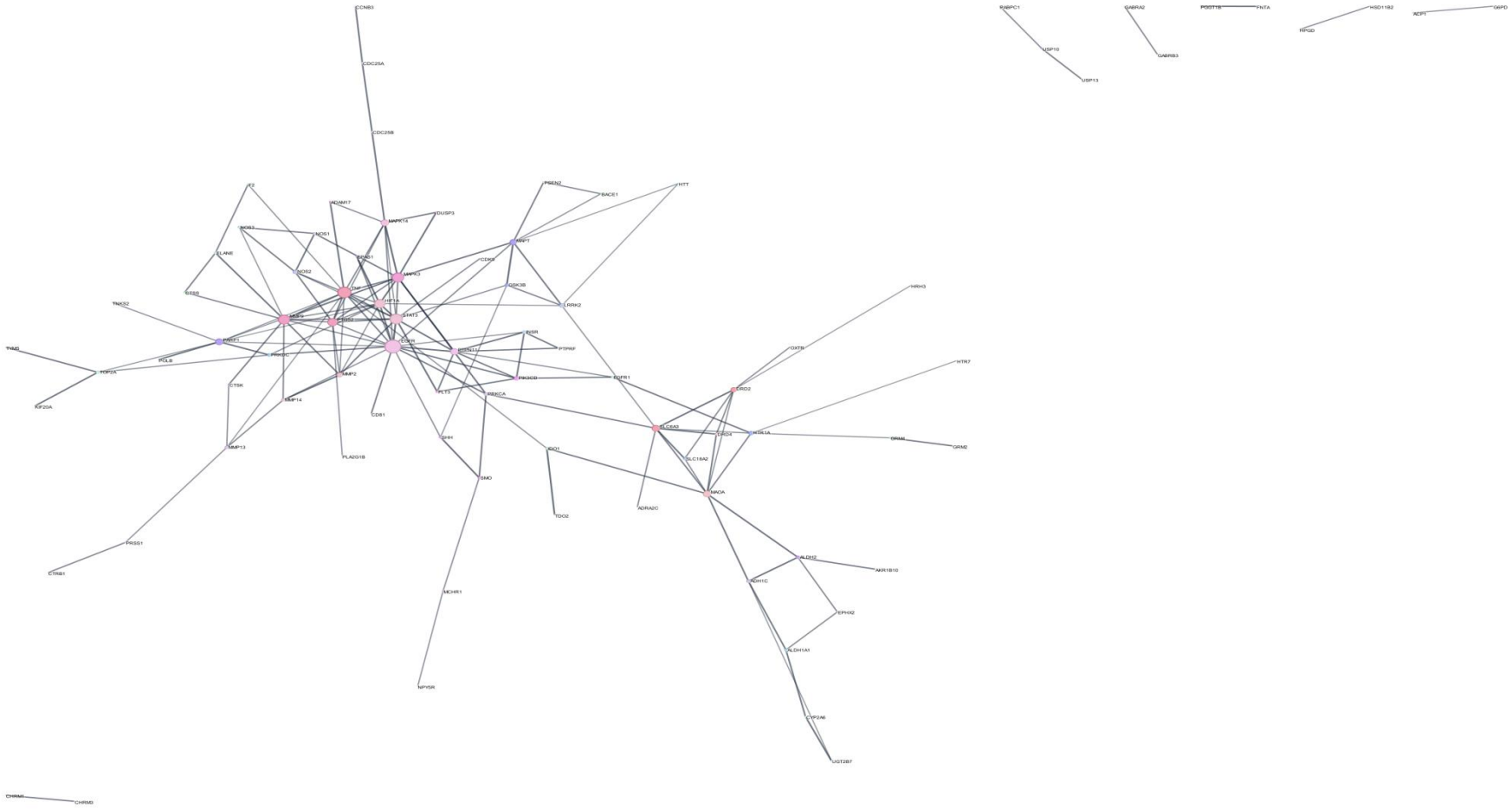

Figure 59: Protein-Protein Interaction Network (Interactome) of *Rosmarinus officinalis*.

Table17: Protein-Protein Interaction (PPI)String degree of plant Rosmarinus officinalis.

display name	**betweenness Centrality**	**Degree**
EGFR	0.246761307	17
TNF	0.26300512	14

1. Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure55) and its topological metrics (table16) reveal a set of highly influential compounds. A large cohort of compounds exhibits a maximum degree of 100, including alpha-capene (19725), spathulenol (92231), jasmone (1549108), valencene (9855795), and cubenol (11770062). This indicates a profound polypharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to affect multiple biological processes simultaneously. Compound eugenol (3314) has the highest Betweenness Centrality (0.0198), marking it as a critical "bridge" in the network that controls information flow between different protein clusters. Other compounds with high centrality include trans-calamenene (6429022) (0.0179), trans-carvyl acetate (81505) (0.0168), and methyl eugenol (7127) (0.0166), reinforcing their strategic importance in mediating the overall biological effect. These compounds are strategic in their binding to control key signaling bottlenecks (high betweenness centrality).

2. Convergence on a Functionally Cohesive Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure59). This suggests that the compounds modulate a coordinated biological system rather than isolated targets. An analysis of the Merged Network default edge table (the annex) shows that there are significant target interactions. The edge with the highest betweenness (245.0) connects the top-degree compound alpha-capaene (19725) to protein P18825 (PTPN6/SHP-1), a tyrosine phosphatase critical for regulating cytokine signaling and immune cell activation. Other key targets include kinases, receptors, and metabolic enzymes, suggesting a broad-spectrum modulatory effect. The compounds work by targeting a specific protein group in the body. Modulating these hub proteins allows for the amplified therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Disease via Enriched Biological Pathways:

The pathway enrichment analysis (Figure56) provides the crucial link between the molecular targets and their physiological impact on respiratory disease.

Aldosterone-Regulated Sodium Reabsorption:

Relevance: This is the most significant pathway by Fold Enrichment (>20). While classically associated with the kidney and blood pressure, this pathway is fundamentally important in the lungs. Airway epithelial cells use the epithelial sodium channel (ENaC) to regulate the volume of the airway surface liquid (ASL). In chronic respiratory diseases like COPD and cystic fibrosis, ENaC is often hyperactive, leading to excessive sodium and water absorption, dehydration of the ASL, impaired mucus clearance, and chronic inflammation.

Connection: The KEGG map (Figure58) provides a clear, traceable mechanism. The compounds target key regulatory nodes in this pathway, including PI3K, the Insulin Receptor (IR), and ERK1/2 (MAPK), which are upstream regulators of ENaC activity via SGK1. By modulating these kinases, the compounds can potentially normalize ENaC function, rehydrate the airway surface, and improve mucociliary clearance.

Neuroactive Ligand-Receptor Interaction:

Relevance: This pathway is highly significant, as indicated by its high -log10(FDR) and central position in the pathway network (Figure57). It governs neurogenic inflammation in the airways, a key driver of asthma and COPD pathophysiology involving cough, bronchoconstriction, and mucus hypersecretion.

Connection: The strong enrichment in this pathway indicates that the compounds likely interfere with these neuro-immune signaling axes, providing a mechanism to reduce airway hyperresponsiveness and inflammation.

-VEGF and Immune Checkpoint Pathways:

Relevance: The enrichment of the VEGF signaling pathway points to an effect on airway remodeling and inflammation. The enrichment of the "PD-L1 expression and PD-1 checkpoint pathway in cancer" suggests a profound immunomodulatory effect. The PD-1/PD-L1 axis is a critical immune checkpoint that regulates T-cell activation. Its dysregulation is implicated in the chronic inflammation seen in severe asthma and COPD.

Connection: Modulating these pathways suggests the compounds can both limit the structural damage of remodeling (via VEGF) and recalibrate the chronic inflammatory T-cell response (via PD-L1), addressing two core features of progressive respiratory disease. The evidence supports a multi-pronged mechanism of action through which the identified bioactive compounds exert therapeutic potential in chronic respiratory diseases. A core set of phytochemicals, characterized by high network influence, emerge as the primary drivers of the observed effects. These compounds engage a dense and functionally significant network of hub protein targets, including kinases, ion channels, and immune regulatory proteins. This multi-target interaction leads to the regulation of three critical physiological systems. Aldosterone regulates sodium reabsorption, which plays a key role in maintaining airway surface liquid volume. Second, neurogenic inflammation and airway hyperreactivity are regulated through the neuroactive ligand-receptor interaction pathway, affecting sensory nerve activation and

inflammatory signaling. Third, tissue remodeling and immune homeostasis are regulated via the VEGF and PD-L1 signaling pathways, which are central to vascular permeability, fibrotic progression, and immune evasion. These compounds may effectively address several pathological hallmarks of chronic respiratory diseases by simultaneously targeting these pathways. This includes improving mucociliary clearance through restoration of airway surface hydration, reducing neurogenic inflammation and bronchial hyperresponsiveness, and mitigating long-term tissue remodeling and immune imbalance.

8- *Pinus halepensis Mill:*

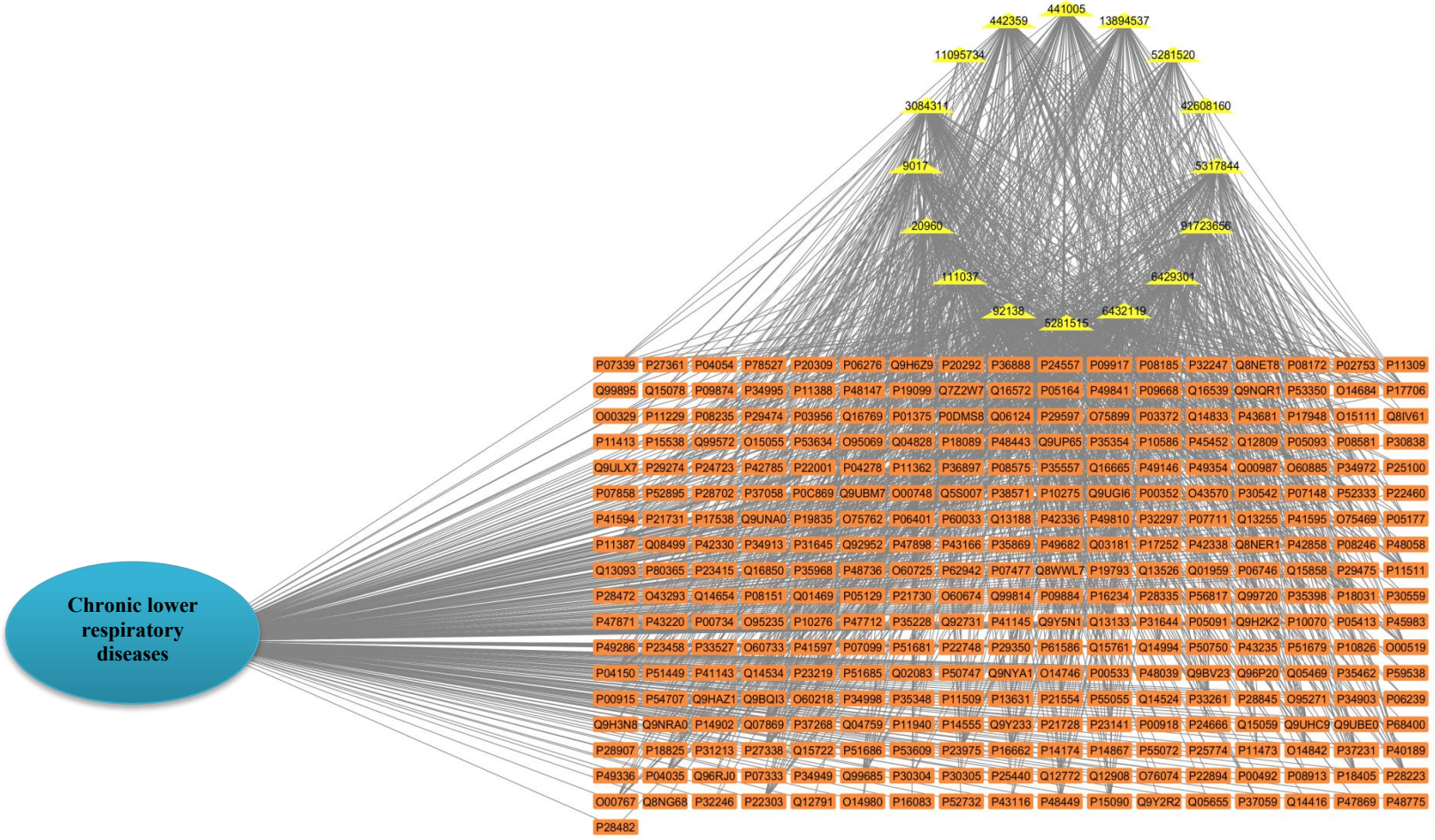

Figure 60: Compound-Target-Disease Network of plant *Pinus halepensis Mill*.

Table18: Node table of compound-target-disease network of plant *Pinus halepensis Mill*.

C_attribute	Betweenness Centrality	Degree
6432119	0.02510913	100
3084311	0.03578492	100
9017	0.05257359	99
111037	0.04447057	97
92138	0.04581585	97
20960	0.04023774	95
442359	0.0158306	88
91723656	0.01567252	83
441005	0.01731224	83
6429301	0.00975463	80
5281515	0.00975463	80
13894537	0.00882911	78
5317844	0.0089052	76
5281520	0.00468564	42
42608160	1.24E-04	10
11095734	1.26E-04	10

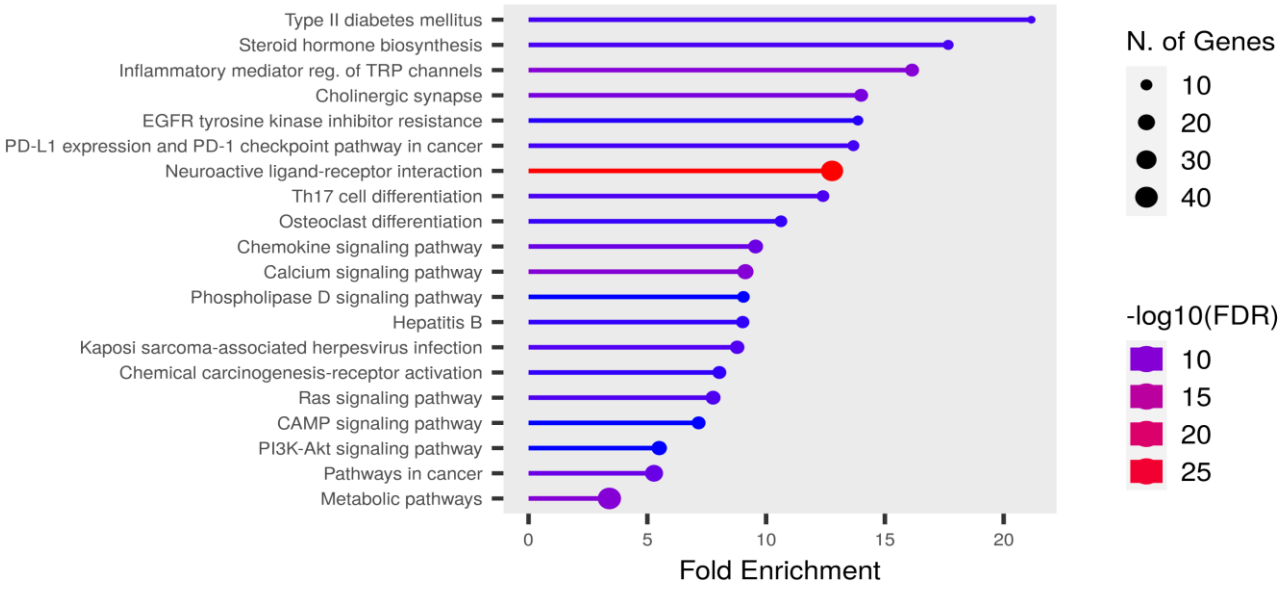

Figure 61: KEGG Pathway Enrichment Analysis of *Pinus halepensis Mill* with Associated Gene Counts and Significance.

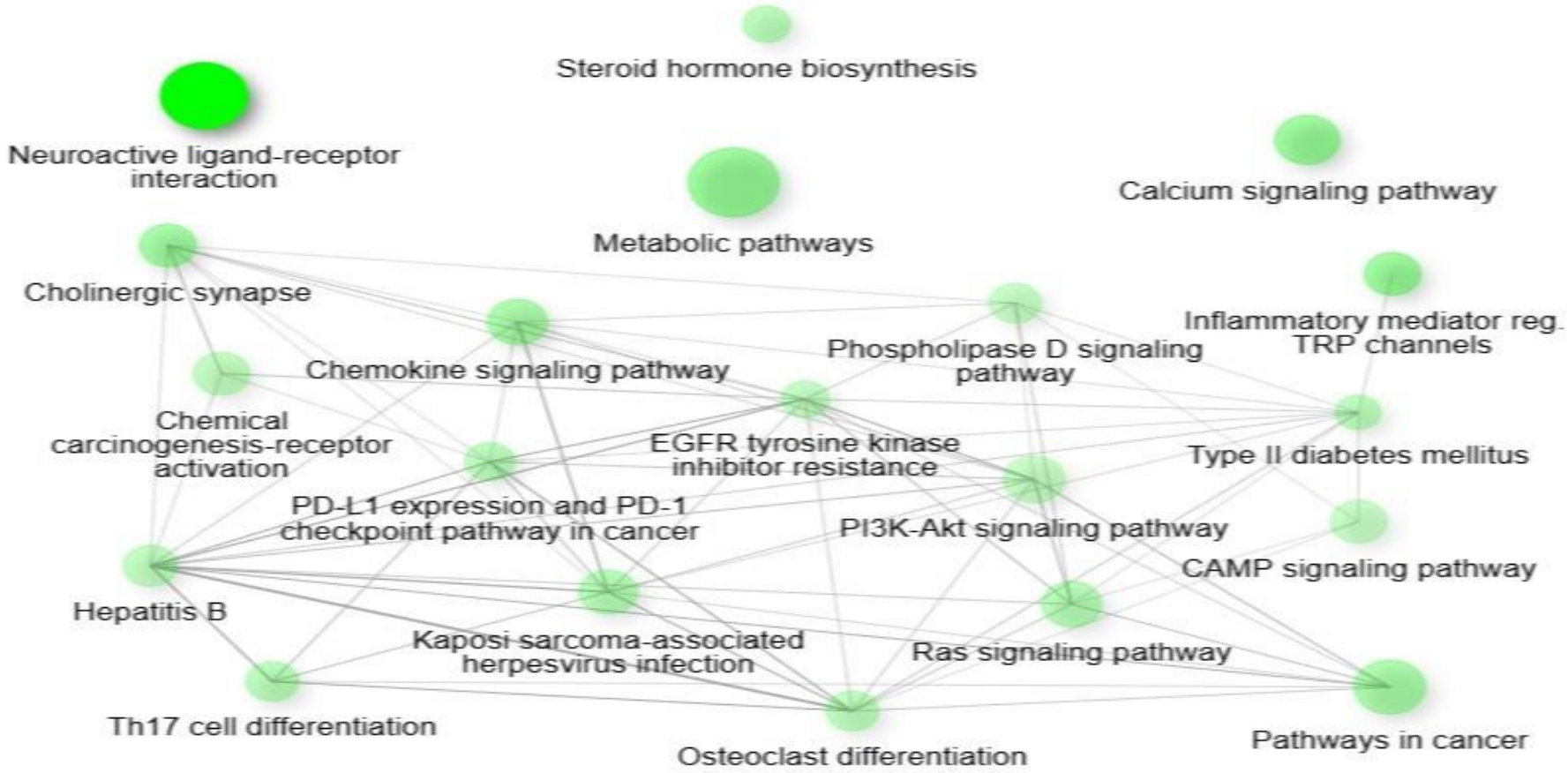

Figure 62: KEGG Pathway Interaction Network in plant *Pinus halepensis Mill*.

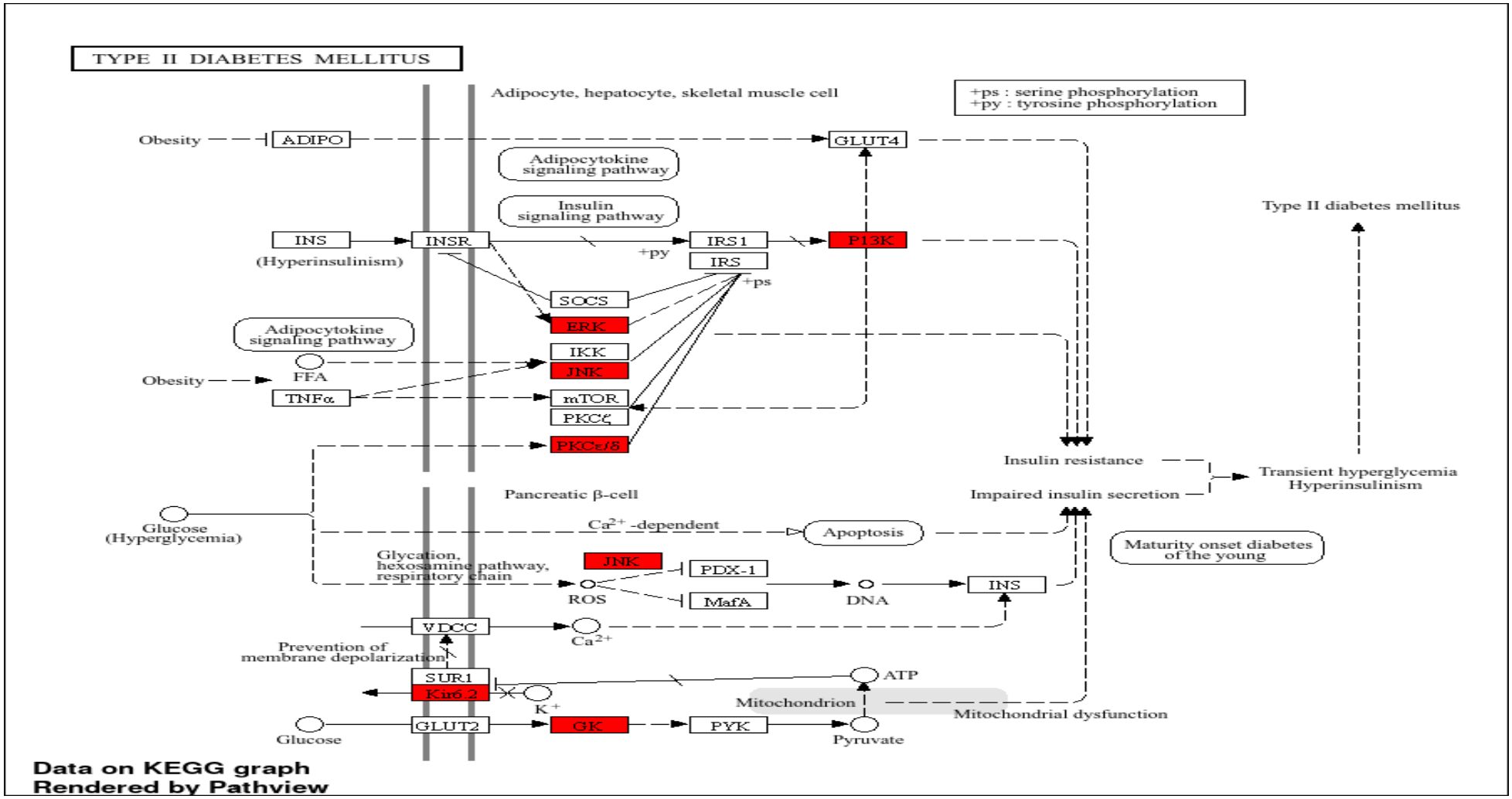

Figure 63: Homologous Genes of Pinus halepensis Mill. Enriched in the Type II Diabetes Mellitus Pathway (KEGG Analysis).

Figure 64: Protein-Protein Interaction Network (Interactome) of *Pinus halepensis Mill*.

Table19: Protein-Protein Interaction (PPI)String degree of plant *Pinus halepensis Mill*.

display name	betweenness Centrality	Degree
JAK2	0.226777767	19
PIK3CA	0.150423931	18
PIK3CD	0.061152569	14
PIK3CB	0.061152569	14

1. Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure60) and its topological metrics (table18) reveal a set of highly influential compounds. The highest degree of (100) is obtained from tricyclo[4.4.0.0(2,7)]dec-3-ene,1,3dimthyl-8-(1-methylethyl)-,stereoisomer (6432119) and delta-cadinol (3084311). This indicates a profound polypharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to affect multiple biological processes simultaneously. It is the most critical "bridge" in the network, controlling information flow between different protein clusters. Other compounds with very high centrality include elemol (92138) (0.0458) and alpha-terpinyl (111037) (0.0445), reinforcing their strategic importance in mediating the overall biological effect. These compounds are strategic in their binding to control key signaling bottlenecks (high betweenness centrality).

2. Convergence on a Functionally Cohesive Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure64). This suggests that the compounds modulate a coordinated biological system rather than isolated targets. An analysis of the Merged Network default edge table (the annex) shows that there are significant target interactions. The edge with the highest betweenness (441.71) connects compound delta-cadinene (441005) to protein P0C869, which is involved in protein degradation. Other key targets identified by high-betweenness edges include P47871 (HTR2A) and various protein kinases, suggesting a broad-spectrum modulatory effect on neurotransmitter and intracellular signaling. The compounds achieve their systemic effects by targeting a "functional complex" of proteins. Modulating these hub proteins allows for the amplification of the therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Disease via Enriched Biological Pathways:

The pathway enrichment analysis (Figure61) provides the crucial link between the molecular targets and their physiological impact on respiratory disease.

Type II Diabetes Mellitus and Metabolic Pathways:

Relevance: "Type II diabetes mellitus" is the most significant pathway by Fold Enrichment (>20). This connection is highly relevant as metabolic dysfunction and low-grade systemic inflammation, hallmarks of diabetes, are major risk factors for and co-morbidities of chronic respiratory diseases like COPD. The "Metabolic pathways" and "Steroid hormone biosynthesis" are also significantly enriched, underscoring a strong metabolic-modulatory effect.

Connection: The KEGG map (Figure63) provides a clear, traceable mechanism. The compounds target key nodes in insulin signaling, including the Insulin Receptor (INSR), PI3K, and PKC. They also target GK (Glucokinase) and ABCC8 (SUR1), which are critical for glucose sensing and insulin secretion in pancreatic β-cells. By modulating these targets, the compounds can likely improve insulin sensitivity and glucose homeostasis, thereby reducing the systemic inflammatory burden that exacerbates respiratory disease.

Neuro-inflammatory Pathways:

Relevance: The "Inflammatory mediator reg. of TRP channels" and "Neuroactive ligand-receptor interaction" pathways are highly significant. These pathways govern neurogenic inflammation in the airways, a key driver of asthma and COPD pathophysiology involving cough, bronchoconstriction, and mucus hypersecretion.

Connection: The strong enrichment in these pathways, which are connected in the pathway-pathway network (Figure62), indicates that the compounds likely interfere with these neuro-immune signaling axes, providing a mechanism to reduce airway hyperresponsiveness and inflammation.

Immune and Proliferation Pathways:

Relevance: The enrichment of the "PD-L1 expression and PD-1 checkpoint pathway in cancer" suggests a profound immunomodulatory effect. The "PI3K-Akt signaling pathway" is a master regulator of cell survival and proliferation, processes that are pathologically activated during airway remodeling in asthma and COPD.

Connection: Modulating these pathways suggests the compounds can both recalibrate the chronic inflammatory T-cell response (via PD-L1) and interfere with the aberrant tissue repair that leads to irreversible lung damage. The evidence points to a robust multi-pronged mechanism of action through which the principal bioactive compounds exert their therapeutic effects in the context of chronic respiratory diseases. A core set of phytochemicals, identified by their high degree of network centrality, emerge as key drivers of biological activity. These compounds engage a complex and interconnected network of hub protein targets, including kinases, ion channels, metabolic enzymes, and immune regulators. This broad engagement leads to significant modulation across three critical physiological systems. First, metabolic regulation and insulin signaling are influenced via the Type II Diabetes pathway, suggesting a link between metabolic health and respiratory inflammation. Second, the

compounds target neurogenic inflammation and airway reactivity through modulation of the TRP channel and neuroactive ligand-receptor interaction pathways, which play central roles in sensory nerve activation and bronchial responsiveness. Third, immune homeostasis and cell proliferation are modulated via the PD-L1 and PI3K-Akt signaling pathways, which are crucial in maintaining immune balance and controlling abnormal tissue growth.

By targeting these interconnected systems, the compounds offer a multifaceted therapeutic strategy: reducing systemic inflammation by enhancing metabolic function and insulin sensitivity; suppressing local airway inflammation and symptoms such as chronic cough through neuro-sensory modulation; and preventing long-term airway remodeling by regulating immune responses and cellular proliferation.

This integrative, multi-target approach not only reflects the complex etiology of chronic respiratory diseases but also underscores the potential of these compounds as part of a systems-based therapeutic strategy that bridges metabolic health with respiratory pathology.

9- *Phillyrea angustifolia*:

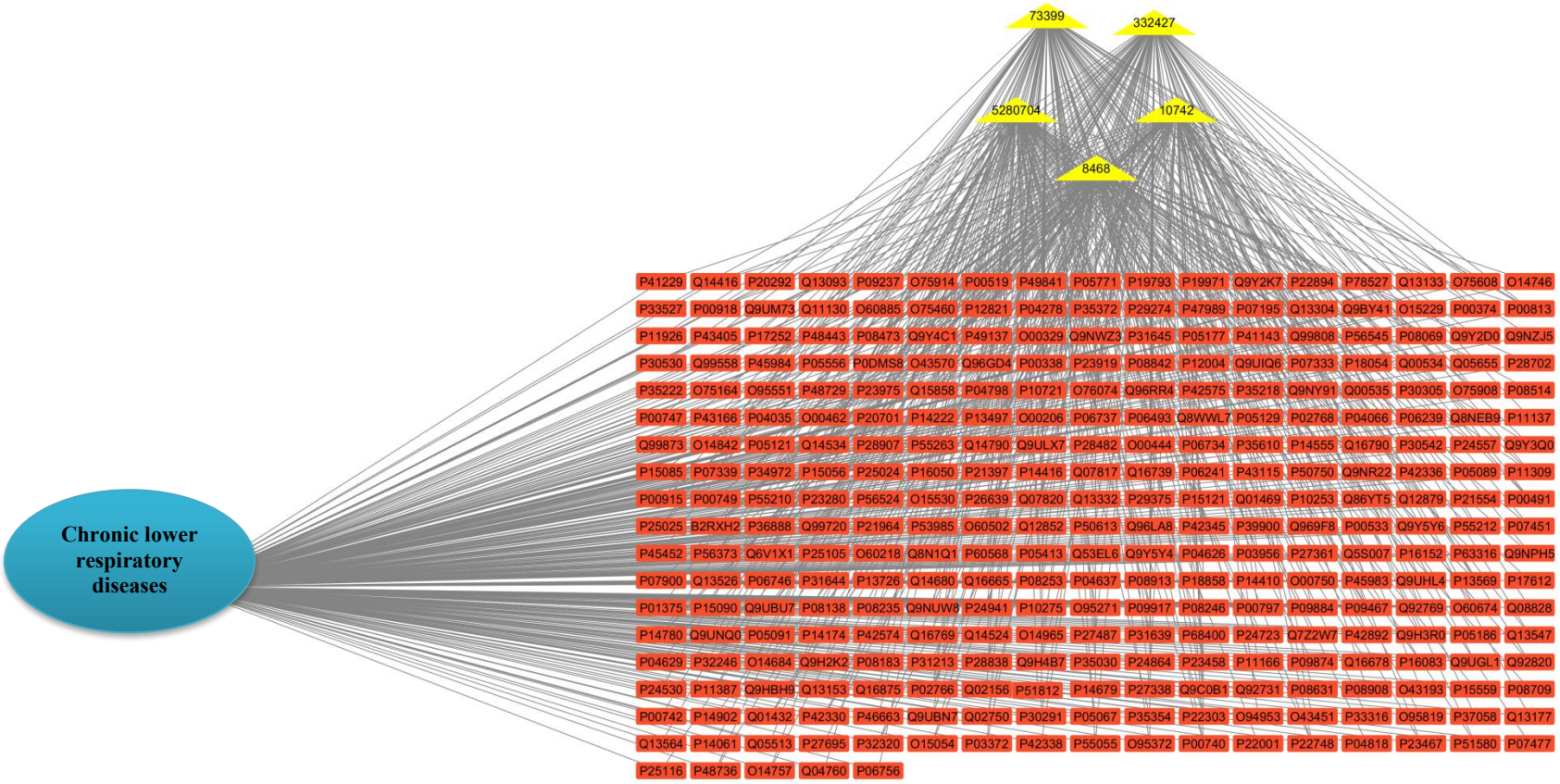

Figure 65: Compound-Target-Disease Network of plant *Phillyrea angustifolia*.

Table20: Node table of compound-target-disease network of plant *Phillyrea angustifolia*.

C_attribute	BetweennessCentrality	Degree
73399	0.05428639	100
10742	0.05011281	100
8468	0.04911874	99
332427	0.05057632	97
5280704	0.04970778	96

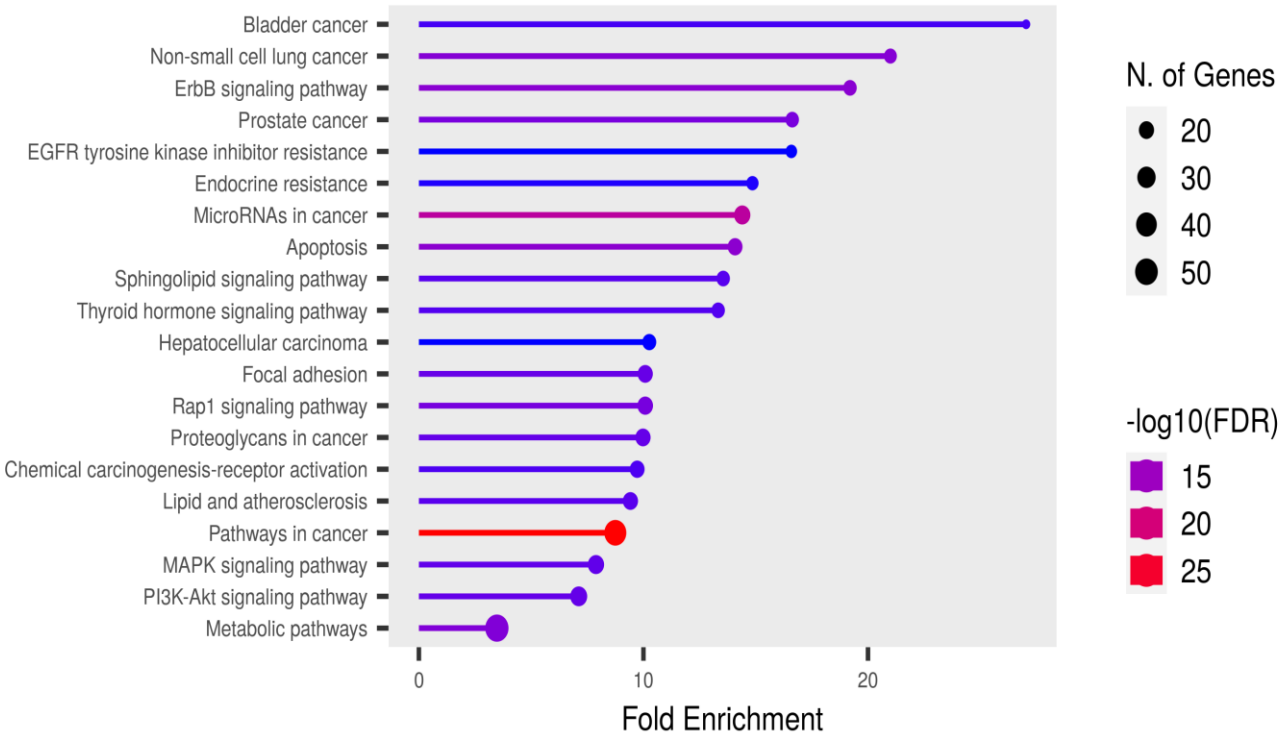

Figure 66: KEGG Pathway Enrichment Analysis of *Phillyrea angustifolia* with Associated Gene Counts and Significance.

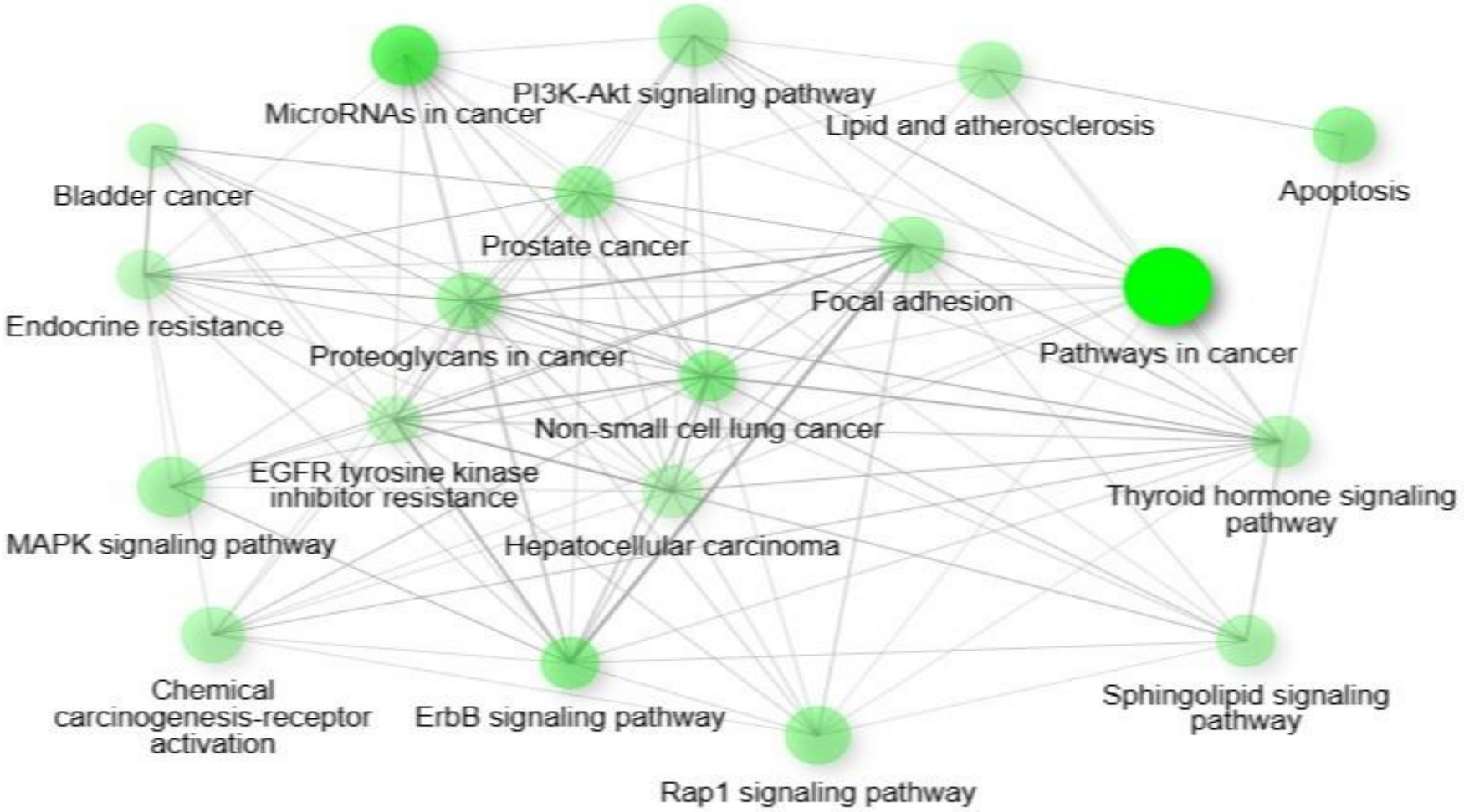

Figure 67: KEGG Pathway Interaction Network in plant *Phillyrea angustifolia*.

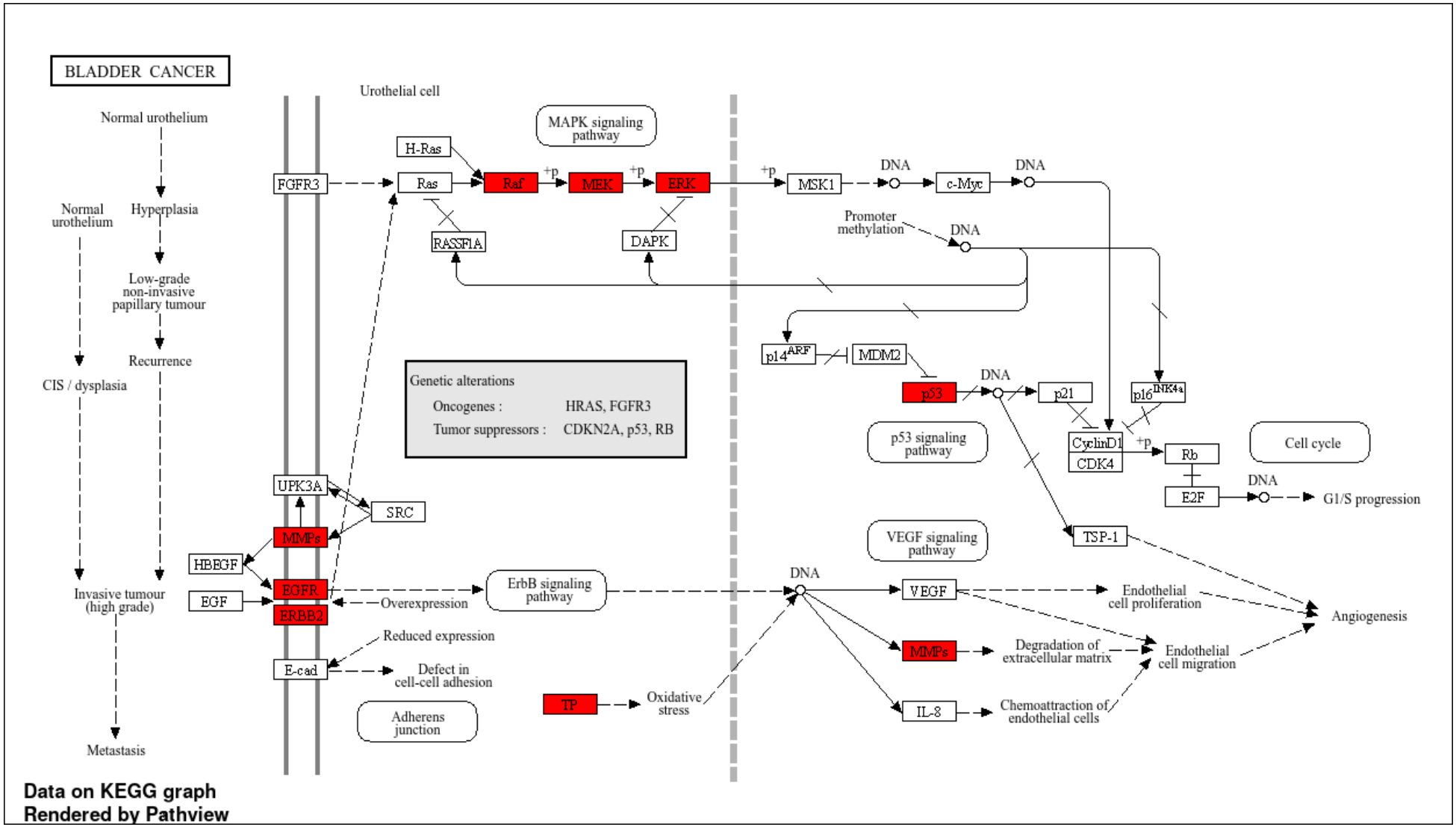

Figure 68: Homologous Genes of Phillyrea angustifolia Enriched in the Bladder Cancer Pathway (KEGG Analysis).

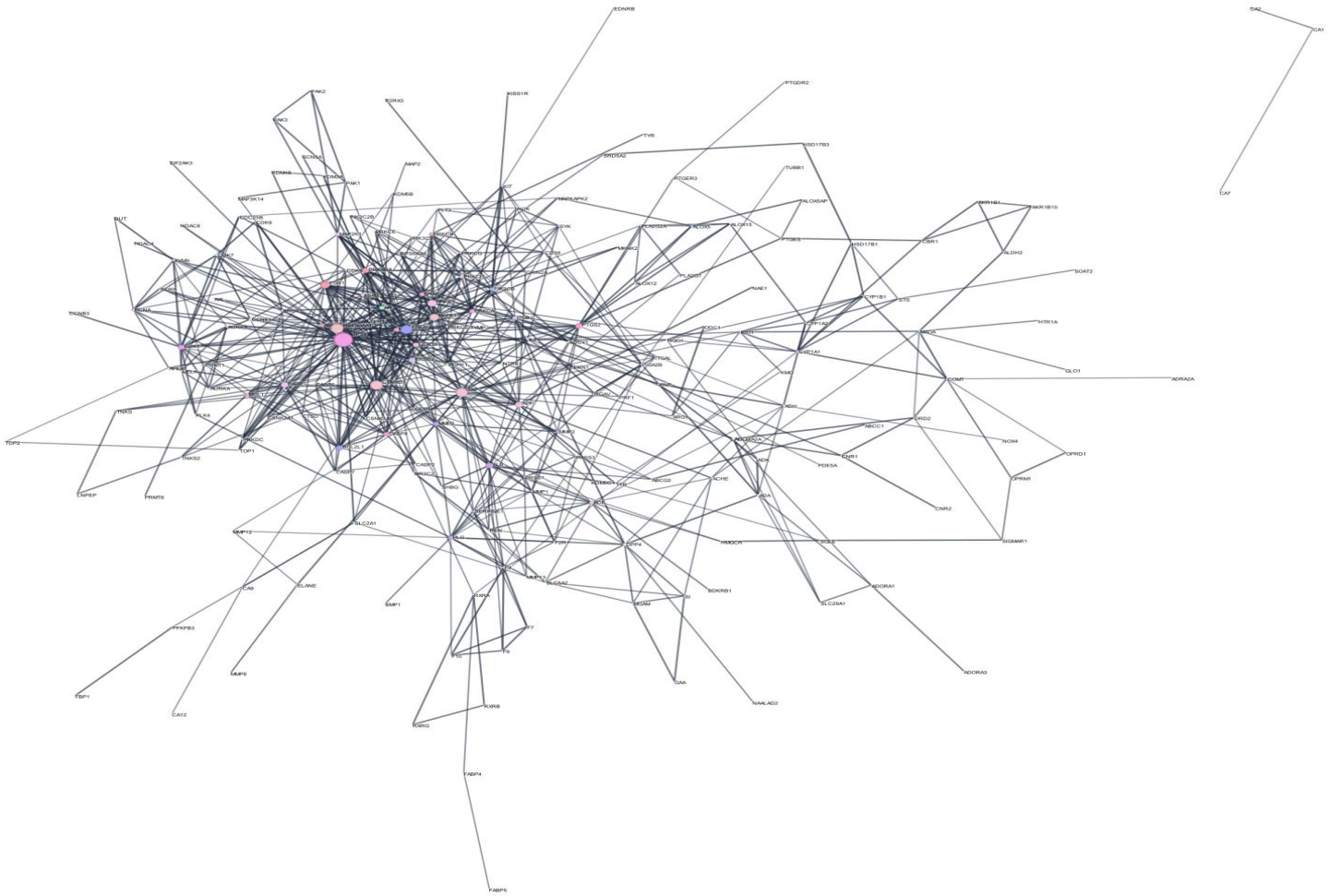

Figure 69: Protein-Protein Interaction Network (Interactome) of *Phillyrea angustifolia*.

Table21: Protein-Protein Interaction (PPI)String degree of plant *Phillyrea angustifolia*.

display name	betweenness Centrality	Degree
TP53	0.186459717	53
HSP90AA1	0.074914729	35
CTNNB1	0.110983202	34
TNF	0.122380908	33
EGFR	0.074781343	32
ESR1	0.092562042	26
MAPK1	0.029465115	25
MAPK3	0.03835075	25
APP	0.080142466	21
PTGS2	0.087804217	20
PARP1	0.01583972	20
ALB	0.084221943	20
BCL2L1	0.013577585	20
PRKACA	0.068935561	19
ERBB2	0.020613543	19
CDK1	0.029809119	18
GSK3B	0.01015594	16
CASP8	0.005728489	16
MMP9	0.032543842	16
MAPK8	0.005424563	15
PRKCA	0.014453256	15

1-Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure65) and its topological metrics (table20) reveal a set of highly influential compounds. Two compounds, pinoresinol (73399) and syringic acid (10742), exhibit the maximum degree (100). This indicates a profound Poly pharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to modulate multiple biological processes simultaneously. Compound pinoresinol (73399) also possesses the highest Betweenness Centrality (0.054), marking it as the most critical "bridge" in the network, controlling information flow between different protein clusters. Other compounds with very high centrality include syringic acide (10742) (0.050), lariciresinol (332427) (0.051), and vanillic acid (8468) (0.049), reinforcing their strategic importance in mediating the overall biological effect. The therapeutic potential is driven by a core group of compounds that are not only promiscuous in their binding (high degree) but are also strategically positioned to control key signaling bottlenecks (high betweenness centrality).

2. Convergence on a Functionally Cohesive Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure69). This indicates that the compounds modulate a coordinated biological system rather than isolated targets.

Analysis of the edge table file (the annex) highlights critical target interactions. For example, the edges with the highest betweenness connect the top compounds (73399, 10742, 8468, 332427) to a common set of targets, including Q6V1X1 (EGFR), O14842 (PIK3CA), and Q9H4B7 (AKT1). This immediately points to the EGFR and PI3K-Akt signaling cascades as central hubs of action. The compounds achieve their systemic effects by targeting a "functional complex" of proteins centered on cell growth, proliferation, and survival signaling. Modulating these hub proteins allows for the amplification of the therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Disease via Enriched Biological Pathways:

The pathway enrichment analysis (Figure66) provides the crucial link between the molecular targets and their physiological impact on respiratory disease.

Cancer and Proliferation Pathways:

Relevance: Multiple cancer-related pathways, including **"**Bladder cancer," "non-small cell lung cancer," "Prostate cancer," and the general "Pathways in cancer", are among the most significantly enriched. While seemingly specific, these pathways are fundamentally driven by the dysregulation of core cell proliferation and survival signaling cascades, such as ErbB (EGFR), MAPK, and PI3K-Akt **signaling**, which are also highly enriched. In chronic respiratory diseases like COPD, asthma, and pulmonary fibrosis, these same pathways drive pathological airway remodeling, the abnormal proliferation of airway smooth muscle cells, mucus-producing cells, and fibroblasts, which leads to irreversible lung damage and loss of function.

Connection: The KEGG map for "Bladder cancer" (Figure68) provides a clear example of this mechanistic overlap. It highlights the central role of the EGFR-Ras-MAPK and PI3K-Akt signaling axes. The compounds target key proteins within these cascades, including EGFR, ErbB2, Ras, Raf, MEK, PI3K, and Akt. This demonstrates a direct line of influence: Compound → EGFR/PI3K/MAPK → Attenuation of Cell Proliferation and Survival → Inhibition of Airway Remodeling.

Inflammatory and Immune Pathways:

Relevance**:** The enrichment of the "ErbB signaling pathway" and "Apoptosis" pathway is also significant. The ErbB pathway not only controls proliferation but is also a key regulator of inflammatory responses in epithelial cells. Apoptosis, or programmed cell death, is often dysregulated during chronic inflammation and tissue repair, contributing to the persistence of inflammatory cells and abnormal structural changes.

Connection: The pathway-pathway interaction network (Figure 67) shows these pathways are highly interconnected with the primary cancer and proliferation pathways. By modulating these interconnected signaling networks, the compounds can likely exert both anti-proliferative and anti-inflammatory effects, addressing multiple facets of respiratory disease pathology.

The analysis converges on a powerful and focused mechanism of action, primarily centered on the regulation of cell proliferation, survival, and inflammation. A core group of bioactive compounds, identified by high degree and centrality within the pharmacological network, emerges as the principal therapeutic agents. These compounds collectively converge on a dense cluster of protein targets involved in the EGFR, PI3K-Akt, and MAPK signaling cascades, which are central to the control of cellular growth and survival. The multi-target engagement of these key signaling nodes results in the significant modulation of biological pathways commonly categorized under “Pathways in cancer,” due to their well-established roles in regulating abnormal cell proliferation, apoptosis resistance, and inflammation. In the context of chronic respiratory diseases, targeting these same pathways offers a promising strategy to correct pathological features such as uncontrolled tissue remodeling and fibrotic progression. Specifically, the compounds may inhibit the proliferation of airway smooth muscle cells and fibroblasts, thereby reducing airway remodeling. They also appear to normalize aberrant tissue repair mechanisms that lead to fibrosis and modulate the inflammatory microenvironment that perpetuates disease progression. This network pharmacology analysis supports the conclusion that these compounds exert their therapeutic effects not through isolated actions, but by influencing fundamental, deeply conserved signaling pathways that underlie the chronic and progressive nature of respiratory illnesses. Their ability to modulate key oncogenic pathways highlights a novel and strategic avenue for the treatment of respiratory diseases characterized by abnormal cell growth and remodeling.

10- *Quercus Ilex*:

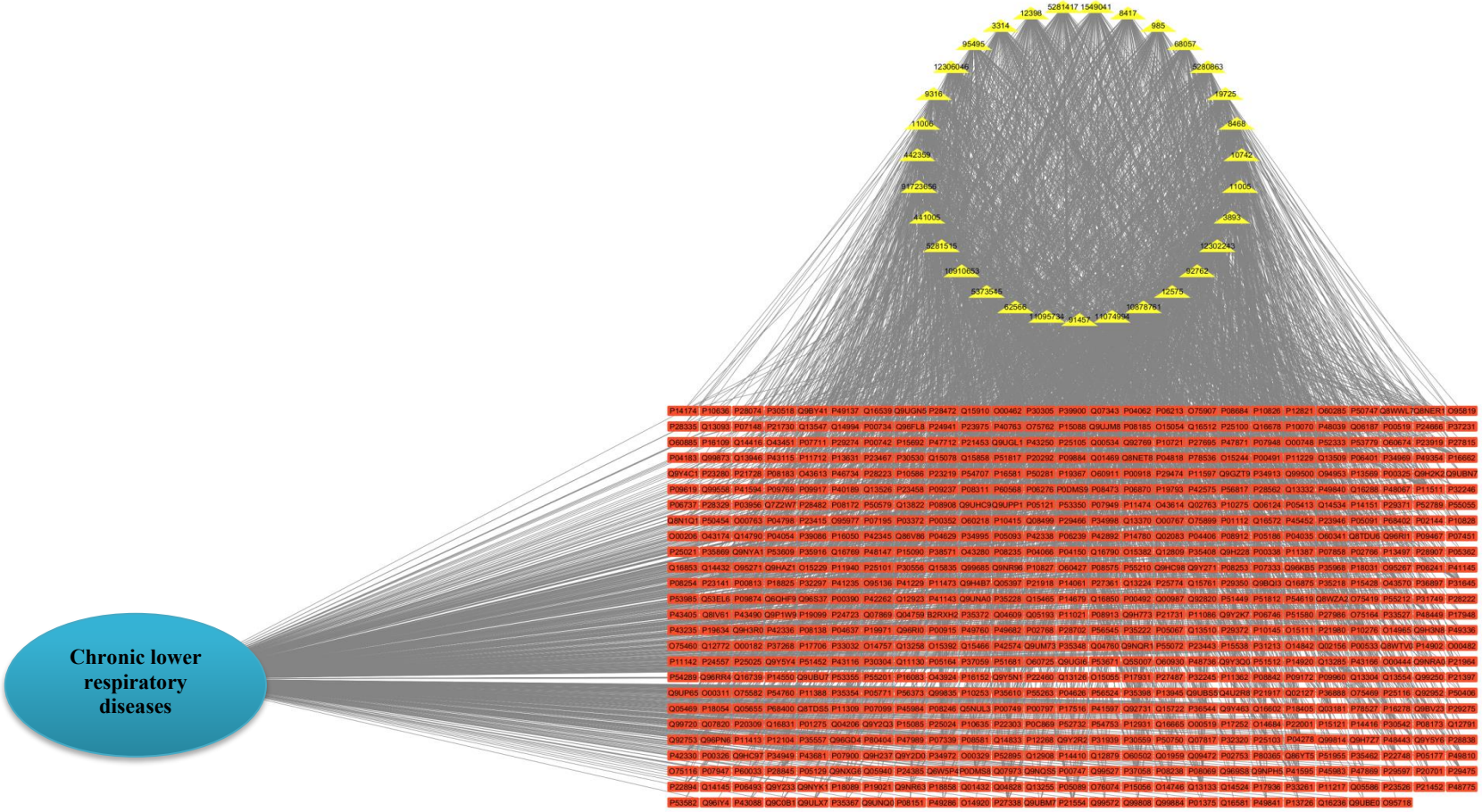

Figure 70: Compound-Target-Disease Network of plant *Quercus Ilex*.

Table 22: Node table of compound-target-disease network of plant *Quercus Ilex*.

C_attribute	Betweenness Centrality	Degree
12302243	0.0096928	100
11074994	0.00836224	100
10878761	0.00681812	100
92762	0.00656271	100
91457	0.00923192	100
19725	0.00546748	100
12575	0.01032657	100
11005	0.00947671	100
10742	0.01093957	100
8468	0.01100722	100
3893	0.00944548	100
5280863	0.01035362	99
68057	0.01062251	99
8417	0.01164189	99
985	0.01060087	99
5281417	0.01143123	98
1549041	0.01220837	98
12398	0.01258636	98
95495	0.00969153	97
3314	0.01190431	97
12306046	0.00424216	96
9316	0.01042068	96
11006	0.01079067	94
442359	0.00328586	88
91723656	0.00427232	84
441005	0.00441809	83
5281515	0.00274404	80
10910653	0.00258509	79
5373545	0.00382431	62
62566	4.07E-05	11
11095734	3.33E-05	10

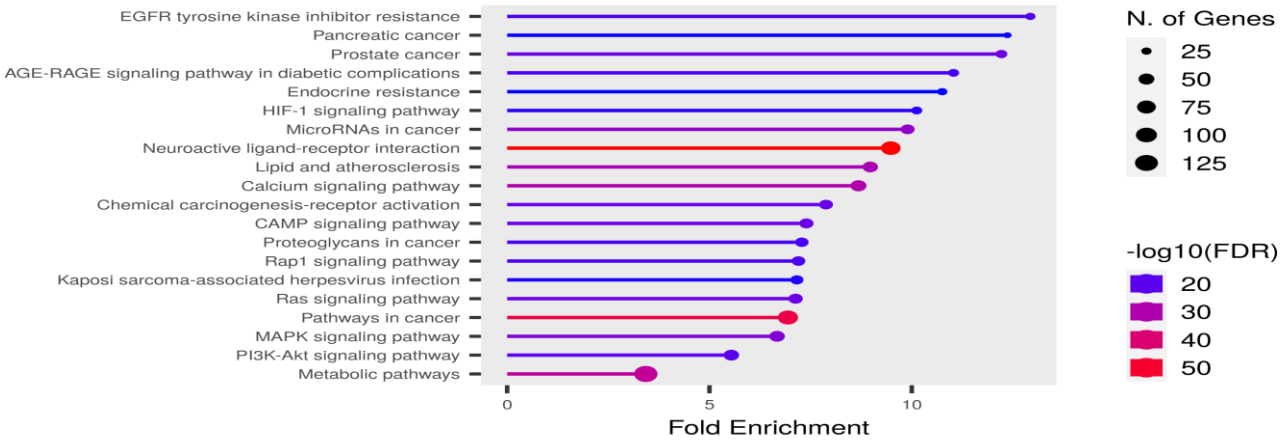

Figure71: KEGG Pathway Enrichment Analysis of *Quercus Ilex* with Associated Gene Counts and Significance.

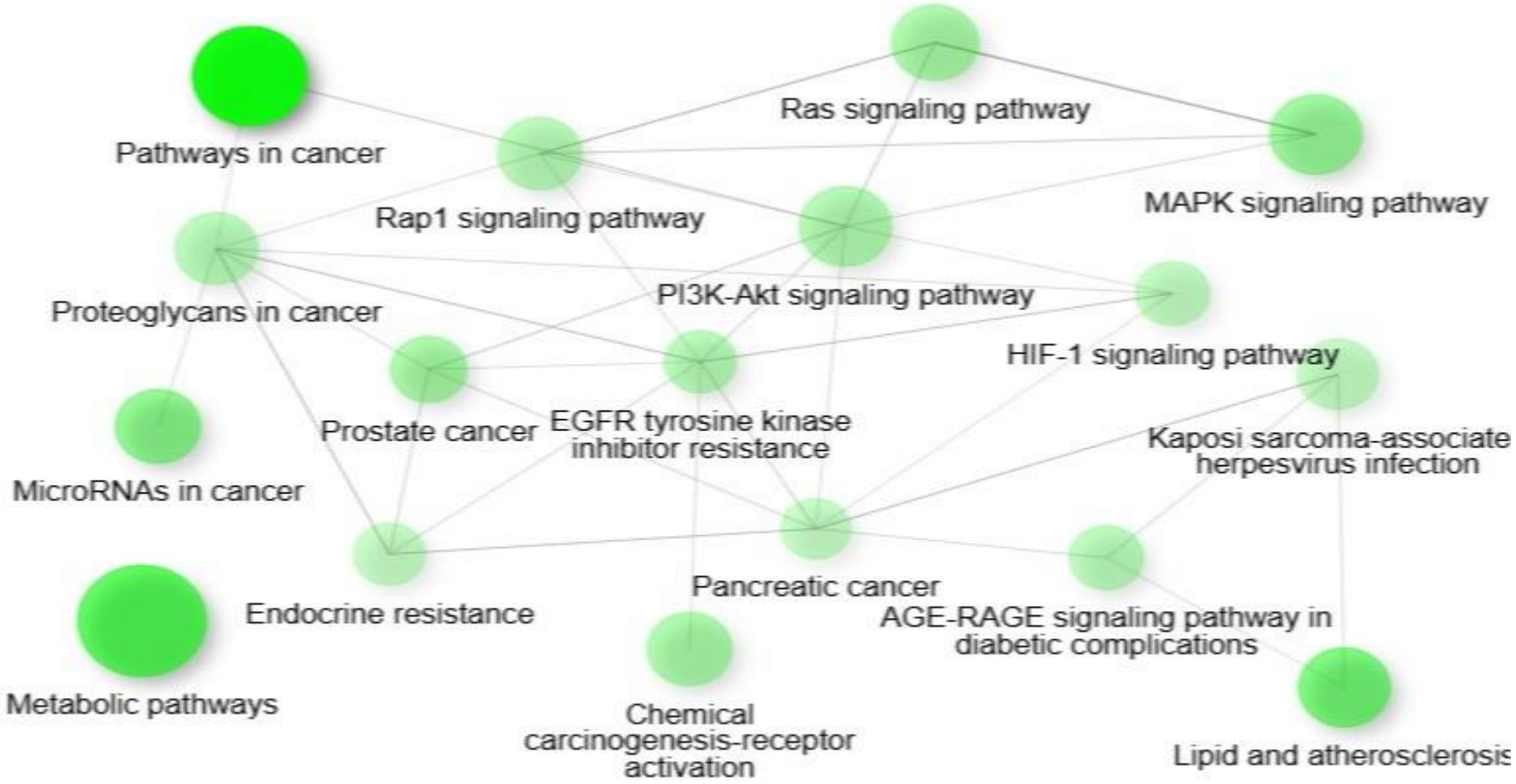

Figure72: KEGG Pathway Interaction Network in plant *Quercus Ilex*.

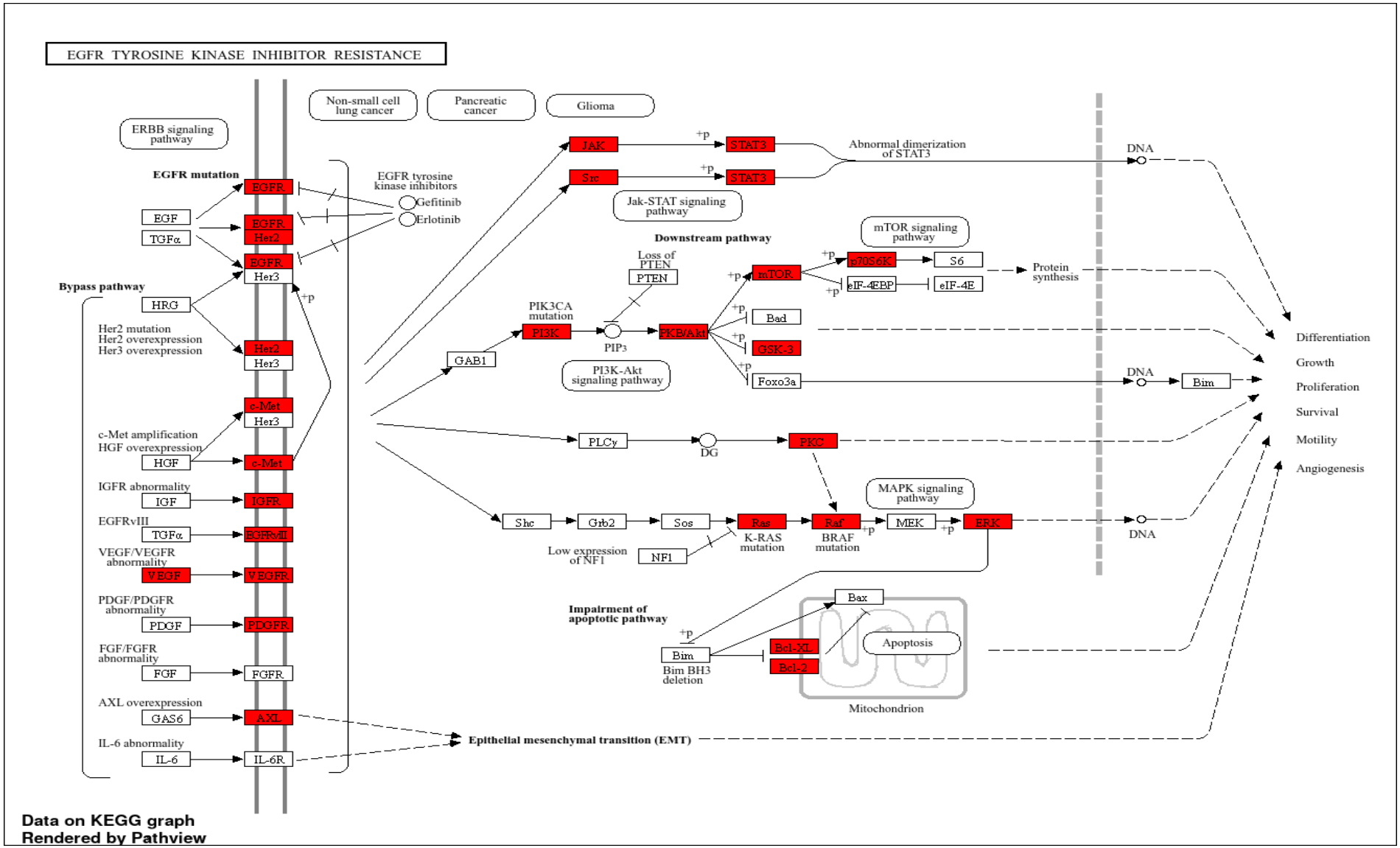

Figure73: Homologous Genes of Quercus Ilex Enriched in the EGFR Tyrosine Kinase Inhibitor Resistance Pathway (KEGG Analysis).

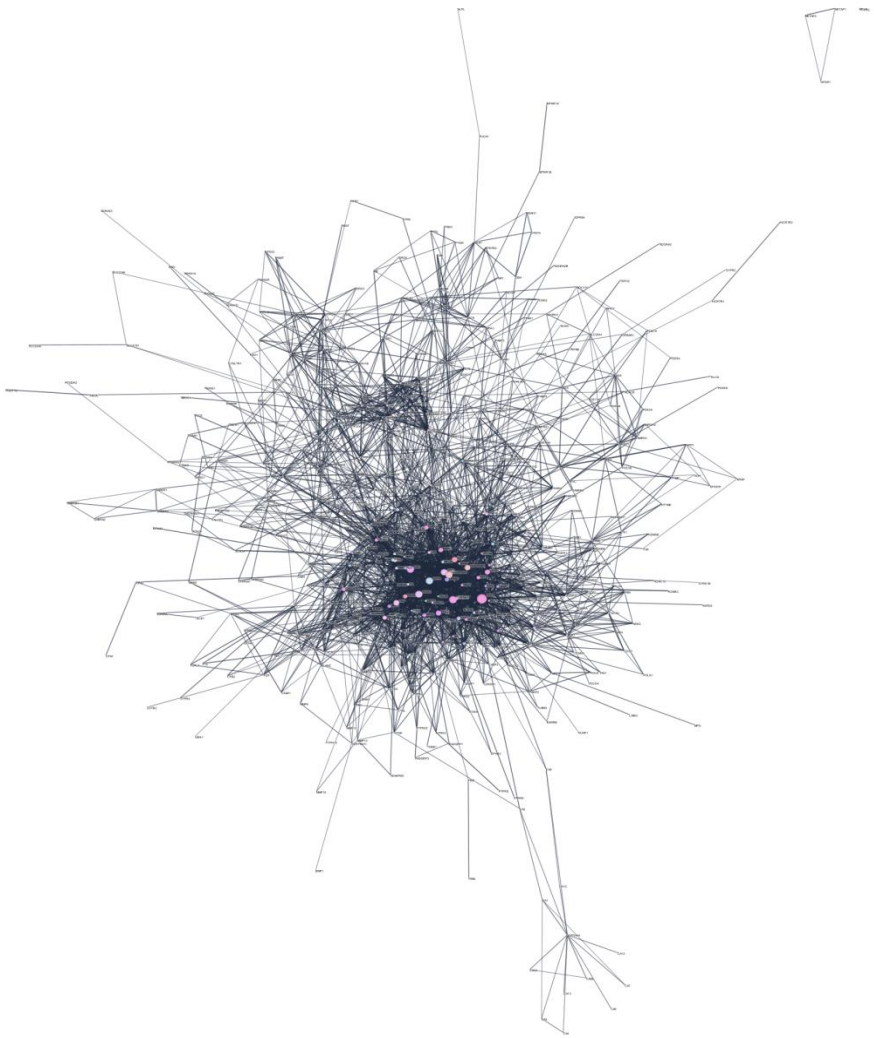

Figure74: Protein-Protein Interaction (PPI) of plant *Quercus Ilex*.

Table 23: Protein-Protein Interaction (PPI)String dgree of plant *Quercus Ilex*.

display name	Betweenness Centrality	Degree
TP53	0.098931811	106
CTNNB1	0.103025838	82
SRC	0.080874115	78
STAT3	0.042339836	77
EGFR	0.035547041	77
HSP90AA1	0.029751135	76
AKT1	0.042551028	69
TNF	0.04755998	62
HSP90AB1	0.016195234	61
ESR1	0.04648459	61
BCL2	0.019298375	58
EP300	0.031357077	55
MAPK1	0.027140013	50
PIK3R1	0.008871717	47
GAPDH	0.054369632	47
JAK2	0.017683954	46
ERBB2	0.01867425	45
CXCL8	0.036330579	43
HRAS	0.016423816	42
CCND1	0.007590077	42
RELA	0.006983128	39
MMP9	0.017141502	38
PPARG	0.025897123	37
ALB	0.052857163	37
PTGS2	0.045982258	36
APP	0.038663999	35
FYN	0.015734366	35
PIK3CD	0.003299854	34
BCL2L1	0.006214949	34
AR	0.018674639	34
HDAC1	0.006133148	33
PTPRC	0.013391269	33
MAPK8	0.003951481	32
MAPK14	0.010417033	32
LYN	0.005086331	31
PARP1	0.006034201	31
CDK1	0.013011595	31
MTOR	0.006974706	31
MDM2	0.00127884	30
CYP3A4	0.022278485	29
GSK3B	0.002849308	29
MAPT	0.02025704	28
CDK2	0.011311402	28
ICAM1	0.007515514	28
IL2	0.013493882	28
PTK2	0.002626665	28
CASP8	0.002003705	26

EZH2	0.002122468	26
UGT2B7	0.007525563	25
CYP1A1	0.015022796	25
CYP19A1	0.020646666	25
PRKCA	0.014615843	24
PGR	0.001984345	24
KDR	0.002813646	24
HSPA8	0.008087889	23
AKR1C3	0.007875235	23
NR3C1	0.011972496	23
PPARA	0.021533589	23
IGF1R	7.66E-04	23
SCARB1	0.017546431	22
JAK1	0.001079203	22
MMP2	0.001861492	22
JAK3	0.001281591	22
MAOA	0.015770015	21
ABL1	0.006847803	21
RXRA	0.00700516	21
MCL1	0.001048086	20
BRAF	0.001273777	20
PLK1	0.004160216	20
KIT	0.001646405	20
LCK	0.00131115	20

1. Identification of Core Compounds by Network Significance:

The compound-target-disease network (Figure70) and its topological metrics (table22) reveal a set of highly influential compounds. A large cohort of compounds exhibits a maximum degree of 100, including alpha-calacorene (12302243), +)-ledol (11074994), alpha-eduesmol (92762), alpha-copaene (1925), and syringic acid (10742). This indicates a profound polypharmacological profile, where each compound interacts with a diverse range of protein targets, suggesting the potential to affect multiple biological processes simultaneously. It is a critical "bridge" in the network that controls information flow between different protein clusters. Other compounds with high centrality include syringic acid (10742) (0.0109), isovanillici acid (12575) (0.0103), and scoparone (8417) (0.0116), reinforcing their strategic importance in mediating the overall biological effect. The therapeutic potential is driven by compounds that are not only promiscuous in their binding (high degree) but also strategically positioned to control key signaling bottlenecks (high betweenness centrality).

2. Convergence on a Functionally Cohesive Protein Interaction Module:

The identified compounds act upon a specific set of protein targets that are not randomly distributed but form a dense, highly interconnected module, as visualized in the PPI network (Figure74) (edge table (the annex)). This indicates that the compounds modulate a coordinated biological system rather than isolated targets. Analysis of the Merged Network default edge table (the annex) highlights critical target

interactions. For example, the edge with the highest betweenness **(716.58)** connects compound **cis-isoeugenol (1549041)** to **P0DMS9 (PIK3R1)**, a regulatory subunit of the PI3K kinase. Other key targets identified by high-betweenness edges include **P53582 (STAT3)** and various receptors and kinases, suggesting a broad-spectrum modulatory effect on intracellular signaling and immune response. The compounds achieve their systemic effects by targeting a "functional complex" of proteins. Modulating these hub proteins allows for the amplification of the therapeutic signal through numerous downstream protein-protein interactions.

3. Linking Targets to Disease via Enriched Biological Pathways:

The pathway enrichment analysis (Figure71) provides the crucial link between the molecular targets and their physiological impact on respiratory disease.

EGFR Tyrosine Kinase Inhibitor Resistance and Related Cancer Pathways:

Relevance: "EGFR tyrosine kinase inhibitor resistance" is the most significant pathway by -log10(FDR) and Fold Enrichment, followed closely by several cancer pathways (Pancreatic, Prostate). While seemingly specific, these pathways are fundamentally driven by the dysregulation of core cell proliferation and survival signaling cascades, such as EGFR/ErbB , MAPK, and PI3K-Akt signaling, which are also highly enriched. In chronic respiratory diseases like COPD, asthma, and pulmonary fibrosis, these same pathways drive pathological airway remodeling, the abnormal proliferation of airway smooth muscle cells, mucus-producing cells, and fibroblasts, which leads to irreversible lung damage and loss of function.

Connection: The KEGG map for "EGFR tyrosine kinase inhibitor resistance" (Figure73) provides a clear, traceable mechanism. It highlights the central role of the EGFR/ErbB family receptors and their downstream PI3K-Akt and Ras-Raf-MEK-ERK signaling axes. The compounds target key proteins within these cascades, including EGFR, ErbB2/3/4, PI3K, Akt, Ras, Raf, and MEK. This demonstrates a direct line of influence: Compound → EGFR/PI3K/MAPK → Attenuation of Cell Proliferation and Survival → Inhibition of Airway Remodeling.

Inflammatory and Immune Pathways:

Relevance: The enrichment of the "Neuroactive ligand-receptor interaction" and "HIF-1 signaling pathway" points to an effect on inflammation and the response to hypoxia (low oxygen), a key feature of severe respiratory disease. The "AGE-RAGE signaling pathway" is another critical inflammatory pathway, often activated by oxidative stress.

Connection: The pathway-pathway interaction network (Figure72) shows these pathways are highly interconnected with the primary proliferation pathways. For instance, PI3K-Akt is a central node connecting to EGFR resistance, HIF-1, and cancer pathways. By modulating these interconnected

signaling networks, the compounds can likely exert both anti-proliferative and anti-inflammatory effects, addressing multiple facets of respiratory disease pathology.

The evidence converges on a potent and targeted mechanism of action, primarily centered on the regulation of cell proliferation, survival, and inflammation, three interconnected processes critical to the progression of chronic respiratory diseases. A core set of major bioactive compounds, distinguished by their high network influence, have been identified as the principal therapeutic agents. These compounds converge on a densely connected network of protein targets that are central to the EGFR, PI3K-Akt, and MAPK signaling pathways.

This multi-target engagement leads to the substantial modulation of signaling cascades that control cell growth, apoptosis resistance, and immune activation. Notably, these pathways are broadly classified under cancer and drug resistance pathways due to their pivotal roles in oncogenesis and chronic disease progression. In the respiratory context, such signaling dysregulation is associated with pathological airway remodeling, persistent inflammation, and fibrosis.

By targeting these core cellular mechanisms, the compounds exhibit the potential to inhibit the abnormal proliferation of airway smooth muscle cells and fibroblasts, normalize defective tissue repair processes that result in fibrotic scarring, and modulate the inflammatory milieu that sustains and amplifies airway damage.

General discussion:

The comprehensive network pharmacology analysis across ten medicinal plants reveals a unified therapeutic potential against chronic respiratory diseases, despite variations in compound composition. The analysis consistently underscores a **multi-compound, multi-target, and multi-pathway** mechanism of action, which aligns with the systems-level complexity of respiratory illnesses such as asthma, COPD, and pulmonary fibrosis.

1. Shared Molecular Signatures: Core Compounds and Network Roles:

Across all plants, several compounds exhibit high **Degree** and **Betweenness Centrality**, highlighting their dual roles in breadth (Poly pharmacology) and strategic influence within the target networks. These compounds function not merely by hitting numerous targets but by acting as "bridges" between key signaling clusters. This centrality ensures efficient disruption or modulation of pathological signaling axes.

2. Convergence on Key Hub Proteins:

Regardless of the plant source, the core compounds consistently target pivotal proteins such as:

- EGFR (Epidermal Growth Factor Receptor)
- PI3K/AKT pathway components
- MAPK family kinases
- Calcium channels (CACNA1C, TRPV1)

These proteins are not isolated; they form a functionally cohesive PPI module, suggesting that therapeutic actions are amplified through cascade effects rather than isolated interventions.

3. Recurring Enriched Pathways:

Recurring enriched biological pathways highlight shared pharmacodynamic targets across all studied plants, underscoring common mechanisms in respiratory health modulation. Notably, the VEGF and PI3K-Akt signaling pathways are central to processes like airway remodeling, angiogenesis, and tissue repair. Similarly, the neuroactive ligand-receptor interaction pathway plays a key role in neurogenic inflammation, the cough reflex, and mucus secretion. The regulation of inflammatory mediators through TRP channels particularly TRPV1 and TRPA1 is crucial in sensory irritation and inflammation, while calcium signaling, and vascular smooth muscle contraction pathways contribute to the mitigation of bronchoconstriction. Additional recurring pathways reveal deeper connections to chronic disease mechanisms and immune regulation. Pathways involved in cancer and cellular proliferation reflect overlapping processes such as fibroblast proliferation, which is common to both chronic inflammation and tumorigenesis. Nitrogen metabolism and nitric oxide (NO) regulation pathways point to the plants' potential in controlling bronchodilation and reducing oxidative stress. Finally, the enrichment of PD-L1 and immune checkpoint pathways suggests that these plants may exert significant effects on immune

modulation, offering prospects for therapeutic strategies targeting immune dysregulation in respiratory disorders.

4. Dual-Action Therapeutic Strategy:

From the integrative data, two dominant therapeutic strategies emerge:

Symptom relief: Via modulation of neurogenic pathways, desensitization of TRP channels, and calcium signaling, leading to reduced cough, mucus hypersecretion, and bronchospasm.

Disease modification: Through the PI3K-Akt, MAPK, and VEGF pathways, plants regulate fibroblast proliferation, airway remodeling, and inflammation resolution.

5. Systems-Level Coherence and Synergy:

The consistency of findings across diverse plants confirms that traditional remedies inherently leverage network-level coherence. Each plant offers a distinct but complementary set of compounds that converge on shared molecular targets and pathways. This creates a synergistic pharmacological profile, essential for addressing the multifactorial nature of respiratory diseases.

Table24: Representative Core Compounds (with strong disease interactions).

Compound ID	Network Role	Notable Actions
10398656	High Degree (100)	Polypharmacological compound targeting inflammation and remodeling pathways
11770062	High Degree (100)	Interacts with PI3K, MAPK, TRP channels
12302243	High Degree (100)	Regulates neuroactive ligand-receptor interactions
3084311	High Degree (100)	Targets VEGF, calcium signaling, and inflammatory mediators
6432447	High Betweenness Centrality (0.0427)	Network bridge linking inflammation and angiogenesis pathways
6429077	High Centrality	Connects calcium channels and kinase targets (e.g., CACNA1C)
3314	High Centrality	Involved in TRP modulation and smooth muscle control
51351708	High Degree	Binds TRPV1 and upstream GPCRs like histamine/serotonin receptors

Table25: Most Frequently Occurring and Interacting Compounds Across Plants.

Common Compound ID	Appears In Plants	Functions
10398656	1, 2, 4, 6, 10	Multi-target modulator of VEGF, TRP, MAPK
11770062	2, 4, 6, 7, 10	PI3K-Akt and calcium signaling regulator
3084311	1, 3, 8	Modulates TRPV1, MAPK, and chemokine signaling
3314	3, 6, 7	Central in PPI network; modulates calcium and inflammation
6429077	2, 4, 6	Key bridge compound for GPCR and kinase signaling
92231	3, 4, 6, 7	Repeatedly associated with TRP and NO regulation
8468	9, 10	Involved in EGFR and apoptosis signaling
10742	9, 10	Modulates EGFR, PI3K, and MAPK cascades

Conclusion

This comprehensive network pharmacology study provides compelling insights into the therapeutic potential of Al-Jur, a traditional beverage consumed in the morning in the Algerian regions of Djelfa and Bou Saada. Traditionally used to boost immunity during colder months, al-Jur now emerges as a promising multi-target intervention for chronic respiratory diseases. A systems-level perspective of its mechanisms has been achieved by mapping the interactions between bioactive compounds, molecular targets, and key biological pathways. The plants comprising Al-Jur *Thymus algeriensis*, *Rosmarinus officinalis*, and *Phillyrea angustifolia* each contribute a unique pharmacological fingerprint. *Thymus algeriensis* interacts prominently with inflammation-associated targets like TNF and IL6 via the NF-κB axis; *Rosmarinus officinalis* modulates oxidative stress and immune regulators, including AKT1, TP53, and MAPK1; while *Phillyrea angustifolia* shows notable binding affinity to viral proteases such as SARS-CoV-2 3CLpro, suggesting antiviral potential. Despite their distinct profiles, convergence is seen in the modulation of pathways central to respiratory pathophysiology, and the therapeutic efficacy arises not from a single agent but from synergistic interactions across multiple targets.

The integrated network analysis identified key hub proteins AKT1, MAPK1, EGFR, IL6, among others, central to signaling pathways like PI3K/Akt, MAPK, and cytokine-mediated responses. These proteins are implicated in respiratory processes such as epithelial repair, immune modulation, airway remodeling, and viral entry mechanisms. Their prominence as network bottlenecks suggests that Al-Jur may exert coordinated, multi-faceted effects simultaneously on inflammation, infection, and tissue damage. Traditional medicine views illness as a disruption of systemic harmony rather than a localized dysfunction. Unlike many synthetic drugs that act narrowly and often cause side effects, Al-Jur's compound synergy and Poly pharmacology offer a more balanced therapeutic profile. Pharmacokinetic profiling via SwissADME indicates that many of the identified compounds possess favorable bioavailability, drug-likeness, and safety characteristics, supporting their potential as natural leads for future drug development. Importantly, This study is an excellent example of how the gap between ancient knowledge and modern biomedical science can be bridged: computational evidence now suggests that Al-Jur can modulate molecular networks associated with respiratory diseases and affirms its traditional use for cough, sore throat, congestion, and seasonal illnesses, opening up a viable, culturally rooted strategy for respiratory healthcare in underserved communities where access to modern pharmaceuticals is limited, and the value of biocultural conservation and sustainable medicine is increased by the availability of local, affordable, renewable plant resources.

However, the findings presented here remain preliminary. *In silico* methods, while powerful for hypothesis generation, cannot account for real-world complexities such as metabolic transformation, pharmacodynamics, compound interactions within full plant extracts, or long-term safety. Experimental

validation is essential to confirm these network-level predictions and improve our understanding of dose, formulation, and efficacy in clinical contexts.

Future directions should go beyond validation, exploring:

- Synergistic studies on whole-plant formulations to capture compound interplay.
- Pharmacokinetic and toxicological assessments under physiological conditions.
- Clinical studies targeting specific respiratory pathologies, including viral infections.
- Integration into public health frameworks, especially in resource-limited settings.

Finally, while the cultural history of al-Jur is important, it can interact disease-relevant biological systems that offers therapeutic promise, which this study outlines as a replicable pathway from traditional use, through computational modeling, to scientific validation for converting ethnomedicines into evidence-based health solutions, and reasserts the continued significance of traditional knowledge while also introducing network pharmacology as an effective method by which natural products can be repurposed in contemporary medicine.

The reference

The reference:

1. Abu-Darwish, M. S., Cabral, C., & Salgueiro, L. (2014). Juniperus phoenicea from Jordan. *Medicinal and Aromatic Plants of the Middle-East*, 241-252.
2. Adjim, I., & Djezzar, R. (2023). *Les alternatives biologiques aux antibiotiques chez les poulets de chair* (Doctoral dissertation, Alger : École Nationale Supérieure Vétérinaire).
3. Alliance Doc. (2024, March 4). *Open Babel*. https://docs.alliancecan.ca/wiki/Open_Babel
4. Andrade, J. M., Faustino, C., Garcia, C., Ladeiras, D., Reis, C. P., & Rijo, P. (2018). Rosmarinus officinalis L.: an update review of its phytochemistry and biological activity. *Future science OA*, *4*(4), FSO283.
5. Atti-Santos, A. C., Rossato, M., Pauletti, G. F., Rota, L. D., Rech, J. C., Pansera, M. R., ... & Moyna, P. (2005). Physico-chemical evaluation of Rosmarinus officinalis L. essential oils. *Brazilian archives of biology and technology*, *48*, 1035-1039.
6. Baranová, B., Gruľová, D., Polito, F., Sedlák, V., Konečná, M., Blaščáková, M. M., ... & Poráčová, J. (2025). Artemisia herba-alba Essential Oil: Chemical Composition, Phytotoxic Activity and Environmental Safety. *Plants*, *14*(2), 242.
7. Barrajón-Catalán, E., Tomás-Menor, L., Morales-Soto, A., Bruñá, N. M., López, D. S., Segura-Carretero, A., & Micol, V. (2016). Rockroses (Cistus sp.) oils. In *Essential oils in food preservation, flavor and safety* (pp. 649-658). Academic Press.
8. Belhouala K, Benarba B. Medicinal Plants Used by Traditional Healers in Algeria: A Multiregional Ethnobotanical Study. Front Pharmacol. 2021 Nov 29;12:760492. doi: 10.3389/fphar.2021.760492. PMID: 34912221; PMCID: PMC8666619.
9. Benkhaira, N., Ech-Chibani, N., & Fikri-Benbrahim, K. (2021). Ethnobotanical survey on the medicinal usage of two common medicinal plants in Taounate Region: Artemisia herba-alba Asso and Ormenis mixta (L.) Dumort. *Ethnobotany Research and Applications*, *22*, 1-19.
10. Bosch, A. A., Biesbroek, G., Trzcinski, K., Sanders, E. A., & Bogaert, D. (2013). Viral and bacterial interactions in the upper respiratory tract. *PLoS pathogens*, *9*(1), e1003057.
11. Boubekeur, S., Messaoudi, M., Awuchi, C. G., Otekunrin, O. A., Sawicka, B., Idjeri-Mecherara, S., ... & Rebiai, A. (2022). Biological properties and polyphenols content of Algerian Cistus salviifolius L. aerial parts. *European Journal of Biological Research*, *12*(2), 163-180.
12. Boufissiou, A., Kadi, I., Benamar-Aissa, B., Boussoussa, H., Harrat, M., & Yousfi, M. (2024). In vitro study of the antioxidant, sun factor protection, antimicrobial, and antifungal activities

with molecular docking of methanolic extracts from leaves and fruit of *Phillyrea angustifolia* L. *3 Biotech*, *14*(2), 41. https://doi.org/10.1007/s13205-023-03877-5

13. Bragina, M. E., Daina, A., Perez, M. A., Michielin, O., & Zoete, V. (2022). The SwissSimilarity 2021 web tool: novel chemical libraries and additional methods for an enhanced ligand-based virtual screening experience. *International Journal of Molecular Sciences*, *23*(2), 811.

14. Caudullo, G., & de Rigo, D. (2016). Juniperus phoenicea. *European Atlas of Forest Tree Species*.

15. Chandran, U., Mehendale, N., Patil, S., Chaguturu, R., & Patwardhan, B. (2016). Network pharmacology. *Innovative approaches in drug discovery*, 127.

16. CHERIET, A., & DIFALLAH, N. (2024). *Enquête ethnobotanique sur la toxicité des Lamiaceae utilisées en médecine traditionnelle dans la wilaya de Tiaret* (Doctoral dissertation, Université ibn khaldoun-Tiaret).

17. Clark, H. L. (2021). The Islamic origins of the French colonial welfare state: hospital finance in Algeria. *European Review of History: Revue européenne d'histoire*, *28*(5-6), 689-717.

18. Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific reports*, *7*(1), 42717.

19. Dassault Systèmes BIOVIA. (2006). *Discovery Studio 2.0* [Software documentation]. Dassault Systèmes.

20. De Rigo, D., & Caudullo, G. (2016)

21. Eberhardt, J., Santos-Martins, D., Tillack, A. F., & Forli, S. (2021). AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. *Journal of Chemical Information and Modeling*, *61*(8), 3891–3898. https://doi.org/10.1021/acs.jcim.1c00203

22. Ekiert, H., Pajor, J., Klin, P., Rzepiela, A., Ślesak, H., & Szopa, A. (2020). Significance of Artemisia vulgaris L.(Common Mugwort) in the history of medicine and its possible contemporary applications substantiated by phytochemical and pharmacological studies. *Molecules*, *25*(19), 4415.

23. El Midaoui, A., Khallouki, F., Couture, R., Moldovan, F., Ismael, M. A., Ongali, B., ... & Lizard, G. (2023). Thymus atlanticus: a source of nutrients with numerous health benefits and important therapeutic potential for age-related diseases. *Nutrients*, *15*(18), 4077.

24. El Omari, N., Guaouguaou, F. E., El Menyiy, N., Benali, T., Aanniz, T., Chamkhi, I., ... & Bouyahya, A. (2021). Phytochemical and biological activities of Pinus halepensis mill., and their ethnomedicinal use. *Journal of Ethnopharmacology*, *268*, 113661.

25. Ellner, J. J. (1988). Management of acute and chronic respiratory tract infections. *The American Journal of Medicine*, *85*(3), 2-5.

26. Faris, N. S. (2014). Respiratory tract bacterial infection etiological agents and susceptibility testing. *European Scientific Journal*, *10*(30).

27. Fekih, N., Allali, H., Merghache, S., Chaïb, F., Merghache, D., El Amine, M., ... & Costa, J. (2014). Chemical composition and antibacterial activity of Pinus halepensis Miller growing in West Northern of Algeria. *Asian pacific journal of tropical disease*, *4*(2), 97-103.

28. Ghani, M. K. (2000). *Knowledge-based approaches in drug/medicinal chemistry: avenues for drug discovery: 4. A qualitative and quantitative understanding of known drug databases*. *J. Chem. Chem.*, *1*(1), 53-60.

29. Gould GS, Hurst JR, Trofor A, Alison JA, Fox G, Kulkarni MM, Wheelock CE, Clarke M, Kumar R. Recognising the importance of chronic lung disease: a consensus statement from the Global Alliance for Chronic Diseases (Lung Diseases group). Respir Res. 2023 Jan 13;24(1):15. doi: 10.1186/s12931-022-02297-y. PMID: 36639661; PMCID: PMC9838069.

30. Gugleva, V., Ivanova, N., Sotirova, Y., & Andonova, V. (2021). Dermal drug delivery of phytochemicals with phenolic structure via lipid-based nanotechnologies. *Pharmaceuticals*, *14*(9), 837.

31. Habtemariam, S. (2016). The therapeutic potential of rosemary (Rosmarinus officinalis) diterpenes for Alzheimer's disease. *Evidence-based Complementary and Alternative Medicine*, *2016*(1), 2680409.

32. Harris, S. (2004). Woody Legumes (excluding Acacias).

33. Hoff, M. (1997). *Anacardiaceae. Flore de la Nouvelle-Calédonie* [Book]. Société Botanique d'Alsace. https://www.researchgate.net/publication/271824794

34. Hope, C. (1962). Respiratory Inadequacy–its study, diagnosis, and treatment. *Res Medica*, *3*(2).

35. Ingale, S. (2023). Network pharmacology approach for validation of traditional claims of Ayurvedic

36. Iorio, F., Saez-Rodriguez, J., & Bernardo, D. D. (2013). Network based elucidation of drug response: from modulators to targets. *BMC systems biology*, *7*, 1-9.

37. Jaouadi, R., Silva, A. M., Boussaid, M., Yahia, I. B., Cardoso, S. M., & Zaouali, Y. (2019). Differentiation of phenolic composition among tunisian thymus algeriensis boiss. Et reut.(lamiaceae) populations: correlation to bioactive activities. *Antioxidants*, *8*(11), 515.

38. Kaufman, J. L. (2016). Acute Respiratory Distress Syndrome.

39. Khalil, S. Y., Youness, E. A., Ghada, B., Chebaibi, M., Mohamed, T., Elbouzidi, A., ... & Allali, A. (2025). Insecticidal Potential of Juniperus phoenicea Essential Oil against Callosobruchus maculatus: Chemical Composition, Biological Evaluation, and Molecular Docking Analysis. *Tropical Journal of Natural Product Research*, *9*(4).

40. Kim, S. (2019). Public Chemical Databases. In *Encyclopedia of Bioinformatics and Computational Biology: ABC of Bioinformatics* (pp. 628–639).

41. Lai, C. C., Shih, T. P., Ko, W. C., Tang, H. J., & Hsueh, P. R. (2020). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International journal of antimicrobial agents*, *55*(3), 105924.

42. Lopes, C. T., Franz, M., Kazi, F., Donaldson, S. L., Morris, Q., & Bader, G. D. (2010). Cytoscape Web: an interactive web-based network browser. *Bioinformatics*, *26*(18), 2347-2348.

43. MAHBOUB, N., LAIB, I., BENNACEUR, D., MERAGHNI, A., & KHERROUBI, H. (2024). PHYTOCHEMICAL PROFILING OF Artemisia herba-alba Asso BY HPLC ANALYSIS AND INVESTIGATION OF THE ANTIOXIDANT AND ANTIBACTERIAL ACTIVITIES. *Annals of Oradea University, Biology Fascicle/Analele Universităţii din Oradea, Fascicula Biologie*, *31*(2).

44. Mahmoudi, Y. (1988). La thérapeutique par les plantes les plus communes en Algérie. *Palais du livre. Blida: Imprimerie MOHLI*, *12*.

45. Makhlouf, F. Z., Squeo, G., Barkat, M., Pasqualone, A., & Caponio, F. (2019). Comparative study of total phenolic content and antioxidant properties of Quercus fruit: flour and oil. *benefits*, *18*, 20.). Quercus ilex in Europe: Distribution, habitat, usage and threats. *European Atlas of Forest Tree Species; San-Miguel-Ayanz, J., de Rigo, D., Caudullo, G., Houston Durrant, T., Mauri, A., Eds*, 152-153.

46. Matsabisa, M. G., Tripathy, S., Dassarma, B., Chabalala, H. P., & Mukherjee, P. K. (2022). African traditional herbal medicine: Addressing standardization and quality control challenges for product development. In *Evidence-Based Validation of Herbal Medicine* (pp. 561-586). Elsevier.

47. Matyga AW, Chelala L, Chung JH. Occupational Lung Diseases: Spectrum of Common Imaging Manifestations. Korean J Radiol. 2023 Aug;24(8):795-806. doi: 10.3348/kjr.2023.0274. PMID: 37500580; PMCID: PMC10400370.

48. Matyga AW, Chelala L, Chung JH. Occupational Lung Diseases: Spectrum of Common Imaging Manifestations. Korean J Radiol. 2023 Aug;24(8):795-806. doi: 10.3348/kjr.2023.0274. PMID: 37500580; PMCID: PMC10400370.

49. Mehmood, A. (2023). Role of ACE-2 Receptors in Multi-System-ic Manifestations of COVID-19. *Clin Surg*, *10*(1), 1-9.

50. Miao, R., Meng, Q., Wang, C., & Yuan, W. (2022). Bibliometric analysis of network pharmacology in traditional Chinese medicine. *Evidence-Based Complementary and Alternative Medicine*, *2022*(1), 1583773.

51. Milia, E., Bullitta, S. M., Mastandrea, G., Szotáková, B., Schoubben, A., Langhansová, L., Quartu, M., Bortone, A., & Eick, S. (2021). Leaves and fruits preparations of *Pistacia lentiscus* L.: A review on the ethnopharmacological uses and implications in inflammation and infection. *Antibiotics (Basel)*, *10*(4), 425. https://doi.org/10.3390/antibiotics10040425

52. Momtazmanesh, S., Moghaddam, S. S., Ghamari, S. H., Rad, E. M., Rezaei, N., Shobeiri, P., ... & Ibitoye, S. E. (2023). Global burden of chronic respiratory diseases and risk factors, 1990–2019: an update from the Global Burden of Disease Study 2019. *EClinicalMedicine*, *59*.

53. Nahida, A. S., & Siddiqui, A. N. (2012). Pistacia lentiscus: A review on phytochemistry and pharmacological properties. *International Journal of Pharmacy and Pharmaceutical Sciences*, *4*(4), 16-20.

54. Nasri, N., Tlili, N., Elfalleh, W., Cherif, E., Ferchichi, A., Khaldi, A., & Triki, S. (2011). Chemical compounds from Phoenician juniper berries (Juniperus phoenicea). *Natural product research*, *25*(18), 1733-1742.

55. National Institute for Occupational Safety and Health (NIOSH**).** *Occupational respiratory diseases*. Centers for Disease Control and Prevention. Retrieved June 13, 2025, from https://www.cdc.gov/niosh/topics/respiratory/default.html

56. Nediani, C., Ruzzolini, J., Romani, A., & Calorini, L. (2019). Oleuropein, a bioactive compound from *Olea europaea* L., as a potential preventive and therapeutic agent in non-communicable diseases. *Antioxidants (Basel)*, *8*(12), 578. https://doi.org/10.3390/antiox8120578

57. Occupational Safety and Health Administration (OSHA). *Occupational lung disease*. U.S. Department of Labor. Retrieved June 13, 2025, from https://www.osha.gov/SLTC/occupational_lung_disease/

58. Oliveros, J. C. (n.d.). *Venny 2.1.0* [Software]. BioinfoGP, CNB-CSIC. Retrieved June 15, 2025, from https://bioinfogp.cnb.csic.es/tools/venny/

59. Pillai, O., Dhanikula, A. B., & Parthasarula, R. (2001). Drug delivery: an odyssey of 100 years. *Current Opinion in Chemical Biology*, *5*(4), 439–446.

60. Piñero, J., Bravo, À., Queralt-Rosinach, N., Gutiérrez-Sacristán, A., Deu-Pons, J., Centeno, E., ... & Furlong, L. I. (2016). DisGeNET: a comprehensive platform integrating information on human disease-associated genes and variants. *Nucleic acids research*, gkw943.

61. Poncet, P., Charpin, D., & Sénéchal, H. (2021). Les Cupressacées des cinq continents. *Revue francaise d'allergologie*, *61*(4), 198-201.

62. Prado, P. R. D., Bettencourt, A. R. D. C., & Lopes, J. D. L. (2019). Related factors of the nursing diagnosis ineffective breathing pattern in an intensive care unit. *Revista Latino-Americana de Enfermagem*, *27*, e3153.

63. Puglielli, G. (2018). Adaptive strategies of Cistus species to Mediterranean stress factors.

64. Rawal, G., Yadav, S., & Kumar, R. (2018). Acute respiratory distress syndrome: an update and review. *Journal of translational internal medicine*, *6*(2), 74-77.

65. Righi, N., Boumerfeg, S., Fernandes, P. A., Deghima, A., Baali, F., Coelho, E., ... & Baghiani, A. (2020). Thymus algeriensis Bioss & Reut: Relationship of phenolic compounds composition with in vitro/in vivo antioxidant and antibacterial activity. *Food Research International*, *136*, 109500.

66. Russo, R., Corasaniti, M. T., Bagetta, G., & Morrone, L. A. (2015). Exploitation of cytotoxicity of some essential oils for translation in cancer therapy. *Evidence-Based Complementary and Alternative Medicine*, *2015*(1), 397821.

67. Satija B, Kumar S, Ojha UC, Gothi D. Spectrum of high-resolution computed tomography imaging in occupational lung disease. Indian J Radiol Imaging. 2013 Oct;23(4):287-96. doi: 10.4103/0971-3026.125564. PMID: 24604929; PMCID: PMC3932567.

68. Sato, S., Isobe, S., & Tabata, S. (2010). Structural analyses of the genomes in legumes. *Current opinion in plant biology*, *13*(2), 146-152.

69. Sayah, K., Marmouzi, I., Naceiri Mrabti, H., Cherrah, Y., & Faouzi, M. E. A. (2017). Antioxidant activity and inhibitory potential of Cistus salviifolius (L.) and Cistus monspeliensis (L.) aerial parts extracts against key enzymes linked to hyperglycemia. *BioMed Research International*, *2017*(1), 2789482.

70. Sharifi-Rad, J., Sureda, A., Tenore, G. C., Daglia, M., Sharifi-Rad, M., Valussi, M., ... & Iriti, M. (2017). Biological activities of essential oils: From plant chemoecology to traditional healing systems. *Molecules*, *22*(1), 70.

71. Shen F, Qin Y, Wang R, Huang X, Wang Y, Gao T, He J, Zhou Y, Jiao Y, Wei J, Li L, Yang X. Comparative genomics reveals a unique nitrogen-carbon balance system in Asteraceae. Nat Commun. 2023 Jul 20;14(1):4334. doi: 10.1038/s41467-023-40002-9. PMID: 37474573; PMCID: PMC10359422.

72. Summers, C., Todd, S. R., Vercruysse, A. G., & Moore, F. A. (2021). *Acute respiratory failure*. National Center for Biotechnology Information. Retrieved from https://www.ncbi.nlm.nih.gov/

73. Szklarczyk D, Nastou K, Koutrouli M, Kirsch R, Mehryary F, Hachilif R, Hu D, Peluso ME, Huang Q, Fang T, Doncheva NT, Pyysalo S, Bork P, Jensen LJ, von Mering C. The STRING database in 2025: protein networks with directionality of regulation. Nucleic Acids Res. 2025 Jan 6;53(D1):D730-D737. doi: 10.1093/nar/gkae1113. PMID:

74. Tahri, D., Elhouiti, F., Ouinten, M., & Yousfi, M. (2020). Historical perspective of Algerian pharmacological knowledge. *Advances in Traditional Medicine*, *20*(3), 279-290.

75. Tahri, D., Seba, M., Elhouiti, F., Ouinten, M., & Yousfi, M. (2021). Traditional Herbal Uses from Algerian Pharmacopoeia against Infectious Diseases. In *Infectious Diseases* (pp. 153-170). Bentham Science Publishers.

76. Tahri, D., Seba, M., Elhouiti, F., Ouinten, M., & Yousfi, M. (2021). Traditional Herbal Uses from Algerian Pharmacopoeia against Infectious Diseases. In *Infectious Diseases* (pp. 153-170). Bentham Science Publishers.

77. Taib, M., Rezzak, Y., Bouyazza, L., & Lyoussi, B. (2020). Medicinal uses, phytochemistry, and pharmacological activities of Quercus species. *Evidence-Based Complementary and Alternative Medicine*, *2020*(1), 1920683.

78. Thibeault, C. (2023). *Valorisation phytochimique et biologique des extractibles de bois de pin blanc* (Doctoral dissertation, Université du Québec à Chicoutimi).

79. Tomou, E. M., Lytra, K., Rallis, S., Tzakos, A. G., & Skaltsa, H. (2022). An updated review of genus Cistus L. since 2014: Traditional uses, phytochemistry, and pharmacological properties. *Phytochemistry Reviews*, *21*(6), 2049-2087.

80. Tuttolomondo, T., La Bella, S., Leto, C., Gennaro, M. C., Calvo, R., & D'Asaro, F. (2017). Biotechnical characteristics of root systems in erect and prostrate habit Rosmarinus officinalis L. accessions grown in a Mediterranean climate. *Chemical Engineering Transactions*, *58*, 769-774.

81. Wang, X., Hu, Y., Zhou, X., & Li, S. (2022). Network pharmacology and traditional medicine: Setting the new standards by combining in silico and experimental work. *Frontiers in Pharmacology*, *13*, 1002537.

82. William Potter, C., 2007. Chapter 25 Respiratory tract viruses. ncbi.nlm.nih.gov

83. Younsi, F., Trimech, R., Boulila, A., Ezzine, O., Dhahri, S., Boussaid, M., & Messaoud, C. (2016). Essential oil and phenolic compounds of Artemisia herba-alba (Asso.): Composition, antioxidant, antiacetylcholinesterase, and antibacterial activities. *International journal of food properties*, *19*(7), 1425-1438.

84. Zerrougui, L., & Bekrar, M. (2019). *Étude phytochimique et potentiel antioxydant d'une plante algérienne du genre Cistus (Cistaceae)* [Mémoire de master, Université non spécifiée]. Google Scholar

85. Zhou, Z., Chen, B., Chen, S., Lin, M., Chen, Y., Jin, S., ... & Zhang, Y. (2020). Applications of network pharmacology in traditional Chinese medicine research. *Evidence-Based Complementary and Alternative Medicine*, *2020*(1), 1646905.

86. ZITOUNI, A., CHEKROUN-BECHLAGHEM, N., GHEMBAZA, N., & BELYAGOUBI-BENHAMMOU, N. (2023). Lentisk fruits (Pistacia lentiscus L.) as sources of phytochemicals with potential health benefits: A review. *Journal of Natural Product Research and Applications*, *3*(01), 27-44.

The annex

The annex01:

The coumpounds of palnts :

CID Pubchem	Thymus algériensis, boiss et reut
79035	Tricyclene
6321405	Isoborneol
17868	alpha-Thujene
6552009	Borneol
6654	alpha-Pinene
6616	Camphene
17100	alpha-Terpineol
6427476	Verbenene
29025	Verbenone
18818	Sabinene
18827	1-Octen-3-ol
14896	beta-Pinene
79044	Delta-2-Carene
26049	Delta-3-Carene
7462	alpha-Terpinene
6989	Thymol
22311	Limonene
2758	1,8-Cineole
5320250	beta-Ocimene, (3Z)-
5281553	beta-OCIMENE, (3E)-
14525	Fenchone
6549	Linalool
180537	6-Camphenol
1252759	alpha-Campholenal
2537	Camphor
19725	alpha-Copaene
62566	beta-Bourbonene
93081	beta-Cubebene
6429301	(Z)-caryophyllene
5281515	Caryophyllene
42608158	Allo-aromadendrene
5317570	Germacrene D
10104370	beta-Bisabolene
441005	Delta-Cadinene
12306048	alpha-Cadinene
5352847	Germacrene D-4-ol
1742210	Caryophyllene oxide
6432447	Longiborneol
10398656	alpha-Cadinol
91752502	Longiborneol acetate
90473619	Caryophyllene acetate
5281761	1-Caffeoyl-beta-D-glucose
440735	Eriodictyol

5281792	Rosmarinic acid
5281793	Salvianolic acid
5281793	Salvianolic acid
95224420	Monomethyl lithospermate
439246	Naringenin
188323	Fenchone
96118	Tetramethyl-scutellarein
10364	Carvacrol

CID Pubchem	Juniperus phoenicea
79035	Tricyclene
6654	alpha-pinene
28930	alpha-fenchene
6427476	verbenene
18818	sabinene
14896	beta-pinene
31253	beta-myrcene
7460	alpha-phellandrene
26049	delta-3-carene
7463	p-cymene
22311	limonene
11142	beta-phellandrene
6428573	cis-linalool oxide
11463	terpinolene
62385	p-cymenene
6549	linalool
98497	alpha-campholene aldehyde
88302	trans-pinocarveol
2537	camphor
61126	verbenol
6432469	isomenthone
11230	4-terpineol
14529	p-cymen-8-ol
17100	alpha-terpineol
61130	myrtenal
10582	myrtenol
8815	estragole
29025	verbenone
330573	cis-carveol
6427102	alpha-fenchyl acetate
8842	citronellol
442495	pulegone
326	cuminaldehyde
8294	linalyl acetate
30248	dihydrocarvyl acetate
6448	bornyl acetate

10364	carvacrol
111037	terpinenyl acetate
442359	alpha-cubebene
1549025	neryl acetate
19725	alpha-copaene
62566	beta-bourbonene
1549026	geranyl acetate
6918391	beta-elemene
5281515	beta-caryophyllene
11095734	aromadendrene
5281520	alpha-humulene
5317570	germacrene d
442393	beta-selinene
10910653	ledene
12306047	alpha-muurolene
6429077	cis-calamenene
441005	Delta-cadinene
8835	citronellyl butanoate
91746579	trans-Cadina-1,4-diene
595385	epizonarene
12302243	alpha-calacorene
92138	elemol
5281519	germacrene b
8888	nerolidol
5352847	germacrene d-4-ol
1742210	caryophyllene oxide
6324	alpha-humulene oxide
91457	beta-eudesmol
92762	alpha-eudesmol
3084331	t-muurolol
10398656	alpha-cadinol
6432025	manoyl oxide
6450812	beta-gurjunene
520909	alpha-himachalene
42608158	allo-aromadendrene
12306046	alpha-amorphene
442351	alpha-chamigrene
11770062	cubenol
519326	13-isopimaradiene
442027	trans-ferruginol
94579	isopulegyl acetate

CID Pubchem	d’Artemisia herba-alba

14896	beta-Pinene
31253	Myrcene
2758	Eucalyptol (or 1,8-cineole)
6549	Linalool
2537	Camphor
10364	Carvacrol
6427512	Isodavanone
5370105	Davana ether
5317570	Germacrene D
519782	Davanone
31677	Unidentified
79035	Tricyclene
17868	alpha-Thujene
6654	alpha-Pinene
6616	Camphene
7462	alpha-Terpinene
22311	Limonene
261491	alpha-Thujone
91456	beta-Thujone
442463	Chrysanthenone
89437	p-Menthan-1-ol
8748	trans-beta-Terpineol
11230	4-terpineol
17100	alpha-Terpineol
84880	trans Myrtanol
6918391	beta-Elemene
5352847	Germacrene D-4-ol
55250274	Isothujol
18818	Sabinene
10703	o-cymene
7463	p-cymene
26049	Delta-3-carene
11463	alpha-terpinolene
29025	Verbenone
88302	trans-Pinocarveol

121719	Pinocarvone
6552009	Borneol
6431301	cis-Chrysanthenyl acetate
10899521	trans-Chrysanthenyl acetate
7439	Carvone
11435490	Myrtenyl acetate
3314	Eugenol
1549018	Jasmone
29025	D-Verbenone
5281515	beta-caryophyllene
3084311	Delta-cadinol
1742210	Caryophyllene oxide
441005	Delta-cadinene
92231	Spathulenol

CID pubchem	Pistacia Lentiscus
79035	tricyclene
6654	alpha-pinene
6616	camphene
18818	sabinene
14896	beta-pinene
31253	beta-myrcene
7460	alpha-phellandrene
10703	o-cymene
7463	p-cymene
11230	L-terpinen-4-ol
7439	Carvone
8163	Undecanone
5281515	Caryophyllen
93081	beta-Cubebene
92231	Spathulenol
10398656	alpha-Cadinol
7461	G-terpinene
11463	alpha-terpinolene
8914	nonanol
31289	nonanal
6552009	borneol
17100	alpha-terpineol
6448	bornyl acetate
8163	2-undecanone
111037	alpha-terpinyl acetate
19725	alpha-copaene

62566	beta-bourbonene
6918391	beta-elemene
5281515	beta-caryophyllene
7193	isoamyl benzoate
5281520	alpha-caryophyllene
42608158	allo-aromadendrene
6432308	G-muurolene
5317570	germacrene D
12306047	alpha-muurolene
10104370	beta-bisabolene
92313	G-cadinene
441005	Delta-cadinene
6429077	calamenene
92138	elemol
1742210	caryophyllene oxide
10704181	humulene epoxide II
11770062	cubenol
160799	epi-Cadinol
3084311	Delta-cadinol
91753455	aromadendrene oxide
1549992	bisabolol
2345	benzyl benzoate

CID pubchem	Cistus salvifolius
31289	nonanal
2537	Camphor
17100	1-alpha-terpineol
6989	thymol
10364	carvacrol
7127	methyl eugenol
1549778	geranyl acetone
51351709	cis-muurola-4(14),5- diene
42608158	allo-aromadendrene
12306047	alpha-muurolene
6427091	cadina-1,4-diene
92138	elemol
91748521	beta-copaen-4-ol
1742210	caryophyllene oxide
6432447	longiborneol
3893	dodecanoic acid
12046149	epi-cubenol
3084331	T-Muurolol
91753440	alpha-muurolol
92762	alpha-eudesmol
10398656	alpha-cadinol
91457	beta-eudesmol
8209	n-tetradecanol

2345	benzyl benzoate
11005	tetradecanoic acid
12366	ethyl hexadecanoate
8221	octadecanol
12403	heneicosane
12405	N-docosane
91748730	3beta-hydroxy- manoyl oxide isomer
442027	trans-ferruginol
625418	trans-ferruginyl acetate
12281309	Cis- totarol

CID pubchem	artemisia campestris
6429323	(z)-salvene
6429324	(e)-salvene
11240513	a-pinene
6616	camphene
31253	myrcene
5315406	yomogi alcohol
7460	a-phellandrene
7462	a-terpinene
7463	p-cymene
22311	limonene
2758	1,8-cineol
68346	artemisia ketone
7410	acetophenone
6428573	cis-linalool oxide
6549	linalool
5319367	cis-p-menth-2-en-1-ol
442463	chrysanthenone
88302	trans-pinocarveol
87839	cis-verbenol
527032	cis-chrysanthenol
6552009	borneol
1254	menthol
14529	p-cymene-8-ol
61130	myrtenal
10582	myrtenol
29025	verbenone
6432474	trans-dihydrocarvone
643779	neral
637566	geraniol
8294	linalool acetate
6452351	trans-myrtanol
638011	geranial
6448	bornyl acetate
30247	lavandulyl acetate
6989	thymol

6584	methyl acetate
10364	carvacrol
81505	trans-carvyl acetate
442359	a-cubebene
3314	eugenol
12303902	a-copaene
1549026	geranyl acetate
62566	b-bourbonene
93081	b-cubebene
7127	methyl eugenol
11095734	aromadendrene
5317570	germacrene d
3083834	ar-curcumene
9855795	valencene
11160	methyl isovalerate
441005	d-cadinene
6429022	trans-calamenene
8888	(z)-nerolidol
92138	elemol
92231	spathulenol
1742210	caryophyllene oxide
65575	cedrol
11770062	cubenol
91457	b-eudesmol
1549108	(z,e)-farnesol
18818	sabinene
5320250	(z)-beta-ocimene
5281553	(e)-beta-ocimene
20055523	cis-sabinene hydrate
6326181	trans-sabinene hydrate
11230	4-terpineol
17100	alpha-terpineol
442393	beta-selinene
519782	davanone
3327	farnesol

CID pubchem	Rosmarinus officinalis
7809	p-xylene
6654	alpha-pinene
6616	camphene
14896	beta-pinene
31253	myrcene
26049	3-Carene
7463	p-cymene
22311	limonene
2758	eucalyptol

7461	gamma-terpinene
11463	terpinolene
6549	linalool
7612	cyclopentadiene
2537	camphor
17100	carvomenthenol
17100	alpha-terpineol
29025	verbenone
176	aceticacid
93009	bornylacetate
5281515	beta-caryophyllene
5281520	alpha-humulene
18818	sabinene
2758	1,8-cineole
11463	alpha-terpinolene
6549	linalool
6427105	pinocamphone
6552009	borneol
11230	terpinen-4-ol
8183	1-dodecene
19725	alpha-copaene
14260	tetradecene

CIDpubchem	Pinus halepensis Mill
17868	alpha-thujene
6654	alpha-pinene
14896	beta-pinene
18818	sabinene
31253	beta-myrcene
26049	3-carene
7462	alpha-terpinene
20960	terpinene 4-acetate
22311	limonene
7460	alpha-phellandrene
5320250	beta-cis-ocimene
11463	alpha-terpinolene
442359	alpha-cubebene
5281515	beta-caryophyllene
5281520	alpha-caryophyllene
79035	tricyclene
6616	camphene
31253	myrcene
8908	hexyle acetate
18756	beta-ocimene
91508	alpha-pinene oxide

6549	linalool
2537	camphor
6552009	borneol
14529	p-cymen-8-ol
17100	alpha-terpineol
111037	alpha-terpinyl acetate
9017	citronellyl acetate
6432119	Tricyclo[4.4.0.0(2,7)]dec-3-ene, 1,3-dimethyl-8-(1-methylethyl)-, stereoisomer
6429301	(z)-caryophyllene
5317844	alpha-guaiene
11095734	aromadendrene
5281520	alpha-humulene
42608158	allo-aromadendrene
91723653	germacrene-d
13894537	bicyclogermacrene
10104370	beta-bisabolene
441005	Delta-cadinene
12315492	beta-sesquiphellandrene
92138	elemol
3084311	Delta-cadinol

CIDpubchem	Phillyrea angustifolia
8468	Vanillic acid
10742	Syringic acid
73399	Pinoresinol
332427	Lariciresinol
486614	Pinoresinol 4-O-beta-d-glucopyranoside
5280637	Luteolin-7-O-glucoside (Cynaroside)
5280704	Apigetrin
5281544	Oleuropein
6450302	Demethyloleuropein
56842347	Oleuropein aglycone
74407576	Isolariciresinol 4â€²-O-beta-d-glucoside

CID pubchem	Quercus Ilex
6184	Hexanal
356	Octane
5281168	trans-2-Hexenal
8130	Heptanal
11240513	a-Pinene
6616	Camphene
14896	beta-Pinene
31253	Myrcene

454	Octanal
7463	p-Cymene
22311	Limonene
957	1-Octanol
11463	alpha-Terpinolene
31289	Nonanal
6552009	endo-Borneol
11230	4-Terpineol
4133	Methylsalicylate
443162	(-)-alpha-Terpineol
9895	beta-Cyclocitral
61124	beta-Cyclohomocitral
3314	Eugenol
68057	1,2,3,4-Tetrahydro-1,1,6-Trimethylnaphthalene
442359	alpha-Cubebene
5373545	1-Mesitylbuta-1,3-diene
19725	alpha-Copaene
95495	6,10-Dimethyl-2-undecanone
62566	beta-Bourbonene
32052	beta-Damascone
638014	beta-Ionone
1549041	cis-Isoeugenol
5281515	trans-Caryophyllene
11095734	Aromadendrene
12306046	alpha-Amorphene
91723653	Germacrene-D
10910653	(+)-Ledene
441005	Delta-Cadinene
12302243	alpha-Calacorene
110745	Palustrol
3893	Dodecanoic acid
1742210	Caryophyllene oxide
11074994	(+)-Ledol
11006	Hexadecane
10878761	Hinesol
91457	beta-Eudesmol
92762	alpha-Eudesmol
12398	n-Heptadecane
11005	Tetradecanoic acid
11635	n-Octadecane
10408	6,10,14-Trimethyl-2-pentadecanone
985	Palmitic acid
12403	n-Heneicosane
5280435	Phytol
9316	9,12,15-Octadecatrienoic acid, methyl ester, (9Z,12Z,15Z)-
74138	1-Docosene
181154	1-Tricosene
82436	1-Tetracosene

528972	1-Pentacosene
29303	1-Hexacosene
528971	1-Heptacosene
87821	1-Octacosene
156989	1-Nonacosene
87639	1-Triacontene
12410	n-Hentriacontane
370	Gallic acid
82755	Hydroxytyrosol
637542	p-Coumaric acid
9064	Catechin
168346974	(-) Epicatechin
107905	Epicatechin gallate
5280863	Kaempferol
5280805	Rutin
12575	Isovanillic acid
151725	3,4-Dihydroxymandelaldehyde
637511	Trans-cinnamaldehyde
5281417	Aesculin (Esculin)
323	Coumarin
8417	Scoparone
5280535	4-Coumaryl alcohol
5281855	Ellagic acid
370	Gallic acid
107957	Catechin hydrate
72	Protocatechuic acid
72	3,4-dihydroxybenzoic acid
3469	Gentisic acid
689043	Caffeic acid
1794427	Chlorogenic acid
10742	Syringic acid
8468	Vanillic acid
637542	P-coumaric acid
445858	Ferulic acid
442428	Naringin
338	Salycilic acid
5281855	Ellagic acid
5280343	Quercetin
439246	Naringenin
5280863	Kaempferol

The annex02:

The last Table of compound plants use:

CID PubChem – Smiles -Bioavailability Score

1-Thymus algeriensis, boiss et reut **:**

CID	SMILES	Bioavailability Score
96118	[H]C1=C(c2c([H])c([H])c(c([H])c2[H])OC([H])([H])[H])Oc2c([H])c(c(c(c2C1=O)OC([H])([H])[H])OC([H])([H])[H])OC([H])([H])[H]	0.55
188323	[H]C1=C(c2c([H])c([H])c(c([H])c2[H])O[H])Oc2c([H])c(c(c(c2C1=O)O[H])OC([H])([H])[H])OC([H])([H])[H]	0.55
90473616	[H]C([H])([H])C(=O)O[C@]12C([H])([H])C([H])([H])C([H])([H])[C@@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]3([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]23[H])C1([H])[H]	0.55
91752504	[H]C([H])([H])C(=O)O[C@]1([H])[C@@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]3([H])[C@]1([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[C@@]23C([H])([H])[H]	0.55
5352847	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])=C([H])[C@](C([H])([H])[H])(C([H])([H])C1([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6432447	[H]C([H])([H])C1(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])[C@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@@]1([H])[C@]3([H])O[H]	0.55
10398656	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
19725	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
62566	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@@]1([H])[C@@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]12C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
93081	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]23[C@@]1([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5317570	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6429301	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55

10104370	[H]C([H])=C(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])[C@]1([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C1([H])[H]	0.55
12306048	[H]C1=C(C([H])([H])[H])[C@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
42608160	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55

2-Juniperus phoenicea :

CID	SMILES	Bioavailability Score
442027	[H]c1c2c(c([H])c(c1C([H])(C([H])([H])[H])C([H])([H])[H])O[H])[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]1([H])C([H])([H])C2([H])[H]	0.55
519326	[H]C([H])=C([H])[C@]1(C([H])=C2C([H])([H])C([H])([H])[C@@]3([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[C@]3(C([H])([H])[H])[C@@]2([H])C([H])([H])C1([H])[H])C([H])([H])[H]	0.55
8835	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])OC(C([H])([H])C([H])([H])C([H])([H])[H])=O	0.55
8888	[H]C([H])=C([H])[C@@](C([H])([H])[H])(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])O[H]	0.55
91457	[H]C([H])=C1C([H])([H])C([H])([H])C([H])([H])[C@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]12[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
92138	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
92762	[H]C1=C(C([H])([H])[H])[C@]2([H])C([H])([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])C([H])([H])C1([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
3084331	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
5352847	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])=C([H])[C@](C([H])([H])[H])(C([H])([H])C1([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
10398656	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
11770062	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
19725	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
62566	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@@]1([H])[C@@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]12C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
442351	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2(C(=C([H])C([H])([H])C([H])([H])C2(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H])C1([H])[H]	0.55

442359	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]23C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
442393	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C(=C([H])[H])[C@]2([H])C1([H])[H]	0.55
520909	[H]C([H])=C1C([H])([H])C([H])([H])C([H])([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C([H])([H])[C@@]12[H]	0.55
595385	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])C1=C(C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5281519	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C(=C(C([H])([H])[H])C([H])([H])[H])C1([H])[H]	0.55
5281520	[H]C1=C([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
5317570	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6450812	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]3([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]3([H])[C@]12[H]	0.55
6918391	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C(=C([H])[H])C([H])([H])[H])C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H]	0.55
10910653	[H]C([H])([H])C1=C2C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]2([H])[C@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@]2([H])C([H])([H])C1([H])[H]	0.55
11095734	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
12306046	[H]C1=C(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
12306047	[H]C1=C(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
42608160	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
91746576	[H]C1=C2[C@@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
6429077	[H]c1c([H])c2c(c([H])c1C([H])([H])[H])[C@@]([H])(C([H])([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])[H]	0.55
12302243	[H]C1=C(c2c([H])c([H])c(c([H])c2[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
6448	[H]C([H])([H])C(=O)O[C@]1([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])[C@@]1(C([H])([H])[H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
8294	[H]C([H])=C([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])OC(C([H])([H])[H])=O	0.55
302	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C	0.55

48	@]([H])(C1([H])[H])OC(C([H])([H])[H])=O	
94579	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])C([H])([H])[C@@]1([H])OC(C([H])([H])[H])=O	0.55
111037	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C1([H])[H])C(C([H])([H])[H])(C([H])([H])[H])OC(C([H])([H])[H])=O	0.55
1549025	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])OC(C([H])([H])[H])=O)C([H])([H])[H]	0.55
1549026	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])OC(C([H])([H])[H])=O)C([H])([H])[H]	0.55
6427102	[H]C([H])([H])C(=O)O[C@]1([H])C(C([H])([H])[H])(C([H])([H])[H])[C@]2([H])C([H])([H])C([H])([H])[C@@]1(C([H])([H])[H])C2([H])[H]	0.55
6428573	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@](C([H])([H])[H])(C([H])([H])[H])O[H])O1	0.55

3-Artemisia herba-alba:

CID	SMILES	Bioavailability Score
519782	[H]C([H])=C([H])[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])([C@]([H])(CC([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])=O)C([H])([H])[H])O1	0.55
6427512	[H]C([H])=C([H])[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])([C@]([H])(CC([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])=O)C([H])([H])[H])O1	0.55
5370105	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C(=C2C([H])=C([H])C(C([H])([H])[H])(C([H])([H])[H])O2)C([H])([H])[H])O1	0.55
3084311	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
5352847	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])=C([H])[C@](C([H])([H])[H])([H])C([H])([H])C1([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
92231	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]12[H])O[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5317570	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6918391	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C(=C([H])[H])C([H])([H])[H])C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H]	0.55
6431301	[H]C1=C(C([H])([H])[H])[C@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@]([H])(C1([H])[H])[C@]2([H])OC(C([H])([H])[H])=O	0.55
10899521	[H]C1=C(C([H])([H])[H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]([H])(C1([H])[H])[C@@]2([H])OC(C([H])([H])[H])=O	0.55
11435490	[H]C1=C(C([H])([H])OC(C([H])([H])[H])=O)[C@@]2([H])C([H])([H])[C@@]([H])(C1([H])[H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
1549018	[H]C(=C([H])C([H])([H])C([H])([H])[H])C([H])([H])C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C1=O	0.55

3314	[H]C([H])=C([H])C([H])([H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])O[H]	0.55

4-Pistacia Lentiscus:

CID	SMILES	Bioavailability Score
92138	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
160799	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
1549992	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C1([H])[H])O[H]	0.55
3084311	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
10398656	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
11770062	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
92231	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]12[H])O[H]	0.55
2345	[H]c1c([H])c([H])c(C(=O)OC([H])([H])c2c([H])c([H])c([H])c([H])c2[H])c([H])c1[H]	0.55
19725	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
62566	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@@]1([H])[C@@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]12C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
92313	[H]C([H])=C1C([H])([H])C([H])([H])[C@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]12[H]	0.55
93081	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]23[C@@]1([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5281520	[H]C1=C([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
5317570	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6432308	[H]C([H])=C1C([H])([H])C([H])([H])[C@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]12[H]	0.55
6918391	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C(=C([H])[H])C([H])([H])[H])C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H]	0.55

12306047	[H]C1=C(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
42608160	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
6429077	[H]c1c([H])c2c(c([H])c1C([H])([H])[H])[C@@]([H])(C([H])([H])C([H])([H])[C@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6448	[H]C([H])([H])C(=O)O[C@]1([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])[C@@]1(C([H])([H])[H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
111037	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C1([H])[H])C(C([H])([H])[H])(C([H])([H])[H])OC(C([H])([H])[H])=O	0.55
7193	[H]c1c([H])c([H])c(C(=O)OC([H])([H])C([H])([H])C([H])(C([H])([H])[H])C([H])([H])[H])c([H])c1[H]	0.55
8163	[H]C([H])([H])C(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H])=O	0.55

5-Cistus salvifolius :

CID	SMILES	Bioavailability Score
442027	[H]c1c2c(c([H])c(c1C([H])(C([H])([H])[H])C([H])([H])[H])O[H])[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])([H])[H])[H]	0.55
12281309	[H]c1c([H])c(c(c2c1[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]1([H])C([H])([H])C2([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])O[H]	0.55
11005	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)O[H]	0.85
91457	[H]C([H])=C1C([H])([H])C([H])([H])C([H])([H])[C@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]12[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
92138	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
		0.55
3084331	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
6432447	[H]C([H])([H])C1(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])[C@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@@]1([H])[C@]3([H])O[H]	0.55
10398656	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
12046149	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([C@]([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55

91753440	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@]1([H])[C@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
91748520	[H]C([H])=C1[C@]2([H])[C@]3([H])[C@]([H])(C([H])([H])[C@@]1([H])O[H])[C@@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@]3([H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
8209	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O[H]	0.55
2345	[H]c1c([H])c([H])c(C(=O)OC([H])([H])c2c([H])c([H])c([H])c([H])c2[H])c([H])c1[H]	0.55
6427091	[H]C1=C2[C@@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
12306047	[H]C1=C(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
42608160	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
51351708	[H]C([H])=C1C([H])=C2[C@@]([H])(C([H])([H])C1([H])[H])[C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
3893	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)O[H]	0.85
1549778	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])C([H])([H])C(C([H])([H])[H])=O)C([H])([H])[H]	0.55
7127	[H]C([H])=C([H])C([H])([H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])OC([H])([H])[H]	0.55

6-Artemisia campestris :

CID	SMILES	Bioavailability Score
519782	[H]C([H])=C([H])[C@@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])([C@]([H])(C(C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])=O)C([H])([H])[H])O1	0.55
8888	[H]C([H])=C([H])[C@@](C([H])([H])[H])(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])O[H]	0.55
65575	[H]C([H])([H])C1(C([H])([H])[H])[C@]2([H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]23C([H])([H])C([H])([H])[C@](C([H])([H])[H])([C@]1([H])C3([H])[H])O[H]	0.55
91457	[H]C([H])=C1C([H])([H])C([H])([H])C([H])([H])[C@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[H])[C@@]12[H])C(C([H])([H])[H])([H])(C([H])([H])[H])O[H]	0.55

92138	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
11770062	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H])O[H]	0.55
3327	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])O[H])C([H])([H])[H])C([H])([H])[H]	0.55
1549108	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])O[H])C([H])([H])[H])C([H])([H])[H]	0.55
92231	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@]2([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])[C@@]12[H])O[H]	0.55
62566	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@@]1([H])[C@@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]12C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
93081	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]23[C@@]1([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
442359	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]23C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
442393	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C(=C([H])[H])[C@]2([H])C1([H])[H]	0.55
5317570	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
9855795	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])([H])C2=C([H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@]2(C([H])([H])[H])C1([H])[H]	0.55
11095734	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55

12303902	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]2(C([H])([H])[H])[C@@]3([H])C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6429022	[H]c1c([H])c2c(c([H])c1C([H])([H])[H])[C@]([H])(C([H])([H])C([H])([H])[C@]2([H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
6448	[H]C([H])([H])C(=O)O[C@]1([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])[C@@]1(C([H])([H])[H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
8294	[H]C([H])=C([H])[C@](C([H])([H])[H])(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])OC(C([H])([H])[H])=O	0.55
30247	[H]C([H])=C(C([H])([H])[H])[C@]([H])(C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])OC(C([H])([H])[H])=O	0.55
1549026	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])C(=C([H])C([H])([H])OC(C([H])([H])[H])=O)C([H])([H])[H]	0.55
81505	[H]C([H])=C(C([H])([H])[H])[C@]1([H])C([H])([H])C([H])=C(C([H])([H])[H])[C@]([H])(C1([H])[H])OC(C([H])([H])[H])=O	0.55
7127	[H]C([H])=C([H])C([H])([H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])OC([H])([H])[H]	0.55
6428573	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C(C([H])([H])[H])(C([H])([H])[H])O[H])O1	0.55
3314	[H]C([H])=C([H])C([H])([H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])O[H]	0.55

7-Rosmarinus officinalis :

CID	SMILES	Bioavailability Score
19725	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5281520	[H]C1=C([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
14260	[H]C([H])=C([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]	0.55
93009	[H]C([H])([H])C(=O)O[C@]1([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])[C@@]1(C([H])([H])[H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
8183	[H]C([H])=C([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]	0.55

8-Pinus halepensis Mill :

CID	SMILES	Bioavailability Score
92138	[H]C([H])=C([H])[C@]1(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]1([H])C(=C([H])[H])C([H])([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
3084311	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])[C@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])O[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
442359	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]23C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
5281520	[H]C1=C([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C1([H])[H]	0.55
5317844	[H]C([H])=C(C([H])([H])[H])[C@@]1([H])C([H])([H])C2=C(C([H])([H])C([H])([H])[C@]2([H])C([H])([H])[H])[C@@]([H])(C([H])([H])[H])C([H])([H])C1([H])[H]	0.55
6429301	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
6432119	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
10104370	[H]C([H])=C(C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H])[C@]1([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C1([H])[H]	0.55
11095734	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
12315492	[H]C([H])=C1C([H])=C([H])[C@]([H])(C([H])([H])C1([H])[H])[C@@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])[H]	0.55
13894537	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])C([H])=C(C([H])([H])[H])C([H])([H])C1([H])[H]	0.55
42608160	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
91723656	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
9017	[H]C(=C(C([H])([H])[H])C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])OC(C([H])([H])[H])=O	0.55

20960	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@](C1([H])[H])(C([H])(C([H])([H])[H])C([H])([H])[H])OC(C([H])([H])[H])=O	0.55
111037	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C1([H])[H])C(C([H])([H])[H])(C([H])([H])[H])OC(C([H])([H])[H])=O	0.55

9-Phillyrea angustifolia:

CID	SMILES	Bioavailability Score
5280704	[H]C1=C(c2c([H])c([H])c(c([H])c2[H])O[H])Oc2c([H])c(c([H])c(c2C1=O)O[H])O[C@@]1([H])[C@@]([H])([C@]([H])([C@@]([H])([C@@]([H])(C([H])([H])O[H])O1)O[H])O[H])O[H]	0.55
332427	[H]c1c([H])c(c(c([H])c1C([H])([H])[C@@]1([H])C([H])([H])O[C@]([H])(c2c([H])c([H])c(c(c2[H])OC([H])([H])[H])O[H])[C@@]1([H])C([H])([H])O[H])OC([H])([H])[H])O[H]	0.55
73399	[H]c1c([H])c(c(c([H])c1[C@]1([H])[C@@]2([H])C([H])([H])O[C@]([H])(c3c([H])c([H])c(c(c3[H])OC([H])([H])[H])O[H])[C@@]2([H])C([H])([H])O1)OC([H])([H])[H])O[H]	0.55
10742	[H]c1c(C(=O)O[H])c([H])c(c(c1OC([H])([H])[H])O[H])OC([H])([H])[H]	0.56
8468	[H]c1c([H])c(c(c([H])c1C(=O)O[H])OC([H])([H])[H])O[H]	0.85

10-Quercus Ilex :

CID	SMILES	Bioavailability Score
52814117	[H]C1=C([H])c2c([H])c(c(c([H])c2OC1=O)O[H])O[C@@]1([H])[C@@]([H])([C@]([H])([C@@]([H])([C@@]([H])(C([H])([H])O[H])O1)O[H])O[H])O[H]	0.55
9316	[H]C(=C([H])C([H])([H])C([H])=C([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)OC([H])([H])[H])C([H])([H])C([H])=C([H])C([H])([H])C([H])([H])[H]	0.55
528086	[H]c1c([H])c(c([H])c([H])c1C1=C(C(c2c(c([H])c(c([H])c2O1)O[H])O[H])=O)O[H])O[H]	0.55

3		
985	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)O[H]	0.85
12398	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]	0.55
11005	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)O[H]	0.85
11006	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]	0.55
91457	[H]C([H])=C1C([H])([H])C([H])([H])C([H])([H])[C@]2(C([H])([H])[H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[C@@]12[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
92762	[H]C1=C(C([H])([H])[H])[C@]2([H])C([H])([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]2(C([H])([H])[H])C([H])([H])C1([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H]	0.55
10878761	[H]C1=C(C([H])([H])[H])[C@]2(C([H])([H])C([H])([H])[C@]([H])(C2([H])[H])C(C([H])([H])[H])(C([H])([H])[H])O[H])[C@@]([H])(C([H])([H])[H])C([H])([H])C1([H])[H]	0.55
11074994	[H]C([H])([H])C1(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])[C@@](C([H])([H])[H])([C@]3([H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])[H])[C@]3([H])[C@@]12[H])O[H]	0.55
8417	[H]C1=C([H])c2c([H])c(c(c([H])c2OC1=O)OC([H])([H])[H])OC([H])([H])[H]	0.55
19725	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]2([H])[C@@]3([H])C1([H])[H]	0.55
62566	[H]C([H])=C1C([H])([H])C([H])([H])[C@]2([H])[C@@]1([H])[C@@]1([H])[C@@]([H])(C([H])([H])C([H])([H])[C@]12C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
441005	[H]C1=C(C([H])([H])[H])C([H])([H])C([H])([H])C2=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]([H])(C([H])(C([H])([H])[H])C([H])([H])[H])[C@]12[H]	0.55
442359	[H]C1=C(C([H])([H])[H])[C@]2([H])[C@@]3([H])[C@@]([H])(C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]23C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
5281515	[H]C([H])=C1C([H])([H])C([H])([H])C([H])=C(C([H])([H])[H])C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])C([H])([H])[C@]12[H]	0.55
10910653	[H]C([H])([H])C1=C2C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])[C@@]2([H])[C@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@]2([H])C([H])([H])C1([H])[H]	0.55

11095734	[H]C([H])=C1C([H])([H])C([H])([H])[C@@]2([H])C(C([H])([H])[H])(C([H])([H])[H])[C@@]2([H])[C@@]2([H])[C@@]1([H])C([H])([H])C([H])([H])[C@@]2([H])C([H])([H])[H]	0.55
12306046	[H]C1=C(C([H])([H])[H])[C@@]2([H])C([H])([H])C([H])([H])C(=C([H])[C@@]2([H])[C@]([H])(C1([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
91723656	[H]C([H])=C1C([H])=C([H])[C@@]([H])(C([H])([H])C([H])([H])C(=C([H])C([H])([H])C1([H])[H])C([H])([H])[H])C([H])(C([H])([H])[H])C([H])([H])[H]	0.55
3893	[H]C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C(=O)O[H]	0.85
12302243	[H]C1=C(c2c([H])c([H])c(c([H])c2[C@@]([H])(C1([H])[H])C([H])(C([H])([H])[H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
95495	[H]C([H])([H])C(C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(C([H])([H])[H])C([H])([H])C([H])([H])C([H])(C([H])([H])[H])C([H])([H])[H])=O	0.55
10742	[H]c1c(C(=O)O[H])c([H])c(c(c1OC([H])([H])[H])O[H])OC([H])([H])[H]	0.56
68057	[H]c1c([H])c2c(c([H])c1C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C2(C([H])([H])[H])C([H])([H])[H]	0.55
5373545	[H]C([H])=C([H])C([H])=C([H])c1c(c([H])c(c([H])c1C([H])([H])[H])C([H])([H])[H])C([H])([H])[H]	0.55
8468	[H]c1c([H])c(c(c([H])c1C(=O)O[H])OC([H])([H])[H])O[H]	0.85
12575	[H]c1c([H])c(c(c([H])c1C(=O)O[H])O[H])OC([H])([H])[H]	0.85
1549041	[H]C(=C([H])C([H])([H])[H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])O[H]	0.55
3314	[H]C([H])=C([H])C([H])([H])c1c([H])c([H])c(c(c1[H])OC([H])([H])[H])O[H]	0.55