REVIEW ARTICLE

Unexplored therapeutic treasure of Himalayan sea buckthorn berry: An opportunity for rejuvenation applications in Ayurveda

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Abstract

Ayurveda captured almost all herbs in its indications for therapeutics from the period of Vadas. More than 700 plants are discussed elaborately in various classics of Ayurveda of different periods. However, it seems that here is a missing link about sea buckthorn alias Amleech (*Hippophae rhamnoides* family *Elaeagnaceae*). This review article is all about morphological characteristic, properties, active constituents, therapeutic spectrum, cosmetic value, nutraceutical value of the plant and its uses for the well-being of humanity. Our objectives are to make this plant beneficial to all humanity as per doctrines of Ayurveda pharmaceutics and therapeutics. We had have searched the available research papers, textbooks, and reference books and summarizes the results related to various properties of sea buckthorn and also emphasizes the aspects that warrant future research in India establishing its activity and utility in preventing diseases related to skin, liver, gastrointestinal, and even cancer. Contemporary researches are indicatives of its various therapeutic properties due to its constituent chemistry such as flavonoids, carotenoides, polyunsaturated fatty acids, vitamins , minerals, Omega 3, 6, 9 and rarest Omega 7 and about 190 bioactive compounds. We can expect many scientific evidence supporting the benefits of the sea buckthorn to maintain health and to cure the diseases by rationalizing it in proper Ayurvedic dosages form for this plant.

Key words: Ayurveda, cosmeceutics, neutraceutics, sea buckthorn, therapeutics

INTRODUCTION

Ayurveda classics are full of descriptions of herbs of medicinal uses. From Veda to Samhita period (5 AD) and onward compilations of medicinal plants known as Nighantus (16 AD) have described all plants material which was used in practice of Ayurveda from *Swarasa* to *Sandhan* dosages form of Ayurveda (different forms of medicines of Ayurveda). However, unfortunately, Ayurvedic scholars have not discussed much about Amleech. Modern researches of this plant revealed many strong pharmacological action of this plant. After knowing all these Ayurvedic scholars started searching about Amleech in Ayurvedic classics. There is a different opinion among Ayurvedists about the identity of Amleech. Some say it is like *Amlavetas*, but few strongly disagree with this conclusion. A minute observation of classics established that Amleech is mentioned in *Bhavprakash Nighantu* in *Amradiphalavarga* where it is described along with *Revandchini*, *Thaikal*, *Chukra*, *Nimbu*. Vaidya Mayaram Aniyalji Suggested all these Himalayan fruits to consider as *Amlavetas*, Because of its close resemblance with *Amlavetas*.[1] Sea buckthorn (*Hippophae rhamnoides L.* – means Shining horse) known by the names as common sea buckthorn. Habitat of Amleech is Leh berry, Tarbu (Lahaul), Dhurchuk (Hindi), Tsetalulu (Ladakh), Chharma, Siberian pineapple, Seaberry, Sandthorn, or Swallowthor.

Hu Sibu Yidian is a classical Tibetan medical book with four volumes and 158 chapters altogether. Thirty chapters deal with sea buckthorn. Its shows it significant in the treatment of

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disorders of the cardiovascular, immune system, anti-senility, anti-inflammation, and anti-radiation effect,[2] on virtue of its phyto-constituencies which are consist biologically active substances with pharmacological effects. During the last few years, research on products of sea buckthorn, that is, medicinal and health products has greatly advanced, and many economic benefits have been gained from it in industries of cosmetics and nutraceutics.

DESCRIPTION

Hippophae is indigenous to the Ladakh region of Jammu and Kashmir, Chamba, Lahaul, Spiti district and Kinnaur of Himachal Pradesh, Kumaon and Garhwal of Uttarakhand and Sikkim. The plant is found gregariously growing along the river sides and moist patches of the cold desert of Himalayas at an altitude of 1600–2500 m.[3]

MORPHOLOGY

The plant is usually a varying sized thorny shrub. The shoot is modified into spines. The leaves are lanceolate-linear and obtuse with peltate and stellate scales on the lower surface. The male plant flowers in clusters at the base of the shoot. The tepals are free and suborbicular. The fruits are subglobose, succulent, and red or orange colored. The seeds are solitary, uniquely lobed, light black, and stony.[4]

DISTINGUISHING FEATURES

Sea buckthorn is a dioecious shrub with an ashen brown colored stem and 2–5 cm long spines. The fruit is a pseudo-berry turning from green to yellow-orange and red on ripening.

Life Cycle

The vegetative buds start sprouting by April as the snow melts. Flowering takes place in July–August and fruiting in August–September.

CONSTITUENTS OF SEA BUCKTHORN

Sea buckthorn has been reported to contain more than 190 bioactive compounds in the seeds, pulp, fruit, and juice.[5]

These compounds include fat-soluble vitamins (A, K, E), 22 fatty acids, 42 lipids, organic acids, amino acids, carbohydrates, Vitamins C, B_1, B_2, B_6, B_{12}, folic acid, tocopherols and flavanoids, phenols, terpenes, and tannins. It also contains twenty mineral elements especially berry contains Al, As, Ca, Cd, Cr, Cu, Fe, K, Mg, Mn, Na, Ni, Pb, Rb, and Zn. Many of the substances that are found in Amleech/sea buckthorn are known to have beneficial effects on health. It is a rich source of omege 3, 6, 7, and 9. It is the only complete plant source that offers every fatty acid and includes a beneficial amount Omega 7 (palmitoelic acid).[6,7] Important phytoconstituents found in plant parts are mentioned in Table 1.

Fruit

The ripe fruit of sea buckthorn is a medicinal food. Results of chromatographic analyses have indicated that the ripe fruit of sea buckthorn contains malic acid, oxalic acid, and another unidentified acid. These organic acids have remitted the toxicity of some medicines such as barbitals and antibiotics, preventing teratogenesis, damages from X-rays and side effects of oxygen therapy.

There are also significant contents of carotenoids (including ßcarotene, ß4, 4biketone-ß-carotene,-carotene, zeaxanthin, lycopene, and polyring-lycopene), progestin, flavoxanthin, cryptoxanthin, violaxanthin, neoxanthin, and Vitamin C, Vitamin K, Vitamin E, (including a, Vitamin E) of which Vitamin C and Vitamin E are the major components of antioxidants.[8] The content of phospholipids in the ripe fruit including lecithin, cephalin, phosphatidylinositol and phosphatidyl is about 0.5%. These substances, as part of the membrane mitochondrion, participate in the electronic migration and the oxidative phosphorylation. It can promote cellular metabolism, and have an anti-fatty liver, anti-cirrhosis effect. There is 0.09-0.36% betaine in the ripe fruit, which is the methylating product of glycine and has anti-ulcer, preventative and curative effects on arteriosclerosis. There are the flavonoids [Table 2] whose main components are leukocyanidin, catechin, flavonol, and trace flavanone. From the flavonol, the isorhamnetin, quassin, and camellin can be isolated. The flavonoids and other phenols can increase the resistance of the human body, retard osmosis of the capillary wall, and prevent Vitamin C from breaking up. The physiological effects of flavonoids on the blood vessel wall

Table 1: Main constituents of Sea buckthorn seed oil, pulp oil, fruit residue oil (values are in mg/100 g)[67]

Ingredients	Seed oil	Pulp oil	Fruit residue oil
Vitamin E	207	171	300-600
Vitamin K	110-230	54-59	-
Carotenoides	30-250	300-870	1280-1860
Total acids	11	38	-
Total flavonoids	-	-	550
Total sterols	1094	721	-
Unsaturated fatty acids (%)	87	67	70
Saturated fatty acids (%)	13	33	30

Table 2: Important flavonoid compound in Sea buckthorn (chemical formula)[68]

Isorhamnetin-3-o-galactorhamnoside
Isorhamnetin-3-o-glucarhamnoside
Isorhamnetin-5-o-gluarabinoside
Isorhamnetin-3-o-glucoglucoside
Isorhamnetin-7-o-rhamnoside
Isorhamnetin-3-o-gluco-7-orhamnoside
Quercitin-7-o-rhamnoside
Kaempferol
2,4-dihydroxy-chalcones-2-oglucoside
Isorhamnetin-3-o-glucoside
Isorhamnetin-3-o-glucoside
Isorhamnetin-3-o-galactoside
Isorhamnetin
Quercitin
Quercitin-3-o-rutin
Quercitin-3-o-glucoside
Quercitin 3-methyl ether
Myricetin

require the participation of Vitamin C; their activity can stabilize Vitamin C in the body, and they can reduce Vitamin C oxidation. These substances also have affects on controlling arteriosclerosis, lowering the cholesterol level, turning hyperthyroidism into euthyroidism and eliminating inflammation.[9] Phenols are effective against oxidation, tumorigenesis, and radiation, and can sustain the activity of many biologically active substances, for example, the anti-tumorigenesis effect of leukocyanidin, the enhancement of X-ray effectiveness in cancer treatment by catechin, and the remarkable antitumor genesis and anti-radiation effect of quassin. Chlorogenic acid and other phenol compounds can facilitate the biosynthesis of gastric acid, stimulate gastric juice secretion, combine with taurine and take part in diuretic action and in strengthening the function of capillaries and at the hypophysis level, regulate thyroid function.

Oil

The sea buckthorn oil [Table 1] extracted from its ripe fruit contains more than 60% of palmitic and palmitoleic acid. The most active biological fractions among them are the unsponified parts, which can co-exist with Vitamin E, carotenoids, beeswax, and the sterols with ß-sitosterol. The ß-sitosterol is considered one of the active compounds used to prevent and cure arteriosclerosis.[10]

Stem

The peel of stem and fruit contains 5-hydroxytryptamine (5-HT), a rare occurrence in the plant kingdom. The 5-HT act as a neurotransmitter and regulate human emotion, blood pressure (BP), body temperature, and hormone level. It can also have important anti-radiation, anti-infection and anti-cancer functions, and can promote coagulation by transforming fibrinogen into fibrin.

Leaves

The leaves contain coumarin, which can strengthen the function of the capillaries, has styptic and anti-coagulation functions, anti-spasmus, anti-vitiligo, anti-turmorigenesis, antinumbness, anti-pyretic effects and can regulate disorders of the gall bladder. Leaves also contain trierpene, whose representative is the ursolic acid which has an effect similar to that of adrenocortical hormone. It can control the actions of sodium (Na^+) and chlorine (Cl^-) and it can cure bronzed skin (hypocorticoidism), heal wounds, ulcer, and inflammation. The leaves contain ß-amyrinoley-lalcohol acid. It can dilate the cardiac and cerebral vessels, facilitate blood circulation and slightly lower the BP.[11]

To sum up, sea buckthorn contains so many biologically active substances beneficial for medicinal and health products.

THERAPEUTIC USE OF SEA BUCKTHORN

Cardiac Diseases

Flavonoids from sea buckthorn acts by activation of nuclear factor (NF)-kappa by stretching cultured cardiac myocytes which improve myocardial function for the treatment of hypertension and chronic cardiac insufficiency.[12] The mechanism of action of flavonoids of sea buckthorn may include reduced stress of cardiac muscle tissue by regulation of inflammatory mediators and reduce the production of pathogenic thrombosis.[13,14] Antioxidant of sea buckthorn juice affects the risk factors such as plasma lipid, low-density lipoprotein, platelet aggregation, and plasma soluble cell adhesion protein concentration for coronary heart diseases.[15-17]

Gastroenterological Diseases

Hippophae is traditionally used in the treatment of gastric ulcers and laboratory studies confirm the efficacy of seed oil for this application. Sea buckthorn oil normalize gastric acid and reduce inflammation by controlling pro-inflammatory mediators. Hexan extract of *Hippophae* found to be active in preventing gastric injury.[18-20] Many of the preparations of sea buckthorn such as ointment, suppositories, liniment, and liquids are used for oral mucosits, rectum mucositis, duodenal ulcers, gastric ulcers.[21]

Antitumor Effect

An alcoholic extract of *Hippophae* that contains flavonoids found to protect the bone marrow from damage due to

radiation and provides fast recovery of bone marrow in cancer patients.[22] Fast recovery of hemopoietic system after chemotherapy is observed with *Hippophae*.[23] The seed oil has been found to enhance nonspecific immunity and to provide anti-tumor effect in preliminary laboratory studies.[24]

5-HT hippophan isolated from sea buckthorn bark inhibited the tumor growth.[25]

Hepatoprotective Activity

Sea buckthorn extract help to normalize liver enzymes, serum bile, acids, and immune system markers involved in liver inflammation and degeneration.[26] Laboratory studies revealed that sea buckthorn oil protects the liver from damaging effects of toxic chemicals such as CCl_4.[27] Sea buckthorn is rich source of Vitamin A, precursor β carotene and unsaturated fatty acids.[6,28,29] Sea buckthorn along with antiviral drug proves effective in treatment of hepatitis B as sea buckthorn shorten the duration of normalizing serum alanine aminotransferase.[30]

Antioxidant, Immunomodulatory Activity

Oxidative damage to cells has been implicated in the pathogenesis of a wide variety of clinical disorders and its broad range of effects in biological systems has drawn attention of many experimental studies.[31,32]

The antioxidant and immunomodulatory properties of sea buckthorn were studied *in vitro* using rat splenocytes, macrophages and C6 glioma cell line and *in vivo* using male albino rats. The alcoholic leaf extract of Seabuckthorn (SBT) (500 g/ml) inhibited chromium-induced free radical production, apoptosis and restored the antioxidant status and mitochondrial transmembrane potential to that of control cells.[33]

The extract alone stimulated interleukin 2 (IL-2) and interferon (IFN) production in the absence of Con A and also inhibited chromium-induced decline in IL-2 and IFN production, it has significant immunomodulatory activity and specifically activates the cell-mediated immune response.[34] The leaf alcoholic extract (100 mg/kg body weight [BW]) protected the animals from chromium-induced oxidative damage.[35] Besides providing protection against chromium induced oxidative injury, the leaf extract also has the capability to protect the glial cells against hypoxia-induced oxidative damage.[36] Triterpenoids had significant inhibitory effect on nitric oxide (NO) production and enhanced radical-scavenging activities.[37] The antioxidant and glucosidase inhibitory activity of the extracts, fractions, and isolated compounds from leaves is well established. The butanol fraction which contained the highest amount of phenolic compounds showed higher radical-scavenging activity and also the most powerful glucosidase inhibitory effect.[38]

In a study, different sea buckthorn extracts, were evaluated for antioxidant activity. The reducing power of the extracts increased in a dose-dependent manner and was highest in 70% methanol extract.[39] Alcoholic fruit extract of plant showed significant cytoprotection against Na^+ nitroprusside-induced oxidative stress in the lymphocytes.[40] The extracts also attenuated the nicotine-induced oxidative stress in rat liver and heart.[41] Total flavonoids content from Hippophae (TFH) provided protection against hydrogen peroxide-induced apoptosis on vascular endothelial cells by lowering the caspase-3 expression.[42]

The *in vitro* and *in vivo* antioxidant properties of seed oil were evaluated by and their observations indicate that *Hippophae* oil has significant antioxidant activity. Seed oil also showed strong inhibition of oxidative damage induced by CCl_4 on mice, increased the activities of antioxidant enzymes and decreased the lipid peroxidation in liver.[43] The leaf extract was found to have significant anti-inflammatory activity in adjuvant-induced arthritis rat model and lipopolysaccharide (LPS)-induced inflammatory response in murine macrophages.[44] In another study, isolated casuarinin from the sea buckthorn leaves was studied for the effect on the tumor necrosis factor (TNF)-induced intercellular adhesion molecule-1 (ICAM-1) expression in a human keratinocytes cell line, pretreatment with casuarinin inhibited TNF-induced protein and messenger RNA expression of ICAM-1 and subsequent monocyte adhesiveness in HaCaT cells[45] (HaCaT cells are the immortalized human keratinocytes and have been extensively used to study the epidermal homeostasis and its pathophysiology).Casuarinin significantly inhibited TNF-induced activation of NF-B, extracellular signal-regulated kinase and p38 mitogen-activated protein kinase in a dose-dependent manner. Pretreatment with casuarinin decreased TNF-induced pro-inflammatory mediators, such as IL-1, IL-6, IL-8, and MP-1 Minimal persistent inflammation. Further, in the murine macrophage cell line, sea buckthorn leaf alcoholic extract significantly inhibited the enhanced production of NO induced by lipopolysaccharide LPS in a dose-dependent manner and by its inhibitory effect on inducible NO synthase activation.[46] Recently, leaf alcoholic extract have shown up-regulated antigen presentation ability of macrophages in aged mice, which exhibited its immune boosting and anti-aging effect.[47] Sea buckthorn berries also showed an immunoprotective effect against T-2 toxin-induced immunodepression in 15-day-old chicks.[48]

Sea buckthorn has been extensively used in oriental traditional medicines for treatment of many inflammatory disorders. Hence, from these observations, the anti-inflammatory and immunomodulatory activities have been scientifically proved.

Anti-stress and Adaptogenic Activity

Sea buckthorn leaf aqueous extract has significant anti-stress and adaptogenic activity.[49] supplementation with its leaf

extract reduced the oxidative stress in liver and muscle of rats during C–H–R exposure and poststress recovery.[50] During severe stressful exposure to C–H–R and poststress recovery, the aerobic metabolism as well as hexose monophosphate pathway is suppressed. The single and five doses of sea buckthorn extract treatment restricted the decrease or better maintained tissue glycogen and enzyme activities, such as hexokinase, phosphofructokinase, citrate synthase and glucose-6-phosphate dehydrogenase, in blood, liver, and muscle, during C–H–R exposure. The studies suggested that leaf aqueous extract treatment caused a trend for shifting anaerobic metabolism to aerobic during multiple stress C–H–R exposure and poststress recovery.[51]

Anti-bacterial and Anti-viral Effects

A phytochemical Hiporamin, possessing a wide spectrum of anti-viral and antimicrobial activities. Hiporamin is a purified fraction of polyphenol fraction, containing monomeric hydrolysable gallo-ellagi-tannins (preferably strictinin, isostrictinin, casuarinin, casuarictin pedunculagin, stachyurin according to the nuclear magnetic resonance spectra). It was found to possess a very strong anti-viral activity and wide range of action against influenza and herpes viruses.[52] It also showed inhibitory effect in a HIV infection in the cell culture and antimicrobial activity. The leaf extract also has a significant anti-dengue activity when evaluated in dengue virus Type 2 infected blood.[53] it also possess antibacterial activity against *Listeria monocytogenes* and *Yersinia enterocolitica*.[54] The antioxidant and antimicrobial effects of the extract implicate its potential for natural preservation. aqueous and hydroalcoholic leaf extracts showed growth inhibiting effect against *Bacillus* cereus, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterococcus faecalis*.[55]

Safety and Toxicity Studies

The fruit extract of SBT has a significant protective role against arsenic-induced oxidative injury.[56] In another study, protective effects of seed oil against injury induced by sulfur dioxide inhalation are evaluated. Administration of sea buckthorn extracts significantly protected from the lethality of sulfur mustard.[57,58] Toxicity studies in animals were carried out using based formulations and extracts. All the biochemical parameters related to fuel metabolism, liver function and renal function and hematological parameters remained within normal limits. In sub-acute toxicity studies of ten and twenty times of maximal effective dose, administration for 14 days, the BW gain and biochemical parameters related to toxicity namely serum bilirubin, creatinine, were unaltered and comparable to controls.[49] No adverse effects of leaf aqueous extracts were observed at a dose of 100 mg/kg BW/day in rats administered for 90 days.[59]

In acute and sub-acute oral toxicity studies, no adverse effects were observed in any of the groups administered with seed oil.[60] Some of phyto actives along with their therapeutics are explained in Table 3.

NEUTRACEUTICAL POTENTIAL OF SEA BUCKTHORN

Sea buckthorn berries, oils and leaves could be considered functional foods due to medicinal and nutritional properties. Due to their functional properties, and unique taste and flavor, *Hippophae* berries can be processed to make juice, candies, jellies, jam, alcoholic or nonalcoholic beverages, or as flavoring of dairy products. The seed and pulp oils of *Hippophae* are used as a source of ingredients in food supplements, such as gelatin, vegetable based capsules, and oral liquids.[61] Leaves are used to produce leaf extracts, tea, tea powder or cosmetics.[62]

Table 3: Some of the bioactives in Sea buckthorn

Phytoconstituents	Medicinal properties
Phytosterols[69]	Improves microcirculation in the skin, anti-ulcer, anti-atherogenic, anti-cancer, regulate inflammatory process
Polyunsaturated fatty acid[70]	Immunomodulatory, neuroprotective, anti-tumor
Organic acids[70]	Lower the risk of heart attack and stroke, anti-ulcer, wound healing, anti-arthritic
Tocopherols[71]	Acts as antioxidant, minimizes lipid oxidation, helps to relieve pain
Vitamin C[71]	Acts as antioxidant and sustain cell membrane integrity Accelerates collagen synthesis
Carotenoids[72]	Acts as antioxidant and helps in collagen synthesis and epithelialization
Vitamin K[73]	Prevents bleeding; promotes wound healing; anti-ulcer effect
Vitamin B complex[73]	Stimulate cell repair and nerve regeneration
Zinc[74]	Strengthen the blood circulation, anti-tumor, aids in cell proliferation, acts as a cofactor for enzymes, and enhances utilization of Vitamin A
Coumarins and triterpenes[75]	Control of appetite, sleep, memory and learning
Polyphenolic compounds[55]	Antioxidant, cytoprotective, cardioprotective, wound healing

At the present there is limited research on feeding *Hippophae* fruits in animal nutrition. Nevertheless, it has been shown that *Hippophae* fruits, seed and leaves are suitable for animal feeding.[63] Sea buckthorn is suitable for poultry also.[64]

COSMECEUTICAL POTENTIAL OF SEA BUCKTHORN

Many countries develops various products of sea buckthorn which has therapeutic and cosmetic values, for example, liquids, powders, plasters, films, pastes, pills, liniment, suppositories, and aerosols. *Hippophae* oil has ultraviolet blocking activity hence used in sun block cream. Beside this plant is used in skin grafting, cosmetology, and treatment of corneal wound.[21] Used in commercially available cosmetic products, like shampoo.[65] Sea buckthorn berry oil is similar to natural skin sebum lipids, and provide important healing and anti-aging benefits to skin. Sea buckthorn oil is anti-inflammatory, anti-microbial, analgesic, and regenerative. Palmitoleic acid, a fatty acid which is the content of sea buckthorn oil is main component of skin. It nourishes the skin and useful in treating skin diseases like atopic dermatitis. This oil mainly diminishes inflammation, disinfecting bacteria, relieving pain, remove blood stasis, increase blood circulation, and improve human immunity and promoting regeneration of tissues. Research on 350 patients treated with sea buckthorn cream revealed the positive therapeutic effect on senile skin wrinkles, melanosis, xanthopsis, and freckles.[66]

CONCLUSION

Ayurvedic scholars of ancient time discovered therapeutic properties of many medicinal plants and suggested several formulations of these plants in different dosages form of Ayurveda. The dosage form of a particular plant was decided by Acharyas on the basis of stages of disease and diseased. After a deep rationale thought, we proposed that for Amleech/sea buckthorn a formation of Ayurvedic *Sneha Kalpana* will be best to have its maximum potency as the rejuvenating medicine of Ayurveda. We invite the attention of all researchers of biomedical field to have a look on therapeutically potent plant and make it available for more common as per principles of Ayurvedic pharmaceutics which ensure quality, safety, and efficacy of plant products.

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