

## Prospective reserves of bioactive compounds and their effect on human health: A review on *Elaeagnus conferta* roxburgh, an edible wild fruit

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### Abstract

Fruits are largely consumed throughout the world; they are not only the sources of energy, but also rich in the sources of nutritive compounds, carotenoids, polyphenols, organic acids etc. Fruits provide an optimal mixture of antioxidants such as vitamins, polyphenols, carotenoids along with complex carbohydrate, protein, fat and fiber. Bioactive compounds are molecules with therapeutic potential and have a positive effect on human health and could reduce the risk of numerous chronic diseases. Bioactive compounds are capable of modulating metabolic processes and possess antioxidant, anti-inflammatory, antifungal, antiviral, antibacterial, anticancer, analgesic and hepatoprotective properties both *in vivo* and *In vitro*. Epidemiological information substantiates that higher the consumption of fruits, lowers the risk of chronic diseases and fosters good health in humans. The following is a review on *Elaeagnus conferta* roxburgh fruits prospective reserves of bioactive compounds and their effect on human health.

**Keywords:** *Elaeagnus conferta*; Bioactive compounds; Antioxidant; Anticancer; Phenolic acid; Health benefits; SAR

### 1. Introduction

Consuming fruits and vegetables are increasing worldwide and the regular intake helps generally to stay away from many diseases including certain chronic diseases as it contains more phytochemicals and nutritional and it is one of the major dietary sources of several antioxidant phytochemicals for human beings. The intake of wild edible fruits are an important source of nutrients and phytochemicals to local communities. Most wild edible fruits are delicious, consumed fresh and are often used in their traditional medicinal practice as they are immune to many diseases. Berries provide significant health benefits because of their high levels of antioxidants, polyphenols, vitamins, minerals, fibers etc. Citrus fruits and lemonoids were indicated to act by preventing heart disease, inflammation and atherosclerosis with their hepatoprotective, antimicrobial, neuroprotective, antioxidants, anti-diabetic properties and also play a pivotal role against several cancers [1]. Fruits provide characteristic health benefits due to the presence of bioactive compounds. *Elaeagnus conferta* roxburgh fruit contains numerous elements, compounds, bioactive compounds and essential fatty acid, which is strange for a fruit. Berry fruits have several bioactive compounds that have antioxidant, anti-inflammatory, cardioprotective and neuroprotective effects[2]. Berry extracts are widely consumed in botanical dietary supplement forms for their potential human health benefits. Many laboratory and animal studies have shown that berries have anticancer, antioxidant, and antiproliferative properties [3]. The purpose of this review is to update the available information regarding the bioactive compounds, health benefits and SAR of *Elaeagnus conferta* roxburgh fruit.

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### 1.1. *Elaeagnus conferta* roxburgh

*Elaeagnus conferta* roxburgh belongs to the family of *Elaeagnaceae*, a thorny climber, densely covered with silvery scale leaves. Fruits are reddish orange in color and fleshy with sour taste. The genus *Elaeagnus* comprises about 70–80 species [4] and it is known by various names as red berries, oleaster, silverberry, Persian olive, autumn olive, Russian olive, thorn olive and wild olive. *Elaeagnus conferta* grows wild in the Indian states of Tamilnadu, Andhra Pradesh, Karnataka, Manipur, Meghalaya, Mizoram, Arunachal Pradesh and Bangladesh, Bhutan, Indonesia, Laos, Malaysia, Myanmar, Nepal, Vietnam, China worldwide.

- Botanical Name: *Elaeagnus conferta* roxburgh, Fl. Ind. 1: 460. 1820.
- Division -Angiospermae
- Class -Eudicots
- Order -Rosales
- Family -Elaeagnaceae
- Genus -*Elaeagnus*
- Species -*conferta*

#### 1.1.1. Common name

Wild Olive, Bastard oleaster, Snake fruit, red berries, oleaster, silverberry, Persian olive, autumn olive, Russian olive, thorn olive and wild olive

#### 1.1.2. Vernacular Name in India

- Tamil -Kurankup-palam, Kulangai Kulari
- Malayalam -Palga, Kattu Munthiringa, angolanga, angola pazham, angolapulli
- Kannada -Halage balli, Hejjala, Halige hannu, Gunnamada Patte Balli
- Irula - Kolaga
- Bengali -Guara
- Marathi -Amgul
- Manipuri -Heiyai
- Assamese -Mirika-tenga, Bon-jar
- Garo -Chhokhutt, Sukhwa
- Khasi -Soh-sng, Soh-khlur, Soh, chhang, Dieng-soh-sang
- Mizo -Sazukpui
- Angami -Pecusi

#### 1.1.3. Chemical and Bioactive Constituents of *Elaeagnus conferta* roxburgh

Wild berries are an additional source of biologically active constituents to human nutrition. The composition of berry fruits depends on the species, degree of ripeness, environmental & climatic conditions and storage time etc. Berries normally contain a diverse range of phytochemicals, most of them are phenolic molecules and include a variety of beneficial compounds, such as vitamins, essential minerals, fatty acids and dietary fibers. Berries are an important source of vitamins to tribal's which includes provitamin A, vitamin C, and B Complex vitamins.

Bioactive constituents of *E. conferta* were assessed and identified 1- Chlorofluoroethane, Cyclopentanone, 2-Methyl n-hexadecanoic acid, 9-Octadecenoic acid, Octadecanoic acid, E-11-Hexadecenal, Hexadecanoic acid-2-hydroxy-1-(hydroxymethyl) ethyl ester, 1,2-Benzenedicarboxylic acid, dioctyl ester, 9,10 anthracenedione, 1,8 dihydroxy-3-methoxy-6-methyl (Parietin) and structures of these have been confirmed by mass analysis [5]. Determination of p-Coumaric acid 321.0 ( $\mu\text{g/gm}$ ), Quercetin 289.0 Ellagic acid 511.0, Kampferol 718.0 were reported [6]. Determination of lipid content of *Elaeagnus conferta* fruit was conducted using conventional and ultrasonic irradiation method. The results indicate that the lipid potential wild fruits under investigation are higher. Hence it will be more beneficial than commonly consumed fruits when a fat rich supplement is required [7]. *Elaeagnus* fruits contains carotenoids, anthocyanin, carbohydrates, lipid, phytic acid, proteins, ascorbic acid, amino acids, flavonoids, minerals, plant sterols, oxalate, catalase, peroxidase, superoxide dismutase which have been used as anti-tumour, anti-microbial, anti-viral, anti-fungal, antioxidant, anti-inflammatory, anti-diabetic and cytoprotective. Bastard oleaster fruits are known for its antirheumatic, haematinic, analgesic properties [8-11]. Kampferol is a strong antioxidant which helps in preventing oxidative damage of cells, lipids, and DNA. It is also known to be a chemopreventive agent [12]. Flavonoids  $11.68 \pm 0.43$  mg/100 mg of lyophilized sample Titratable acidity  $2.3703 \pm 0.0004$  /100 g fruit sample Total lipids From pulp  $3.5 \pm 0.04$  /100 g sample Sugars Total Carbohydrates  $39.00 \pm 0.40$  mg/100 mg of lyophilized sample Total reducing sugars

35.00± 0.40 mg/100 mg of lyophilized sample Non reducing sugars 4.0± 0.05 mg/100 mg of lyophilized sample Total starch content 8.25± 0.03 mg/100 mg of lyophilized sample[13].

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## 2. Bioactive compounds

### 2.1. Phenolic Acids

The term “phenolic acids” generally describes the phenolic compounds having one carboxylic acid group. Plant phenolics are vital in human dietary, epidemiology evidence indicates fruits and vegetables that are rich in antioxidants significantly reduces the risk of many oxidative stress allied diseases viz. diabetes, cancers and cardiovascular.

Free and total phenol of *Elaeagnus conferta* fruit was determined by colorimetric method and reported 2.88 + 0.06 mg/100mg of lyophilized sample Total phenolics 6.08 ± 0.85 mg/100 mg of lyophilized sample respectively [13].

### 2.2. Beta -carotene

The name beta carotene comes from the Greek “beta” and Latin “carota”. It is the yellow/orange pigment that gives vegetables and fruits rich colors. H. Wachenroder crystallized beta carotene from carrot roots in 1831, and came up with the name “carotene”.

Beta-carotene is a carotenoid, known to have antioxidants and other effects. Beta carotene is a precursor of vitamin A. Human body converts beta carotene into vitamin A (retinol). We need vitamin A for good vision, eye health, healthy skin and immune system. Beta carotene may slow down cognitive decline and keep lungs healthy as people get older. The β carotene content of *Elaeagnus conferta* pulp was determined and expressed as 16.00± 0.45 mg/100mg of lyophilized sample by Dandge et al.[13] and Valvi et al.[8], 2014 investigated and reported the carotenoid content of mature and ripened *Elaeagnus conferta* fruit as 8.4 ± 0.003 and 2.14 ±0.001.

### 2.3. Ascorbic acid

Ascorbic acid is a water soluble vitamin, which is an essential micronutrient to human beings and helps for carnitine and normal metabolic function. Humanbeing can not synthesize ascorbic acid, it must be obtained through diet, which is abundantly found in fresh fruit, particularly in citrus fruit. Lack of vitamin C in the diet causes the deficiency disease scurvy. Vitamin C content varies in the species by numerous factors viz. region, Weather condition, climate, ripeness etc.

Dandge et al. determined the ascorbic acid content from the *Elaeagnus conferta* fruit and reported the value as 8.2± 0.40 mg/100 g. Vaishali J.Khilari et al [14] reported the amount of ascorbic acid content in *Elaeagnus conferta* as 13.2mg/100g, while Wu et al[15] reported 35.2 mg/kg dry weight of the dry fruit of *Elaeagnus conferta*. N. Devachandra et al [16] reported Vitamin C of the fruit content ranges from 7.00 to 17.00 mg/100g. Jin et al [17] reported 12.53mg/100 g.

### 2.4. Lycopene

More recently, lycopene has attracted considerable attention because of its association with a decreased risk of certain chronic diseases, including cardiovascular diseases and cancers . Considerable efforts have been expended to identify its biological and physicochemical properties. Methanol-chloroform extract of fruit of *E. conferta* was prepared to estimate carotenoid content and results have indicated that lycopene and βcarotene are the two major carotenoids in the flesh of *E. conferta* Roxb., and their content differed markedly between two genetic genotypes[18].

### 2.5. Minerals

The mineral elements are involved in various important physiological and biochemical processes in humans by affecting water and electrolyte balance, metabolic catalysis, oxygen binding, and hormone functions. Mineral nutrients are scientifically recognized as potentially essential constituents for human health as they play an important role in development of bones and teeth and provide strength to muscles in humans.

*Elaeagnus conferta* are rich in both macro and micronutrients. The major mineral elements found in *Elaeagnus conferta* are Sodium, Phosphorus, Potassium, Calcium, Magnesium, Iron, Manganese, Copper,Zinc and Nitrogen.

**Table 1** Comparison of Mineral composition

Na	K	Ca	Mg	P	Fe	Mn	Cu	Zn	N	Reference
7250 mg/kg	879 mg/kg	1090 mg/kg	846.4 mg/kg	1390 mg/kg	85.2 mg/kg	56.4 mg/kg	-	-	-	[15]
6.7 ± 0.3	233.5 ± 2.3	5.8 ± 0.3	-	-	-	-	-	-	-	[19]
184.3 ±0.57 mg/100g	1338.6 ±3.2	280.1 ±0.78	140.1 ±1.12	1.29 ±0.08	21.33 ±0.58	3.80 ±0.08	0.94 ±0.04	5.51 ±0.01	0.57 ±0.015	[20]

### 3. Health benefits

Evidence is growing worldwide that edible berries are playing an important role in tribal diets. Various phytochemicals from *Elaeagnus conferta* roxburgh fruit function as antioxidants, anticancer agent. Bioactive compounds of berries possibly block the entry of microorganisms by preventing them from adhering to the human cells. Epidemiological studies correlate ROS (Reactive Oxygen Species) values with DNA damage, heart diseases, cancer, and other chronic and degenerative diseases [21]. The beneficial health effects of fruit phytochemicals are associated with the neutralization of these ROS molecules. Due to this fact, an increase in the fruit consumption has been observed in the decade. However, analyzing the beneficial effects of berry phytochemicals and their absorption is to be considered on priority.

#### 3.1. Antioxidant Properties

Antioxidants have different effects when consumed by humans; they help to control blood pressure or blood sugar influencing substances, or can act as agents with anticarcinogenic, immunity-supporting, antibacterial, antifungal, antiviral, cholesterol-lowering, antithrombotic or anti-inflammatory properties [22].

Overproduction of oxidants in humans can cause oxidative stress, which is associated with chronic diseases; therefore, increased consumption of fruits and vegetables containing high levels of antioxidants could prevent or slow the oxidative stress caused by free radicals [23]. Different studies have demonstrated that phenols and flavonoids contribute to a higher extent than vitamin C, carotenoids, and others to the antioxidant capacity of fruits. An antioxidant is a substance that inhibits the oxidation of other molecules; it protects the body from free radicals. Beta carotene is an antioxidant like all other carotenoids. Several studies indicate that antioxidants through diet help people's immune systems, protect against free radicals, and lower the risk of developing cancer and heart disease. The number and position of hydroxyl groups in a particular phenolic compound is responsible for the variation in their antioxidant potential. Polyphenols are generally effortlessly absorbed in the intestine, the other modes are radical quenching via electron donation and singlet oxygen quenching are also known for the antioxidant activity of phenolic acids.

Vitamin C readily scavenges reactive oxygen and nitrogen species, such as superoxide and hydroperoxyl radicals, aqueous peroxy radicals, singlet oxygen, ozone, peroxy nitrite, nitrogen dioxide, nitroxide radicals, and hypochlorous acid [24], thereby effectively protecting other substrates from oxidative damage. Methanolic extract of *E. conferta* is an effective antioxidant. Free radical scavenging activity of extract was assayed by DPPH in terms of inhibitory concentration (IC<sub>50</sub>), effective concentration (EC<sub>50</sub>) and antiradical power (ARP). It has been investigated that fruit of *E. conferta* can reduce free radical generation at a concentration of IC<sub>50</sub>: 0.060, EC<sub>50</sub>: 2.61, ARP: 38.44 [25].

#### 3.2. Anticancer Properties

Epidemiologic studies suggest that consumption of a phytochemical-rich diet, which includes fruits and vegetables, contributes toward reducing the risk for certain types of human cancers [26]. Berry bioactive phenolics impart anticancer effects through various complementary and overlapping mechanisms of action including the induction of metabolizing enzymes; modulation of gene expression; and their effects on cell proliferation, apoptosis, and subcellular signaling pathways. A large number of laboratory and animal studies have shown that berries have anticancer properties [27].

#### 3.3. Hepatoprotective Properties

The rate of ethanol clearance from blood varies in individuals. If not metabolized properly, it can lead to liver damage and functional changes in gastrointestinal epithelial cells as well as other deleterious effects. Hepatic alcohol

dehydrogenase (ADH) and aldehyde dehydrogenase ALDH) are key enzymes responsible for the metabolism of ethanol into acetate for subsequent oxidation and elimination from the liver [28]. The effect of *E. conferta* Roxb dry fruit powder on the activities of ADH and ALDH was evaluated. A 30-min pretreatment with the extract at 400 and 800 mg /kg led to a faster clearance of blood alcohol after the alcohol ingestion. The concentration of blood alcohol at 4 h after alcohol intake decreased by 21.2% in mice pretreated with 800 mg kg<sup>-1</sup> of the extract. These results suggest that pretreatment with the fruit powder might expedite blood alcohol removal by promoting the activities of ADH and ALDH [29].

### 3.4. Insecticidal activity

Mosquitoes transmit a number of pathogens that cause diseases such as malaria, dengue, chikungunya, and filariasis in humans. T. R. Prashith Kekuda et al. [30] evaluated the larvicidal activity of *E. conferta* fruit against II and III instar larvae of *Anopheles* sp. and reported fruit extract of *E. conferta* caused 100% mortality of all larval stages of *Anopheles* species.

**Table 2** Insecticidal activity

Extract	Larval Stage	Total Number of Larvae	Number of Dead Larvae	Mortality of Larvae %
<i>E Conferta</i>	II	20	20	100.00
	III	20	20	100.00

### 3.5. Antibacterial Activity

Bacterial diseases are common in humans and are considered critical at times. Plants have been considered as potential alternatives for antibiotics. Plant based formulations are cheaper and locally available. Antibacterial potential of *E. Conferta* fruit has been investigated by T. R. Prashith Kekuda et al. [30] and markable antibacterial activity against a range of pathogenic bacteria were noticed.

**Table 3** Antibacterial activity

Test Bacteria	Zone of Inhibition in cm
<i>S. aureus</i>	1.7
<i>B. subtilis</i>	2.0
<i>E. coli</i>	1.9
<i>P. eruginosa</i>	2.2
<i>P. syringe</i>	2.0
<i>X. campestris</i>	2.1
<i>S. typhi</i>	1.9

### 3.6. Antifungal Activity

Exploring botanicals with antifungal activity has been increased continuously, because of several drawbacks that are associated with the use of synthetic fungicides. Studies have shown that extracts from fruits possess antifungal activity. T. R. Prashith Kekuda et al. [30] investigated the antifungal activity of fruit extract of *E. conferta* and found effective to more extent against the mycelial growth of *Rhizopus* sp. (52% inhibition) when compared to *Curvularia* sp. (35% inhibition)

**Table 4** Antifungal activity

Fungi	Colony Diameter in cm	
	<i>E. Conferta</i>	Control
<i>Curvulari sp.</i>	2.25	3.50
<i>Rhizopus sp.</i>	3.30	7.00

#### 4. Structure–activity relationship (SAR) studies in *Elaeagnus conferta* roxburgh fruit bioactive compounds in respect of human diseases

*Elaeagnus conferta* roxburgh fruits are plentiful with various bioactive compounds including phenolic acids, flavonoids, carotenoids, vitamins- provitamin A, C, E and K, minerals sodium, potassium, calcium and magnesium and dietary fibers which play a critical role in human health. Though numerous reports describing the biological activities and compositions of fruit bioactive compounds are available, only limited studies focus on the structure activity relationships between the chemical compounds and their biological activity.

##### 4.1. Phenolic Acids

Plant phenolics are vital in human dietary, epidemiology evidence indicates fruits and vegetables that are rich in antioxidants significantly reduces the risk of many oxidative stress allied diseases viz. diabetes, cancers and cardiovascular. Phenolic acid compounds play a pivotal role as antioxidants and also can reduce the oxidative stress-induced tissue damage due to chronic diseases and anticancer activities. Cancer is one of the major health problems around the world, and according to a report of WHO approximately more than twice as many people die every year from cancer than AIDS, malaria, and tuberculosis together, whereas it is expected that these numbers will soar 80% by 2030 [31]. Even though several mechanisms are known for the antioxidant activity (due to the reactivity of phenol moiety) of phenolic acids, radical scavenging via hydrogen atom donation is believed as the main method. Most of the phenolics act at different points to cure or inhibit the different types of cancer [32].

##### 4.2. Flavonoids

Flavonoids, one of the largest groups of phenolic compounds studied extensively, have been known to play a significant role in various biological activities including antioxidant, antimicrobial, antimutagenic, cytotoxic and anticancer activities [33]. Quercetin, the most abundant plant flavonols, is active in several cancers, neurodegenerative and cardiovascular diseases. Its chemical modification has led to novel derivatives with improved biological effects, better bioavailability and antioxidant properties. Recently, a study investigated O-substituted quercetin derivatives revealing monochloro pivaloyl quercetin and chloro naphthoquinone quercetin as potential therapeutics against chronic diseases like diabetes and neurodegenerative disorders [34]. Another interesting study suggested that quercetin therapy might improve heat stroke outcomes in rats by attenuating excessive hyperthermia as well as myocardial injury [35]. The phenolic compounds were analyzed by liquid chromatography (Agilent Technologies 1200 series) and reported 289 microgram/gram of Quercetin in *Elaeagnus conferta* roxburgh fruit by Rajaram P. Patil [36]. Myricetin, a plant flavonoid abundant in fruits, has been well known to act as an effective therapeutic against diabetes mellitus [37]. A new study on mice revealed that myricetin ameliorated memory deficits thereby acting as an effective drug target for Alzheimer's disease [38]. It was reported that myricetin induces apoptosis and enhanced cytotoxicity in ovarian cancer cell lines, proving potential against ovarian cancer, the most lethal gynecological cancer [39]. Myricetin in *Elaeagnus conferta* roxburgh fruit had been confirmed using mass analysis by Valvi SR et al. [5]

##### 4.3. Carotenoids

Dietary carotenoids are tetraterpenoids primarily from fruits and vegetables and possess varied health benefits.  $\alpha$ -carotene,  $\beta$ -carotene,  $\gamma$ -carotene and lycopene are precursors of vitamin A which also possess beneficial effects apart from antioxidant activity. *In vitro* cell culture experiments have shown that carotenoids inhibit cell proliferation, transformation and micronucleus formation as well as modulating expression of certain genes. These properties are consistent with a protective effect against carcinogenesis [40]. One of the earliest discoveries in this respect was that certain carotenoids, *In vitro*, increased gap junctional communication in a dose-dependent manner [41]. Since this early study, there has been a wealth of investigations on individual carotenoids and their effect on cancers.

#### Abbreviations

- IC – Inhibitory Concentration
- EC- Effective Concentration
- ADH – Alcohol Concentration
- ALDH – Aldehyde Concentration
- SAR – Structure Activity Relationship
- QSAR – Quantitative Structure Activity Relationship
- ARP- Anti Radial Power
- ROS – Reactive Oxygen Species

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## 5. Conclusion

An effort has been made to summarize the recent updates on *Elaeagnus conferta* roxburgh fruit bioactive compounds, their medicinal properties, the structure activity relationship of the compounds with relation to diseases. The use of all these biological activities presented in this review related to berry bioactive phenolics and flavonoids might promote the development of alternative berry compounds for the prevention and control of various diseases and disorders. Further research is needed on this subject related to plant breeding and genetic approaches at the interface with the synthesis of compounds for nutrition and health benefits. Advanced computational tools like molecular docking, QSAR studies, pharmacophore, *In vitro* and *in vivo* assays would undoubtedly enable the efficient use of fruit bioactive compounds as therapeutic and nutraceutical agents in the near future.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

The authors declare that they have no competing interests.

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