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Review Article

Advances in the Genus *Pyracantha*: From Traditional Healing to Modern Therapeutics

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ABSTRACT

Pyracantha (Rosaceae family) is the name of evergreen shrub plants that are widely spread in Asia and Europe, and it is traditionally utilized in folk remedy to treat several diseases. Various species for example *Pyracantha crenulata, Pyracantha fortuneana, Pyracantha coccinea, Pyracantha koidzumii and Pyracantha angustifolia* possess nutritional and medicinal importance. The current review provides information about ethno medicinal uses, phytochemicals composition, and pharmacological properties of *Pyracantha* species. Bioactive compounds that include flavonoids, phenolic acids, polysaccharides, triterpenoids, organic acids, anthocyanins, carotenoids, vitamins, and minerals have been identified in *Pyracantha* during phytochemical studies. The genus *Pyracantha* possess strong antioxidant, anti-inflammatory, antimicrobial activity, antibacterial, antidiabetic, antihypertensive, anticancer, photoaging, analgesic, anti-hyperlipidemic and hepatoprotective activities *in vitro* and *in vivo* models.

Keywords: Anticancer, Antidiabetic, Antihypertensive, Antioxidant, Bioactive compounds, *Pyracantha*.

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INTRODUCTION

Pyracantha is a type of genus shrubs that belong to the *Rosaceae* family, Amygdaloideae subfamily and Rosales order. The total number of the species present in this genus ranges between 7-10 species, and these plants are also known as firethorn plants. The *Pyracantha* is a term derived from two Greek words 'pyr' which means fire and 'acantha' which means thorn indicating the plant's sharp thorns and bright, fiery fruits.[1-3]

Plants of the *Pyracantha* genus are evergreen or semi-evergreen and are widely distributed in Asia, Europe, and the Himalayan regions. In India, species such as *Pyracantha* are found in the temperate Himalayan belt, growing naturally in forests, hillsides, and along roadsides.[4,5]

Morphologically, *Pyracantha* plants are dense, bushy shrubs with hard woody stems and strong thorns. The leaves are small to medium-sized, oval or lance-shaped, and dark green with a glossy surface. During the spring season, the plants produce numerous small white flowers arranged in clusters. These flowers later develop into berry-like fruits that turn red, orange, or yellow in autumn and winter. The fruits of *Pyracantha* are rich in natural pigments and remain attached to the plant for long periods, making them important for ecological balance as they serve as food for birds and small animals. Although the fruits are not commonly consumed by humans in raw form, they are used in some regions in the processed form such as jam and jelly.[1]

Pyracantha has a long history of use in traditional and folk medicine where fruits, leaf and bark have found various applications. In Himalayan and Chinese traditional practices, *Pyracantha* species are used to manage conditions like digestive disorders, inflammation, infections, and wound healing. It is also used as diuretic and tonic properties. The plants are also believed to strengthen the heart and improve blood circulation.[2,6,7]

The genus *Pyracantha* is rich in various phytochemical constituents that contribute to its medicinal and therapeutic properties. Different species of *Pyracantha* have been reported many numbers of secondary metabolites i.e. flavonoids (quercetin, kaempferol, rutin), polyphenols (chlorogenic acid, caffeic acid, ferulic acid, gallic acid), triterpenoids (ursolic acid, oleanolic acid, pyracrenic acid), and these components represents broad range of biological activities, such as antioxidant, anti-inflammatory, antimicrobial, anticancer and antidiabetic activities.[8-11]

Some Species of genus *Pyracantha*

The various species of *Pyracantha* genus has been shown in Table 1.

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Pyracantha coccinea M. Roem

- **Synonyms:** *Cotoneaster Pyracantha* (L.) Spach, *Crataegus Pyracantha* Pers., *Mespilus Pyracantha* (L.) All.[1]
- **Common names:** Scarlet firethorn, firethorn, Red firethorn.[1]

Geographical Distribution

Pyracantha coccinea indigenous to certain areas of southern and central Italy. It is also found across the Anatolian parts of Turkey, as well as in northern Iran, Crimea, Southern Europe and the Caucasus. Since the 16th century, this evergreen shrub has also been widely cultivated in Northern Italy as an ornamental species for gardens.[1,3]

Botanical Description

This plant is a thorny shrub that can grow up to about 5 meters tall. Its twigs are thin and soft, with fine hairs when young, but they become smooth and reddish-brown as they mature. The leaves are long and narrow, ranging from oblong to lance shaped and are about 25-30 mm in length. Their edges have small, saw-like teeth. The flowers are creamy white and appear in small, closely packed clusters.[1,2]

Traditional Uses

Pyracantha coccinea has been traditionally used in Europe for medicinal purposes, particularly as a heart soother. The leaves have historically been used in Turkey for treating diarrhea and urinary diseases. The fruit is eaten for medicinal purposes and are used for the treatment of dysentery and various stomach complaints. Plant extracts have also demonstrated promise in traditional medicine practices for conditions such as hypertension and diabetes. It is used in regulation of the menstrual cycle and relief from constipation.[2,12]

Reported phytoconstituents

The reported phytoconstituents present in *Pyracantha coccinea* M. Roem. had been shown in Table 2 and some chemical structures presented in Figure 1.

Reported pharmacological activities

The reported pharmacological activities of *Pyracantha coccinea* M.Roem. such as antioxidant, antibacterial, analgesic, cytotoxic activity, antimutagenic are shown in Figure 2 and Table 3.

Antioxidant Activity

The anti-oxidant ability of the fruit extracts from *Pyracantha coccinea* was determined by using DPPH free radical scavenging method by comparing the efficacy of ethanol and methanol isolates at various concentrations that is 0.25, 0.5, 1, and 2 mg/mL, where ascorbic acid served as the control. The findings revealed in which DPPH scavenging activity was increasing with an increase in the concentration of the extract. At 0.25 mg/mL concentration, the ethanol extract confirmed 40.65±2.41% inhibition, while the methanol extract exhibited 29.38±0.97%, while the ascorbic acid inhibited DPPH by 82.25±1.13%. At a concentration of 0.5 mg/mL, the ethanol and methanol extracts had 58.99±0.86% and 46.35±1.68% inhibition, respectively, and ascorbic acid demonstrated 90.93±1.38% inhibition. At 1 mg/mL, the scavenging activity rose to 74.29±1.96% and 55.51±2.80% for the ethanol and methanol extracts, respectively, compared to 94.43±0.47% for the standard. At 2 mg/mL, scavenging effect was 80.61±1.04% of the ethanol extract and 65.29±1.65% in the methanol extract, while ascorbic acid had a scavenging effect of 96.48±0.46%. Thus, the ethanol extract exhibited comparatively better DPPH scavenging effect than the methanol extract, but it was less effective than the standard antioxidant ascorbic acid.[23]

Antimicrobial activity

The Minimum inhibition concentration of the fruit aqueous extract and FeNPs of fruit extract on Gram-negative (*Y. pseudotuberculosis* ATCC 911, *E. coli* ATCC 25922, *P. vulgaris* ATCC 13315, and *P. aeruginosa* ATCC 43288) and Gram-positive (*S. pyogenes* ATSC 19615, *S. aureus* ATCD 25923, and *B. subtilis* ATCB 6633) bacteria were determined by the fluid micro-dilution procedure. Different concentrations of the fruit extracts were varied between 90 to 0.17 mg/mL, and the nanoparticles were evaluated in a range of 60 to 0.05 mg/mL. Fruit extract showed activity against all tested bacteria, where MIC values of 1.25-40 mg/mL, being most effective against *Yersinia pseudotuberculosis* (MIC 1.25 mg/mL). Biosynthesis of FeNPs resulted in much better antimicrobial activities of fruit extract, with MIC of 0.75 mg/mL for most bacteria and 0.375 mg/mL for *Pseudomonas aeruginosa*. In comparison with the crude extract, FeNPs were 53-fold higher activity opposed to *P. aeruginosa, S. aureus*, and *P. vulgaris*, 27-fold higher activity against *S. pyogenes*, and 13-fold higher effect opposed to *E. coli*.[24]

Antiproliferative activity

Antiproliferative activity of methanol and ethanolic fruit extract of *Pyracantha coccinea* fruits was studied using A549 cells by (3-(4,5-dimethylthiazole-2-yl)-2,5-Diphenyltetrazolium Bromide assay (MTT). Various concentrations of 25, 50, 100, and 200 µg/mL of both extracts were used for study. The findings revealed that both the methanol and ethanol extract have dose-dependent antiproliferative activity, as cell proliferation decreased with an increase in the concentrations of the extracts. Between the two extracts, the ethanol extract has high antiproliferative activity than the methanol extract at all the concentrations used.[15]

Larvicidal Activity

Methanolic fruit extract of *Pyracantha coccinea* against second instar Culex larvae has been investigated. Five concentrations of the fruit extract (62.5, 125, 250, 500, and 1000 ppm) have been tested, and their larvicidal activity has been determined at 24, 48, 72, and 96 hr of exposure period. The extract exhibited both dose and time-dependent influence on the larvae mortality. The values of LC_{50} and LC_{90} were 32110.12 ppm and 808,652.32 ppm, correspondingly. From these results, it could be concluded that the methanolic fruit extract of *Pyracantha coccinea* is characterized by the larvicidal activity on Culex larvae.[25]

Cytotoxic Activity

The cytotoxicity potential of Silver Nanoparticles (AgNPs) and Zinc Nanoparticles (ZnNPs) prepared through the extract of the fruit was evaluated by MTT assay using C6, HT29, MCF7, and L929 cell lines from American Type Culture Collection (ATCC). Different concentrations of the nanoparticles, including 0, 6, 12, 25, 50, and 100 µM, were applied to the cells, and the absorbance at 540 nm was measured to determine cell viability. The positive control for the test was represented by cisplatin. The IC_{50} value for the MCF7 cell line was 65.88±7.07 µM, while that for cisplatin was 26.34±3.72 µM, which is much lower, demonstrating that cisplatin is more potent against MCF7 cells. Conversely, when HT29 cells were tested, it became clear that the nanoparticles have much stronger antiproliferative properties than cisplatin. Thus,

Table 1: Various species of *Pyracantha* with Traditional uses.

Sl. No.	Species	Synonyms	Common names	Distribution	Traditional uses	References
1.	Pyracantha coccinea	*Cotoneaster Pyracantha* (L.) Spach, *Crataegus Pyracantha* Pers., Mespilus *Pyracantha* (L.) All.	Scarlet firethorn	Native to southern Europe, Turkey, Western Asia	Used to cure diarrhea. Having cardiac, diuretic and tonic properties.Used as heart soother.	[1,4]
2.	Pyracantha angustifolia	Cotoneaster angustifolius	Narrowleaf firethorn, Woolly firethorn	Native to southwest China, widely naturalized in SouthAfrica, Australia, New Zealand	It is used to treat body pains. Used for gastrointestinal ailments.	[1,12]
3.	Pyracantha fortuneana	Possible syn.*P. crenatoserrata*	Broad-leaf firethorn	China, Japan and several temperate countries.	Used against toothache, pain, swelling.	[1,10]
4.	Pyracantha crenulata	*Mespilus crenulata* D. Don, *Cotoneaster crenulatus* K.Koch	Himalayan firethorn, Nepalese firethorn or Hawthorn	Himalayan region including India, Nepal, Bhutan, Pakistan, China and Myanmar.	Used to treat hypertension, earaches, constipation, anemia. Used for menstrual disorders.	[1,2,13]
5.	Pyracantha koidzumii	*Cotoneaster koidzumii* Hayata	Taiwan firethorn	Native to Taiwan	Used to treat stomach-related problems	[14]
6.	Pyracantha atalantioides	Sportella atalantioides	Gigg's firethorn	Native to central and southern china	Used to treat general health.	[1,4]
7.	Pyracantha crenatoserrata	*P. fortuneana*,*Photinia crenatoserrata*,*P. crenulata* var. *yunnanensis*,*P. gibbsii* var. *yunnanensis*,*P. Yunnanensis*	Huo ji	Native to southwestern China	It is used in the preparation of beverages, jams and fermented products.	[15]

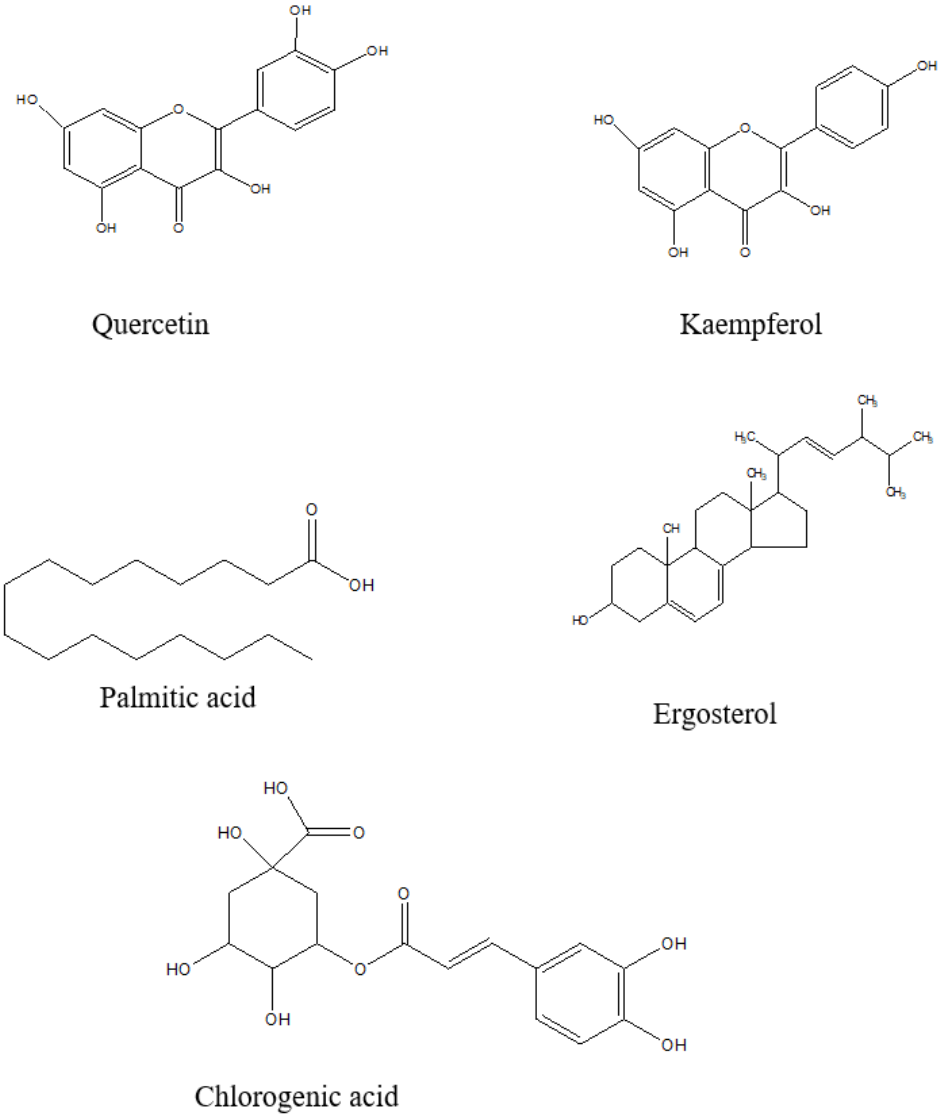

Figure 1: Chemical structure of phytoconstituents present in *Pyracantha coccinea*.

the IC_{50} value of cisplatin in relation to HT29 cells was 49.07±6.30 µM, while those of AgNPs and ZnO NPs were 8.87±0.63 µM and 19.31±2.01 µM, respectively.[26]

Analgesic activity

Ethanol, chloroform, ethyl acetate and n-hexane extract of leaves were used for the determination of analgesic effect using formalin-induced pain test. The ethanol extract of leaves was administered orally at the doses of 100 and 300 mg/kg. The chloroform, ethyl acetate and n-hexane extract were tested at doses of 30 and 100 mg/kg. Diclofenac was used as a standard drug with dose 25 mg/kg. The ethanol extract significantly reduces pain score, while the chloroform and ethyl acetate extracts produced the strongest effect and n-hexane extract shows weaker analgesic effect.[27]

Antiinflammatory Activity

Anti-inflammatory potential of successively extracted chloroform, ethyl acetate, n-hexane and ethanol leaf extracts was done through carrageenan-induced paw edema experiment on rats. The ethanolic extract of leaves was given in 100 and 300 mg/kg doses. Chloroform, ethyl acetate and chloroform extract was given in 30 and 100 mg/kg doses. Diclofenac is used as standard drug in 25 mg/kg dose. The control rats showed about 0.45cm^3 paw edema after 3 hr. Reduction in paw edema by ethanolic extract was 0.30cm^3 and 0.25 cm^3 at 100 and 300 mg/kg. Chloroform and ethyl acetate extracts showed significant reduction in edema (p<0.001) while no significant result came from n-hexane fraction.[27]

Pyracantha angustifolia

- **Synonyms:** *Cotoneaster angustifolius*.[1]

- **Common names:** Narrow leaf firethorn, slender firethorn, Woolly firethorn.[1]

Geographical Distribution

It is a woody shrub belonging to the Rosaceae family and originates from China. It commonly grows in grasslands, shrub-covered areas, and mountainous habitats, and is commonly found along roadsides at heights of 1600-3000 m.[2,32]

Botanical Description

The plant can grow to a height of 4 m and has thorny branches. The leaves are long and narrow, measuring around 15 to 50 mm in length and 4 to 8 mm in width. The flowers are white, about 8 mm across, and grow together in small clusters that are 2-4 cm wide. The fruits are small berries, orange to red in colour, about 5-8 mm in size.[1,33]

Traditional uses

Pyracantha angustifolia is traditionally used to treat earache, menstrual problems and constipation. Its ethnomedical uses highlight its importance in local healing traditions, pointing to its potential therapeutic effects beyond its pharmacological characteristics. In addition the plant has also been useful in traditional medicine for treatment of various stomach diseases, to get better digestion, to enhance blood flow and to cure ailments including diarrhea, dysentery and hemostasis, suggesting ethnomedical importance of the plant in contributing to overall health.[2,34]

Table 2: **Reported phytoconstituents of *Pyracantha coccinea* M. Roem.**

Category	Identified compounds	References
Flavonoids	Quercetin, kaempferol, rutin, cyanidin derivatives	[11,16-18]
Phenols	Chlorogenic acid, gallic acid	[11,19]
Lipids and fatty acid derivatives	Linolenic acid, palmitic acid	[20]
Phytosterols and vitamins	β-sitosterol, ergosterol, stigmasterol, δ-tocopherol, α-tocopherol, Vitamin k, Vitamin D	[20,21]
Others	Pyracrenic acid, fortuneanosides.	[11,22]

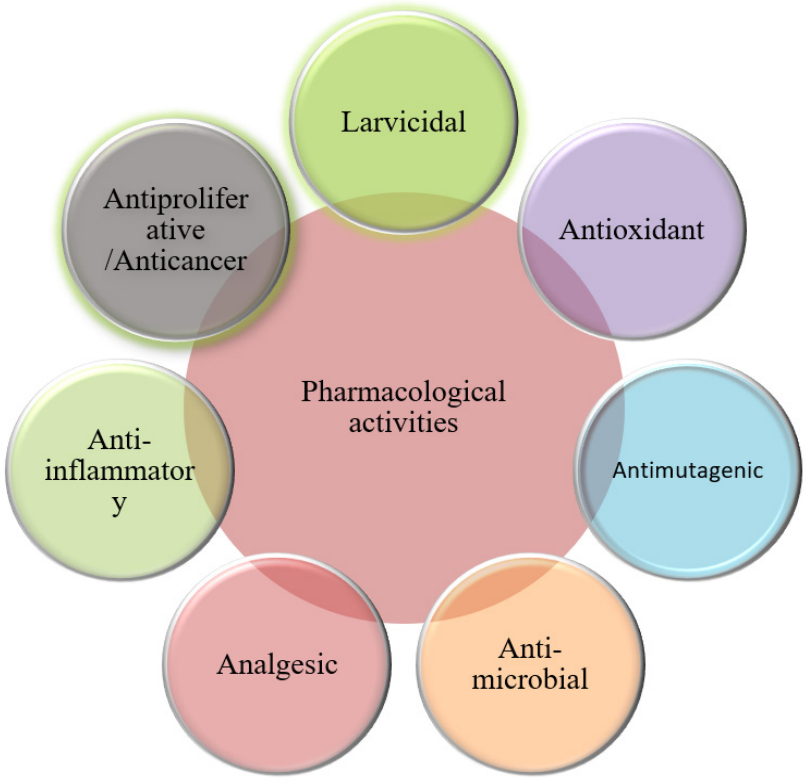

Figure 2: Reported pharmacological activities of *Pyracantha coccinea* M.Roem.

Table 3: Reported pharmacological activities of *Pyracantha coccinea* M.Roem.

Sl. No.	Activities	Plant part	Method	Model	Therapeutic profile/ results	References
1.	Antioxidant	Fruits	Green synthesis of iron nanoparticles; ABTS, DPPH, TPC, TFC, TAC.	*In vitro* antioxidant assays	Fe-NPs showed stronger antioxidant activity than the fruit extracts.	[24,28]
2.	Anti-microbial	Fruits	Green synthesis of iron nanoparticles; microdilution.	Antibacterial assays	Iron-nanoparticles shows significant antimicrobial activity than the fruit aqueous extract.	[24]
3.	Antioxidant	Fruits	Different solvent extracts; ABTS, DPPH, Phenolic and flavanoid assays.	*In vitro* chemical assays	Water extract shows highest falavnoids, phenolics, ABTS and DPPH activity.	[29]
4.	Anti-microbial	Fruits	Agar well diffusion method.	*In vitro* microbial assays	Extract shows strongest activity against *Bacillus cereus* and *Pseudomanas aeruginosa*.	[29]
5.	Antinociceptive / analgesic	Leaves	Formalin induced pain test	Wistar rats	It showed strongest analgesic effect.	[27]
6.	Anti-inflammatory	Leaves	Ethanolic extract and n-.hexane, chloroform, ethyl acetate fractions; HPTLC, carrageenan induced paw edema.	Wistar rats	Ethanolic, ethyl acetate, and chloroform fractions significantly reduced carrageenan paw edema chloroform fraction was strongest.	[27]
7.	Anti-proliferative	Fruit	A549 cancer cell line	*In vitro*	Antiproliferative activity increased with concentration.	[15]
8.	Antibacterial	Leaves and fruits (silver nanoparticles)	Disk diffusion and broth dilution method.	Bacterial strains	Synthesized silver exhibited significant antibacterial activity with bactericidal effect and were slightly more effective against gram-negative bacterial strains than positive strains.	[30]
9.	Anti-microbial	Fruits	Disc diffusion method	*In vitro* against 45 bacteria and 3 yeasts	It shows antimicrobial activity against 22 microorganisms.	[31]

Sl. No.	Activities	Plant part	Method	Model	Therapeutic profile/ results	References
10.	Larvicidal	Fruits	Methanol extract; larvicidal bioassay	*Culex pipiens* larvae	Fruit methanol extract showed larvicidal activity against second-instar mosquito larvae.	[25]
11.	Anticancer	Fruits (AgNPs and ZnNPs)	MTT cell viability assay, followed by flow cytometry, apoptosis assay and cell cycle analysis.	L929 (mouse fibroblast); MCF-7 (breast cancer); HT-29 (colon cancer); C6 (glioblastoma)	Both AgNPs and ZnNPs showed significant cytotoxicity against MCF-7 and HT-29 cells, but no significant cytotoxic effect against C6 glioblastoma cells.	[26]

Abbreviations: DPPH: 2,2-diphenyl-1-picrylhydrazyl; ABTS: 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; TPC: total phenolic content; TFC: total flavonoid content; TAC: total alkaloid content; HPTLC: high-performance thin-layer chromatography; NPs: nanoparticles; AgNPs: silver nanoparticles; ZnNPs: zinc nanoparticles.

Reported phytoconstituents

The reported phytoconstituents present in *Pyracantha angustifolia* including phenolic compounds, flavanoids, vitamins, etc. are shown in Table 4 and chemical structures are shown in Figure 3.

Reported pharmacological activities

The reported pharmacological activities of *Pyracantha angustifolia* are antimelanogenesis, antibacterial, anticancer, antigastric ulcer, etc are shown in Figure 4 and Table 5.

Antimelanogenesis activity

The inhibition of melanogenesis from *Pyracantha angustifolia* was determined through the use of B16F10 murine melanoma cell line. Extracts of leaves, branches, and fruit obtained from ethanol were tested at 100 and 250 µg/mL concentration. The positive control Arbutin (500 µg/mL) was employed. Treatment of cells with leaf extract at 100 µg/mL caused an approximate 32.4% reduction in melanin content without any cytotoxic effects. HG and CH were identified as major bioactive components. These compounds inhibited melanogenesis through the reduction of tyrosinase activity, down regulation of TYRP-1 and TYRP-2, and intracellular ROS.[34]

Antioxidant Activity

The anti-oxidant activity was determined via DPPH method using ethanol extract of leaves, twigs and fruits of *Pyracantha angustifolia*. Various concentrations of extract, i.e., 100 and 250 µg/mL, were tested and compared to the standard ascorbic acid. It was found that ethanol extract possessed the highest antioxidant activity.[34]

Antibacterial activity

The antibacterial activity of biosynthesized Silver Nanoparticles (AgNPs) from *Pyracantha angustifolia* was determined through the agar disc diffusion test against 10 bacteria pathogens. The MIC of AgNPs was determined by testing AgNP solution in DMF at 10, 20, 40, and 80 mg/mL. The synthesized AgNPs had the potential to display broad-spectrum antibacterial activity, which was observed from the inhibition zone of 10.0±1.15 mm to 23.3±0.66 mm. The highest antibacterial activity was demonstrated by AgNPs towards *Clavibacter michiganensis* (23.3±0.66 mm), *Erwinia carotovora* (22.3±0.57 mm) and *Curtobacterium flaccumfaciens* (21.0±0.57 mm).[36]

Anticancer activity

The anticancer activity of *Pyracantha angustifolia* was used the fruit extract prepared with 70% ethanol. The efficiency of the preparation was tested on the human breast cancer (MDA-MB-231) and Human Hepatocellular Carcinoma (HepG2) cell lines while MCF10A human mammary epithelial cells served as a control. The cells were exposed to the concentrations of the extract 10, 40, 160, and 320 µg/mL for 2 4, 48, and 72 hr. Anticancer activity was determined with the help of the alamar Blue cell viability assay, while the flow cytometry was used to evaluate the cell cycle arrest. In addition, the caspase-3/7 and caspase-9 activity assays, qRT-PCR analysis of the apoptosis-related genes, and the Reactive Oxygen Species (ROS) determination were applied in order to determine the mechanisms of the effects. The extract demonstrated significant concentration-dependent antiproliferative effect using an IC_{50} value of 21.91±2.10 µg/mL for the human breast cancer cells and 28.41±4.53 µg/mL for the HepG2 cells, while its activity towards the normal MCF10A cells was minimal. Treatments, especially those at 40 and 320 µg/mL, produced arrest of cell cycle at G2/M

phase, accompanied by increase in Sub-G1 population, activation of caspase-3/7 and caspase-9, up-regulation of pro-apoptotic genes like p53, Caspase-3, Caspase-7, PARP, and PUMA, as well as decrease in intracellular reactive oxygen species production via elevation of antioxidant enzymes production. These results indicate that *Pyracantha angustifolia* fruits have considerable selective anticancer activity.[37]

Antigastric ulcer activity

The anti-gastric ulcer effect of *Pyracantha angustifolia* leaf extract was studied on Wistar rats (both males and females with age between 7-9 weeks and weight range between 180-200 g). The rats were treated using leaf extract with doses of 150, 300, and 600 mg/kg orally, whereas cimetidine was standard drug for anti-ulcer effect. The gastric pH was measured to study the gastroprotective effect. The results of the gastric pH in different groups of rats after the treatment with 150, 300, and 600 mg/kg were 2.58±0.23, 3.12±0.49, and 3.89±0.49 respectively. The highest pH value belonged to the rats receiving cimetidine, and it was equal to 5.79±0.46.[38]

Antiinflammatory activity

Pyracantha angustifolia fruit extracts' ability to reduce inflammatory reactions was investigated in LPS-induced RAW 264.7 cells. Ethanol (PE) and hot-water (PW) extracts were assessed for their effect on NO production at 0.0625, 0.125, 0.25, 0.5, and 1.0 mg/mL concentrations. Cytotoxicity of either extract was not observed at any of these concentrations. The ethanol extract significantly inhibited NO production in a dose-dependent manner, with significant decreases in TNF-α secretion and iNOS and TNF-α gene expressions, especially at 0.5 and 1.0 mg/mL. Hot water extract also displayed anti-inflammatory action, but its potency was less significant from ethanol extract.[39]

Pyracantha fortuneana

- **Synonyms:** *P. crenatoserrata*.[1]
- **Common names:** Broadleaf firethorn (Australia).[40]
- **Geographical Distribution:** It is found in the area ranging from Eastern Asia to Southern Europe.[41]

Botanical Description

The plant having small bush which attains a length of 1-3 m. The leaves have broader apex, narrower basal end, with a shape between oval and elongated, measuring around 1.5 to 6 cm in length and 0.5 to 2 cm in width. The plant bears white flowers and produces small, bright red fruits.[1]

Traditional Uses

The fruits are consumed for improving digestion, lowering body temperature, relieve thirst and improve blood circulation. Roots of *P. fortuneana* used in herbal medicine for arresting hemorrhage, reduce swelling and treat toothache. It is used in Chinese medicine to treat dyspepsia and dysentery. Its fruits are recommended for oral use and externally for sore relief. This has been accepted as source of food by the Ministry of National Health of China.[42,43]

Reported phytoconstituents

The reported phytoconstituents identified from *Pyracantha fortuneana* include flavonoids, polyphenols, phtyosterols, lipids are shown in Table 6 and some chemical structures are shown in Figure 5.

Reported pharmacological Activities

The reported pharmacological activities of *Pyracantha fortuneana* such as antioxidant, antimutagenic, anticancer, antithrombocytopenia, antiphotoaging, antihyperlipidemic are shown in Figure 6 and Table 7.

Antioxidant activity

The anti-oxidant potential was measured using DPPH free radicals scavenger analysis. Fifty microlitres of the fruit extract from each of methanol, acetone, and ethanol (50%, 70%, and 90%) were used and the absorbance was measured at 517 nm. Among the various extracts tested, 50% acetone extract possessed

Table 4: Reported phytoconstituents of *Pyracantha angustifolia*.

Category	Identified compounds	References
Phenolic and flavonoids	p-hydroxybenzoic acid, hesperidin, rutin, myricetin, morin, quercetin, kaempferol.	[2,34,35]
Lipids and sterols	Palmitic acid, methyl ester, ergosterol, β-sitosterol	[2]
Vitamins	Vitamin D, vitamin k, α-tocopherol, Vitamin C, retinol	[34,35]
Sugars	Arabinose, fructose, glucose, sucrose, maltose	[34]
Minerals	Calcium, sodium, potassium, iron, manganese, magnesium, zinc	[34]

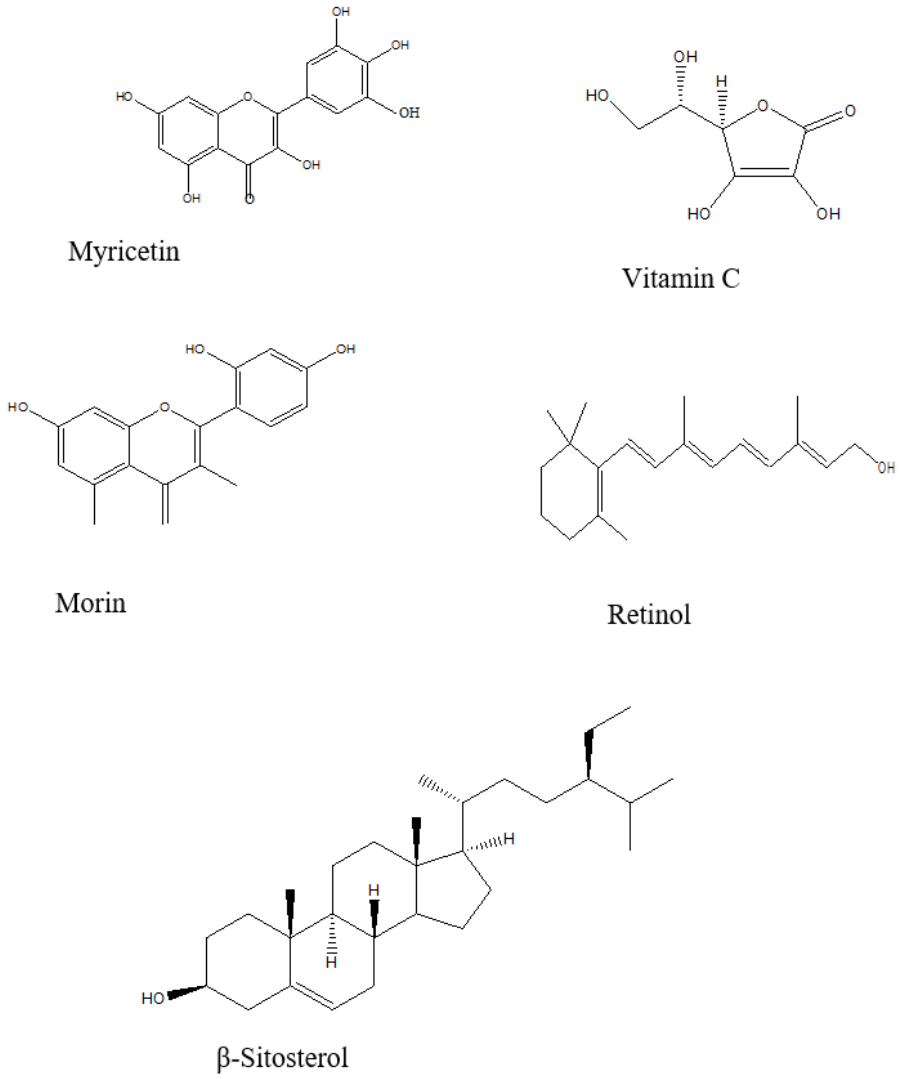

Figure 3: Chemical structure of phytoconstituents present in *Pyracantha angustifolia.*

the highest DPPH scavenging effect, having the least IC_{50} value (0.61±0.08 mg/mL), followed by 70% acetone extract (0.69±0.02 mg/mL) and 50% ethanol extract (0.79±0.09 mg/mL). The poorest scavenging effect was found in 90% ethanol extract (IC_{50}=2.54±0.18 mg/mL).[53]

Antidiabetic activity

Antidiabetic properties of polysaccharides obtained from *Pyracantha fortuneana* fruit using different drying procedures, which include natural, hot air, infrared, freeze, microwave vacuum, and Freeze Microwave Vacuum Drying (FMVD) were investigated *in vitro* using α-glucosidase inhibition and BSA-glucose non-enzymatic glycation models. Various concentrations of polysaccharides were tested for antidiabetic effect, in which 8 mg/mL was used for antiglycation experiments, whereas α-glucosidase inhibition was determined as IC_{50}. The polysaccharides obtained using FMVD showed the most significant dual antidiabetic activities, presenting the lowest IC_{50} value of α-glucosidase inhibition (0.51 mg/mL), 62.27% inhibition of fructosamine formation at 8 mg/mL, and AGE inhibition IC_{50} of 3.48 mg/mL. Moreover, FMVD showed the highest yield of polysaccharides (6.22%) and uronic acid contents (45.48%). Thus, it could be concluded that freeze microwave vacuum drying is very effective in improving the structure and antidiabetic activity of polysaccharides.[54]

Anticancer activity

The anticancer activity of Selenium-*Pyracantha* Polysaccharide (Se-PFP) isolated from *Pyracantha fortuneana* on MDA-MB-231 triple negative breast cancer cells as well as BALB/c nude mouse xenograft model was investigated. The *in vitro* study involved treatment of the cancer cells with Se-PFPs at concentrations of 0, 50, 100, 200, and 400 μg/mL over 24 to 48 hr, while *in vitro* apoptosis and cell cycle analysis mainly used 100 and 400 μg/mL. Furthermore, the *in vivo* study was done by administering tumor-bearing mice with 100 and 400 mg/kg/day dose for

30 days. Se-PFPs showed significant anti-cancer action in a dose-dependent manner as they caused decrease in cell viability to 40% and 25% of the controls at 200 and 400 µg/mL after 24 hr. In the mice, the treatments reduced tumor size from 1365.5 mm^3 (controls) to 895.8 mm^3 (100 mg/kg) and 284.5 mm^3 (400 mg/kg) and tumor weights from 3.6 g to 2.6g and 1.4 g respectively, without affecting the body weight, it demonstrates the potent anticancer activity with low toxicity.[55]

Antiphotoaging activity

Polysaccharides from the fruit of *Pyracantha fortuneana* were characterized by structural analysis and studied for their anti-photoaging activity via oxidative stress, apoptosis, MAPK signaling pathway, and lifespan studies in HaCaT cells injured by UVB and *C. elegans* injured by UVB. The fruit polysaccharides effectively decreased oxidative stress and apoptosis levels, increased mitochondrial membrane potential, inhibited MAPK phosphorylation, upregulated tight-junction proteins, and extended the lifespan of UVB-injured *C. elegans*.[56]

Antihyperlipidemic activity

The antihyperlipidemic properties of flavonoid and saponin fractions obtained from *Pyracantha fortuneana* fruits have been investigated using a free fatty acid (300 µM)-induced L02 human hepatocyte cell line model and a 15 mM glucose-induced *Caenorhabditis elegans* model. PFF and PFS were applied at 100, 200, and 400 µg/mL concentrations on L02 cells and 200, 400, and 800 µg/mL in *C. elegans*. For the assessment of lipid deposition, an Oil Red O staining test was performed, whereas TG, TC, and LDL were measured to assess the lipid metabolism. It was found that both PFF and PFS decreased intracellular lipid deposition and reduced TG, TC, and LDL levels dose dependently compared with the untreated hyperlipidemic models. In addition, it was found that the treatments increased lipid metabolism-related genes expression, such as SIRT1 and CPT-1, which means that the fatty acid β-oxidation and lipid metabolism were improved. These results indicate the presence of significant antihyperlipidemic properties in flavonoid and saponin fractions obtained from *P. fortuneana* fruits.[57]

Antimutagenic activity

The effectiveness of Selenium-Rich Polysaccharides of *Pyracantha fortuneana* (Se-PFPs) in terms of their ability to exhibit antimutagenic effects was studied in mice. Treatment of animals with Se-PFPs in doses of 1.35, 2.7, and 5.4 g per kilogram of body weight. Administration of Se-PFPs resulted in the dose-dependent reduction of DNA damage induced by cyclophosphamide. Se-PFPs enhanced the action of enzymes

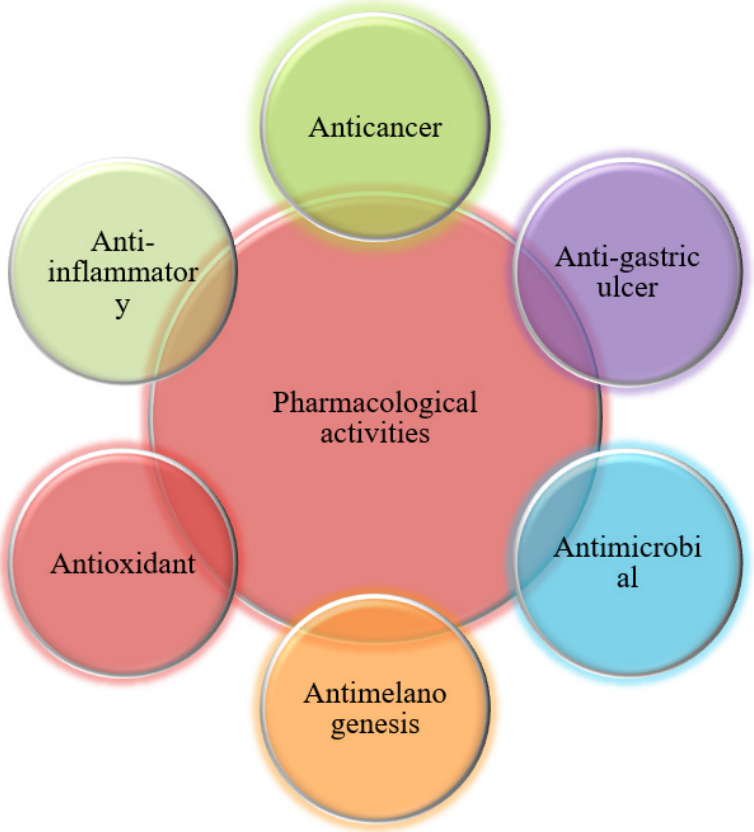

Figure 4: Reported pharmacological activities of *Pyracantha angustifolia*.

Table 5: Reported pharmacological activities of *Pyracantha angustifolia*.

Sl. No.	Activities	Plant part	Method	Model	Therapeutic profile/results	References
1.	Anti-melanogenesis	Leaves	TYR inhibition assay	*In vitro* (B16F10 cells)	Inhibited melanin, TYR activity, TYRP-1/2 expression	[34]
2.	Antioxidant	Leaves	DPPH, ABTS	*In vitro*	Strong radical-scavenging activity	[34]
3.	Antioxidant	Fruit	DPPH, ABTS	*In vitro*	High radical scavenging activity	[35]
4.	Anti-inflammatory	Fruit	Nitric oxide production and cytokine secretion inhibition	*In vitro* (RAW 264.7 macrophage cells)	Inhibited NO, TNF-α, INOS / TNF-α mRNA	[35]
5.	Anti-bacterial	Leaves and fruits	Disc diffusion	*In vitro* (silver nanoparticles)	High activity against *E. caratovora, C. michiganensis*	[36]
6.	Anticancer	Fruit	Cell viability assay	*In vitro* (breast carcinoma and hepatocellular cell lines)	Maximum inhibition of cancer cells	[37]
7.	Antioxidant	Aerial parts	DPPH	*In vitro*	High phenolic/ flavanoid content	[39]
8.	Anti-gastric ulcer	Leaves	Gastric ulcer induction	*In vivo* (rats)	Reduced ulcer index and acidity	[38]

Abbreviations: DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2′ -azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); TNF-α, tumour necrosis factor-alpha.

(SOD and GPx) and suppressed CYP1A1/CYP1A2, responsible for activation of carcinogens.[58]

Immunoprotective

The immunoprotective properties of PFPs were investigated in the model of Cyclophosphamide (CTX)-induced immunosuppressed mice. Mice were treated with PFPs orally administered dose of 100, 200 and 300mg/kg body weight/day, while the immunosuppression was induce by cyclophosphamide administration. The immunoprotective effect of PFPs was evaluated based on spleen and thymus indices, splenocyte proliferation, natural killer cells activity, $CD4^+$ and $CD8^+$ T-lymphocyte populations, $CD4^+$/$CD8^+$ ratio, cytokine production (IL-2, IL-6, TNF-α), Nrf2 expression in splenocytes and antioxidant enzymes activities. PFPs caused a dose-dependent immunoprotective effect that was characterized by an increase in spleen and thymus indices, improvement of splenocyte proliferation and NK cells activity, improvement of $CD4^+$/$CD8^+$ T-lymphocyte ratio, stimulation of IL-2 production, and reduction of pro-inflammatory cytokines (IL-6 and TNF-α). Moreover, PFPs upregulated the expression of Nrf2 and enhances potential of antioxidants, such as SOD and GPx. Thus, these findings have confirmed the immunoprotective and immunomodulating activity of PFPs.[59]

Pyracantha koidzumii

- **Synonyms:** *Cotoneaster koidzumii* Hayata.
- **Common Names:** Taiwan firethorn, Formosa firethorn.

Geographical Distribution

It is mainly indigenous to Taiwan and Aastern Asia parts. It has been introduced into various countries such as Australia, the US and pacific islands due to its ornamental importance.[14]

Botanical Description

It is a thorny shrub usually 2-4 m tall. Leaves are small, glossy dark green, narrowly elliptic to oblong in shape. The plant produces numerous small white bisexual flowers blooming during late spring. Its fruits are small, round pomes that ripen to orange-red or scarlet-red and often remain on the plant throughout winter.[14]

Traditional Uses

It is used for stomach related problems and disgestive comfort. It is also used in cosmetics.[2]

Reported phtyoconstituents

The bioactive compounds like flavanoids, phenolic compounds, tannins present in the *Pyracantha koidzumii* are shown in Table 8 and Figure 7.

Reported pharmacological activities

The reported activities on *Pyracantha koidzumii* including tyrosinase inhibition, antifungal, antibiolfilm activity are presented in Table 9.

Tyrosinase inhibition

Fresh fruits of *Pyracantha koidzumii* were treated with 95% ethanol extraction and isolation process was done to identify the active compounds. Human Epidermal Melanocytes (HEMn) were utilized to determine the skin whitening effect. Firstly, the cell proliferation was analyzed via WST-8 test at a concentration of 100 μM for 24 hr. Afterwards, non-cytotoxic compounds were evaluated in their ability to inhibit tyrosinase activity at 100 μM for 24 hr by using 2 mM L-DOPA as substrate and arbutin (2.5 mM) as positive control. The top two potent compounds were investigated further for their abilities to reduce the melanin levels, tyrosinase activity, protein and gene expression (MITF and PAX3) at concentrations of 60, 80, and 100 μM. Among 13 isolated compounds, compound 13 displayed the highest inhibitiory effects on tyrosinase activity and skin whitening activities. The compound inhibited the tyrosinase action and melanin production in human melanocytes. Compound 13 inhibited the expressions of tyrosinase, TRP-2, MITF, and PAX3 genes with increasing concentration.[14]

Antifungal Activity

Antifungal effect of Copper Nanoparticles (CuNPs) produced from *Pyracantha koidzumii* leaves against non-albicans Candida such as *Candida krusei, Candida tropicalis*, and *Candida glabrata* was studied. Fungal suspensions (0.5 McFarland) were prepared and subjected to antifungal testing with CuNPs at the concentration range from 0.24 to 500 μg/mL. Nystatin was used as positive control. The MIC, MFuC, and MFC of the CuNPs were determined by broth micro-dilution method. It is evident that the CuNPs exhibit good potential towards the tested antifungal *C. strains. C. krusei* and *C. glabrata* strains were found more susceptible having MIC of 0.48 μg/mL than *C. tropicalis* having MIC of 0.97 μg/mL. MFuC of *Candida krusei, Candida tropicalis* and *Candida glabrata* were 1.9 μg/mL, 31.2 μg/mL and 15.6 μg/mL, respectively. For MFC, they were 3.8 μg/mL, 62.4 μg/mL and 31.2 μg/mL, respectively.[69]

Antibiofilm Activity

The antibiofilm potential of CuNPs prepared using *Pyracantha koidzumii* extract was determined using the modified method. Sterile polystyrene 1 cm^2 pieces were inoculated into 24-well microtiter plates. In each well, 0.5 mL of standard fungal suspension (0.5 McFarland) and 0.5 mL of CuNPs solution were used. Negative control contained 0.5 mL of fungal suspension and 0.5 mL of RPMI-1640 medium. The microtiter plates were incubated for 24 hr at 37°C . Following incubation, polystyrene sheet was carefully taken out from the wells and washed twice with PBS. Attached biofilms were then stained with 0.5% Crystal Violet (CV) for 20 min and later again rinsed with PBS to eliminate any unbound stain, air-dried for 30 min, and morphology was observed using light microscope 40× magnification and recorded using the AmScope T720 Series Infinity microscope. Biofilm inhibition was observed for all the tested non-albicans Candida strains following treatment. Biofilm fragmentation to microcolonies was evident upon treatment with 31.2 μg/mL of CuNP in *C. glabrata*. In *C. tropicalis*, treatment with 62.4 μg/mL led to reduced biofilm formation but still retained denser clusters and pseudohyphae. The highest antibiofilm effect was achieved when *C. krusei* was treated with 3.8 μg/mL leading to biofilm fragmentation to thin and discontinuous strands.[70]

Table 6: Reported phytoconstituents of *Pyracantha fortuneana*.

Plant part	Chemical compounds	References
Fruit	Quercetin, hyperoside, caffeic acid, ferulic acid, ursolic acid, oleanolic acid, veratric acid, sinapoylglucose, cyanin, delphinidin, epigallocatechin, isoorientin, rutin, chlorogenic acid, cyanin.	[44-46]
Leaf	Vanillin, arbutin, 2-hydroxybenzoic acid, FA, caffeic acid 3-O-glucuronide, 2-oxopomolic acid, pomolic acid, methyl palmitate.	[47-50]
Root	Chrysin-5-glc, chrysin, noprwogonin-5-glc, dihydrokaempferol, dihydroquercetin, pinocembrin, sakuranin, dihydrowogonin.	[47]
Bark	Pyracrenic acid.	[51]
Flower	Eugenol, germacrene D, isoledene, isophorone, jasmone, cadinene, cyclododecane, docosane, tricosane, farnesol.	[47,52]

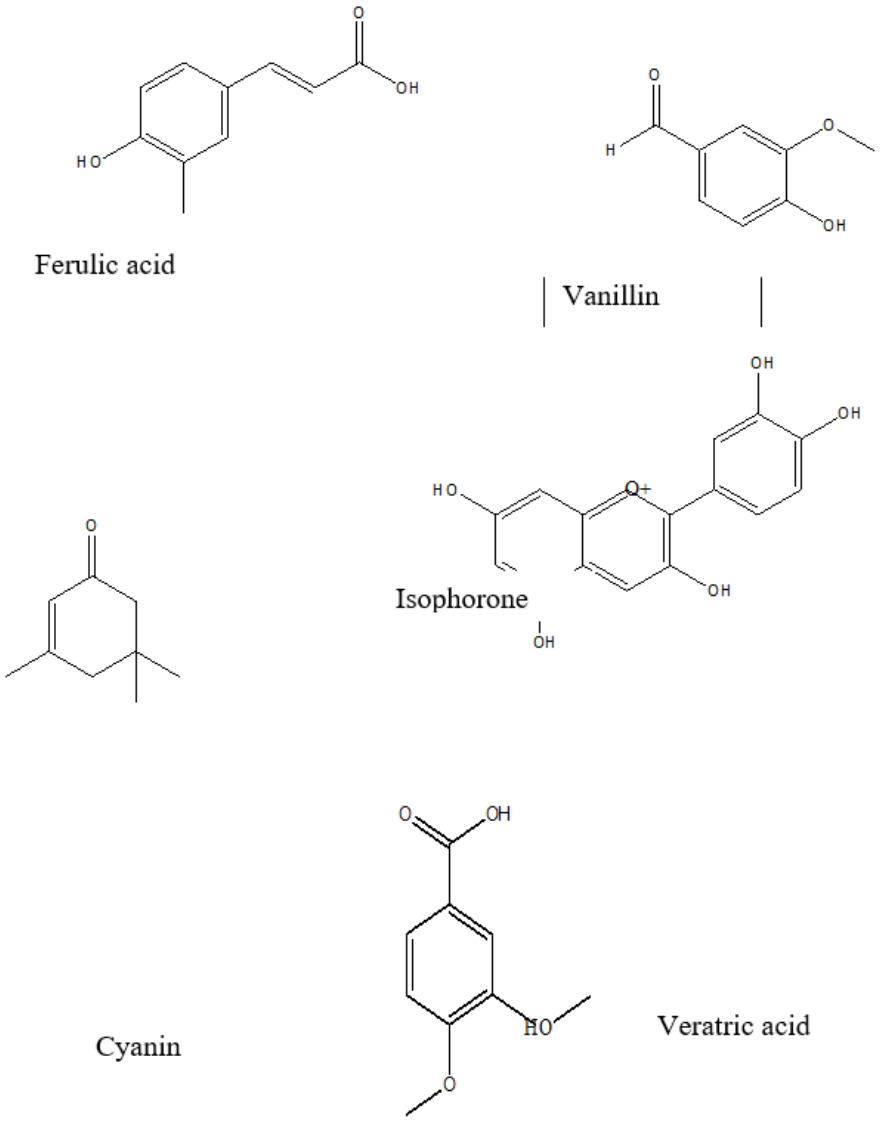

Figure 5: Chemical structure of phytoconstituents present in *Pyracantha fortuneana*.

Cytotoxic activity

For the study of toxicity of the CuNPs isolated from *Pyracantha koidzumii*, the Human Hepatocellular Carcinoma (HepG2) cell line was chosen. Cultivation of HepG2 cells was done under conditions with EMEM, which included 10% of fetal bovine serum, 1% of non-essential amino acids, 1% of sodium pyruvate and 1% of antibiotic-antimycotic solution at 37°C and 5% CO_2 atmosphere. Among 80-90% confluence, cells were removed using 0.25% trypsin-EDTA solution. Subsequently, cells were introduced to CuNPs in the concentration range of 0.24 to 250 µg/mL for 24 hr. The cell viaHbility was estimated with the help of Fluorescein Diacetate (FDA) fluorometric test by addition of 0.016 mg/mL FDA for 5 min at room temperature. Measurement of fluorescence was performed at the wavelengths of 488 nm of excitation and 533 nm of emission; normalization of results was done using the protein amount determined according to Lowry. In terms of cytotoxicity, the *Pyracantha koidzumii*-based CuNPs exhibited relatively moderate concentration-dependent cytotoxicity towards HepG2 cells. Under low concentration ranges of 0.24 to 3.9 µg/mL, the nanoparticles showed good cytocompatibility with high viability of 93%. With the increase in concentration to 7.81 µg/mL, there was marked decrease in cell viability to about 44%. Based on this, the cytotoxicity at high concentration could be attributed to the presence of phenolic compounds such as quercetin, rutin, and hyperoside in the aqueous extract of the plant.[69]

Pyracantha crenulata

- **Synonyms:** *Mespilus crenulata* D. Don, *Cotoneaster crenulatus* K. Koch, *Pyracantha chinensis* M. Roem, *Crataegus crenulata* Roxb.[71]
- **Common Names:** Ghingharu (Saini *et al.*,2026), Himalayan firethorn, Nepalese firethorn or Hawthorn (Guglani *et al.*,2022), Ghangaru, Gangaru, Kaathgedi.[71]

Geographical Distribution

Pyracantha crenulata is mainly distributed across the Himalayan belt, extending from the Sutlej region of India to Bhutan, and it is also native to China. The plant commonly grows at elevations between 800-2500 m. In Uttrakhand, it is widely found between 1000-2600 m altitude, especially in districts such as Almora, Nainital, Champawat, Tehri and Pithoragarh. The species is also present in the Himalayan foothills of Himachal Pradesh, Jammu and Kashmir, the Northeastern hill regions of India, and Nepal, where it generally occurs between 1600-2500 m elevation.[71] This perennial shrub prefers mountainous habitats with good drainage and sufficient sunlight, and it is frequently observed in temperate forests and alpine meadow ecosystem s. The shrub is able to survive under diverse climatic conditions to subtropical environments, demonstrating its ecological adaptability. Due to its extensive occurance in Himalayan regions, *Pyracantha crenulata* has been traditionally used in herbal medicine for many years. Its broad geographical distribution may also influence variations in its phytochemical composition and therapeutic properties.[72]

Botanical description

Pyracantha crenulata is an evergreen shrub known for its unique botanical and structural features. Morphologically, plant usually reaches a height of about 1.5-3 m and develops many branches. Its thick, upright growth creates a dense shrub covered with shiny green leaves. The name 'firethorn' comes from the sharp thorns present on the branches. It is a thorny, woody shrub that usually grows to a height of 2-5 m and is native to the Himalayan foothill

Figure 6: Reported pharmacological activities of *Pyracantha fortuneana*.

Table 7: Reported pharmacological activities of *Pyracantha fortuneana*.

Sl. No.	Activities	Plant part / preparation	Method	Model	Therapeutic profile/ results	References
1.	Antioxidant	Fruit extract with different solvents	DPPH, ABTS, FRAP, Fe^{3+} reducing power, radical scavanging assays	*In vitro* chemical assay	Multiple fruit extract showed antioxidant activity; water extract had strongest DPPH and ABTS scavenging, ethyl acetate had highest FRAP, and polysaccharides also showed strong antioxidant capacity.	[60-62]
2.	Anti-diabetic /α-Glucosidase inhibitory	Fruit extracts, fruit proanthocyanidins, fruit polysaccharides	Enzyme inhibition assay, solvent optimization, spectroscopy, docking	*In vitro* enzyme model	50% and 70% acetone fruit extracts showed strongest α-glucosidase inhibition; fruit proanthocyanidins showed very potent non-competitive inhibition with IC_{50} value 0.15±0.01 µg/mL; acidic and FMVD polysaccharides also showed strong inhibition.	[53,54 63]
3.	Anti-diabetic	Fruit	Preventive feeding study with metabolic phenotyping, serum metabolomics, gut microbiota profiling	High-fat /high-sugar diet + STZ- induced type 2 diabetic SD rats	Fruit pre-intervrention improved glucoe tolerance, insulin sensitivity and supporting anti-diabetic potential *in vivo*.	[64]
4.	Anti-cancer (breast cancer)	Selenium-containing fruit polysaccharides	Cell-growth assay, cell-cycle/apoptosis proteins, xenograft study	MDA-MB-231 TNBC cells; mouse xenograft model	Selenium- polysaccharides inhibited TNBC cell growth by G2 arrest, increased p53/Bax/Puma/Noxa and caspase-3/9 activity, reduced xenograft tumor growth, and enhanced doxorubicin cytotoxicity without body-weight loss.	[65]
5.	Anti-cancer (ovarian cancer)	Fruit polysaccharides, polysaccharid-iron complex	Cytotoxicity, apoptosis, ROS, mitochondrial membrane potential, DNA damage assays	Human SKOV3 ovarian carcinoma cells	Polysaccharides induced ROS, mitochondrial depolarization, DNA damage, and apoptosis in SKOV3 cells; the polysaccharide-iron complex also showed cytotoxicity and apoptosis-inducing effects.	[66]

Sl. No.	Activities	Plant part / preparation	Method	Model	Therapeutic profile/ results	References
6.	Anti-photoaging	Fruit polysaccharides	Structural characterization and oxidative stress, apotosis, MAPK and lifespan assays	UVB-damaged HaCaT cells; UVB-injured *C. elegans*	Purified fruit polysaccharide reduced apotosis and oxidative stress, improved mitochondrial membrane potential, lowered MAPK phospholyration, repaired tight-junction protein expression and extended lifespan in UVB-injured *C. elegans*.	[67]
7.	Anti-bacterial	Fruit polyphenols	Ultrasonic-assisted polphenol extraction, MIC and zone of inhibition testing	*Straphylococcus aureus* and *Escherichia coli*	Hydro-alcoholic fruit polyphenols inhibited *S. aureus* and *E. coli* with 10 and 20 mg/mL and ZOI are 7.4 and 6.8 mm respectively.	[68]
8.	Anti-hyperlipidemic	Fruit flavanoid fraction and saponin fraction	Lipid accumulation assay, ROS/ MDA assays, gene-expression analysis	FFA-induced LO2 cells; high-glucose *C. elegans*	Flavanoid and saponin fractions induced lipid droplets, ROS, MDA, and lipid deposition and upregulated nrf2/ARE, CPT-1 and SIRT1-related lipid metabolism pathways.	[57]
9.	Hypolipidemic / antiobesity	Fruit extract	Preventive and therapeutic rodent study; cell assays for constituent activity	Rodents; Hep G2 cells	Fruit extract decreased body weight, TG, TC, LDL-C and MDA, while increasing HDL-C, GPx, and SOD; quercetin, rutin and procyanidins increased LDL receptor activity and apolipoprotein-A1 in Hep G2 cells.	[66]
10.	Anti-mutagenic	Selenium containing fruit -polysaccharides	Micro-nucleus assay, chromosomal aberration assay, liver antioxidant and CYP4501A analysis	*In vivo* (Mice)	Selenium -polysacharides inhibited cyclophosphamide induced micronucleus formation, increased liver SOD and GPx, and reduced CYP4501A activity.	[58]
11.	Platelet -protective / anti-thrombocytopenia	Fruit extract, ethyl acetate fraction	Fractionation, platelet counts, bleeding/clottiong measures, transcriptomics	Chemotherapy-induced thrombocytopenia mice	Fruit extract and mainly ethtyl acetate fraction increased platelet counts by 48.7%, reduced bleeding volume, mitigated organ injury, and upregulated hematopoietic lineage pathways.	[67]

Sl. No.	Activities	Plant part / preparation	Method	Model	Therapeutic profile/ results	References
12.	Immunoprotective	Fruit polysaccharides	Organ index measurement, splenocyte proliferation, NK- cell assay, cytokines, oxidative stress markers	*In vivo* (mice)	Polysaccharides increased thymus and spleen indices, stimulating splenocyte proliferation, NK activity, CD4+/CD8+ ratio, and IL-2, while lowering IL-6, TNF-α, and oxidative stress markers; Nrf2 expression increased.	[59]

Abbreviations: DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); IC_{50}, half-maximal inhibitory concentration; MIC, minimum inhibitory concentration; ROS, reactive oxygen species; TNF-α, tumour necrosis factor-alpha; STZ, streptozotocin; FMVD, freeze-microwave vacuum drying; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SOD, superoxide dismutase; GPx, glutathione peroxidase; Nrf2, nuclear factor erythroid 2-related factor 2; CPT-1, carnitine palmitoyltransferase 1; SIRT1, sirtuin 1; MAPK, mitogen-activated protein kinase; TNBC, triple-negative breast cancer.

regions.[72] The colour of the leaves is dark green, smooth in texture and taper towards the tip, measuring about 2.5-4.0 cm long and 1.0-2.2 cm wide. They are generally elliptical to ovate in shape. One distinctive feature of the leaves is their delicately toothed edges, which create a scalloped or crenulated pattern, inspiring the species name *crenulata*.[71] The plant bears white compound corymb inflorescences containing many bisexual flowers. Each flower consists of 20 stamens, a central ovary, and is enclosed by five sepals and five petals. The plant flowers between march and may.[72] Its fruit are small, pome-like juicy berries that ripen from July to September. Each berry weighs nearly 250 mg and changes in colour from orange to bright red on maturation.[73]

Traditional Uses

Pyracantha crenulata has long been valued in Southeast Asian countries for both its traditional medicinal applications and it is used as a food resource.[72] It has been traditionally applied to managing several cardiovascular diseases, including heart failure, weakened heart muscles, high blood pressure. In addition, its fruits are known to exhibit antispasmodic, diuretic, calming and blood vessel-dilating effects. Its leaves are used for making herbal tea. Leaves are used like appetizer, vasodilator and soothing.[71] It is used for treating malaria.[74] Leaves are also used in case of burns. It is used as a starter, vasodilator and soothes. It is used in treating malaria. Paste of leaf helps in case of burns.[75]

Reported phytoconstituents

The phytoconstituents like phenols, flavanoids, triterpenoids, phytosterols, tannins present in *Pyracantha crenulata* are shown in Table 10 and some chemical structures are presented in Figure 8.

Reported pharmacological activities

The reported activities including analgesic, antidiabetic, antibacterial, antihypertensive, antiurolithogenic are shown in Figure 9 and Table 11.

Analgesic activity

The analgesic effect of Hydroethanolic filtrate obtained from leaf and fruit of *Pyracantha crenulata* in Wistar rats via oral route of administration at doses of 100 and 300 mg/kg. The effects were evaluated using the tail immersion, tail flick, Eddy's hot plate, and the formalin-induced pain response model, with diclofenac sodium (25 mg/kg) being used as the control drug. Both extracts significantly increased reaction latency in thermal nociception tests and decreased pain responses in both neurogenic and inflammatory phases of the formalin test with increasing concentration manner, where increased dose produced maximal effect, which was equal to the effect of diclofenac. Also, molecular docking and molecular dynamics studies have shown that gallic acid, which is one of the main phytoconstituents in the extracts, is responsible for the analgesic activity through inhibitory effect on Cyclooxygenase-2 (COX-2) enzyme and interaction with μ-opioid receptor.[80]

Antidiabetic activity

The antidiabetic effect of sequential n-hexane, ethyl acetate, ethanolic, and aqueous extracts of fruit was analyzed by *in vitro* α-amylase and α-glucosidase enzyme at different concentrations varying between 10 to 100 μg/mL, where acarbose served as the control drug. The effects of the extract on the two enzymes were dose-dependent, with the ethanolic extract displaying maximum potency. With respect to α-amylase enzyme inhibition, the ethanolic extract displayed 73.22±0.56% inhibition at a concentration of 100 μg/mL, whereas the IC_{50} of acarbose was 33.34 μg/mL. For the α-glucosidase enzyme inhibition activity, the ethanolic extract showed 77.94±1.47% inhibition at 100 μg/mL and value of IC_{50} was 30.09 μg/mL, while the IC_{50} of acarbose was 24.86 μg/mL.[81]

Antioxidant activity

The anti-oxidant potential of lyophilized leaves ethanol extract of *Pyracantha crenulata* was analyzed using DPPH method. Various

doses of filtrate ranging from 200, 400, 600, 800, and 1000 µg/mL, were tested against the standard ascorbic acid. DPPH radical scavenging activity of extract was seen to be depending on the concentration of the sample. IC_{50} of freeze-dried leaf extract was determined with value of 12.73 µg/mL while that of standard AA was comparatively lower, 8.10 µg/mL. It is evident from the results that the extract possessed good antioxidant effect but was less potent from the standard one.[78]

Antibacterial activity

Antibacterial activity of *Pyracantha crenulata* fruit was tested through the *in vitro* disc diffusion technique using ethanolic fruit pulp extract against 10 bacterial species. The extract displayed remarkable antibacterial property, showing the greatest zones of inhibition against *S. flexneri* (18 mm), *E. coli* (17 mm), and *S. pyogenes* (15 mm). These results suggest that the ethanolic fruit extract of *P. crenulata* displays good antibacterial property against pathogenic bacteria.[13]

Antiurolithogenic activity

Antiurolithiogenic activity of *Pyracantha crenulata* fruit was conducted using fresh fruit juice and 70% hydro-alcoholic (alcohol) extracts in ethylene glycol-induced urolithiasis in male albino rats. Both extracts orally administered to the rats at a dose of 250 mg/kg BW for prophylactic and therapeutic effect, whereas Cystone was taken as the standard drug at a dosage of 750 mg/kg. Hydro-alcoholic extract possessed significant activity where it caused a reduction of urinary oxalate from 2.61±0.17 to 0.86±0.01 mg/dL, calcium from 3.85±0.18 to 2.03±0.24 mg/dL and phosphate from 6.82±0.13 to 3.40±0.26 mg/dL. It also reduced renal oxalate content from 4.85±0.11 to 2.18±0.03 mg/g, calcium from 4.94±0.21 to 2.82±0.21 mg/g and phosphate from 3.88±0.11 to 1.80±0.06 mg/g. In addition, renal functions improved through reduction in blood urea nitrogen from 52.67±0.46 to 40.31±0.22 mg/dL, serum creatinine from 0.98±0.08 to 0.60±0.03 mg/dL and uric acid from 3.48±0.11 to 2.00 mg/mL.[82]

Table 8: Reported phtyoconstituents of *Pyracantha koidzumii*.

Plant part	Chemical compounds	References
Fruits	Quercetin, rutin, helicioside B, garcimangosone D, 2-Hydroxyaucparin, 9-Hydroxyeriobofuran, 3,6-Dihydroxy-2,4-dimethyoxydibenzofuran, Fortuneanoside L, isoquercetin.	[14]

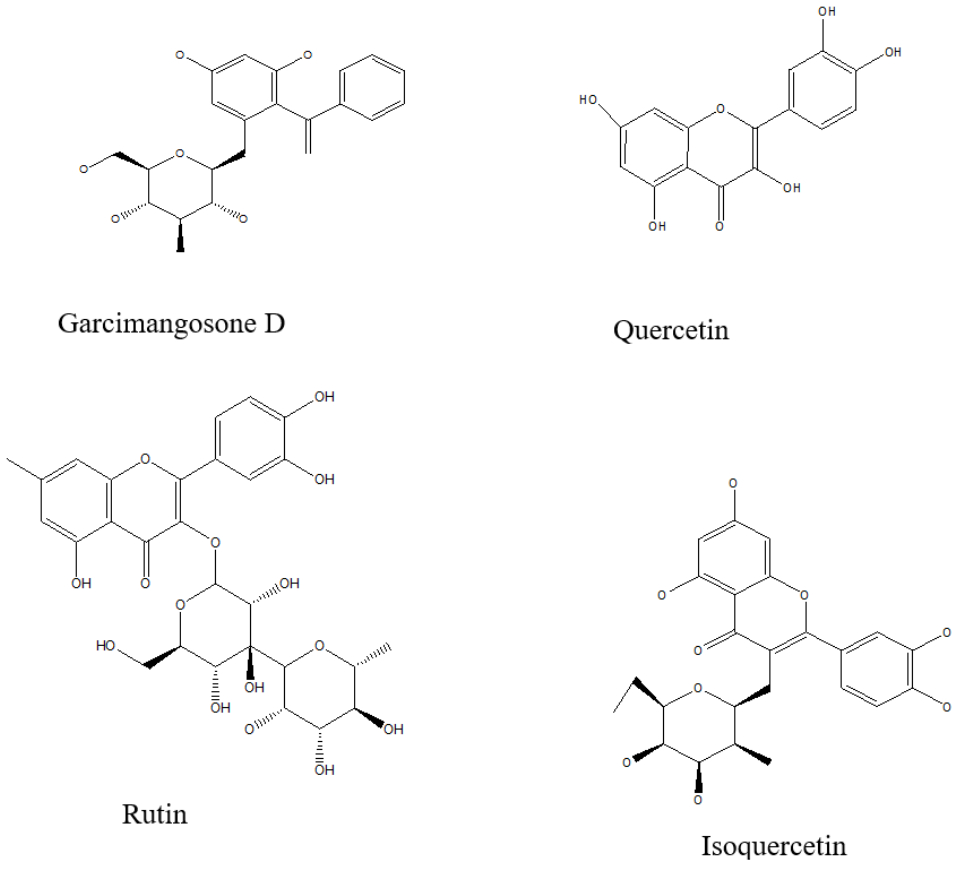

Figure 7: Chemical structure of phytoconstituents present in *Pyracantha koidzumii*.

Table 9: Reported pharmacological activities of *Pyracantha koidzumii*.

Sl. No.	Activities	Plant part / preparation	Method	Model	Therapeutic profile/ results	References
1.	Tyrosinase inhibition/ whitening	Fruit	Bioassay- guided isolation from ethanol fruit exctract, cellular-tyrosinase, protein, mRNA, and enzyme-kinetic assays.	Human Epidermal Melanocytes (HEMn)	Ethanol fruit extract showed cellular tyrosinase- inhibitory activity and new compound 13 was the most potent, inhibiting cellular tyrosinase activity.	[14]
2.	Tyrosinase inhibition mechanism	Fruit-derived isolated compounds	Lineweaver-Burk enzyme kinetics using isolated compound 13	Enzyme assay with L-DOPA substrate	Compound 13 exhibited an uncompetitive mixed type inhibition against L-DOPA, with a reported K_m value of 0.262 Mm.	[14]
3.	Antifungal activity	Silver nanoparticles of aqueous leaf extract	Green synthesis of CuNPs and deteremination of their antifungal potential by minimum fungistatic and fungicidal concentration assays.	Clinical isolated *Candida krusei, Candida tropicalis* and *Candida glabrata*	Activity was species-dependent MFuC/MFC were 1.9/3.8 µg/mL for *C. krusei*, 31.2/62.4 µg/mL for *C. tropicalis* and 15.6/31.2 µg/mL for *Candida glabrata.*	[69]
4.	Antibiofilm activity	Copper nanoparticles	Crystal violet biofilm assay with exopolysaccharide and oxidative stress asseseement	Non- albiacans Candida isolates	Copper nanoparticles markedly reduced biofilm biomass, decrfeased exopolysaccharide production and increased suspectability to oxidative stress across isolates.	[70]
5.	Antifungal mechanism	Copper nanoparticles	Calcofluor white-propidium iodide staining	Candida cells	CuNPs caused cell-wall disruption at fungistatic concentrations.	[69]
6.	Cytotoxic activity	Copper nanoparticles	HepG2 cytotoxicity assay	HepG2 cells	Showed moderate cytotoxicity in HepG2 cells with IC_{50} 7.81 µg/mL, indicating a narrow *in vitro* safety margin.	[69]

Abbreviations: MIC, minimum inhibitory concentration; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); IC_{50}, half-maximal inhibitory concentration.

Antihypertensive Activity

This study aimed to investigate the antihypertensive activity of fruit beverage prepared from *Pyracantha crenulata* was evaluated in Wistar male rats using normotensive and cadmium chloride (1 mg/kg, i.p.)-induced hypertensive models. In the non-invasive normotensive model, oral administration of the beverage at 1.0, 1.5, and 2.0 mL/rat produced a biphasic reduction in mean arterial blood pressure, with the hypotensive effect persisting for up to 5 hr, while heart rate remained unchanged, indicating that the beverage lowered blood pressure without causing significant cardiac depression. In the invasive hypertensive model, intravenous administration of 25, 50, and 100 µL/

rat significantly reduced blood pressure, with the 100 µL/rat dose maintaining the antihypertensive effect for up to 4 hr in cadmium chloride-induced hypertensive rats. It concluded that the fruit beverage possesses significant antihypertensive activity, which was attributed mainly to its high flavonoid and antioxidant content, supporting its potential use as a natural cardioprotective and antihypertensive formulation.[5]

Anticancer Activity

Anti-cancer activity of *Pyracantha crenulata* were investigated using biologically synthesized Silver Nanoparticles (AgNPs) made by reducing silver nitrate with the assistance of the extract from leaves of the plant. The antitumor activity was tested *in vitro* on liver cancer cells called Hep-2 with the help of Sulphorodamide B (SRB) and MTT assays. The AgNPs were measured at 10 µg/mL concentration whereas Cyclophosphamide monohydrate (5 µg/mL) was taken as the standard control compound. The AgNPs showed high cytotoxic activity resulting in 78.45% inhibition of Hep-2 cells in SRB test and 75.62% inhibition in MTT test while the corresponding values for Cyclophosphamide were 85.0% and 82.23%, respectively.[83]

Neuroprotective

Pyracantha crenulata was tested for its neuroprotective effect using a hydroalcoholic extract of the whole plant using Soxhlet extraction in methanol: water (1:1) ratio. Neurotoxicity was created by administering Aluminium Chloride ($AlCl_3$, 100 mg/kg/day) in oral way to adult male Wistar rats for 21 days to create memory deficit similar to Alzheimer's disease. Hydroalcoholic extract of *Pyracantha crenulata* was orally given at doses of 250 and 500 mg/kg/d, while rivastigmine (5 mg/kg/day) was used as the standard drug. Tests used in evaluating memory and learning included MWM (Moris water maze) test and EPM (Elevated plus maze) test. Biochemical and histopathological studies were also carried out on the animals. Treatment with the extract of *P. crenulata*, especially 500 mg/kg dose, significantly enhanced

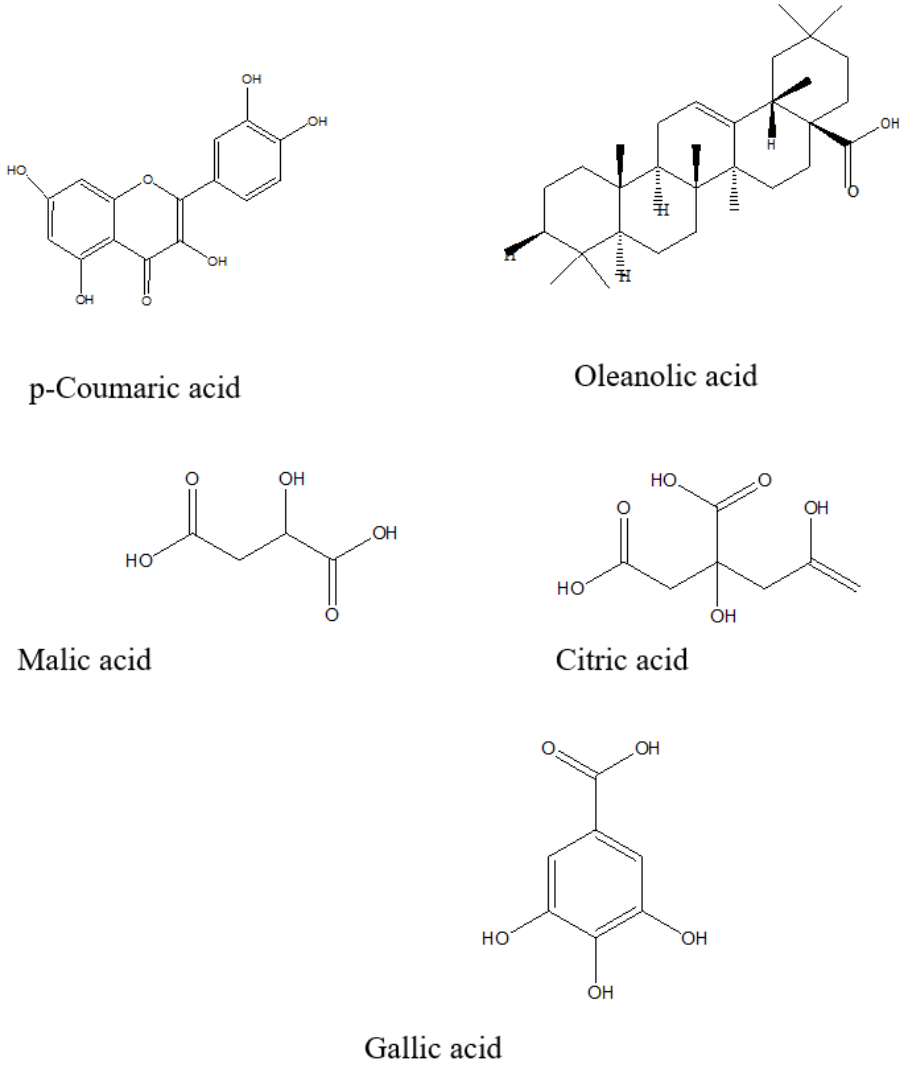

Figure 8: Chemical structure of phytoconstituents present in *Pyracantha crenulata*.

Table 10: Reported phytoconstituents of *Pyracantha crenulate*.

Category	Reported compounds	References
Phenolic compounds	Gallic acid, chlorogenic acid, caffeic acid, ferulic acid, p-Coumaric acid	[2,13,76]
Flavanoids	Quercetin, kaempferol, rutin, hyperoside, isoquercetin	[2,13]
Triterpenoids	Ursolic acid, oleanolic acid	[71,77]
Phytosterols	β -sitosterol, stigmasterol	[2]
Tannins	Hydrolysable and condensed tannins	[78]
Organic acids	Malic acid, citric acid	[13]
Vitamins	Vitamin C, β-Carotene	[4,79]
Minerals	Potassium, magnesium, iron, phosphorus	[13]

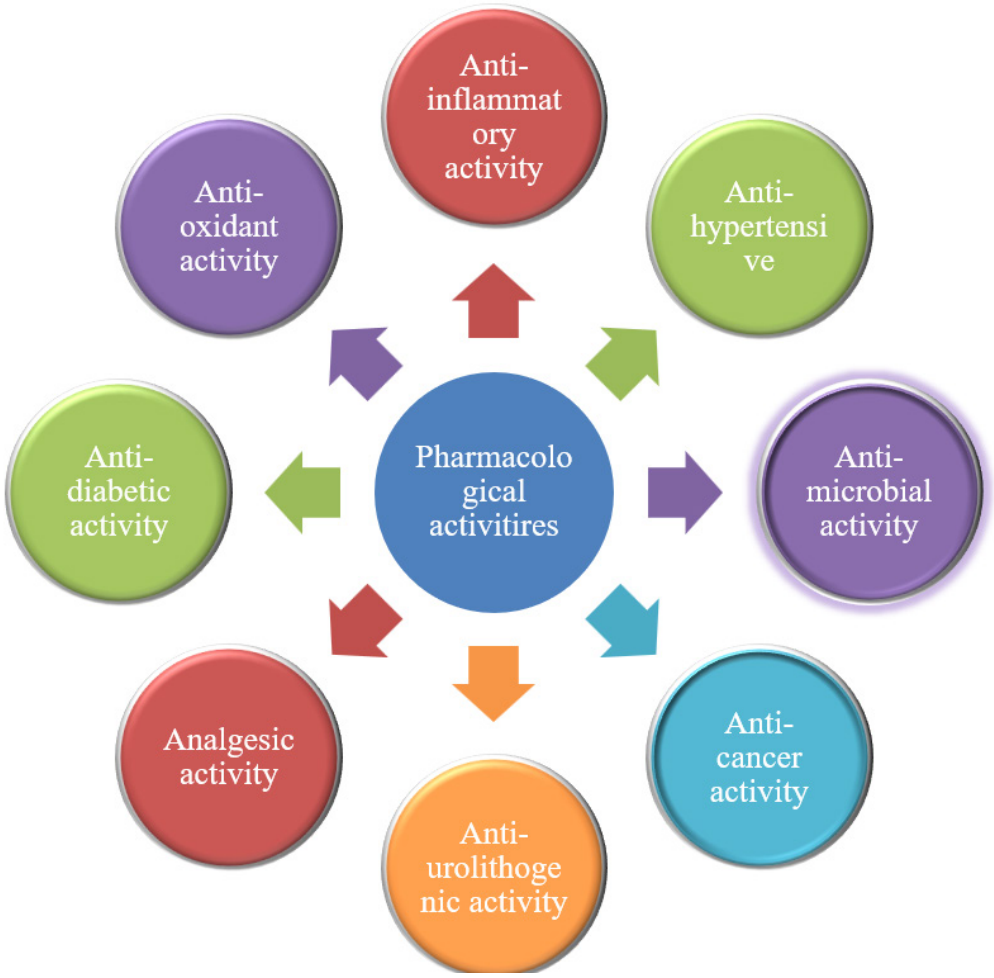

Figure 9: Reported pharmacological activities of *Pyracantha crenulata*.

spatial learning and memory, elevated SOD levels from 3.88±0.37 to 6.54±0.35 µmol/mg protein, decreased Acetylcholinesterase (AChE) levels from 0.39±0.018 to 0.26±0.026 ng/g protein and lowered Myeloperoxidase (MPO) levels from 196.38±5.25 to 125.61±9.24 U/L when compared with disease control.[73]

DISCUSSION

The available literature indicates that *Pyracantha* species possess a broad phytochemical profile, including flavonoids, phenolic acids, triterpenoids, polysaccharides, organic acids, vitamins, minerals, and other specialized metabolites. The reported composition varies according to species, plant part, geographical origin, extraction method, and experimental

Table 11: Reported pharmacological activities of *Pyracantha crenulata*.

Sl. No.	Activities	Plant part	Method	Model	Therapeutic profile/results	References
1.	Analgesic/ antinociceptive	Leaves and fruits	Hydroethanolic extraction, behavioral analgesia assay, docking /dynamics.	wistar rats, tail immersion, tail flicl, hot plate, formalin paw test.	Leaf and fruit extracts significantly reduced nociception through central and peripheral mechanisms, effects were compareable to diclofenac, with gallic acid docking to COX-2 and mu-opoid receptor.	[80]
2.	Anti-diabetic	Fruits	Successive soxhlet extraction in n-hexane, ethyl acetate, ethanol, water; inhibition assays.	α-amylase and α-glucosidase assays (*in vivo*).	Extracts inhibited both enzymes dose-dependently; the ethanol fruit extract was most active with IC_{50} 44.79 µg/mL for α-amylase and 30.09 µg/mL for α-glucosidase, comparable to acarbose	[81]
3.	Antioxidant	Leaves	Lyophilized leaf extract; radical scavenging assays.	*In vitro* ABTS and DPPH assays.	Leaf extract showed strong anti-oxidant activity with IC_{50} 10.61 µg/mL in ABTS and 12.73 µg/mL in DPPH, alongside high phenolic, tannin and flavanoid content.	[78]
4.	Antioxidant	Leaves	Compound isolation by column chromatography; DPPH assay; docking.	*In vitro* DPPH assay; *in silico* CDK2 docking.	Six compounds were isolated; compound Cc-4 showed the strongest antioxidant activity with IC_{50} 15.734 µg/mL and favouarble docking and ADME profiles.	[84]
5.	Anti-urolithogenic	Fruits	Alcohol and juice extracts; prophylactic and curative dosing.	Male albino rats with ethylene glycol-induced urolithiasis.	Both juice and alcohol extracts lowered renal deposition of stone-forming constituents, reduced calcium oxalate precipitation, improved kidney function and showed cytoprotectrive effects.	[82]
6.	Anti-hypertensive	Fruits	Herbal beverage formulation from fruit juice.	Hypertensive snd normotensive rat models; cadmium chloride-induced hypertension.	The fruit beverage exhibited antihypertensive effects by reducing blood pressure in both hypertensive and normotensive rat models.	[5]
7.	Anti-inflammatory	Bark	Isolation of pyracrenic acid; fertile egg method; oral rat test.	Fertile egg assay; rats for granulation tissue formation.	Pyracrenic acid showed dose-dependent anyti-inflammatory activity in the fertile egg method and inhibited granulation tissue formation at 50mg/kg in rats.	[4]

Sl. No.	Activities	Plant part	Method	Model	Therapeutic profile/results	References
8.	Antimicrobial	Fruits	Disc diffusion method	10 bacterial strains and 3 fungal strains.	Ethanol extract Shows strongest antimicrobial activity.	[76]
9.	Anti-bacterial	Fruits	Disc diffusion method	*In vitro* against Shigella, *E. coli, Streptococcus* pyrogens.	Ethanolic fruit extract exhibited strongest antibacterial activity against food-poisioning associated microorganism.	[13; 74]
10.	Cytotoxic/ anticancer	Leaves	Green synthesis of silver nanoparticles from aqueous leaf extract, MTT assay.	Liver cancer Hep-2 cells.	Biosynthesis AgNPs from leaf extract strongly inhibited liver cancer cell growth in the MTT assay.	[83]
11.	Neuroprotective	leaves	Morris water maze and elevated plus maze.	Rats	Extract showing activity with dose dependent manner with the highest dose exhibiting the greatest improvement in memory performance.	[72]

Abbreviations: MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; DPPH, 2,2-diphenyl-1-picrylhydrazyl; ABTS, 2,2′ -azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); IC_{50}, half-maximal inhibitory concentration; AgNPs, silver nanoparticles; COX-2, cyclooxygenase-2; CDK2, cyclin-dependent kinase 2.

conditions. *Pyracantha fortuneana* has been comparatively well investigated for polysaccharides, antioxidant, antidiabetic, anticancer, antihyperlipidemic, immunoprotective, and anti-photoaging effects, whereas *P. coccinea and P. crenulata* have also demonstrated diverse biological activities. *P. angustifolia and P. koidzumii* show promising antioxidant, antibacterial, antimelanogenesis, tyrosinase-inhibitory, antifungal, antibiofilm, and anticancer activities, although the evidence base is smaller.

Most reported pharmacological evidence remains preclinical, with a substantial proportion derived from *In vitro* assays and animal models. The studies summarized in this review support the therapeutic potential of *Pyracantha*, but differences in plant material, extraction procedures, doses, models, and outcome measures limit direct comparison among studies. Further work should therefore emphasize authenticated and standardized plant material, validated phytochemical profiling, isolation of bioactive constituents, mechanistic studies, toxicity evaluation, pharmacokinetic characterization, and well-designed preclinical and clinical investigations. The development of standardized extracts and modern delivery systems may also improve reproducibility and translational potential.

CONCLUSION

The genus *Pyracantha* is a remarkable genus of medicinal and ornamental plants, which has great ethnopharmacological importance. This review emphasizes the richness of *Pyracantha* species regarding variety, geographical distribution, and phytochemical composition. There are numerous reports on the presence of various classes of secondary metabolites, including flavonoids, phenolic acids, triterpenoids, organic acids, polysaccharides, anthocyanins, carotenoids, and others, among different *Pyracantha* species. The current scientific literature proves the wide spectrum of pharmacological activity of this genus, such as anti-oxidant, antimicrobial, anti-inflammatory, antidiabetic, antihypertensive, carcinogentioc, hepatoprotective, immunomodulatory, anti-photoaging, and woundhealing properties. All the mentioned data prove the high medicinal value of *Pyracantha* species and their great effect as a source of photochemical constituents for the development of pharmaceuticals and nutraceuticals.

Although there have been some promising developments in the research, the genus *Pyracantha* has not been studied sufficiently enough. It seems that most of the research was performed only on several species, namely, *Pyracantha fortuneana, Pyracantha coccinea, Pyracantha crenulata, Pyracantha angustifolia*, and some other species such *as Pyracantha atalantioides* and *Pyracantha koidzumii* have not been paid so much attention yet. Moreover, the majority of pharmacological experiments are based on *In vitro* and animal models, but there is no human trial available yet.

The standardization of the material, the profiling of phytochemicals, the characterization of active substances, the evaluation of pharmacokinetics, the toxicity studies, and the investigation of molecular mechanisms are also needed. The differences in the procedures of extractions, the plant parts used, the geographic origin, and the experimental conditions make the comparison of data from different studies difficult as well. Future

investigation should be explored the isolation and identification of new active substances, at advanced metabolomics and molecular research, as well as at developing standard extracts of high quality. Preclinical and clinical studies should be conducted to validate medicinal potential of *Pyracantha* species and determine their safety profiles. Additionally, nanotechnology, green synthesis methods, and new technologies of drug delivery could help to increase the bioavailability of *Pyracantha* extracts. The conservation and sustainable utilization of *Pyracantha* genetic resources should be ensured in order to make these plants available for medicinal and commercial use in the future. In conclusion, it can be stated that the evidence obtained shows that *Pyracantha* genus is characterized by high phytochemical diversity and medicinal potential.

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ABBREVIATIONS

ABTS: 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); **AChE:** Acetylcholinesterase; **AgNPs:** Silver nanoparticles; **CDK2:** Cyclin-Dependent Kinase 2; **COX-2:** Cyclooxygenase-2; **CuNPs:** Copper nanoparticles; **DPPH:** 2,2-Diphenyl-1-picrylhydrazyl; **EPM:** Elevated plus maze; **FeNPs:** Iron nanoparticles; **FMVD:** Freeze-microwave vacuum drying; **GPx:** Glutathione peroxidase; **HPTLC:** High-performance thin-layer chromatography; **IC_{50}:** Half-maximal inhibitory concentration; **iNOS:** Inducible nitric oxide synthase; **LPS:** Lipopolysaccharide; **MAPK:** Mitogen-activated protein kinase; **MIC:** Minimum inhibitory concentration; **MPO:** Myeloperoxidase; **MTT:** 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; **MWM:** Morris water maze; **NPs:** Nanoparticles; **Nrf2:** Nuclear factor erythroid 2-related factor 2; **PUMA:** p53 upregulated modulator of apoptosis; **ROS:** Reactive oxygen species; **SIRT1:** Sirtuin 1; **SOD:** Superoxide dismutase; **STZ:** Streptozotocin; **TFC:** Total flavonoid content; **TNF-α:** Tumour necrosis factor-alpha; **TNBC:** Triple-negative breast cancer; **TPC:** Total phenolic content; **ZnNPs:** Zinc nanoparticles.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Riya Rajput: Literature search and manuscript drafting. **Sumitra Singh:** Cnceptualization, critical revision of the manuscript and **Bhawna Parmar:** literature review. **Rakesh K. Sindhu:** Cnceptualization, Supervision, critical revision, and All authors approved of the manuscript for publication.

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