Chapter 8
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A Comprehensive Analysis of the Medicinal Use of Bioactive Secondary Metabolites from the Genus *Ehretia*

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ABSTRACT

The roughly 150 species of plants that make up the genus *Ehretia* are primarily found in tropical regions of North America, Africa, Australia, and Asia. They have long been used as traditional and folk remedies in China, India, and Japan to cure a wide range of illnesses. Pharmacological investigations verified that the genus's crude extracts or specific components had anti-snake venom properties in addition to antioxidant, anti-inflammatory, antibacterial, anti-arthritic, anti-tubercular, and anti-allergic properties. Based on the available literature up to February 2024, summery of secondary metabolites that have been identified from several species of *Ehretia* in this literature. Chapter concentrated on the known biological activities of the *Ehretia* plants and covered them in detail here, in addition to their traditional therapeutic usage.

Keywords: Ehretia; traditional & medicinal importance; essential oil; biological activities; future prospects.

1. INTRODUCTION

There are over 150 species in the genus *Ehretia,* which is a member of the Boraginaceae family [1]. Tropical regions of Asia, Africa, Australia, Europe, and North America are home to a large number of species [2]. Every species of

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Ehretia is a shrub (*E. rigida*) or a tree (*E. acuminata*) [3]. In China, Japan, and India, traditional medicines are made from leaves, barks, roots, branches, fruits, and heartwoods [3a]. Some species have small fruits that are visited by a wide range of opportunistic avian frugivores, and because of their low fibre content and in vitro fermentation properties, some of these species may be useful as supplemental feed for ruminant livestock and wild animals [4]. Numerous species of the genus *Ehretia* have been described for India, including *Ehretia* leavis Roxb, *Ehretia acuminata* R.Br, and *Ehretia microphylla* [5]. Due to these species' excellent responses in a wide range of biological activities, they are employed in numerous herbal and traditional medicines in China and India. Phenolic acids, lignans, flavonoids, nitrile glycosides, quinonoids, steroids, triterpenoids, and pyrrolizidine alkaloid have all been linked to the *Ehretia* genus [6]. Numerous *Ehretia* species have been shown to have anti-bacterial, anti- inflammatory, and anti-diabetic properties. This genus has several significant species, including *E. longiflora, E. leavis, E. acuminata, E. microphylla*, and *E. obtusifolia [3a]*.

This article represents the findings of a thorough investigation of the chemotaxonomy, secondary metabolites, biological activities, and pharmacological applications of this genus up to 2024, which will aid in future research and potential applications of the plants. In an effort to provide the most recent information available, some chemical constituents and activities have been published.

2. TRADITIONAL AND MEDICINAL IMPORTANCE OF SOME SPECIES OF GENUS *EHRETIA*

For the past few decades, China, India, and Japan have been using various plants in the genus *Ehretia* in a wide range of traditional herbal and Chinese medicines.

Table 1. Traditional and medicinal importance of some species of genus *Ehretia*

Botanical name	Common name	Part used	Traditional use	Reference
Ehretia acuminata *R.Br.*	Pudila, Nara, Koda	1. Leaves 2. Bark 3. Root	The extract of the leaves mixed with water and taken orally once daily for 2-3 days to cure acute dysentery.	[7]
Ehretia leavis *Roxb.*	Chamror (Punjab). Kuptaa, Datarangi (Maharashtra.)	1. Leaves 2. Root 3. Bark 4. Fruit	Bark is used internally and as gargle in throat infections, inner bark of *E. laevis* is used as food**.**	[8]
Ehretia microphylla *Lam.*	Pala.	1. Leaves 2. Root	Dried leaves used in stomachic, decoction of the leaves is used as cure for coughs and is prescribed for the treatment of cyaniding with bloody discharge and for dysentery.	[9]
Ehretia obtusifolia. Hochst. ex A.DC		1. Leaves 2. Thin branches	Decoction of leaves and bark in Malaria.	[10]

Botanical name	Common name	Part used	Traditional use	Reference
Ehretia cymosa		1. Leaves 2. Bark	Different parts of plant are use in Diarrhea.	[11]
Ehretia amoena		1. Leaves 2. Bark 3. Root	Plant works against trypanosomiasis	[12]

3. PHYTOCONSTITUENT PRESENT IN GENUS *EHRETIA*

Numerous phytoconstituents, including phenolic acids, flavonoids, benzoquinones, cyanogenetic glycosides, fatty acids, and other significant compounds, are found in the species that make up the genus *Ehretia.*

3.1 Phenolic Acids

Natural bioactive substances like secondary metabolites and antioxidants may be found in plants. The therapeutic agent and secondary metabolite found in medicinal plants are phenolic acids. Fruits and vegetables have special tastes and health-promoting qualities because of phenolic chemicals. Because dietary phenolics have antioxidative and potentially anticarcinogenic properties, there is currently a lot of interest in their effects.

Table 2. Phenolic compounds present in genus *Ehretia*

S.no	Phenolic acid	Species	Reference
1.	Buddlenol B	*E. ovalifolia*	[13]
2.	Cinnamic acid	*E. thyrsiflora*	[14]
3.	Ehletianol D	*E. ovalifolia*	[13]
4.	(E)-ethyl caffeate	*E. thyrsiflora*	[15]
5.	Caffeic anhydride	*E. obtusifolia*	[8]
6.	Icariside E5	*E. ovalifolia*	[11]
		E. thyrsiflora	[14]
7.	Lithospermic acid B	*E. thyrsiflora*	[14]
8.	Methyl 2-O-feruloyl-1a-O-vanillactate	*E. obtusifolia*	[9]
9.	Methyl rosmarinate	*E. obtusifolia*	[9]
		E. thyrsiflora	[13]
10.	p-hydroxybenzoic acid	*E. thyrsiflora*	[13]
11.	Rosmarinic acid	*E. obtusifolia*	[9]
		E. thyrsiflora	[14]
12.	Trans-4-hydroxycyclohexyl-2-O-p- coumaroyl-β-D-glucopyranoside	*E. obtusifolia*	[9]
13.	Ehletianol C	*E. ovalifolia*	[12]
14.	*Trans*-ferulic acid	*E. thyrsiflora*	[14]

3.2 Flavonoids

More than 6,000 compounds have been identified as belonging to the flavonoid class, which is further divided into several subclasses: flavonols (such as rhamnazin, myricetin, kaempferol, and quercetin), flavones (such as apigenin, luteolin, and tangeretin), flavanones (such as hesperetin, naringenin, and eriodictyol), flavanols (such as catechins and epicatechins), anthocyanidins (such as yaniding, delphinidin, and malvidin), and isoflavones (such as genistein, daidzein, and glycitein).

Table 3. Flavonoids present in plants of genus *Ehretia*

S.no	Flavonoids	Species	Reference
1.	Apigenin	*E. ovalifolia*	[15]
2.	Hyperoside	*E. thyrsiflora*	[14]
3.	Kaempferol-3-*O*-α-*D*-arabinoside	*E. thyrsiflora*	[13]
4.	Kampferol-3-*O*-β-*D*-galactopyranoside	*E. thyrsiflora*	[14]
5.	Quercetin-3-*O*-α-*D*-arabinoside	*E. thyrsiflora*	[13]
6.	Ovalifolin	*E. ovalifolia*	[15]

3.3 Fatty Acids

Although a vast array of fatty acids are synthesized by plants, only a small number are significant and frequently occurring phytoconstituents. Since fatty acids produce a significant amount of ATP during metabolism, they are crucial dietary sources of fuel for animals.

Table 4. Fatty acids present in plants of genus *Ehretia*

S.no	Fatty acid	Species	Reference
1.	Araneosol	*E. ovalifolia*	[15]
2.	Di (octadecyl) phthalate	*E. thyrsiflora*	[16]
3.	Tetradecenoic acid 2, 3-dihydroxypropyl ester	*E. thyrsiflora*	[17]
4.	(10*E*, 12*Z*, 15*Z*)-9-hydroxy-10, 12, 15-octadecatrienoic acid methyl ester	*E. dicksonii*	[18]
5.	2-methoxyl benzoic acid octyl ester	*E. thyrsiflora*	[17]

3.4 Benzoquinones

Quinones are a class of secondary metabolites generated from plants, and within the kingdom of plants, benzoquinones are extensively dispersed and are primarily found in higher plants, including those belonging to the families Polygonaceae, Rubiaceae, Leguminosae, Rhamnaceae, Labiatae, and Boraginaceae.

Table 5. Benzoquinones present in plants of genus *Ehretia*

S.no	Benzoquinone	Species	Reference
1.	Cyclomicrophyllone	*E. microphylla*	[8]
2.	Dehydromicrophyllone	*E. microphylla*	[8]
3.	Ehretianone	*E. buxifolia*	[19]
4.	Microphyllone	*E. microphylla*	[8,19]
5.	1,4-naphthoquinone lewisone	*E. laevis*	[20]
6.	Ehretiquinone	*E. longiflora*	[21]

3.5 Glycosides

Important secondary metabolites called glycosides are present in the chemical components. Nonetheless, the composition of the sugar moieties frequently affects the biological actions of glycosides.

Table 6. Glycosides present in plants of genus *Ehretia*

S.no	Glyciside	Species	Reference
1.	Simmondsin	*E. philippinensis*	[22]
2.	Ehretioside B	*E. philippinensis*	[23]
3.	Polyalcohol	*E. philippinensis*	[23]

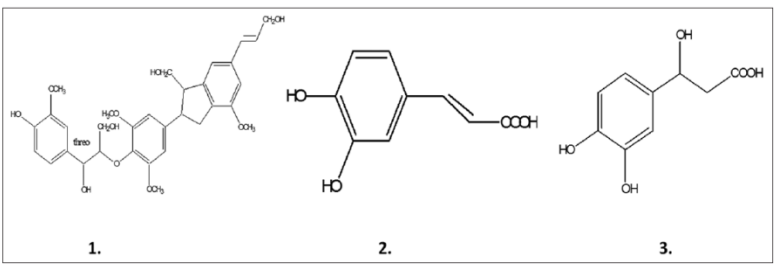
4. OTHER IMPORTANT CONSTITUENTS EXTRACT FROM GENUS *EHRETIA*

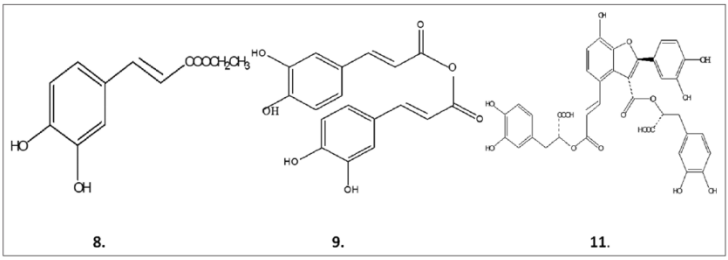
Numerous other significant components have also been identified from various plant sections, including the leaves, bark, fruit, and roots of the genus *Ehretia.*

Table 7. Important phytoconstituents present in plants of genus *Ehretia*

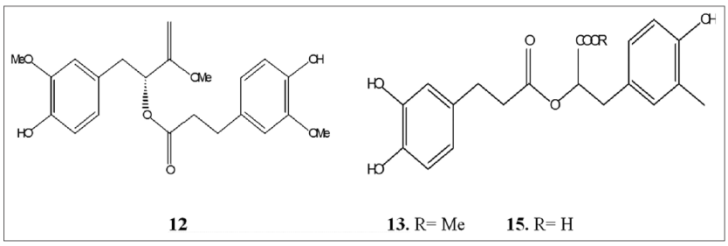
S.no	Compound	Species	Reference
1.	Bauerenol	*E. laevis*	[24]
2.	β-sitosterol	*E. laevis*	[24]
3.	Daucosterol	*E. thyrsiflora*	[17]
4.	Stigmasterol	*E. buxifolia*	[25]
5.	Stigmastanol	*E. buxifolia*	[25]
6.	Ehretiolide	*E. longiflora*	[26]
7.	Ehreticoumarin	*E. longiflora*	[26]

5. CHEMICAL STRUCTURE OF COMPOUND PRESENT IN *EHRETIA* GENUS [32]

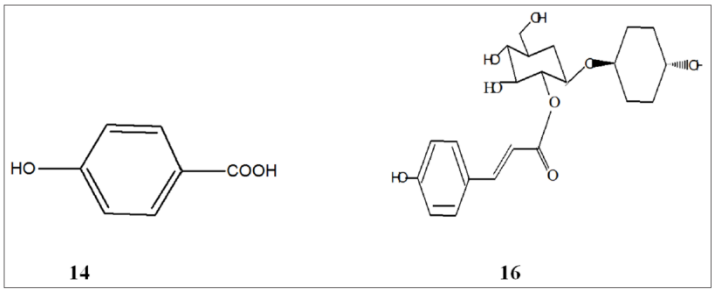




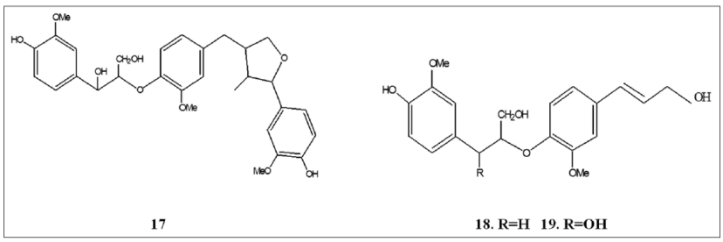
8. **9.** **11.**



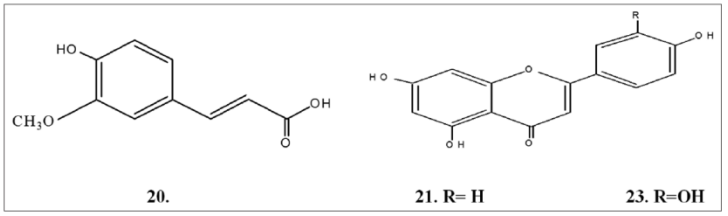
12 **13.** R= Me **15.** R= H



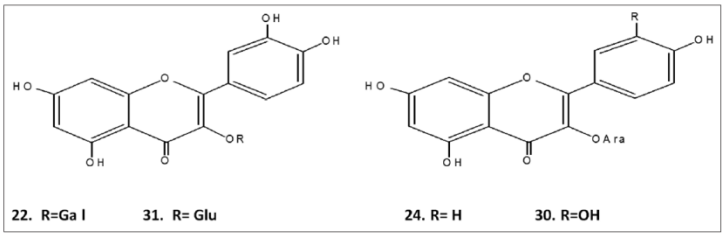
14 **16**



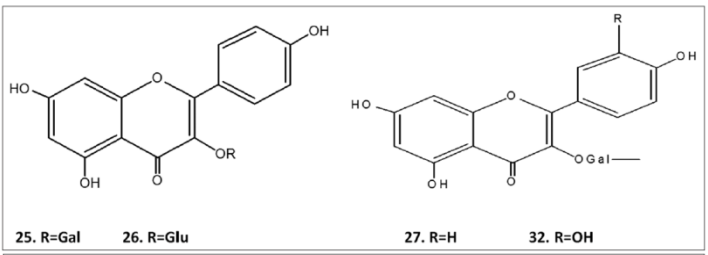
17 **18.** R=H **19.** R=OH



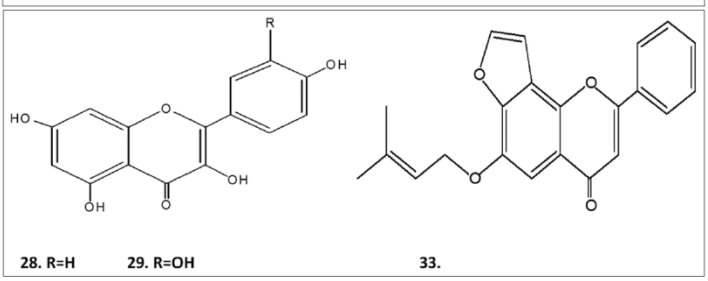
20. **21.** R= H **23.** R=OH



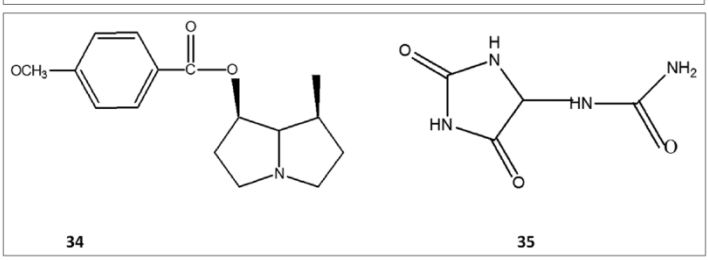
22. R=Ga l **31. R= Glu** **24. R= H** **30. R=OH**



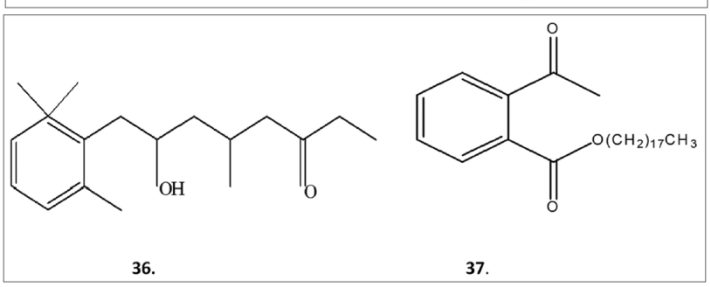
25. R=Gal **26. R=Glu** **27. R=H** **32. R=OH**



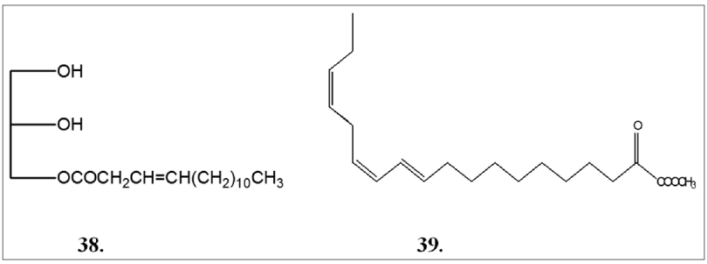
28. R=H **29. R=OH** **33.**



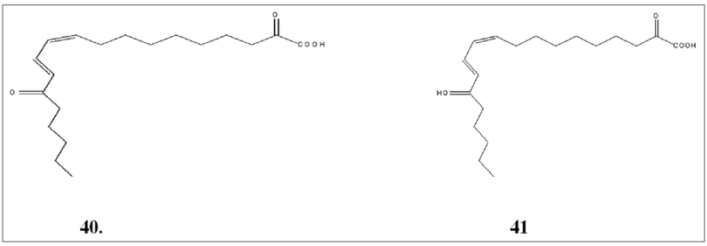
34 **35**



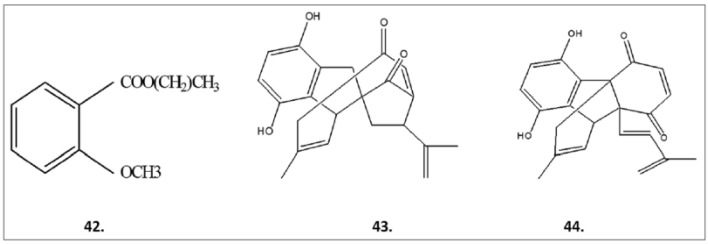
36. **37.**



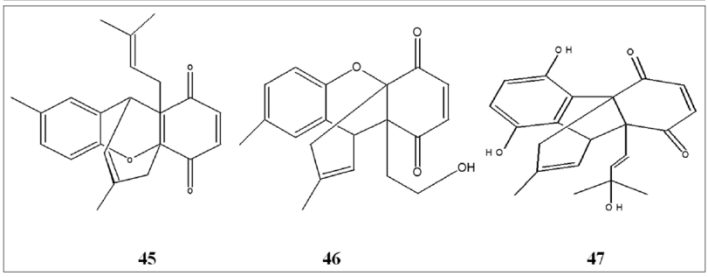
38. **39.**



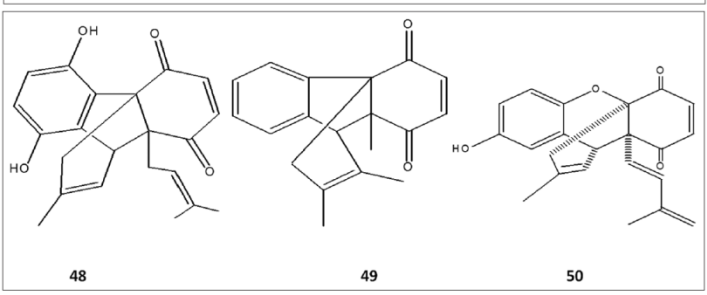
40. **41**



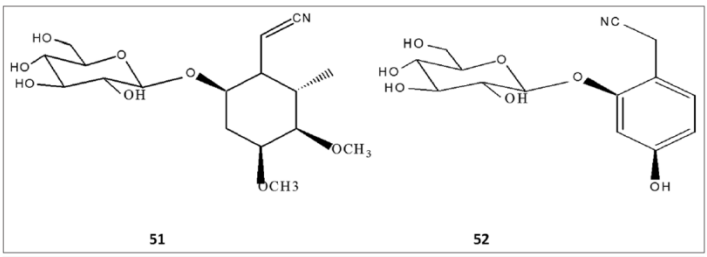
42. **43.** **44.**



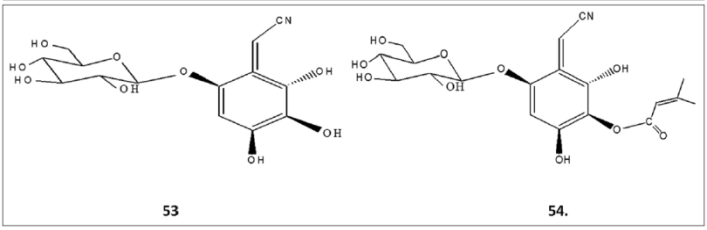
45 **46** **47**



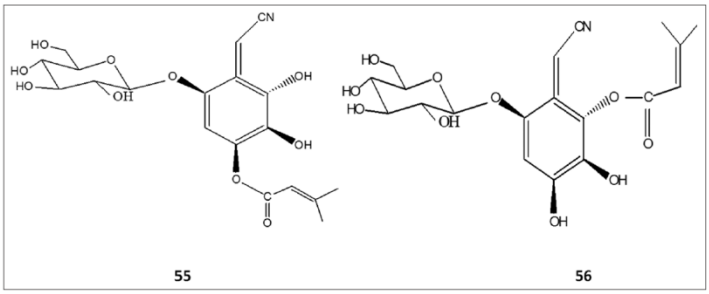
48 **49** **50**



51 52



53 54.



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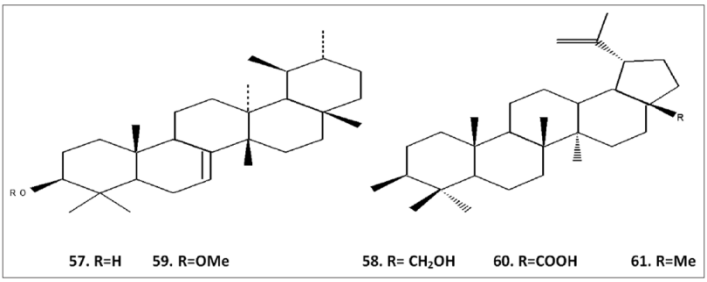
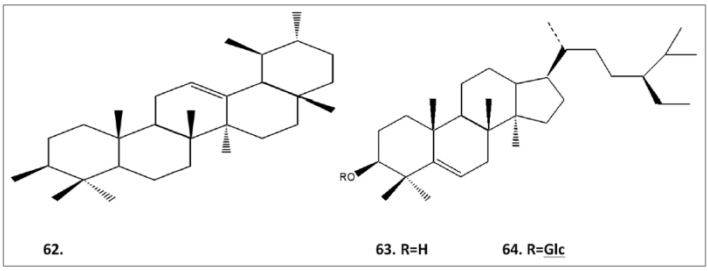


57. R=H 59. R=OMe 58. R= CH_2OH 60. R=COOH 61. R=Me



62. 63. R=H 64. R=Glc

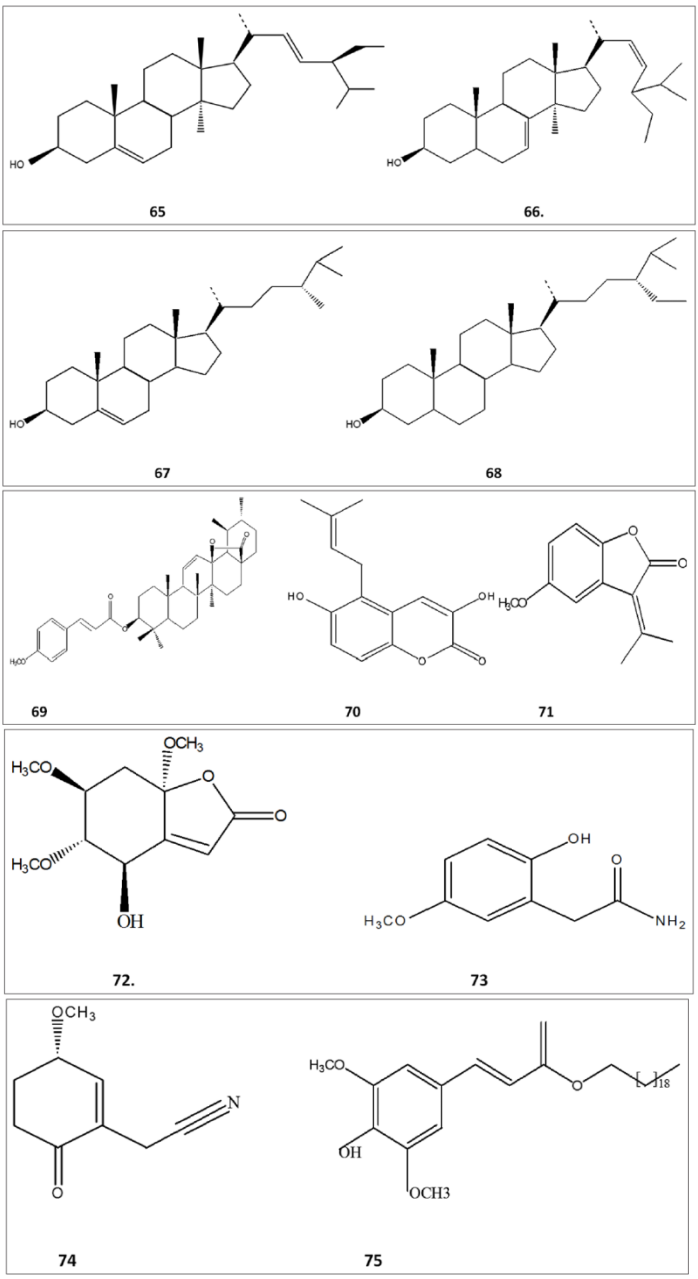


Fig. 1. Compounds isolated from genus *Ehretia*

5.1 Essential Oil

Essential oil obtained through hydrodistilation from the leaves of *E. cymosa*. Certain chemical components were extracted from the essential oil, which was primarily made up of sesquiterpene hydrocarbon molecules, by comparing their mass spectra with those of NIST. Kaur et al. 2024 extracted essential oil from *E. acuminata* fruit and GC\MS study revealed that chemical constituents found in oil was biologically active.

Table 8. Compound separated from essential oil

S.no	Compound	Reference
1.	Linalool	[27]
2.	*trans*-Sesquisabinene hydrate	[27]
3.	Methyl salicylate	[27]
4.	*o*-tert-Butylphenol	[27]
5.	β-Ylangene	[27]

6. SOME SPECIES OF GENUS *EHRETIA*

Ehretia leavis ***Ehretia microphylla***

Ehretia aspera ***E. longiflora***

E. anacua ***E. obstulifolia***

E. acuminate ***E. dicksonii***

Fig. 2. Important Species of genus *Ehretia*

7. BIOLOGICAL ACTIVITIES OF DIFFERENT SPECIES OF GENUS *EHRETIA*

Numerous Ehretia species exhibit a variety of biological properties, including anti-oxidant, anti- inflammatory, anti-becterial, anti-airthritic, and anti-snake venomous properties.

7.1 Antioxidant Activity

Numerous substances that are found in plants naturally have been classified as either active oxygen scavengers or free radicals. The 1-butanolic and chloroform fractions of the leaves and the ethyl acetate fraction of the fruits in *E. serrata* demonstrated significant anti-free radical activity. These compounds exhibit a notable antioxidant response.

Table 9. Different species having Antioxidant potential of genus *Ehretia*

S.no	Species	Part used	Reference
1.	*E. thyrsiflora*	leaves	[26]
2.	*E. laevis* Roxb	leaves	[28]
3.	*E. serrata*	leaves	[28]
4.	*E. laevis* Roxb	fruit	[29]
5.	*E. tinifolia*	fruit	[30]
6.	*E. microphylla*	aerial part	[11]

7.2 Anti-inflammatory Activity

An outline of the inflammatory process could be an event series that happens in reaction to noxious stimuli, infection, or trauma. Redness, heat, swelling, discomfort, and loss of function are the traditional indicators of inflammation.

Table 10. Different species having Anti-inflammatory potential of genus *Ehretia*

S.no	Species	Part used	Reference
1.	*E. dicksonii*	leaves	[18]
2.	*E. obtusifolia*	leaves	[19]
3.	*E. laevis* Roxb	leaves	[31]
4.	*E. longiflora*	root	[21]

7.3 Anti-bacterial Activity

Methanol, chloroform, and aqueous solvent extracts of *E. leavis* leaves have all demonstrated remarkable antibacterial activity. Chloroform and aqueous methanolic extract had strong antibacterial action against both gramme positive and gramme negative bacteria when compared to methanol.

Table 11. Different species having Antibacterial potential of genus *Ehretia*

S.no	Species	Part used	Reference
1.	*E. laevis Roxb*	leaves	[32]
2.	*E. abyssinica r.br.*	leaves	[33]
3.	*E. microphylla*	leaves	[31]

8. CONCLUSION AND FUTURE PROSPECTS

Numerous components of the genus *Ehretia* exhibit a wide range of biological and pharmacological properties, including anti-allergic, anti-trypanosomal, anti-airthritic, and anti- snake venom properties. Even though many *Ehretia* species have been used for a long time as traditional medicines in Australia, North America, and Asia, and despite the fact that many chemistry and pharmacology studies on *Ehretia* have been conducted, the authors offer some viewpoints here in an effort to shed light on related research that may be done on *Ehretia* in the future.

First off, there are notable variations in the primary secondary metabolites of the rather large genus Ehreia. These molecules were extensively described from *E. longiflora, E. leavis, E. microphylla, E. obtusifolia, E. thyrsiflora, E. buxifolia, E. philippinensis, E. dicksonii*, and *E. ovalifolia*; however, no reports for the other investigated species, *E. alba, E. angolensis, E. bakeri, E. coerulea, E. dichotoma, E. dolichandra, E. exsoluta, E. hainanensis, E. javanica, E. latifolia*, and *E. papuana,* were discovered. Nine different species can be found in South Africa [32].

As native to India, plants of this genus have the potential to be a significant source of money for the country if researchers and industry take advantage of this potential for highly pharmacological application by conducting additional study to support prior findings.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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- National Faculty Development Programme on Current Research and Innovation Trends in Sciences & Technology. 2024.
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- Abha Shukla, Amanpreet Kaur*. A Systematic Review of Traditional Uses Bioactive Phytoconstituents of Genus Ehretia. Asian journal of pharmaceutical and clinical research. 2018,11(6) 88-100.
- Amanpreet Kaur*, Abha Shukla, Rishi Kumar Shukla. Comparative Evaluation of ABTS, DPPH, FRAP, Nitric Oxide Assays for Antioxidant Potential, Phenolic & Flavonoid Content of Ehretia acuminata R. Br. Bark. International Research Journal of Pharmacy 2018, 9(12) 100-104.

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