

A SYSTEMATIC REVIEW OF TRADITIONAL USES BIOACTIVE PHYTOCONSTITUENTS OF GENUS *EHRETIA*

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ABSTRACT

The plants of the genus *Ehretia* composed of about 150 species mainly distributed in tropical Asia, Africa, Australia, and North America. They have been used as traditional and folk medicines to treat various ailments in Japan, India, and China for a long time. Previous phytochemical screenings demonstrated that the *Ehretia* plants mainly contain fatty acids, phenolic acids, flavonoids, cyanogenetic glycosides, and benzoquinones and other constituents from different chemical classes. The pharmacological studies confirmed that the crude extracts or individual compounds from the genus showed antioxidant, anti-inflammatory, antibacterial, antiarthritic, antitubercular, and antiallergic activities, as well as anti-snake venom property. In this review, we presented a summary of the secondary metabolites isolated from different species of *Ehretia* based on the published literatures up to March 2017. In addition to the traditional medicinal use of *Ehretia* plants, we focused on the known biological activities of the plants and discussed them in detail here.

Keywords: *Ehretia*, Traditional and medicinal importance, Essential oil, Antiparasitic activity, Future prospects.

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INTRODUCTION

Ehretia genus has around 150 species belongs to the family Boraginaceae [1-3]. Many species are mainly distributed in tropical Asia, Africa, Australia, Europe, and Northern America [4-14]. All species of *Ehretia* are trees (*Ehretia acuminata*) and shrubs [15] (*Ehretia rigida*). The leaves, barks, roots, branches, fruits, and heartwoods are used as the traditional medicines in China, Japan, and India. Some species produce small fruits are visited by a broad variety of opportunistic avian frugivores, and some species could be a valuable supplementary feedstuff for ruminant livestock and wild animal due to its *in vitro* fermentation characteristics as well as low fiber [15-19]. In India, genus *Ehretia* is reported for many species such as *Ehretia laevis* Roxb., *E. acuminata* R.Br [20], and *Ehretia microphylla* [21,22]. These species are used in many herbal and traditional medicines in India and China because of their good response in many biological activities. *Ehretia* genus has reported the presence of phenolic acids, lignans, flavonoids, nitrile glycosides, quinonoids, steroids, triterpenoids, and pyrrolizidine alkaloid [23,24]. Many species of *Ehretia* genus are reported for anti-inflammatory, antidiabetic, and antibacterial activity. Some important species of this genus are *Ehretia longiflora*, *E. laevis*, *E. acuminata*, *E. microphylla*, and *Ehretia obtusifolia*.

In an effort to provide the up-to-date information of the genus *Ehretia*, in previous, some chemical constituents and activities have published up to 2010 [25], and this article represents the results of an extensive investigation of the chemotaxonomy, secondary metabolites, biological activities, and pharmacological applications of this genus up to 2017, which would assist further researches and potential applications of the plants.

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

Different plants of genus *Ehretia* are widely used traditionally in many herbal and Chinese medicines from last few decades in China, India, and Japan [26,27] (Table 1).

CHEMICAL CONSTITUENT PRESENT IN GENUS *EHRETIA*

Species present under the genus *Ehretia* contains many phytoconstituents such as - phenolic acids, flavonoids, benzoquinones,

cyanogenetic glycosides, fatty acids, and some other important compounds.

Phenolic acids

Plants are potential sources of natural bioactive compounds such as secondary metabolites and antioxidants. Phenolic acids are the secondary metabolites and therapeutic agent present in medicinal plant. Phenolic compounds confer unique taste and health-promoting properties found in vegetables and fruits. The effect of dietary phenolics is currently of great interest due to their antioxidative and possible anticarcinogenic effect (Table 2).

Flavonoids

Flavonoids are the polyphenolic compounds among secondary metabolites in different parts of plants that possess a wide range of biological activities. They are present in fruits, vegetables, nuts, spices, and herbs and derived products such as wine, tea, and chocolate. The flavonoid class includes more than 6000 compounds as found in nature and comprises several subclasses including flavonols (e.g., quercetin, kaempferol, myricetin, and rhamnazin), flavones (e.g., apigenin, luteolin, and tangeretin), flavanones (e.g., hesperetin, naringenin, and eriodictyol), flavanols (e.g., catechins and epicatechins), anthocyanidins (e.g., cyanidin, delphinidin, and malvidin), and isoflavones (e.g., genistein, daidzein, and glycitein) (Table 3).

Alkaloids

Alkaloids are quite important secondary metabolites of plants. They are internal constituents of plants so-called biomolecules. Uses of alkaloids primarily mean their use in health care. They act as lifesaving drugs in various serious disorders such as heart failure, blood pressure, and cancer. Several alkaloids isolated from natural herbs exhibit antimetastasis and antiproliferation effects on various types of cancers such as vinblastine and camptothecin and have already been successfully developed into anticancer drugs. Lycorine, indicine n-oxide, alstonine, cocaine, quinine, and quinidine are some alkaloids present in plants (Table 4).

Fatty acids

Plants synthesize a huge variety of fatty acids although only a few are major and common phytoconstituents. Fatty acids are

Table 1: Traditional uses of genus Ehretia

| Botanical name | Common name | Part used | Traditional use | References |
|---|---|------------------|--|------------|
| <i>Ehretia acuminata</i> R.Br. | Pudila, Nara, Koda | 1. Leaves | 1. The extract of the leaves mixed with water | [28] |
| | | 2. Bark | and taken orally once daily for 2–3 days to cure acute dysentery | [29] |
| | | 3. Root | 2. Bark juice used in sores on tongue and fever | |
| <i>Ehretia laevis</i> Roxb. | Chamror (Punjab). Kuptaa, Datarangi (Maharashtra) | 1. Leaves | 1. Leaves juice is applied in ulcer, skin disease, and headache | [30] |
| | | 2. Root | 2. Root used in venereal diseases | [31] |
| | | 3. Bark | 3. Bark is used internally and as gargle in throat infections, inner bark of <i>E. laevis</i> is used as food | [32] |
| | | 4. Fruit | 4. Fruit used in infections of urinary passages, diseases of lungs and spleen | |
| <i>Ehretia microphylla</i> Lam. | Pala. | 1. Leaves | 1. 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 | [33] |
| | | 2. Root | 2. Root in cachexia and syphilis; an antidote to vegetable poisoning | |
| <i>Ehretia obtusifolia</i> . Hochst. ex A.DC | | 1. Leaves | 1. Decoction of leaves and bark in Malaria | [34] |
| | | 2. Thin branches | | |
| <i>Ehretia cymosa</i> | | 1. Leaves | 1. Different parts of plant are used in diarrhea | [35] |
| | | 2. Bark | 2. The extract of leaves used in Malaria | |
| <i>Ehretia amoena</i> | | 1. Leaves | 3. Bark and leaves used in epilepsy | |
| | | 2. Bark | 1. Plant works against trypanosomiasis | [36] |
| | | 3. Root | | |

Table 2: Phenolic acids separated from genus Ehretia

| S. no | Phenolic acid | Species | References |
|-------|---|------------------------|------------|
| 1. | Buddlenol B | <i>E. ovalifolia</i> | [37] |
| 2. | Caffeic acid | <i>E. thyrsoiflora</i> | [38] |
| 3. | Danshensu | <i>E. thyrsoiflora</i> | [39] |
| 4. | Cinnamic acid | <i>E. thyrsoiflora</i> | [39] |
| 5. | Ehletianol A | <i>E. ovalifolia</i> | [37] |
| 6. | Ehletianol B | <i>E. ovalifolia</i> | [37] |
| 7. | Ehletianol D | <i>E. ovalifolia</i> | [37] |
| 8. | (E)-ethyl caffeate | <i>E. thyrsoiflora</i> | [40] |
| 9. | Caffeic anhydride | <i>E. obtusifolia</i> | [34] |
| 10. | Icariside E5 | <i>E. ovalifolia</i> | [37] |
| | | <i>E. thyrsoiflora</i> | [39] |
| 11. | Lithospermic acid B | <i>E. thyrsoiflora</i> | [39] |
| 12. | Methyl 2-O-feruloyl-1a-O-vanillactate | <i>E. obtusifolia</i> | [34] |
| 13. | Methyl rosmarinic acid | <i>E. obtusifolia</i> | [34] |
| | | <i>E. thyrsoiflora</i> | [38] |
| 14. | p-hydroxybenzoic acid | <i>E. thyrsoiflora</i> | [38] |
| 15. | Rosmarinic acid | <i>E. obtusifolia</i> | [34] |
| | | <i>E. thyrsoiflora</i> | [39] |
| 16. | Trans-4-hydroxycyclohexyl-2-O-p-coumaroyl-β-D-glucopyranoside | <i>E. obtusifolia</i> | [34] |
| 17. | Ehletianol C | <i>E. ovalifolia</i> | [37] |
| 18. | 1-(4-hydroxy-3-methoxyphenyl)-2-{2-methoxy-4-[1-(E) propen-3-ol]-phenoxy}-propane-3-diol (erythro) | <i>E. ovalifolia</i> | [37] |
| 19. | 1-(4-hydroxy-3-methoxyphenyl)-2-{2-methoxy-4-[1-(E) propen-3-ol]-phenoxy}-propane-1, 3-diol (threo) | <i>E. ovalifolia</i> | [37] |
| 20. | Trans-ferulic acid | <i>E. thyrsoiflora</i> | [39] |

E. ovalifolia: *Ehretia ovalifolia*, *E. thyrsoiflora*: *Ehretia thyrsoiflora*, *E. obtusifolia*: *Ehretia obtusifolia*

important dietetic sources of fuel for animals because, when metabolized, they yield large quantities of ATP (Adenosine triphosphate). Many types of cell can use either fatty acids or glucose for this purpose. Long-chain fatty acids are not capable to cross the blood–brain barrier and so cannot be used as fuel by the cells of the central nervous system (Table 5).

Benzoquinones

Quinones, a type of plant-derived secondary metabolites and benzoquinones, are widely distributed in the plant kingdom and mainly exist in higher plants, such as those from the Polygonaceae, Rubiaceae,

Leguminosae, Rhamnaceae, Labiatae, and Boraginaceae families, among others. Moreover, a number of benzoquinones show significant biological activities such as anticancer and antibacterial activities (Table 6).

Glycosides

In the chemical constituents occur in a glycoside are important, secondary metabolites. However, biological activities of glycosides are, in many cases, susceptible to the nature of sugar moieties. They are an essential resource of natural medicine, health food, cosmetics, and food supplements (Table 7).

Table 3: Flavonoids separated from from genus Ehretia

| S. no | Flavonoids | Species | References |
|-------|--|----------------------|------------|
| 21. | Apigenin | <i>E. ovalifolia</i> | [40] |
| 22. | Hyperoside | <i>E. thyriflora</i> | [39] |
| 23. | Luteolin | <i>E. ovalifolia</i> | [40] |
| 24. | Kaempferol-3-O- α -D-arabinoside | <i>E. thyriflora</i> | [38] |
| 25. | Kaempferol-3-O- β -D-galactopyranoside | <i>E. thyriflora</i> | [39] |
| 26. | Kaempferol-3-O- β -D-glucopyranoside | <i>E. thyriflora</i> | [39] |
| 27. | Kaempferol-3-O-arabinosylgalactoside | <i>E. thyriflora</i> | [39] |
| 28. | Kaempferol | <i>E. thyriflora</i> | [38] |
| 29. | Quercetin | <i>E. thyriflora</i> | [38] |
| 30. | Quercetin-3-O- α -D arabinoside | <i>E. thyriflora</i> | [38] |
| 31. | Quercetin-3-O- β -D-glucopyranoside | <i>E. thyriflora</i> | [39] |
| 32. | Quercetin-3-O-arabinosylgalactoside | <i>E. thyriflora</i> | [39] |
| 33. | Ovalifolin | <i>E. ovalifolia</i> | [40] |

E. ovalifolia: *Ehretia ovalifolia*, *E. thyriflora*: *Ehretia thyriflora*, *E. obtusifolia*: *Ehretia obtusifolia*

Table 4: Alkaloids separated from from genus Ehretia

| S. no | Alkaloids | Species | References |
|-------|------------|----------------------|------------|
| 34. | Ehretinine | <i>E. aspera</i> | [41] |
| 35. | Allantoin | <i>E. thyriflora</i> | [42] |

E. aspera: *Ehretia aspera*, *E. thyriflora*: *Ehretia thyriflora*

Table 5: Fatty acids separated from from genus Ehretia

| S. no | Fatty acid | Species | References |
|-------|---|----------------------|------------|
| 36. | Araneosol | <i>E. ovalifolia</i> | [40] |
| 37. | Di (octadecyl) phthalate | <i>E. thyriflora</i> | [42] |
| 38. | Tetradecanoic acid 2, 3-dihydroxypropyl ester | <i>E. thyriflora</i> | [42] |
| 39. | (10E, 12Z, 15Z)-9-hydroxy-10, 12, 15-octadecatrienoic acid methyl ester | <i>E. dicksonii</i> | [43] |
| 40. | (9Z, 11E)-13-oxo-9, 11-octadecadienoic acid | <i>E. dicksonii</i> | [43] |
| 41. | (9Z, 11E)-13-hydroxy-9, 11-octadecadienoic acid | <i>E. dicksonii</i> | [43] |
| 42. | 2-methoxybenzoic acid octyl ester | <i>E. thyriflora</i> | [42] |

E. ovalifolia: *Ehretia ovalifolia*, *E. thyriflora*: *Ehretia thyriflora*, *E. dicksonii*: *Ehretia dicksonii*

Table 6: Benzoquinones separated from genus Ehretia

| S. no | Benzoquinone | Species | References |
|-------|-----------------------------|-----------------------|--------------|
| 43. | Cyclomicrophyllone | <i>E. microphylla</i> | [33] |
| 44. | Dehydromicrophyllone | <i>E. microphylla</i> | [33] |
| 45. | Ehretianone | <i>E. buxifolia</i> | [44] |
| 46. | Allomicrophyllone | <i>E. microphylla</i> | [33] |
| 47. | Hydroxymicrophyllone | <i>E. microphylla</i> | [33] |
| 48. | Microphyllone | <i>E. microphylla</i> | [33] [45] |
| 49. | 1,4-naphthoquinone lewisone | <i>E. laevis</i> | [46] |
| 50. | Ehretiquinone | <i>E. longiflora</i> | [47] |

E. microphylla: *Ehretia microphylla*, *E. buxifolia*: *Ehretia buxifolia*,
E. laevis: *Ehretia laevis*, *E. longiflora*: *Ehretia longiflora*

Table 7: Glycosides separated from genus Ehretia

| S. no | Glycoside | Species | References |
|-------|----------------------------|--------------------------|------------|
| 51. | Simmondsin | <i>E. philippinensis</i> | [48] |
| 52. | Ehretioside B | <i>E. philippinensis</i> | [48] |
| 53. | Polyalcohol | <i>E. philippinensis</i> | [48] |
| 54. | Ehretioside Al | <i>E. philippinensis</i> | [48] |
| 55. | Ehretioside A ₂ | <i>E. philippinensis</i> | [48] |
| 56. | Ehretioside A ₃ | <i>E. philippinensis</i> | [48] |

E. philippinensis: *Ehretia philippinensis*

Table 8: Some other constituents separated from genus Ehretia

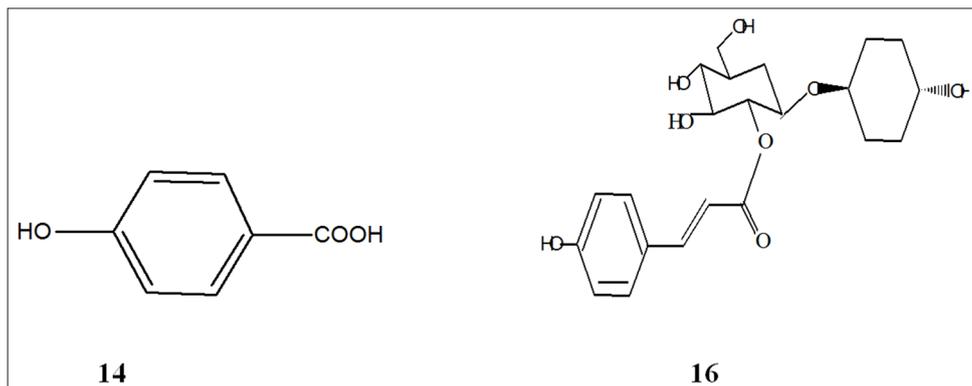
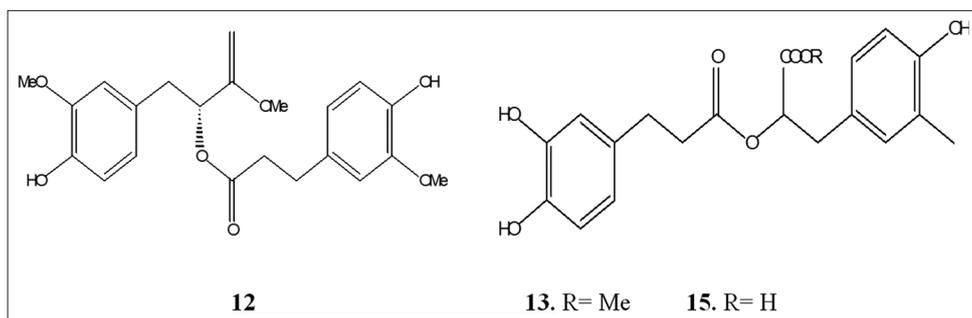
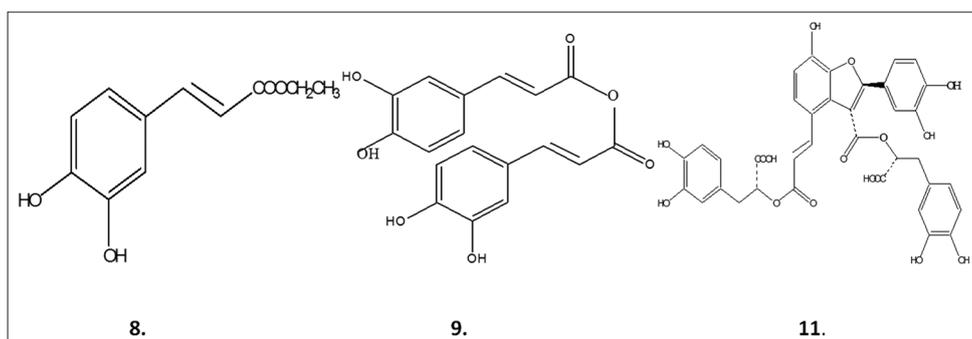
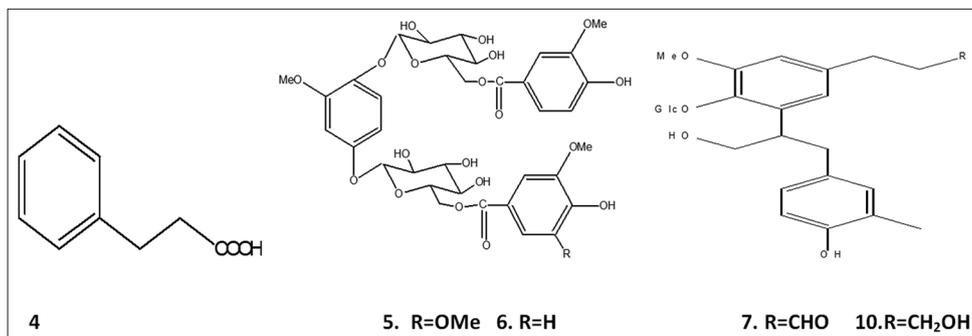
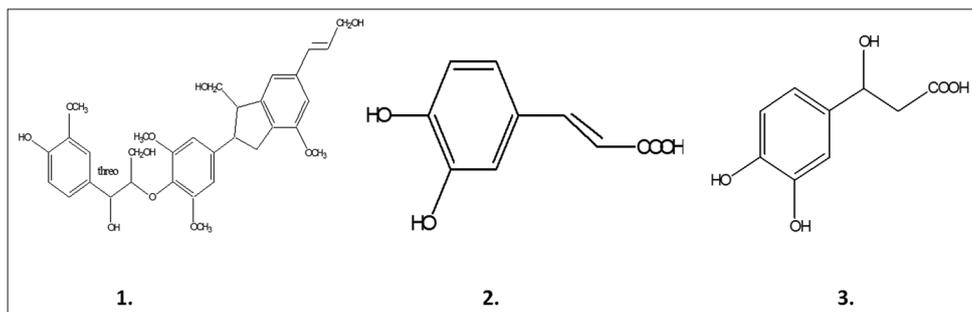
| S. no | Compound | Species | References |
|-------|-----------------------|----------------------|------------|
| 57. | Bauerenol | <i>E. laevis</i> | [49] |
| 58. | Betulin | <i>E. laevis</i> | [49] |
| 59. | Bauerenol acetate | <i>E. laevis</i> | [49] |
| 60. | Betulinic acid | <i>E. laevis</i> | [49] |
| 61. | Lupeol | <i>E. laevis</i> | [49] |
| 62. | α -amyrin | <i>E. laevis</i> | [49] |
| 63. | β -sitosterol | <i>E. laevis</i> | [49] |
| 64. | Daucosterol | <i>E. thyriflora</i> | [42] |
| 65. | Stigmasterol | <i>E. buxifolia</i> | [44] |
| 66. | α -spinasterol | <i>E. buxifolia</i> | [44] |
| 67. | Campesterol | <i>E. buxifolia</i> | [44] |
| 68. | Stigmastanol | <i>E. buxifolia</i> | [44] |
| 69. | Ehretiolide | <i>E. longiflora</i> | [47] |
| 70. | Ehreticoumarin | <i>E. longiflora</i> | [47] |
| 71. | Ehretilactone A | <i>E. longiflora</i> | [47] |
| 72. | Ehretilactone B | <i>E. longiflora</i> | [47] |
| 73. | Ehretiamide | <i>E. longiflora</i> | [47] |
| 74. | Ehretine | <i>E. longiflora</i> | [47] |
| 75. | Ehretiate | <i>E. longiflora</i> | [47] |

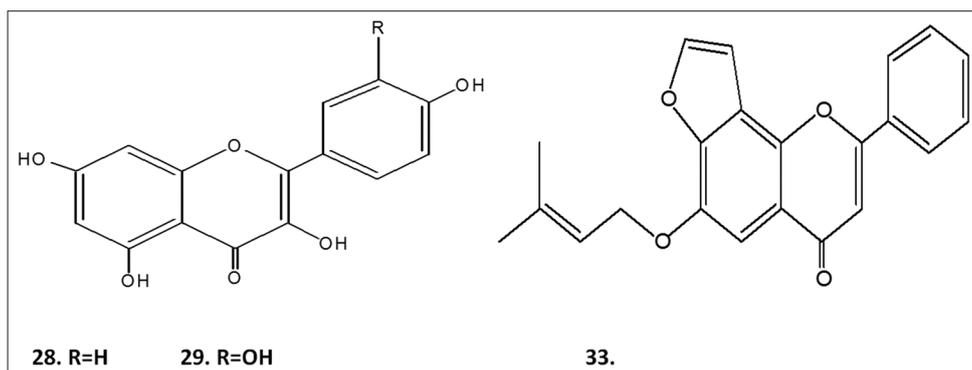
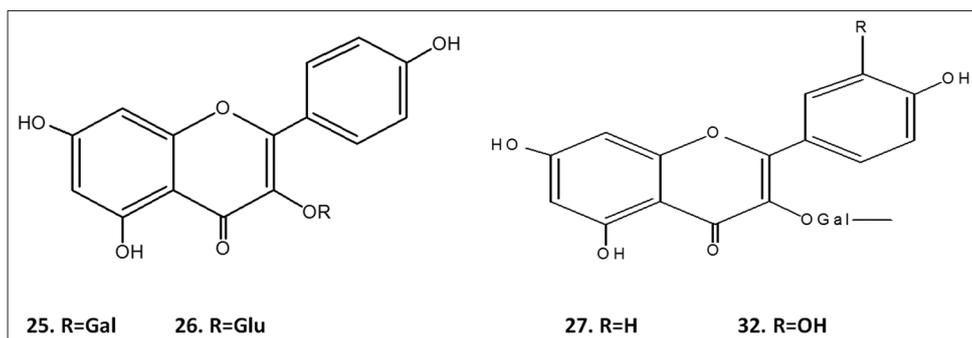
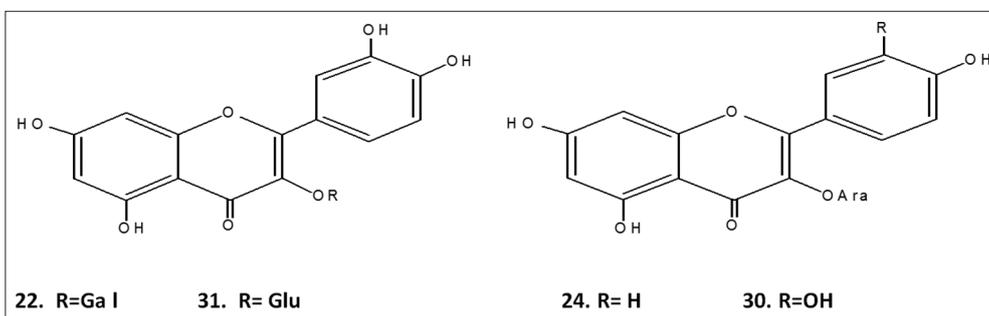
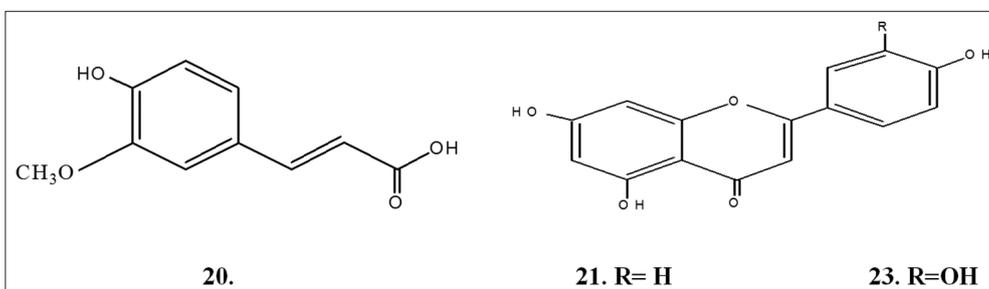
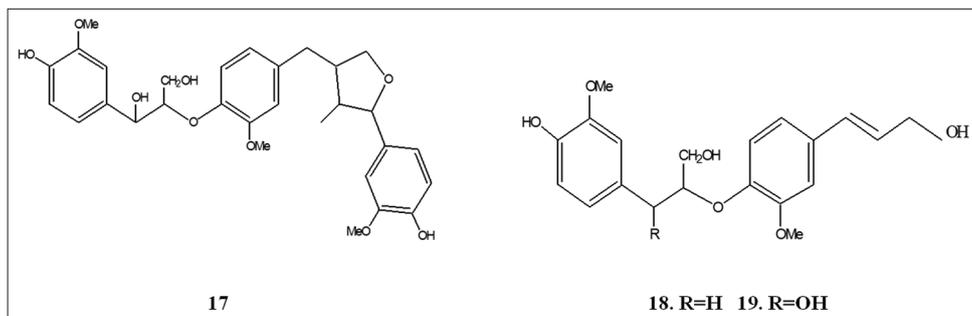
E. laevis: *Ehretia laevis*, *E. thyriflora*: *Ehretia thyriflora*, *E. buxifolia*: *Ehretia buxifolia*, *E. longiflora*: *Ehretia longiflora*

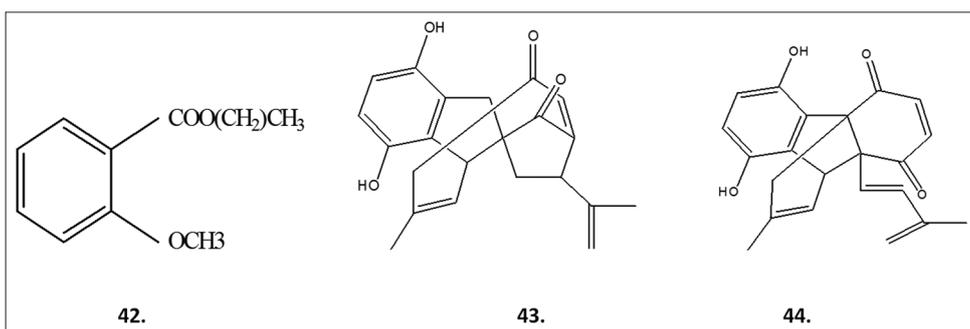
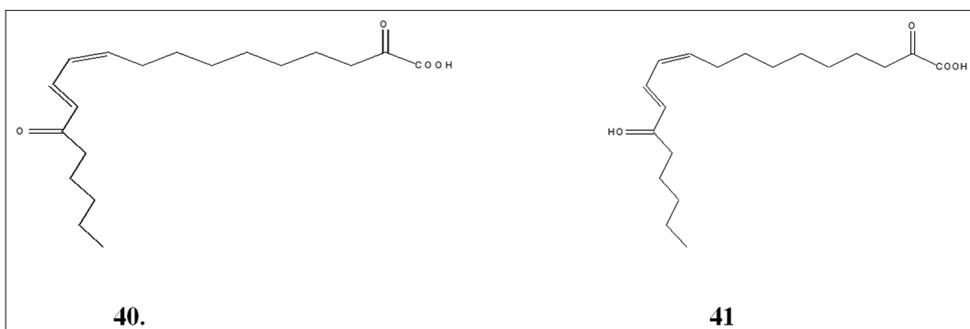
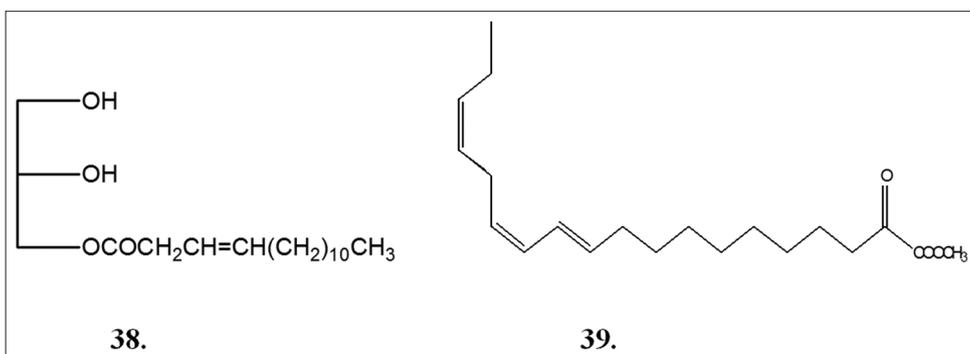
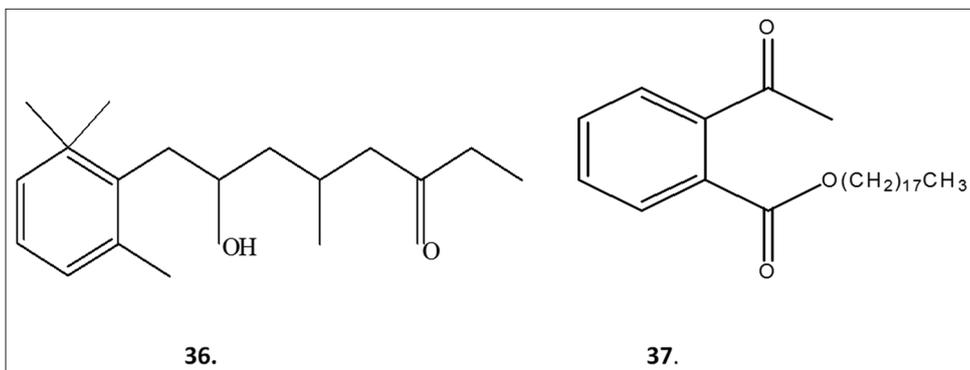
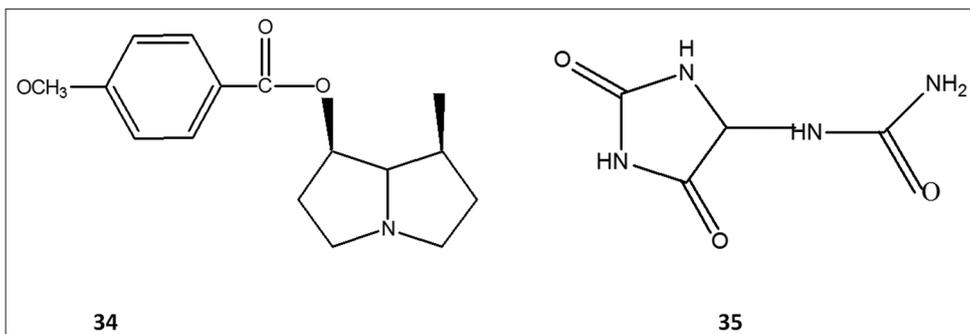
OTHER IMPORTANT CONSTITUENTS EXTRACT FROM GENUS EHRETIA

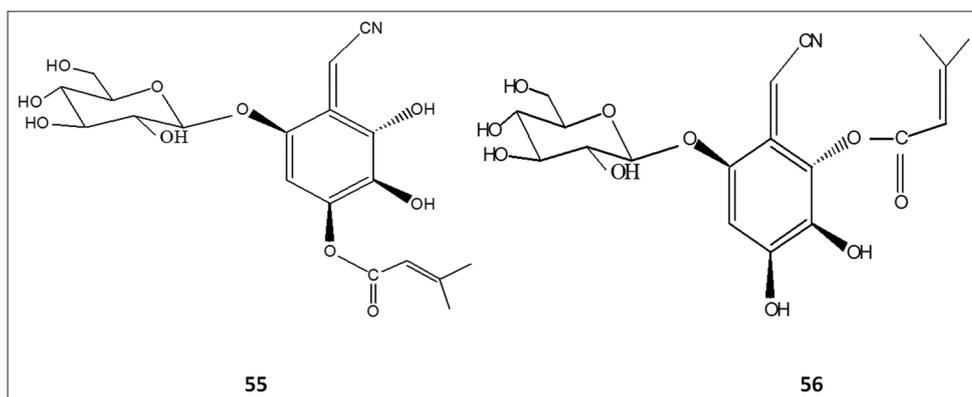
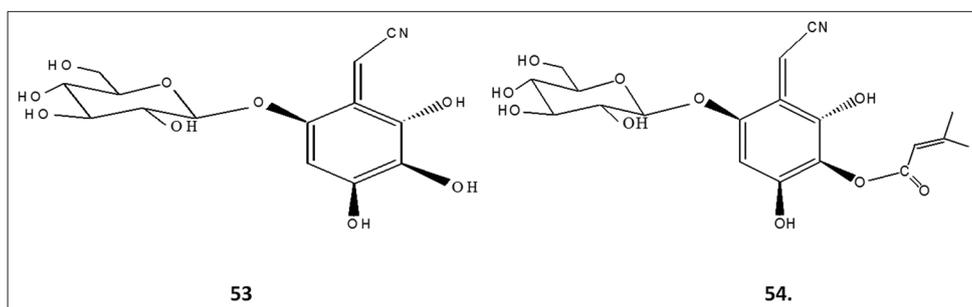
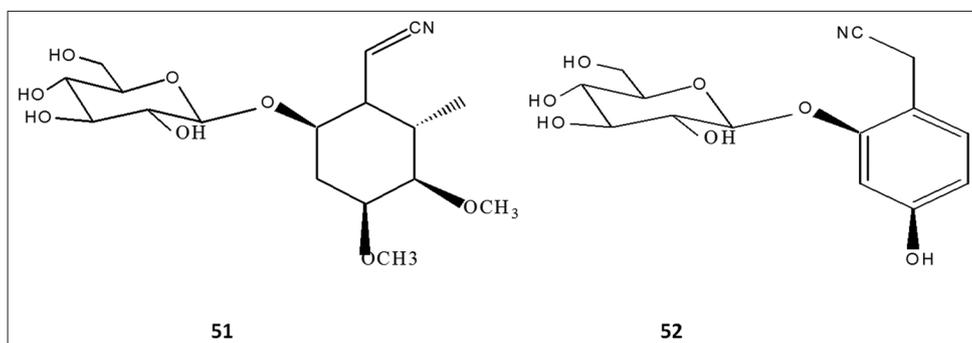
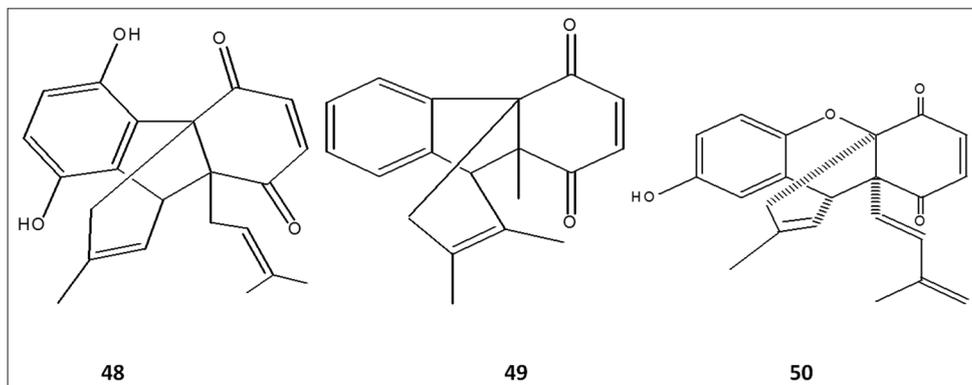
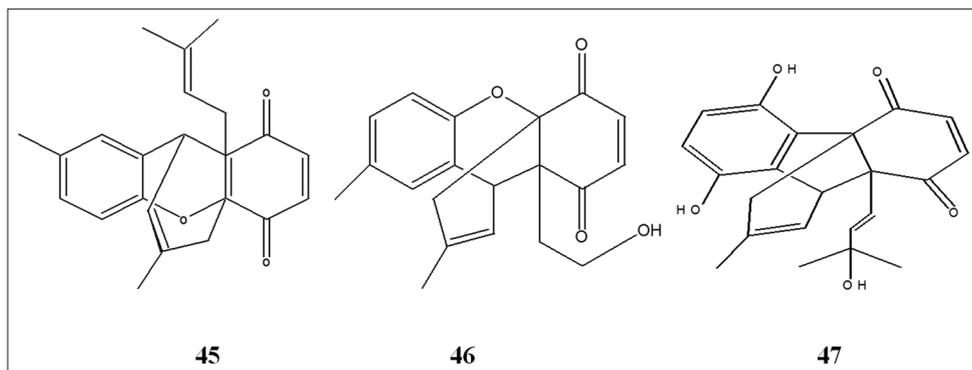
Many other important constituents are also reported from different parts such as leaves, bark, fruit, and root of plants of *Ehretia* genus (Table 8).

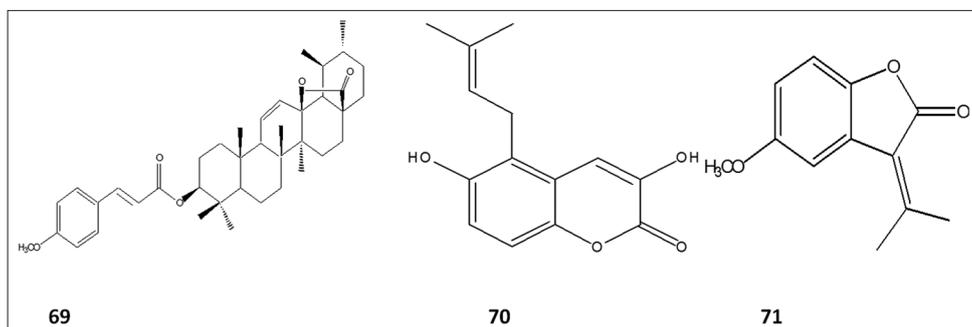
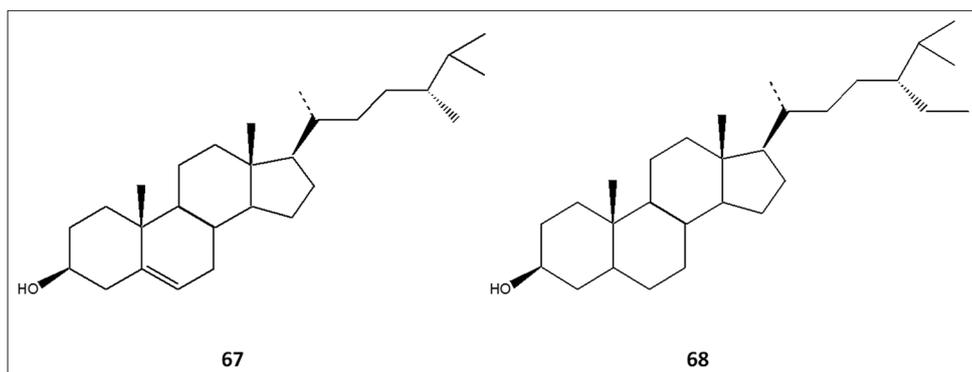
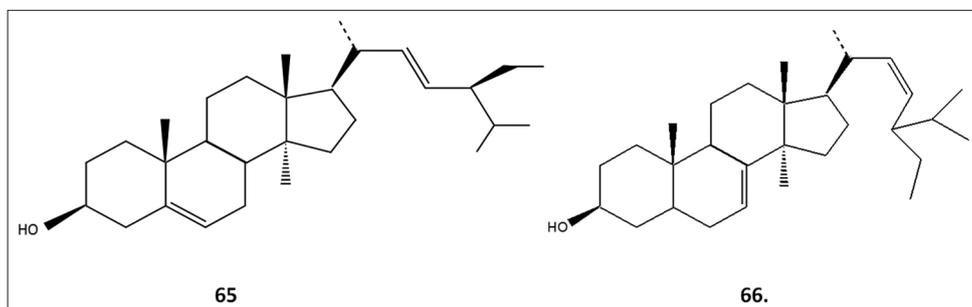
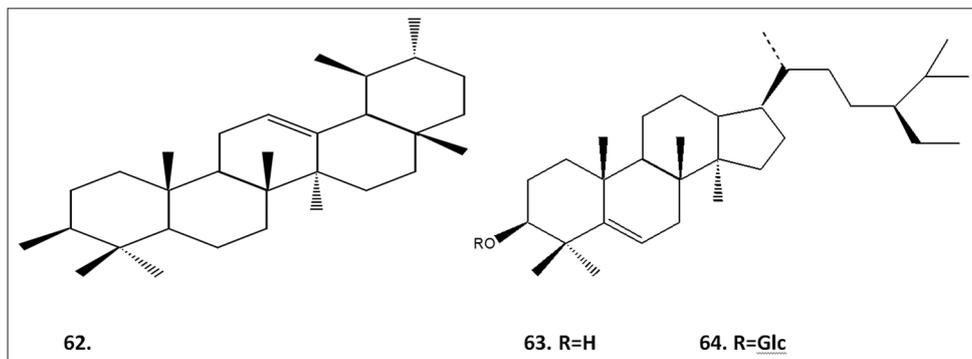
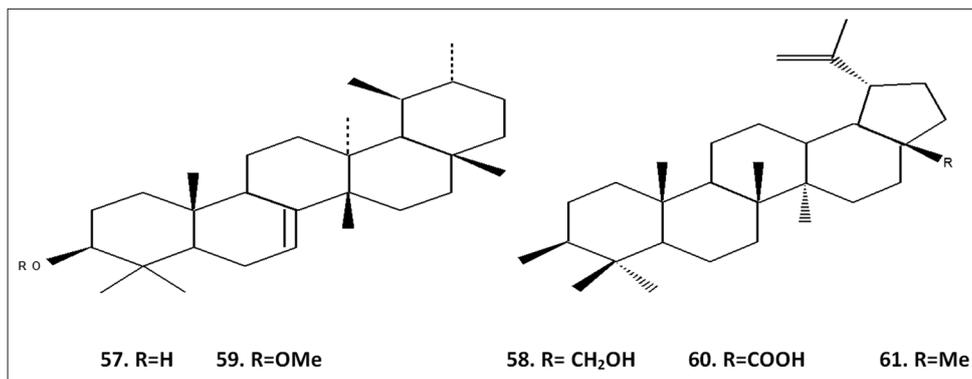
CHEMICAL STRUCTURE OF COMPOUND PRESENT IN EHRETIA GENUS (FIGS. 1-75)

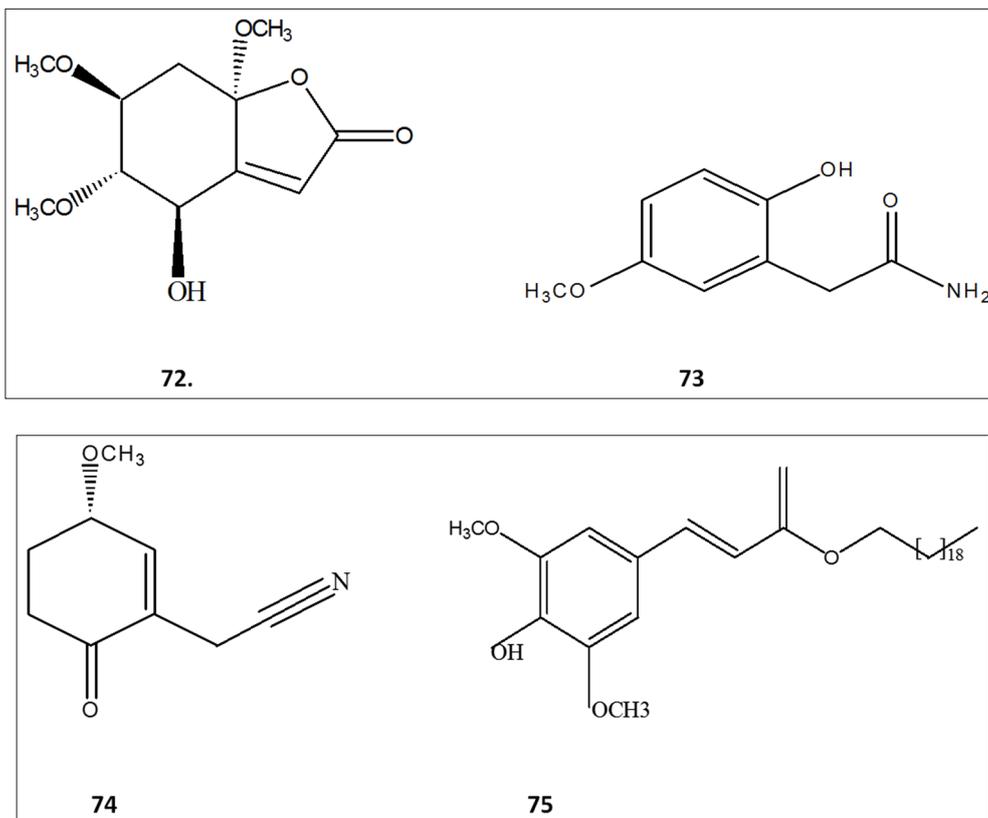












Essential oil

Essential oil extracted from leaves of *Ehretia cymosa* by hydrodistillation. Some chemical constituents separated by comparison of their mass spectra with NIST from essential oil which mainly comprised sesquiterpene hydrocarbon compounds.

The other classes of compounds identified in these essential oils were monoterpenes, alcohols, phenylpropanoids, esters, and fatty acids. In addition, some of the studied volatile oils have exhibited biological activities such as antimicrobial, phytotoxicity, insecticidal, and cytotoxicity (Table 9).

SOME SPECIES OF GENUS *EHRETIA*





BIOLOGICAL ACTIVITIES OF DIFFERENT SPECIES OF GENUS *EHRETIA*

Many species of genus *Ehretia* show different biological activities such as antioxidant, antibacterial, anti-inflammatory, antiarthritic, and anti-snake venom activities.

Antioxidant activity

Many compounds, naturally occurring from plant sources, have been identified as free radical or active oxygen scavengers. Recently, interest has increased substantially in finding naturally occurring antioxidant for use in foods or medicinal materials to replace synthetic antioxidants, which are being restricted due to their side effects such as carcinogenicity. Natural antioxidants can protect the human body from free radicals and retard the progress of many chronic diseases as well as decelerate lipid oxidative rancidity in foods. In *Ehretia serrata*, 1-butanolic and chloroform fractions of leaves and ethyl acetate fraction of fruits showed appreciable results against free radical. 12 compounds including six phenolic acids and six flavonoids, rosmarinic acid, cinnamic acid, icariside E5, ferulic acid, α -hydroxydihydrocaffeic acid, lithospermic acid B, isoquercitrin, hyperoside, trifolin, astragalol, kaempferol 3-O-arabinosylgalactoside, and quercetin 3-O-arabinosylgalactoside were first isolated from *Ehretia thyrsoiflora* and have a significant response of antioxidant (Table 10).

Anti-inflammatory activity

The inflammatory process may be outline a sequence of events that occur in response to noxious stimuli, infection, or trauma. The classic signs of inflammation are redness, heat, swelling, pain, and loss of function. The issue of inflammation that underlines these manifestations are induced and regulated by a large number of chemical mediators including eicosanoids, kinins, complement proteins, histamine, and monokines (Table 11).

Antiallergic activity

Allergic disorders such as rhinitis, sinusitis, atopic dermatitis, asthma, pollenosis, and food allergy are the most common cause of human disease. There are a number of pharmacological agents available for the treatment of allergic conditions such as asthma and allergy rhinitis, and we also focus antiallergic activity as an essential step to the development of effective antiallergic agent. Some species of *Ehretia* genus have compounds such as dimeric prenylbenzoquinones, nitrile glucosides, and rosmarinic acid show antiallergic effect (Table 12).

Anti-bacterial activity

All extracts of *E. laevis* leaves (methanol, chloroform, and aqueous solvent) have revealed excellent antibacterial activity. When compared to methanol, chloroform, and aqueous methanolic extract showed the high antibacterial activity on Gram-positive and Gram-negative bacteria, and aqueous extracts show the high antibacterial activity on Gram-negative than Gram-positive. Some other species also show positive respond against antibacterial activity (Table 13).

Antitubercular activity

In human being, tuberculosis is a contagious infectious disease primarily caused by *Mycobacterium tuberculosis*. Although regimens exist for treating tuberculosis, they are far from ideal. Development of efficient strategies for the treatment of human tuberculosis has posed a challenge, considering the increase in infections associated with the human immunodeficiency virus and immunocompromised patients. Phytoconstituents have been used in traditional treatment of many diseases; however, careful investigation of these constituents has not been undertaken with respect to treatments of tuberculosis. Two compounds ehretiolide and prenylhydroquinone have extracted from root of *Ehretia longiflora* are responsible for antitubercular activity (Table 14).

Anti-snake venom activity

Snakebite is an important cause of morbidity and mortality and is one of the major health problems in India and other Asian countries. *Ehretia buxifolia* claimed to be useful in treating snake poison. The present study evaluated the potential antivenom effect *Ehretia* genus. A compound ehretianone has isolated from MeOH extract from *E. buxifolia* is responsible for anti-snake venom activity (Table 15).

Antiarthritic activity

Arthritis is an inflammatory disorder involving damage of joints. There are over a hundred different forms of arthritis, of which rheumatoid arthritis, osteoarthritis, and psoriatic arthritis are the most common. The treatment of any systemic disorder with allopathic drugs causes moderate-to-severe adverse effect that could cause death. Hence, alternative systems of medicine are being explored to treat diseases. *E. laevis* treatment supports antiarthritic activity. Of the three parts such as stem, leaf, and bark and fruit employed, the leaf extract was the most effective. This antiarthritic respond may be due to the presence of active constituents such as hexadecanoic acid (palmitic acid), oleanenic acid, and other fixed oils (Table 16).

Antitrypanosomal and antiprotozoal activity

Sleeping sickness, leishmaniasis, Chagas disease, and malaria are infectious diseases caused by unicellular eukaryotic parasites "protozoans." The available drugs for the treatment of trypanosomiasis and protozoans are old, expensive, and less effective, associated with severe adverse reactions and face the problem of drug resistance. This situation underlines the urgent need for the development of new safe, cheap, and effective drugs for the treatment of parasitic disease. The search for new antitrypanosomal and antiprotozoal agents in this study is based on ethnomedicine. *E. amoena* show weak antitrypanosomal potential with ethanol extract of leaves, bark, and root. *E. acuminata* show antiprotozoal activity with methanol extract of leaves (Table 17).

Antidiabetic activity

Diabetes mellitus, one of the fastest-growing health problems, is concerned about the use of antihyperglycemic drugs because of undesirable pathological conditions, for example, the adverse effect of metformin is gastrointestinal discomfort, pioglitazone with bladder cancer and heart failure, and sulfonylureas with hypoglycemia and weight gain. There are the ethnobotanical studies of medicinal plants used in the treatment of diabetes mellitus in many countries. A lot of genus have already reported for effective respond of antidiabetic

potential, but a few species of genus *Ehretia* are reported for antidiabetic activity yet. A species of *E. laevis* shows antidiabetic potential using multiwalled carbon nanotubes paste electrode in electrochemical measurement (Table 18).

Cardiotonic activity

Carmona retusa (*E. microphylla*) has a high potential in fighting the growth and multiplication of cancer cells. However, there are no scientific data on the use of this plant on cardiotonic activity. Hence, this study was carried out to evaluate the effect of aqueous extract of various aerial parts of *C. retusa* on isolated frog's heart. The activity of the aqueous extract was found to be effective (Table 19).

CONCLUSION AND FUTURE PROSPECTS

The genus *Ehretia* contains abundant ingredients displaying extensive biological and pharmacological functions such as anti-snake venom, antiarthritic, antitrypanosomal, and antiprotozoal activity, and antiallergic activities. Despite that many *Ehretia* species have been used as the traditional medicines in Australia, North America, and Asian countries for long time, and numerous studies on chemistry and pharmacology have been conducted, the authors propose herein a few opinions with an attempt to shed light on the related investigations on *Ehretia* in future.

Table 9: Compound separated from essential oil

| S. no | Compound | References |
|-------|--------------------------------------|------------|
| 1. | Linalool | [35] |
| 2. | <i>trans</i> -Sesquisabinene hydrate | [40] |
| 3. | Methyl salicylate | [40] |
| 4. | <i>O</i> - <i>tert</i> -Butylphenol | [40] |
| 5. | β Ylangene | [40] |
| 6. | β -Damascenone | [40] |
| 7. | β -Cedrene | [40] |
| 8. | β -Caryophyllene | [40] |
| 9. | Trans- α -Bergamotene | [40] |
| 10. | Isocaryophyllene | [40] |
| 11. | ar-Curcumene | [40] |
| 12. | β -Bisabolene | [40] |
| 13. | Oxygenated monoterpenes | [40] |
| 14. | Sesquiterpene hydrocarbons | [40] |

Table 10: Antioxidant activity of genus Ehretia

| S. no | Species | Part used | References |
|-------|-----------------------------|------------------|--------------|
| 1. | <i>Ehretia thyrsoiflora</i> | Leaves | [50] |
| 2. | <i>Ehretia laevis</i> Roxb. | Leaves | [51] [52] |
| 3. | <i>Ehretia serrata</i> | Leaves and fruit | [53] |
| 4. | <i>Ehretia laevis</i> Roxb. | Fruit | [54] |
| 5. | <i>Ehretia tinifolia</i> | Fruit | [55] |
| 6. | <i>Ehretia microphylla</i> | Aerial part | [56] |

Table 11: Anti-inflammatory activity of genus Ehretia

| S. no | Species | Part used | References |
|-------|------------------------|-----------|------------|
| 1. | <i>E. dicksonii</i> | Leaves | [43] |
| 2. | <i>E. obtusifolia</i> | Leaves | [34] |
| 3. | <i>E. laevis</i> Roxb. | Leaves | [57] |
| 4. | <i>E. longiflora</i> | Root | [47] |

E. dicksonii: *Ehretia dicksonii*, *E. obtusifolia*: *Ehretia obtusifolia*, *E. laevis*: *Ehretia laevis*, *E. longiflora*: *Ehretia longiflora*

Foremost, *Ehretia* is a relatively vast genus, and there are considerable differences in their major secondary metabolites, these molecules were intensively described from *E. longiflora*, *E. laevis*, *E. microphylla*, *E. obtusifolia*, *E. thyrsoiflora*, *E. buxifolia*, *E. philippinensis*, *E. dicksonii*, and *E. ovalifolia*, while no reports were found for 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*. There are nine species found in South Africa *E. coerulea*, *E. amoena*, *E. obtusifolia*, *E. namibiensis* subsp. *kaokoensis*, *E. namibiensis* subsp. *namibiensis*, *E. alba*, *E. rigida* subsp. *rigida*, *E. rigida* subsp. *silvatica*, and *E. rigida* subsp. *nervifolia*. Recently, a new species of *Ehretia retro serrata* is reported in China [67].

Second, great efforts were devoted to explore the study of *E. microphylla* which indicate great potential of antibacterial and a recent research has done in India which shows *Ehretia microphylla* helps in treating irregular ovulation disorders and promotes fertility in female [68]. In Bangladesh, *E. microphylla* used in traditional medicinal treatment of various forms of cancer, and it is expected that scientific studies on this plants shall lead to discovery of novel anticancer compounds [66,69,70]. *E. microphylla* used widely in the traditional Philippine medicine and considered most promising for large-scale culture. Advice is given on vegetative propagation culture, harvesting, and storage (where appropriate), based on the results of preliminary trials [71].

E. laevis used as masticatories by the ethnic communities in India [72]. Unexplored wound healing property has shown by *E. laevis*. The best part is its leaves are effective, and hence, plenty of material is available without requirement of uprooting of plant [73]. Many researches have done by Indian scientists to improve the germination of multipurpose trees like *E. laevis* [74]. Molecular study has also done on some species to better understand the properties of genus *Ehretia* [75]. Recently, a research has done on *Ehretia tinifolia* which show positive response against diabetic complications, atherosclerosis, and cardiovascular diseases [76].

These properties have created a sense of conservation reservation and cultivation of the plant. The treatment is also very economic as only

Table 12: Antiallergic activity of genus Ehretia

| S. no | Species | Compound | References |
|-------|-------------------------------|--|------------|
| 1. | <i>Ehretia philippinensis</i> | Nitrile glucosides, rosmarinic acid, methyl rosmarinat | [48] |
| 2. | <i>Ehretia microphylla</i> | Rosmarinic acid | [58] |

Table 13: Anti-bacterial activity of genus Ehretia

| S. no | Species | Part used | References |
|-------|---|-----------|------------|
| 1. | <i>Ehretia laevis</i> Roxb. | Leaves | [57,59] |
| 2. | <i>Ehretia abyssinica</i> r.br. Ex fresen | Leaves | [60] |
| 3. | <i>Ehretia microphylla</i> | Leaves | [61] |

Table 14: Antitubercular activity of genus Ehretia

| S. no | Species | Part used | Reference |
|-------|----------------------|-----------|-----------|
| 1. | <i>E. longiflora</i> | Root | [47] |

E. longiflora: *Ehretia longiflora*

Table 15: Anti-snake venom activity of genus Ehretia

| S. no | Species | Part used | Reference |
|-------|---------------------|------------|-----------|
| 1. | <i>E. buxifolia</i> | Root, Bark | [44] |

E. buxifolia: *Ehretia buxifolia*

Table 16: Antiarthritic activity of genus Ehretia

| S. no | Species | Part used | Reference |
|-------|------------------------|-----------|-----------|
| 1. | <i>E. laevis</i> Roxb. | Leaves | [62] |

E. laevis: *Ehretia laevis*

Table 17: Antitrypanosomal and antiprotozoal activity of genus Ehretia

| S. no | Species | Part used | References |
|-------|---------------------|--------------------|------------|
| 1. | <i>E. amoena</i> | Leaves, root, bark | [36,63] |
| 2. | <i>E. acuminata</i> | Leaves | [64] |

E. amoena: *Ehretia amoena*, *E. acuminata*: *Ehretia acuminata*

Table 18: Antidiabetic activity of genus Ehretia

| S. no | Species | Part used | Reference |
|-------|------------------|-----------|-----------|
| 1. | <i>E. laevis</i> | Leaves | [65] |

E. laevis: *Ehretia laevis*

Table 19: Cardiotoxic activity of genus Ehretia

| S. no | Species | Part used | Reference |
|-------|-----------------------|-------------|-----------|
| 1. | <i>E. microphylla</i> | Aerial part | [66] |

E. microphylla: *Ehretia microphylla*

paste is to be prepared in aseptic condition. The study revealed that no antibiotic work required, and hence, the immunological study of patient was not hampered; similarly, there were huge savings in the medical expenditure which is very important in developing country like India [77]. This research has confirmed the antimicrobial potentials of *E. laevis* supporting its application as a preventive remedy for various microbial diseases of hard tissues in the oral cavity [59].

Plants of this genus as a native to India can become a great source of income for the nation if this potential for highly pharmacological use exploited by the researchers and industries by undertaking further research to corroborate earlier studies.

AUTHOR'S CONTRIBUTIONS

Amanpreet Kaur: Conceptualization of paper, compilation full literature, and wrote manuscript. Abha Shukla: Reviewing and checking of the manuscript and contributed in enhancing the standard of the manuscript.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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