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Review Article


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Phytochemistry, Pharmacological Actions and Market Formulations of Sea Buckthorn (*Hippophae rhamnoides* L.): A Comprehensive Review



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ABSTRACT

Plants have been utilized for the treatment of various diseases for ages because of their plethora of pharmacological actions and almost inferior side effects. Among all medicinal plants sea buckthorn also came into the limelight because of its unique appearance and valuable phytoconstituents as well as medicinal properties. The sea buckthorn known as *Hippophae rhamnoides* L. belonging to family Elaeagnaceae is a berries-bearing plant. This review explores the plant profile, phytochemistry, pharmacological activities including: *in vivo*, *in vitro*, clinical studies of the plant and market preparation till date of sea buckthorn. The data was collected by comprehensively searching various scientific search engines i.e. PubMed, Google Scholar, web of science etc. According to literature plant contains various phenolic and non-phenolic secondary metabolites and nutrients. Majorly plants contain Carotenoids, Triterpenoids, Phenolic compounds i.e. Kaempferol, quercetin, gallic acid, Catechin, Epicatechin, Gallo catechin etc. Apart from these different parts of the plants also contains Lipids, Proteins, fatty acids, sterols; volatile compounds, Amino acids, Proteins, Sugars, Pectin, Vitamins (C, E, B, K1, D, A, folic acid) Macro and trace elements (potassium, magnesium, calcium, iron, sodium, manganese, zinc, copper, nickel). Sea buckthorn is known for its antioxidant, anti-cancer, antidiabetic, hepatoprotective, wound healing, anti-bacterial, anti-viral etc. pharmacological properties. In conclusion, the elaborate tapestry of sea buckthorn's phytochemistry and its multifaceted pharmacological actions has illuminated a promising path for both nutritional and therapeutic exploration. However, the paper's identification of substantial data gaps will spur more research and development, particularly for the creation of nutraceuticals and herbal medicines based on sea buckthorn.



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1 .INTRODUCTION

The sea buckthorn (*Hippophae rhamnoides* L.) is a species that bears berries. It is a hardy shrub belongs to family Elaeagnaceae^[1]. Sea buckthorn is commonly known as Sand Thorn, Dhurchuk, Chumaa, Tarwaa, Sirmaa etc. Around 100 species in three genera are found primarily in the Northern Hemisphere's moderate geographical latitudes ^[2].*Hippophae rhamnoides* Linn is a deciduous, thorny willow-like plant species native to Europe and Asia that grows in the freezing heights of the Himalayas. Its generic name, *Hippophae*, derives from the practice of feeding sea buckthorn to horses in ancient Greece in order to give them glossy coats (Greek: hippos—horse; pharos—shiny)^[3-4]. It is a pioneer plant that loves low humidity, alluvial gravel, wet landslips, and riverfront habitats, with brown rusty-scaly shoots ^[5]. Seaberries are shrubs or small trees that grow to sizes of 3 to 4 meters. They are trees with simple, alternate leaves that vary generally silver-gray in color and bloom without a crown. Seaberry branches are frequently coated with several stiff thorns. Seaberries are anemophilous and dioecious. Male plants have flower buds that are 2-3 times larger than female plants. ^[2]

Hippophae rhamnoides Linn currently expands seven species: ^[7]

- i. subsp. *sinensis*
- ii. subsp. *yunnanensis*
- iii. subsp. *turkestanica*
- iv. subsp. *mongolica*
- v. subsp. *caucasina*
- vi. subsp. *carpatia*
- vii. subsp. *fluviatilis*

In vitro and *in vivo* human and animal studies of sea buckthorn have shown a number of bioactive chemicals in leaves, roots, seeds, and berries called seaberries or Siberian pineapples, and oil derived therefrom; these compounds have a broad spectrum of anti-inflammatory effects, anticancer, antioxidant, and antiatherosclerosis.



Figure 1: *Hippophae rhamnoides* Linn plant



Figure 2: Dried Berries of *Hippophae rhamnoides* Linn

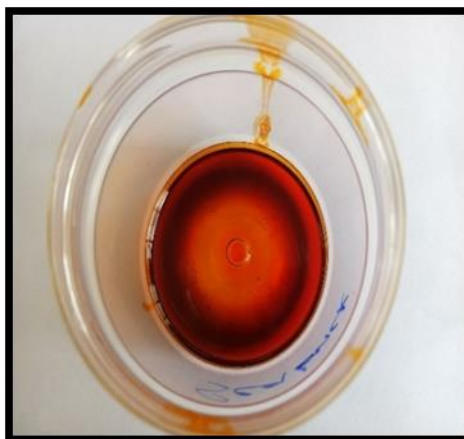


Figure 3: Extract of *Hippophae rhamnoides* Linn

2. Material and Methods:

In this review we explored the plant profile, phytochemistry, and pharmacological activities including: *in vivo*, *in vitro*, clinical studies of the plant and market preparation, to date of sea buckthorn. The data was collected by comprehensively searching various scientific search engines i.e. PubMed, Google Scholar, web of science, Science direct etc.

3. Plant profile

3.1 Geographical Distribution

Hippophae rhamnoides, *H. salicifolia*, and *H. tibetana* are the predominant seabuckthorn species in India. Of these, *H. rhamnoides* is widely distributed in India^[6-5]. The *Hippophae rhamnoides* Linn is widely distributed in European and Asian countries like India, China, Pakistan, Russia, Nepal, etc. ^[5]. Sea buckthorn (*Hippophae rhamnoides*) grows naturally in six valleys: Leh, Nubra, Changthang, Suru, Lahaul, and Spiti. And, is also found in a few pockets of Nathula in Sikkim. Seabuckthorn has been mapped in Himachal Pradesh, Lahaul Spiti, and Ladakh regions in Jammu and Kashmir using remote sensing and GIS.^[6]

3.2. Vernacular name^[7].

English	Sallow-thorn, Sea buckthorn
French	Argousier, Argoussier
German	Stech-dorn
Ladakh	Sirna, Tasru, Tsarana, Tsarap
Lahoul	Sirna, Tasru, Tsarana, Tsarap
North-wester	Chuk, Chuma, Dhurchuk, Tarwa
Pangi	Suak
Punjab	Amb, Bautphut, Kalabisa, Kando, Milech, Miles, Rul, Sirma, Suts, Starbu, Tarru, Tsarap, Tsarnang, Tsarmaniechak, Tserkar, Tswak
Tibet	Starbu
United-provinces	Chuma, Dhurchuk, Tarwa
Bhotia	Tarwa
Dutch	Duindown
Piti	Sirna, Tasru, Tsarana, Tsarap
Italian	Olivella spinosa and ventrie marina
Russian	Oblepicha
Swedish	Havtorn

3.3. Taxonomic classification of *Hippophae rhamnoides* Linn^[8]

The taxonomic classification of *Hippophae rhamnoides* Linnis given in the table:

Kingdom	Plantae
Sub kingdom	Phanerogamia
Division	Angiospermae
Class	Dicotyledons
Subclass	Monochalamydae
Series	Daphnales
Family	Elaeagnaceae
Genus	<i>Hippophae</i>
Species	<i>rhamnoides</i> Linn

3.4. Morphological and microscopic character

The Elaeagnaceae family includes the unique herb and fragrant plant known as sea buckthorn. The plant may reach heights of 2 to 6 meters and is a small to medium-sized deciduous tree or big shrub. The main stem is covered with thick, rough bark, while the juvenile branches are smooth, grey to light ash in color, and have needle-shaped thorns. Thorns, which range in length from 2.5 to 5.0 cm, begin to form on 2- or 3-year-old plants in almost all *Hippophae* species. Pollen-producing flowers first arise before leaves^[9]. The leaves are silver-gray on the upper side, alternating, thin, and 4–6 cm long. On wood that is two years old and has undergone differentiation over the previous growth season, flower buds generally develop. A sea buckthorn fruit weighs between 200 and 500 milligrams. A single dicotyledonous brownish-black seed is also present in the berry or fruit. The seed has two different layers of the Testa, which are produced from the outer and inner integument of the ovule, and is about 4.3 mm long and 2.4 mm broad. It has a furrow all the way around the seed body^[12]. The inner layer of the seed is thin and fibrous in appearance, while the outer coating is thick, hard, and brownish-black in color. The seed coat's overall thickness ranges from 0.1 to 0.2 nm.

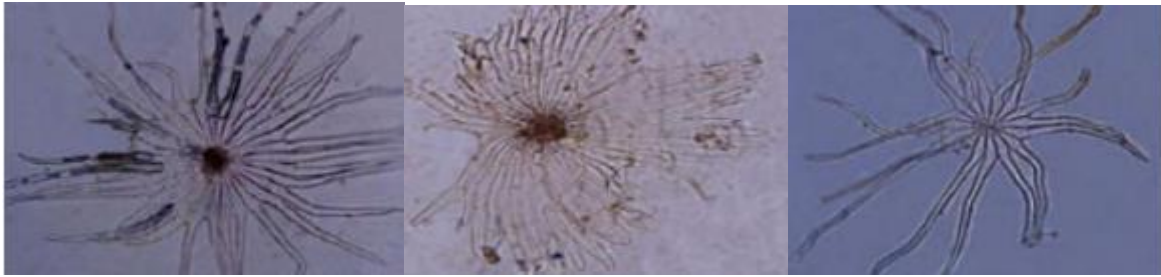


Figure 4: Powder microscopy of *Hippophae rhamnoides* Linn leaf.

Powder microscopy showed the existence of many forms of trichomes, included stellate, peltate, as well as a mix of the both stellate-peltatetrichomes, as well as palisade cells and fractured xylem arteries in the wounded epidermis^[10].

3.5. Bioactive compounds of sea buckthorn

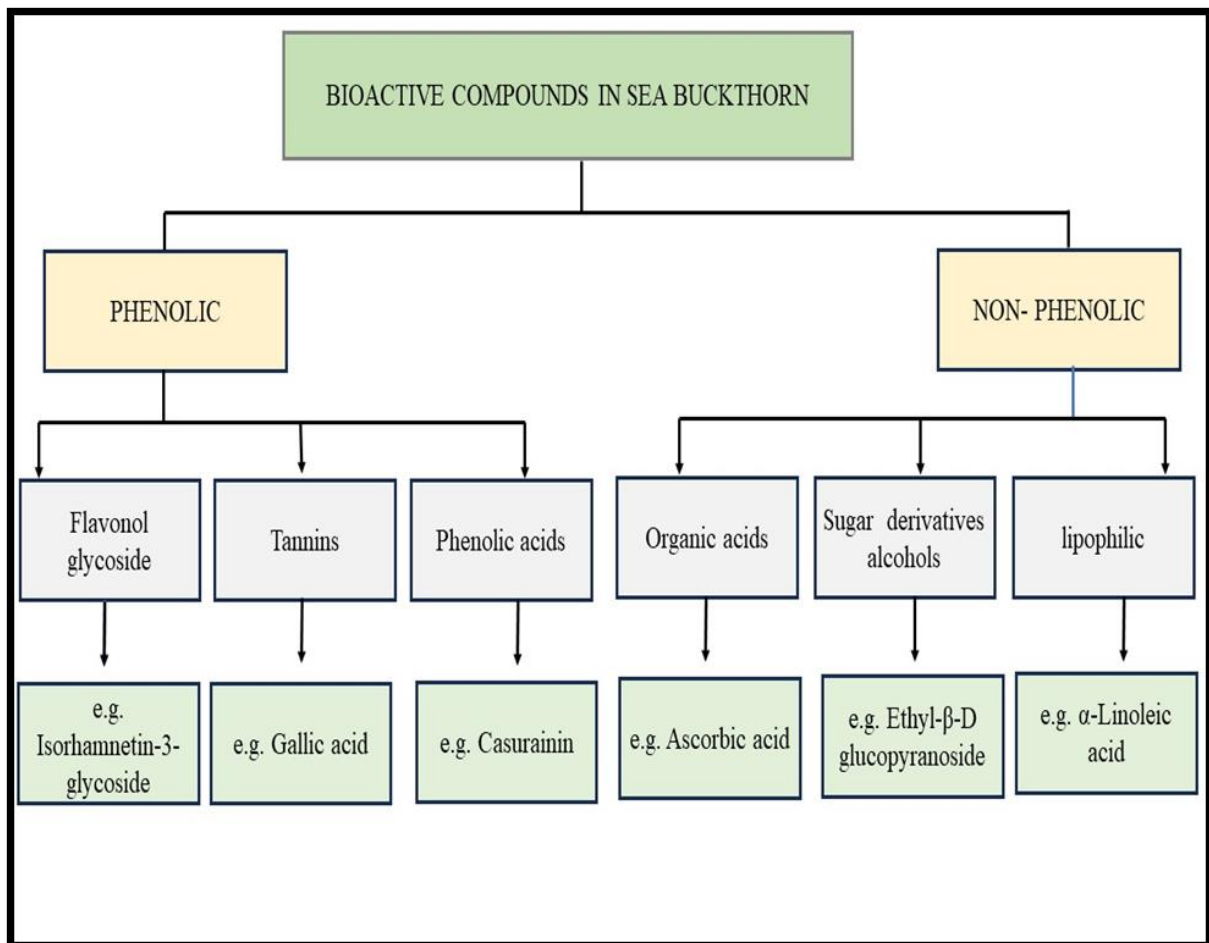


Figure 5: Bioactive compound in *Hippophae rhamnoides* Linn.

3.6. Physical and chemical parameters of *Hippophae rhamnoides* Linn^[5]

Color	Yellow, orange orange-red
Shape	Round, oval, ovoid
Fruit weight	10-16 gm /100 berries;
Fruit juice extraction rate	64- 75 %
Vitamin C in fruit juice	1161.1- 1302.5 mg/100 gm
Vitamin A in fruit juice	0.75 mg/100 gm
Carotenoids in fruit juice	7.2 -7.4 mg/100 gm
Soluble solids in fruit juice	15.92 -17.66
Carotenoid in fruit residue oil	1570 mg/100 gm
Total flavone in fruit juice	365 -885 mg/100 gm
Total flavone in fresh fruit	354 mg/100 gm
Protein in fruit	34.6 %
Total sugar	6.29 %
Organic acid	4.35%
Sodium	41.28 mg/kg fruit
Potassium	1499.96 mg/kg fruit
Calcium	383 mg/kg fruit
Iron	11.68 mg/kg fruit
Magnesium	47.7 mg/kg fruit
Zinc	0.94 mg/kg fruit
Phosphorus	0.02 %
Seed	6.54 %
Oil in seed	10.37- 19.51 %
Vitamin E in seed oil	101.5-277.6 mg/100 gm
Vitamin C in seed	149 mg/100 gm
Protein in seeds	21.66 %

3.7. Major Phytoconstituents of sea buckthorn ^[3]

Sr no	Phytoconstituents	Medicinal properties
01	Tocopherols	Act as antioxidants, minimize lipid oxidation, and help to relieve pain.
02	Carotenoids	Act as antioxidants, help in collagen synthesis and epithelialization
03	Vitamin K	Prevents bleeding, promotes wound healing, shows anti-ulcer effects
04	Vitamin C	Acts as an antioxidant sustains cell membrane integrity, accelerates collagen synthesis
05	Vitamin B complex	Stimulates cell repair and nerve regeneration
06	Phytosterols	Improve microcirculation in the skin, show anti-ulcer, anti-atherogenic, and anti-cancer effects, regulate inflammatory processes
07	Polyphenolic compound	Show antioxidant, cytoprotective, and cardioprotective effects, promote wound healing
08	Polyunsaturated fatty acids (PUFA)	Immunomodulatory, neuroprotective, and anti-tumor activity
09	Organic acids	Lower the risk of heart attack and stroke, show anti-ulcer effects, promote wound healing, anti-arthritic
10	Coumarins and triterpenes	Control of appetite, promote sleep, memory, and learning
11	Zinc	Strengthens blood circulation, aids in cell proliferation reveals anti-tumor effects, acts as a cofactor for enzymes, enhances the utilization of vitamin-A -A

4. Chemical composition of the whole plant of sea buckthorn

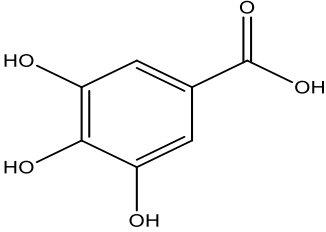
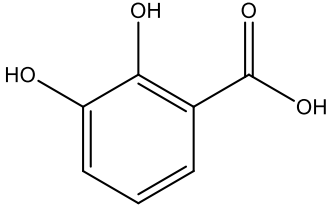
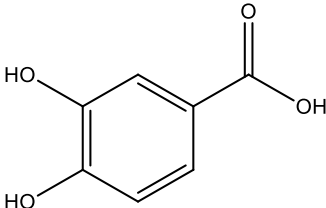
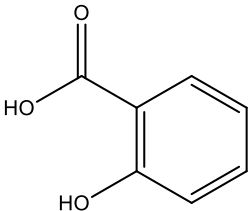
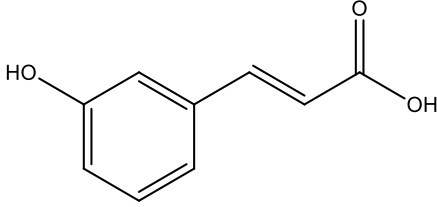
Sr. no.	Part of <i>Hippophae rhamnoides</i> Linn	Chemical composition	References
01	Fruits (berries)	<p>Carotenoids; β-Cryptoxanthin, Lycopene, γ-Carotene, β-Carotene β-Cryptoxanthin esters, Zeaxanthin, Zeaxanthin esters lipids; Phosphatidylcholine, Phosphatidylglycerol, Phosphatidylethanolamine, Digalactosyldiacylglycerol, Monogalactosylacylglycerol Oleanolic acid; Ursolic acid, 19-α-Hydroxyursolic acid, Dolicoic acid Carbohydrates; Carbohydrate 2-O-Methyl-L-chiro- inositol(L-quebrachitol), Chiro-inositol, Myo-inositol Tocopherols; α-Tocopherol, β-Tocopherol, γ-Tocopherol, δ-Tocopherol, α-Tocotrienol, β-Tocotrienol, γ-Tocotrienol</p> <p>Phenolic compounds; sterols; fatty acids; volatile compounds, Lipids, Amino acids, Organic acids, Proteins, Sugars, Pectin, Vitamins (C, E, B, K1, D, A, folic acid) Macro and trace elements (potassium, magnesium, calcium, iron, sodium, manganese, zinc, copper, nickel)</p>	[11-12-14-15-16]

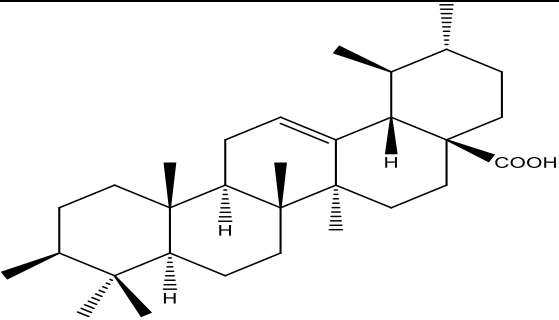
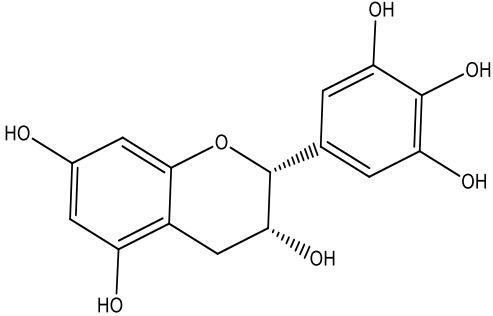
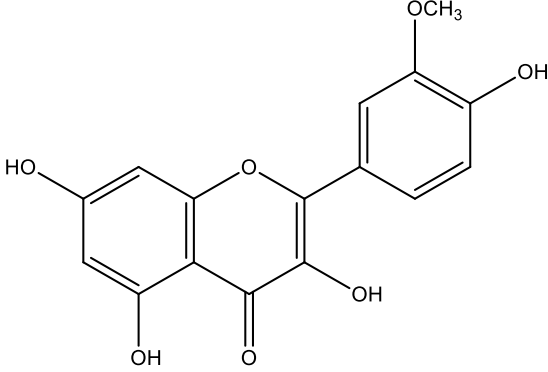
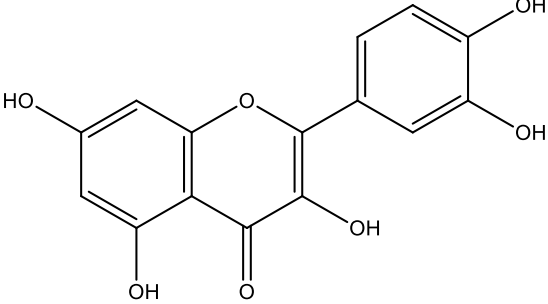
02	Leaves	<p>Flavanol's; Isorhamnetin, Isorhamnetin 3-O-[O-β-D-glucopyranosyl-(1→6)- β-D-glucofuranose] Kaempferol, Kaempferol 3-O-(6-O-p-coumaroyl)-β-D-glucoside (tiliroside) Quereetin; Quercetin 3-O-β-D-glucopyranoside (isoquercitrin), Quercetin 3-galactoglucoside Myricetin Phenolic acids; Gallic acid (3,4,5-trihydroxy benzoic acid) Tannins; 6-O-Galloyl-1,3-O-hexahydroxydiphenoyl-β-D-glucose(hipporhamninn), Strictinin, Isostrictinin, Elaeagnatin A Pterocarinin A Hippophaenins A Hippophaenins B, Stachyurin, Casuarinin, Casuarictin, Pedunculagin Vitamins (E, folic acid) Calcium, magnesium, potassium, Carotenoids, Amino acids, Chlorophyll, Proteins, Pectin</p>	[13-14-15]
03	Seed	<p>Carotenoids, Phenolic compounds, Lipids, Proteins, fatty acids Catechin, Epicatechin, Gallo catechin, Epigallocatechin, Catechin-(4α→2)-phloroglucinol Catechin(4α-8) catechin, Catechin(4α-8) epicatechin</p>	[15-11-16]
04	Roots	<p>Carotenoids, Phenolic compounds, Lipids, Proteins</p>	[12]
05	Branch, Bark	<p>Catechin, Epicatechin, Gallo catechin, Epigallocatechin, Catechin-(4α→2)-phloroglucinol Triterpenoids;</p>	[15-17]

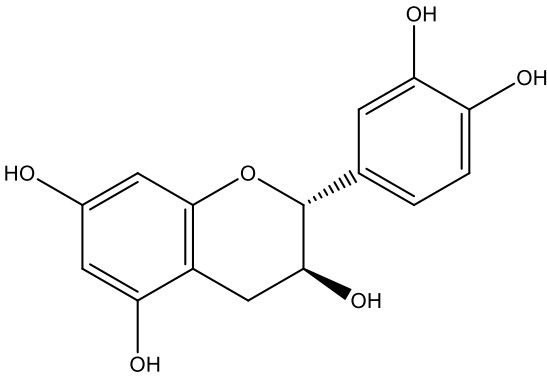
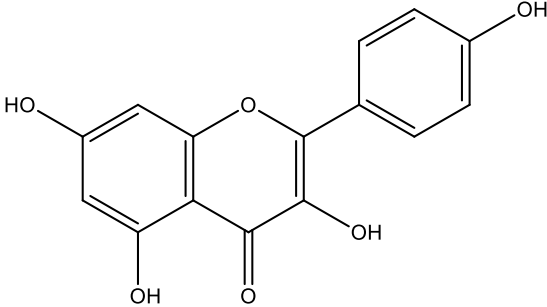
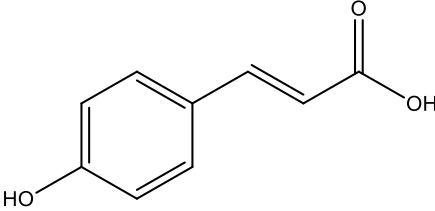
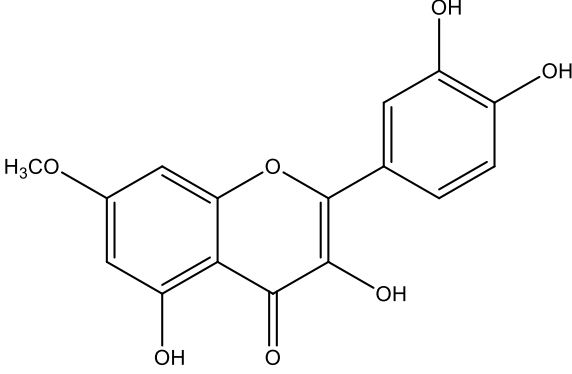
		<p>2-O-Trans-p-coumaroyl maslinic acid, 2-O-Caffeoyl maslinic acid</p> <p>Oleanolic acid;</p> <p>3-O-Trans-p-coumaroyloleanolic acid, 3-O-Caffeoyl oleanolic acid, Ursolic acid</p>	
06	Juice	<p>Flavanols;</p> <p>Isorhamnetin, Isorhamnetin 3-O-rutinoside, Isorhamnetin 3-O-glucoside, Isorhamnetin 7-O-rhamnoside, Isorhamnetin 3-O-glucoside-7-O-rhamnoside</p> <p>Quercetin;</p> <p>Quercetin 3-O-rutinoside, Quercetin 3-O-glucoside, Flavon-3-ols;</p> <p>Catechin, Epicatechin</p> <p>Phenolic acids;</p> <p>Gallic acid (3,4,5-trihydroxybenzoic acid), Protocatechuic acid (3,4-dihydroxybenzoic acid)</p> <p>Ascorbic acid</p>	[18]
07	Pomace	<p>Flavanol's;</p> <p>Isorhamnetin 7-O-α-L-rhamnoside, Isorhamnetin 3-O-β-D-glucoside-7-O-α-L-rhamnoside, Isorhamnetin 3-O-β-D-sophoroside-7-O-α-L-rhamnoside, Isorhamnetin 3-rutinoside-7-rhamnoside, Isorhamnetin 3,7-diglucoside, Isorhamnetin 3-pentoside-7-rhamnoside, Isorhamnetin rhamnosylglucoside, Isorhamnetin 3-coumaroylglucosylglucoside-7-rhamnoside, Isorhamnetin 3-hydroxy feruloyl-glucosylglucoside-7-rhamnoside</p> <p>Kaempferol 3-O-β-D-sophoroside-7-O-α-L-rhamnoside, Kaempferol rutinoside,</p>	[19-15-20]

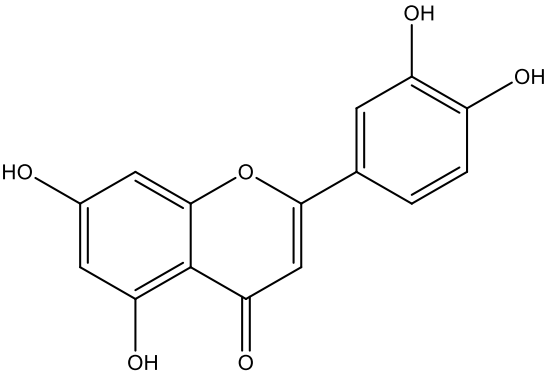
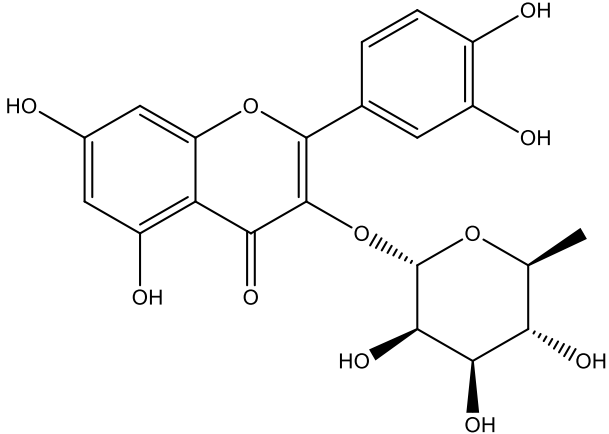
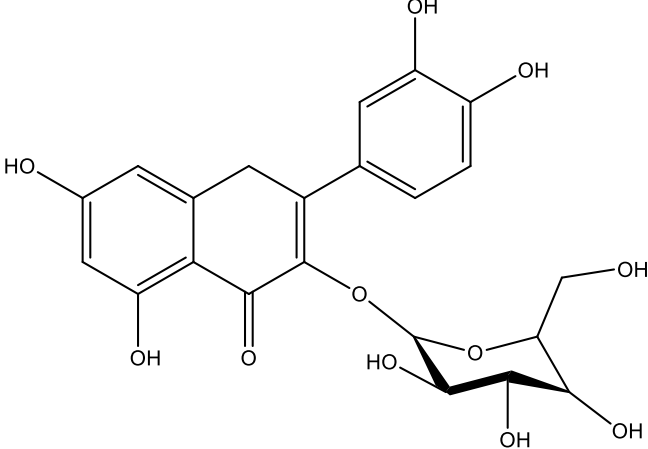
		<p>Kaempferol 3-glucoside-7-rhamnoside, Kaempferol 3-rutinoside-7-rhamnoside, Kaempferol 3-glucosyl-glucoside-7-rhamnoside, kaempferol 3-rhamnosyl-glucoside-7-rhamnoside, Kaempferol dirhamnosylglucoside, Kaempferol diglucosylrhamnoside, Kaempferol 3-hydroxyvanilloylglucosylglucoside-7-rhamnoside</p> <p>Quercetin 3-O-rutinoside, Quercetin 3-sophoroside-7-rhamnoside, Quercetin, Quercetin diglucosylrhamnoside Quercetin 3-coumaroylglucosylglucoside-7-rhamnoside, Quercetin dimethyl ether 3-hydroxyferuloylglucosyl, glucoside-7-rhamnoside, Quercetin dimethyl ether 3-caffeoylglucosylglucoside-7-rhamnoside</p> <p>Myricetin rutinoside, Myricetin dimethyl ether rutinoside, Catechin, Epicatechin, Gallo catechin, Epigallocatechin, Catechin-(4α→2)-phloroglucinol, Epicatechin-(4β→2)-phloroglucinol</p>	
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5. Structure of phytoconstituents

Class of compound	Compound	Structure	Reference
Phenol	Gallic acid		[21]
Phenol	pyrocatechuic acid		[21]
Phenol	Protocatechuic acid		[21]
Phenol	Salicylic acid		[21]
Phenol	m-coumaric acid		[21]

<p>Triterpenoid</p>	<p>Ursolic acid</p>		<p>[17]</p>
<p>Flavonoid</p>	<p>Epigallocatechin</p>		<p>[17]</p>
<p>Flavonoid</p>	<p>Isorhamnetin</p>		<p>[22]</p>
<p>Flavonoid</p>	<p>Quercetin</p>		<p>[7]</p>

<p>Flavonoid</p>	<p>Catechin</p>		<p>[17]</p>
<p>Flavonoid</p>	<p>Kaempferol</p>		<p>[7]</p>
<p>Phenol</p>	<p>p-Coumaric acid</p>		<p>[21]</p>
<p>Flavonoid</p>	<p>Rhamnetin</p>		<p>[7]</p>

<p>Flavonoid</p>	<p>Luteolin</p>	 <p>The structure shows a flavone core with hydroxyl groups at positions 5, 7, and 8 on the A-ring, and hydroxyl groups at positions 3' and 4' on the B-ring.</p>	<p>[23]</p>
<p>Flavonoid</p>	<p>Quercetin 3-rhamnoside</p>	 <p>The structure shows a flavone core with hydroxyl groups at positions 5, 7, and 8 on the A-ring, and hydroxyl groups at positions 3' and 4' on the B-ring. A rhamnose sugar is attached to the 3-position of the flavone core via an ether linkage.</p>	<p>[23]</p>
<p>Flavonoid</p>	<p>Quercetin 3-galactoside</p>	 <p>The structure shows a flavone core with hydroxyl groups at positions 5, 7, and 8 on the A-ring, and hydroxyl groups at positions 3' and 4' on the B-ring. A galactose sugar is attached to the 3-position of the flavone core via an ether linkage.</p>	<p>[23]</p>

6. Traditional uses

- *Hippophae rhamnoides* Linn is a common component in traditional Asian medicine. Traditional uses for this plant included gastrointestinal illnesses, coughs, colds, and menstrual diseases^[28].
- In medical applications, several Sea buckthorn (SBT) medicinal formulations have been used to treat stomach ulcers, burns, mouth inflammation, and radiation damage^[25].
- Sea buckthorn berries were included in the Chinese Pharmacopoeia as a remedy for increasing blood circulation, digestion, and coughing.
- In Russia, the use of sea buckthorn oil for the treatment of eye conditions has been recorded. Using sea buckthorn oil, many eye conditions such as corneal lesions, dark adaption, and visual acuity were treated. Historically, sea buckthorn has been used to treat a variety of illnesses, including atopic dermatitis, platelet aggregation, and dry eye. etc.^[26].
- Traditional Chinese medicine (TCM): In China, sea buckthorn has been used in traditional medicine for over a thousand years. In TCM, the oil from sea buckthorn berries is believed to have healing properties and is used to treat skin conditions, promote digestion, and support the respiratory system^[11].

7. Pharmacological uses

7.1. Antioxidant properties

It is compounds that inhibit or delay the oxidation of other molecules by inhibiting the initiation or propagation of oxidative chain reactions. The antioxidant effect refers to the enhancement of antioxidant enzyme activity and the inhibition of related activities of Oxidase. Free radicals can be generated by redox and peroxide ions of transition metals (iron and copper). Therefore, the production of antioxidant enzymes is promoted, and reduced the formation of oxidase and metal ions can achieve a good antioxidant effect^[3].

7.2. Cardiovascular disease

Polyphenols called flavonoids are found naturally in a variety of fruits and vegetables, including sea buckthorn. Isorhamnetin and quercetin are the flavonoids that are most prevalent in sea buckthorn fruit and leaves^[27]. According to reports, flavanols' antioxidant capabilities reduce the incidence of cardiovascular illnesses. Total sea buckthorn flavonoids

have protective properties against tumors, oxidative damage, cardiac ischemia and reperfusion, and aging [28].

7.3. Diabetes

An endocrine system metabolic condition is diabetes. It makes it difficult for individuals to manufacture and utilize insulin in the body as intended, which raises blood glucose levels. [3]. Many scientists have looked at how sea buckthorn could help with diabetes therapy. An example investigated the effects of an aqueous extract of sea buckthorn seed residues on serum glucose, lipid profiles, and antioxidant parameters in streptozotocin-induced diabetic rats. Four groups of rats were examined: a normal control group, a diabetic control group, a diabetic group supplemented with 5 mg/kg body weight of glibenclamide (reference drug), and another a diabetic group supplemented with 400 mg/kg body weight of sea buckthorn seed residue extract. The extract significantly lowered the levels of serum glucose, triglyceride, and nitric oxide in diabetic rats [29].

7.4. Antitumor effect

An initiator (7,12-dimethylbenz[a]anthracene) and a promoter (12-O-tetradecanoylphorbol-13-acetate (TPA)) of mouse carcinogenesis were used to show the anticancer action of sea buckthorn extract. A triterpenoid (Uric acid) and three phenolic components (catechin, Gallo catechin, and epigallocatechin) extracted from sea buckthorn have been demonstrated to inhibit TPA-induced inflammation [30].

7.5. Gastrointestinal effect

The therapeutic potential of sea buckthorn for gastrointestinal disorders has been studied [31]. Oral administration of CO₂-extracted seed and pulp oil was used as a pre-trial treatment for groups of rats with artificially generated stomach ulcers. The sea buckthorn oils' therapeutic and preventative benefits were investigated. Consuming sea buckthorn oil has been shown to hasten the recovery of stomach ulcers brought on by acetic acid [3].

7.6. Wound Healing

The historic usage of sea buckthorn for skin regeneration has given way to its use in contemporary medicine. Omega-3, 6, and 7 useful unsaturated fatty acids, natural antioxidants, vitamins E and K, carotenoids, and phytosterols are all abundant in sea buckthorn fruit and seed oil. These substances work together to safeguard cell membranes

and improve cell regeneration. The skin contains palmitoleic acid, which is used to treat burns and promote wound healing. According to certain reports, sea buckthorn oil can both prevent and treat several forms of stomach ulcers, chronic cervicitis, and atopic dermatitis^[32].

7.7. Antimicrobial and Antiviral Properties

Both antiviral and antibacterial activities are present in sea buckthorn. The antibacterial activity of sea buckthorn berry extracts was investigated by Chaman and colleagues^[31]. using the hole-plate diffusion technique. According to the findings, methanol extract (100 mg/mL) produced a rather strong antibacterial response, whereas other extracts only produced a modest zone of inhibition against all of the tested microorganisms. Infection with the Dengue virus triggers an antiviral response in sea buckthorn as well. There is no direct therapy for the dangerous infection known as dengue fever. Human blood-derived macrophages infected with Dengue virus type-2 were used to evaluate *H. rhamnoides* leaf extract and compare it to the widely used antiviral medication Ribavirin. It is possible that *H. rhamnoides* leaf extract has strong anti-dengue action and might be utilized to treat dengue fever because it was similarly efficient at preserving the cell viability of dengue-infected cells as Ribavirin^[33].

7.8. Food application

Many food items already include sea buckthorn. The most often consumed sea buckthorn-based goods include juices, jams, wines, pies, and liquors. The fruits may be used to produce reviving drinks due to their strong acidity, whilst the leaves are utilized to make teas^[32].

8. *In vitro* study of sea buckthorn

Part of plant	Concentration	Cell line	Outcome	Reference
Edible berry	10–50 µl/ml of medium	Stomach, prostate, intestine, and breast cell lines	Inhibit cancer cell proliferation and suppress TNF-induced activation of NF-Kb	[8]
Edible berry	< 0.1–2% (v/v) of medium	Human colon and liver cancer cell lines (h Caco-2 and Hep G2 cells)	Anti-proliferative effects	[34]
Fruit and berry	0.025–0.5% medium	MCF-7 (breast cancer cells) and HT29 (colon cancer cells)	Inhibition of proliferation of cancer cell	[35-8]
Isorhamnetin (Hippophae rhamnoides L.)	25–300 µg/ml of medium (IC50 = 75 µg/ml)	BEL-7402 (human hepatocellular carcinoma cells)	Antitumor activity	[22]
Isorhamnetin (Hippophae rhamnoides L.)	10–320 µg/ml	A549 (cancer cells of lungs)	Anti-proliferative effects	[36]
Isorhamnetin (sea buckthorn fruits)	20 and 40 µ molar	Human colorectal cancer cells (HT 29, HCT116, and SW480)	Anti-proliferative action	[37]
Procyanidins (SBT seeds)	10–60 µg/ml	Human breast cancer MDA-MB-231 cells	Induce apoptosis via inhibiting FAS	[36]
Leaves	10–100 µg/ml	Human breast cancer MDA-MB-231 cells	Antitumor activity	[38]
Leaves	0.62–62 µg/ml	Glioma cells	Inhibit proliferation and promote apoptosis	[39]

9. *In vivo* study of sea buckthorn

Part of the plant used	Animals used	Doses	Outcome	References
Whole plant	Mice	1.7 and 0.2 μ mol/ear	Antitumor properties	[44-40]
Berries	Mice	50–200 mg/kg, intragastric once a day daily for 14 days	Decrease carcinogen-induced forestomach and skin tumorigenesis	[42]
Fruit or berries	Mice	Sea buckthorn juice (300 ml) was given orally to mice for 5 or 10 days	Decrease carcinogen-induced forestomach and skin tumorigenesis	[45-41] Click or tap here to enter text.
Sea buckthorn seed oil	Dog	5 ml per animal, twice a day	Increase ROS-induced oxidative stress	[42]
SBT oil	Wistar albino male rats	HR oil (1 mg/kg BW)	CCl ₄ -induced hepatic damage by regulating the levels of aspartate aminotransferase	[43]
Hexane extract of sea buckthorn berry	Rats	1 ml/kg bw orally (gavage) prior to induction of ulcer	Decrease carcinogen-induced forestomach	[44]
Seed oil and pulp oils (CO ₂ extra.)	Rats	3.5 ml/kg bw/d and 7 ml/kg bw/d prior to/after induction of ulcer for 7 or 12 d, orally	activation of the cell-mediated immune response.	[45]
Aqueous extract of sea buckthorn dried leaves	Rat	100 mg/kg orally	Increase ROS-induced oxidative stress	[46]
Aqueous extract of sea buckthorn seed	Rat	400 mg/kg b. w.	Antidiabetic effect (Type-1 diabetic)	[47]
Sea buckthorn berry	229 healthy adults	28g	Increase in circulating flavanol concentration; no effect on total, HDL, LDL	[48]

			cholesterol, and triacylglycerol	
Sea buckthorn fruit powder	Hypertensive stroke-prone rats	0.7g/kg	Improvement in metabolic processes and reduction in hypertensive stress	[49]
Sea buckthorn seed extract	Sucrose-fed rats	150mg/kg	Decrease in blood pressure, hyperinsulinemia, and dyslipidemia	[50]
Sea buckthorn seed oil	Rabbits fed on high cholesterol diet	1ml	Reduction in LDL, atherogenic index, and increase in HDL and vasorelaxant activity	[51]
Sea buckthorn seed residue extract	Diabetic rats	400mg/kg	Reduction in serum glucose, triglycerides, and nitric oxide levels	[47]
Sea buckthorn oil	12 healthy normolipidemic men	5g	No change in plasma lipids and glucose; decrease in platelet aggregation	[52]

10. Clinical studies

- Traditional wisdom and previously published information provide the foundation for the medical use of SBT in humans. The long-standing use of SBT oil for the treatment of stomach ulcers has been supported by laboratory research. SBT seed oil has also undergone clinical evaluation for ulcers and chronic cervicitis. A clinical investigation including 30 patients with partial cervix erosion was carried out. SBT seed oil was used topically on every patient for 90 days, and curiously, after 30 days, every patient was cured [25].
- Different research was conducted on infants with ulcerative stomatitis between the ages of 4 months and 12 years. Wonderfully, 55 of 60 children were treated after 3-5 days of treatment with SBT seed oil used topically, while chronic cases were cured after 8 days of treatment [8].
- A study was done on twenty healthy people who were given a placebo/SBT juice for eight weeks, and the results showed that SBT juice supplementation reduced the risk of

coronary heart disease due to the powerful antioxidants included in SBT juice. In another research, patients with ischemic heart disease were given total flavonoids from SBT for six weeks, and the results showed that the patients had lower cholesterol and increased cardiac function [51-8].

- A four-month double-blind placebo-controlled trial was undertaken on 49 atopic dermatitis patients who were given SBT seed oil, SBT pulp oil, or paraffin oil daily. Dermatitis was considerably treated by SBT pulp oil administration over the follow-up period [17].

- A clinical trial was also conducted on 05 women who had urogenital tract disorders. For 12 weeks, the patients were given 06 capsules per day of standardized SBA25 Omega 7 SBT oil (extracted by supercritical CO₂) containing 3g SBT oil, and all five chronic vaginal inflammation cases improved. Twenty-five female Sjogren's syndrome patients (aged 37-66; average age 52.2) with typical symptoms of itching, liquid discharge, burning, and dryness in the vaginal tract were studied in a placebo-controlled double-blind, cross-over research. The patients were randomly assigned to receive SBA 24 Omega 7 sea buckthorn oil or fractionated coconut oil capsules for three months, and the results concluded that the SBA 24 Omega 7 sea buckthorn oil capsules had favorable benefits [52].

- A clinical experiment was done to determine whether SBT berry oil ingestion can alleviate the symptoms of dry eye syndrome. The research included 100 people (aged 20 to 75 years) who experienced dry eye symptoms. The SBT oil was added with 2 g twice a day for three months (ClinicalTrials.gov Identifier: NCT00739713). Approximately 100 participants were recruited for the current clinical trial, and the study was completed with 86 participants. Finally, during the cold season, SBT oil alleviated dry eye symptoms and decreased tears [52-53].

- A clinical investigation was carried out on 41 obese children aged 10 to 18 years. SBT pulp oil treatment was administered at a dose of 800 mg per day for two months as therapy. Finally, SBT pulp oil reduces atherosclerosis by lowering triglycerides, blood pressure, and cholesterolemia, as well as resistance, oxidative stress, and inflammation [53].

- A human-randomized, controlled, double-blind longitudinal research including 32 control subjects and 74 hypertensive and hypercholesterolemic subjects (n = 74) was carried out. SBT seed oil and a placebo sunflower oil were both consumed orally for 30 days. The

outcomes showed that SBT seed oil is effective in lowering cardiovascular risk factors and dyslipidemia. (54)This human trial is registered in the Clinical Trial Registry of India as clinical trial registration number—CTRI/2015/11/006368^[52].

11. Toxicity studies

SBT seed oil exhibited effectiveness in protecting against the toxicity of Sulphur dioxide inhalation. also documented the significant antioxidant protection provided by SBT extracts against Sulphur mustard. By increasing antioxidant activity, the SBT fruit extract also demonstrated beneficial efficacy against heavy metal (arsenic) toxicity, but the extract was unable to remove arsenic from the cells via chelation. ^[55-56]. Animals have been used in a variety of toxicity studies for extracts and formulations based on SBT. According to the acute toxicity investigation, the LD50 for SBT extract was 10 g/kg. Additionally, a subacute toxicity study was carried out, and the outcomes showed that it is safe. In addition, the extract's safety was determined in light of the presence of heavy metals in the extract^[57]. In subacute investigations, SBT was administered orally for 14 days at doses of 1 and 2 g/kg once daily. The results of the study showed an increase in body weight, but toxicity-related parameters like serum bilirubin and creatinine remained unchanged when compared to control animals. They also revealed that an aqueous extract of SBT leaf given to rats at a dose of 100 mg/kg bw/day once daily for 90 days had no negative side effects. In both the subacute and acute oral toxicity assays conducted on rats, CO₂-SFE-extracted seed oil of SBT was likewise shown to be non-toxic.(58)Aqueous extract of sea buckthorn fruit administered to four groups of rats (0, 100, 250, or 500 mg/kg in a single dose/day for 90 days) revealed no treatment-related changes in mean body weight, organ/body weight ratio, histological, hematological, or biochemical markers. Over 90 days, rats treated with 250 and 500 mg/kg aqueous extract of sea buckthorn berries increased plasma glucose levels. The results suggest that there isn't any information on its toxicity. As a result, it is a nutritional supplement that is safe to use when accompanied by a prescription from a physician or clinical dietician^[59].

12. List of *Hippophae rhamnoides* Linn goods available in the market ^[60]

Sea buckthorn oil soft gel	Frakenbiochem co., ltd. [Shandong, China]
Fructus <i>Hippophae</i> extract	Rui heng industry co., ltd. [China]
Sea buckthorn pulp oil	Inner Mongoliayuhangren hi-tech industrial co., ltd. [province: Inner Mongolia, China]
Sea buckthorn seed oil	Hebei shenxing sea buckthorn health products co., ltd. [China]
Immune-enhancing ingredients	Shanghai brightol international co., ltd. [province: Shanghai, China]
Fish oil soft gel capsule & lecithin soft gel capsule	Qingdao dacon trading co., ltd. [province: Shandong, China]
Sea buckthorn berry oil sea buckthorn seeds	Beijing powdery food co., ltd. [province: Beijing, China]
Oil capsule (y-o-04)	Youchain group co., ltd. [province: Hebei, China]
Shenxing sea buckthorn xinzhan oral liquid	Hebei shenxing sea buckthorn health products co., ltd. [province: Hebei, China]
Organic sea buckthorn fruit oil soft capsule	Hebei shenxing sea buckthorn health products co., ltd. [province: Hebei, China]
Organic sea buckthorn berry/fruit powder	Hebei shenxing sea buckthorn health products co., ltd. [province: Hebei, China]
Sea buckthorn fruit oil capsules-1	Jinan sea buckthorn trade co., ltd. [Province: Shandong, China]
Jinan sea buckthorn trade co., ltd. [province: Shandong, China]	Jinan sea buckthorn trade co., ltd. [Province: Shandong, China]
Sea buckthorn seed oil capsule	Wutai mountain sea buckthorn co., ltd. [Province: Shanxi, China]
Sea buckthorn berry powder	Shijiazhuang yiling pharmaceutical co., ltd. [province: Beijing, China]
Sea buckthorn powder	Shijiazhuang yiling pharmaceutical co., ltd. [province: Beijing, China]
Spirulina	Dechen nutrachem co., ltd. [province: Shandong, China]
Sea buckthorn seed oil (flu-s003)	Inner Mongolia prosperous earth trade co., ltd. [province:

	Inner Mongolia, China]
Sea buckthorn seed oil (flu-s004)	Inner Mongolia prosperous earth trade co., ltd. [province: Inner Mongolia, China]
Sea buckthorn oil	Guangzhou honsea sunshine bio science & technology co., ltd. [province: Guangdong, China]
Sea buckthorn seed oil capsule (hy-08003)	Beijing huiyuan group youyu co., ltd. [province: Shanxi, China]
Sea buckthorn gallicsoft gel (Perfect (China) co., ltd. [province: Guangdong, China]
Sea buckthorn fruit oil	Wutai mountain sea buckthorn co., ltd. [province: Shanxi, China]
Fruit juice concentrate	Heilongjiang provincial hongri trading co., ltd. [province: Heilongjiang, China]
Sea buckthorn effervescent tablets	Nanjing union biotech co., ltd. [province: Jiangsu, China]
Frozen sea buckthorn berry	Conseco sea buckthorn co., ltd. [province: Beijing, China]
Digestive support herbal candy	Candy manufacturer inc. [province: Guangdong, China]
Capsules of nutrient products	Shanghai hong hao chemicals co. Ltd. [province: Shanghai, China]
Menov`aheyeqianzi slimming herbs capsule	Panda international trade co., limited [province: Hong Kong, China]
Soft gel capsule [2010-08-17]	Sunrise nutrachem group [province: Shandong, China]
Skin whitening product	Chifeng wedge pharmaceutical co., ltd. [province: Inner Mongolia, China]

CONCLUSION

The available literature on sea buckthorn reveals that historically plant has been used to cure a variety of conditions, including gastrointestinal illnesses, coughs, colds, and menstrual diseases, stomach ulcers, burns, mouth inflammation, radiation damage, atopic dermatitis, platelet aggregation, and dry eye. During collection of data from various search engines various parameters i.e. plant profile, phytochemistry, pharmacological activities including: in vivo, in vitro, clinical studies of the plant and market preparation till date of sea buckthorn were studied. *Hippophae rhamnoides* contains various phenolic and non-phenolic secondary

metabolites i.e. carotenoids, triterpenoids, kaempferol, quercetin, gallic acid, Catechin, Epicatechin, Gallo catechin etc. The pharmacological effects of sea buckthorn include antioxidant, anti-cancer, hepatoprotective, wound healing, anti-bacterial, antiviral, etc. In conclusion, the extensive literature on the phytochemistry and diverse pharmacological effects of sea buckthorn has revealed a promising avenue for nutritional and therapeutic research, notably for the development of sea buckthorn-based nutraceuticals and herbal medications.

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