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Important Therapeutic Uses of Sea Buckthorn (*Hippophae*): A Review

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Abstract: Sea buckthorn is a deciduous species, widely distributed all over the world, including Pakistan. It contains different kinds of nutrients and bioactive substances such as vitamins, carotenoids, flavonoids, polyunsaturated fatty acids, free amino acids and elemental components etc. These components vary substantially among populations, origins or subspecies, however their presence is more important for the health of individual. The clinical trials and scientific studies during the 20th century confirm medicinal and nutritional value of sea buckthorn. The present study describe some areas of research that have been important points, for example in cancer therapy, cardiovascular diseases, treatment of gastrointestinal ulcers, skin disorder and as a liver protective agent. A lot of research work is still need to clarify the mechanism of curing these conditions in molecular and cellular levels.

Key words: *Hippophae*, medicinal importance, flavonoids, fatty acid, antioxidants

INTRODUCTION

Hippophae (Sea buckthorn) is a deciduous spiny species widely distributed throughout the temperate zone of Asia, including Pakistan, Europe and all over the subtropical zones of especially at high altitude. This plant has been cultivated by some ancient plant-breeder[1]. The ancient Greeks used it in a diet for racehorses; hence it gets the botanical name *Hippophae* which means shiny horse. The clinical trials and scientific studies conducted during the 20th century in several countries confirm medicinal and nutritional value of sea buckthorn. The references to medicinal use of sea buckthorn were found in the ancient Greek texts attributed to Theophrastus and Dioskorid and in classic Tibetan medicinal texts, including "the RGyud Bzi" (The Four Books of Pharmacopoeia) dated to the times of Tang Dynasty (618-907 AD). Herbal remedies made of sea buckthorn are most frequently used for the treatment of diseases of skin and digestive system[2]. Traditional use of sea buckthorn oil to promote the recuperation of skin injuries and support the healing of skin diseases, well agrees with the data of modern clinical studies. Sea buckthorn oil is widely used to promote the recovery of various skin conditions, including eczema, burns, bad healing wounds, skin damaging effects of sun, therapeutic radiation treatment and cosmetic laser surgery. The preparations from the berries are also utilized to prevent gum bleeding, to help recuperate mucous membranes of the stomach and other organs[3,4]. The health problems (cancer, digestive ulcers, skin diseases, cardiovascular symptoms etc) are growing fast in the whole world especially in the developing countries and their therapy by synthetic medicine is very costly or side affected. The use of phytochemical or ingredients from *Hippophae* or other medicinal plants is a safe way for combating these conditions. The present study review over the available literature on some of the important therapeutic uses of *Hippophae*, so as to obtain a clear concept over the medicinal importance of *Hippophae* for the future research.

Chemistry and phytochemistry: The wide chemical and phytochemical composition of sea buckthorn has recently reviewed by Zeb[4] and Beverage[5] and was found to varies with the origin, climate and method of extraction[6]. Indian Summer juice gave an average pH of 3.13 and an average titratable acidity of 1.97% calculated as malic acid[3,7]. In general *H. rhamnoides* contains vitamin C[8-10], mineral elements[9-12], monosaccharides sugars[4,10,13], organic acids[5,10,12], free amino acids[11,12], large amount of carotenoids and vitamin E[14-16], volatile compounds[10,17] (Table 1) and different flavonoids (Table 2), quercetin, myricetin and kaempferol[18], fatty acids[19], triacylglrcerol, glycerophospholipids[20], phytosterols[21], zeaxanthin esters[22], alpha-tocopherol[23] and phenolic compounds[24]. The oil content of the whole fresh berries, including seeds, varied from 2 to 11% and of the seeds from 4 to 17%. On an average, only 10-20% of the oil is in the seeds, the proportion of which never exceeded that of the pulp oil[10,17,20]. A variety of other important nutrients are also present in the sea buckhorn products, which are beneficial for human health. Further research is needed to explore

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Table 1: Main constituents of sea buckthorn oils from seed, fruit pulp (juice) and fruit residue after removing juice[4]

	Concentration (mg/100 g)		
Ingredient	Seed oil	Pulp oil	Fruit residue oil
Vitamin E	207	171	300-600
Vitamin K	110-230	54-59	-
Carotenoids	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 compounds in Sea buckthorn[28]

Chemical formula
Isorhamnetin-3-O- galactorhamnoside
Isorhamnetin-3-O-glucoside
Isorhamnetin-3-O-glucorhamnoside
Isorhamnetin-5-O-glucoarabinoside
Isorhamnetin-3-Oglucoglucoside
Isorhamnetin-7-O-rhamnoside
Isorhamnetin
Isorhamnetin-3-O-gluco-7-Orhamnoside
Myricetin
Quercitin-3-O-rutin
2,4-dihydroxy-chalcones-2-Oglucoside
Quercitin
Isorhamnetin-3-O- galactoside
Isorhamnetin-3-O-gluco-(166) Glucoside
Quercitin-3-O-glucoside
Quercitin-7-O-rhamnoside
Quercitin-3-methyl ether
Kaempferol

Table 3: Some important medicinal properties of *Hippophae*

Medicinal property	Subject	SBT product	Reference
Anticancer	Rat	Oil	29
Antimutagenic	Mouse	Oil	31
Immunological antitumor	Rat	Oil	34
Non-specific immunity	Rat	Oil	30, 65
Protection against radiation	Rat	Oil	32, 58
Cardiovascular diseases	Rat, Human	Oil	25-29
Antioxidant in coronary heart disease	Human	Juice	44, 46
Reducing fat and antioxidant	Human	Oil	38
Arterial thrombosis	Mouse	Oil	40
Atherosclerosis	Human	Oil	45
Gastric ulcer	Rat	Oil	47-52
Treatment of liver fibrosis	Human	Oil	53, 54
Protective effect of liver injury	Human	Oil	55
Treatment of chronic hepatitis	Human	Oil	56
Skin burning	Human	Oil	57
Atopic dermatitis	Human	Oil	59-62
Other skin diseases	Rat, Human	Oil	64, 65

the chemical changes occur in these nutrients during various types of handling and usage.

Medicinal uses of *Hippophae*: Medicinal properties of sea buckthorn has been ascribed to its important phytochemical, like flavonoids, carotenoids, fatty acids, etc. It has been found that beta-carotene[25,26], flavonoids, fatty acids etc, are important medicinal phytochemicals. Sea buckthorn has been shown to have a potent antioxidant activity[27,28]. Both the flavonoids and the oils from sea buckthorn have several potential applications[1,4,28]. There are several areas of research that have been important points for their use: as an aid to patients undergoing cancer therapy; a long-term therapy for reduction of cardiovascular risk factors; treatment of gastrointestinal ulcers; internal and topical therapy for a variety of skin disorder and as a liver protective agent and a remedy for liver cirrhosis (Table 3).

Cancer therapy: The literature describing the role of *Hippophae* in prevention and control of cancer is limited, however certain analysis of the known experimental research information on anticancer by *Hippophae* available at present[29,30]. The inhibition of *Hippophae* oil on the cancer cells was not as effective as the positive medicine, for example, the cancer inhibition rate of phosphamide was twice as much as *Hippophae*, The possible mechanisms of antimutagenic action of the sea buckthorn oil, have been discussed[31]. Most of the work done in this area has been with laboratory animals. Reports on the potential of a *Hippophae* extract (an alcohol extract, which would mainly contain the flavonoids) to protect the bone marrow from damage due to radiation; this study also showed that the extract might help faster recovery of bone marrow cells[32]. In China, a study was done to demonstrate faster recovery of the hemopoietic system after high dose chemotherapy in mice fed the sea buckthorn oil[33]. The seed oil has been found to enhance non-specific immunity and to provide anti-tumor effects in preliminary laboratory studies[34,35]. Studies on the effects of vitamins from other diet sources on cancer therapy in amphibian and other animals has established[36], however well-designed clinical studies with sea buckthorn are needed to validate its effects and exact mechanism on cancer patients in humans.

Cardiovascular therapy: *Hippophae* is used as anti-cardiovascular medicine[37,38]. In a double blind clinical trial, 128 patients with ischemic heart disease were given total flavonoids of sea buckthorn at 10 mg each time, three times daily, for 6 weeks. The patients had a decrease in cholesterol level and improved cardiac function; also they had fewer anginas than those receiving the control drug. No harmful effect of sea buckthorn flavonoids was noted in renal functions or hepatic functions. The mechanism of action may include reduced stress of cardiac muscle tissue by regulation of inflammatory mediators[39]. In another laboratory animal study, the flavonoids of sea buckthorn were shown to reduce the production of pathogenic thromboses in mouse[40]. Some simple formulas based on sea buckthorn have been developed recently which is intended for use in treatment of coronary heart disease and sequelae of heart attack and stroke, through

improving blood circulation and restoring cardiac function. An Immuno-histochemical method was used to assess the inhibitory effect of total flavonoids of *Hippophae* on the activation of NF-kappa-B by stretching cultured cardiac myocytes. The results supported that the blockade of activation of NF-kappa-B might be a potential access to the improvement in myocardial function with the use of total flavonoids of *Hippophae* for treatment of hypertension and chronic cardiac insufficiency[41].

Recent studies show that the major factors leading to the atherosclerosis are the lipid oxidation damage and anti-oxidation treatment could significantly inhibits the atherosclerosis formation and the incidence of coronary heart disease have a close relation with HDL cholesterol[42]. This was observed in 230 abnormal blood fat cases and 190 cases with all information, among them 102 cases were selected as treatment group (dried *Hippophae* emulsion) and 92 cases as the control group. All patient were treated for 12 consecutive weeks and the blood fat were checked at 4, 8, 12 weeks after treatment. The results showed that 4 weeks after treatment, the dried *Hippophae* emulsion could decrease the total cholesterol in the blood, the arteriosclerosis index [(TC-HDL)/HDL] and increase the high-density lipoprotein (HDL). After treatment, TC decreased average 19.2%, (TC-HDL)/HDL decrease average 28.2% and HDL increase average 18.1%, eight weeks after treatment, the triglycerides content decreased significantly, average decreasing 20.1%. The net is that dried *Hippophae* emulsion could adjust the abnormal blood fat and have anti-oxidation function[43].

There is increasing evidence to support the hypothesis that free radical-mediated oxidative processes contribute to atherogenesis[44,45]. More recently the ability of antioxidant nutrients to affect cell response and gene expression has been reported *in vitro*, providing a novel mechanistic perspective for the biological activity of antioxidants. Sea buckthorn (*Hippophae rhamnoides* L.) is a rich source of antioxidants both aqueous and lipophilic, as well as polyunsaturated fatty acids. It was found that antioxidants rich sea buckthorn juice affects the risk factors (plasma lipids, LDL oxidation, platelet aggregation and plasma soluble cell adhesion protein concentration) for coronary heart disease in humans[44,46].

Gastrointestinal ulcers: Gastric ulcers are growing fast in human being, especially in the developing countries like Pakistan, due to unfavorable and non-assessed diet, ignorance, carelessness. *Hippophae* is traditionally used in the treatment of gastric ulcers and laboratory studies confirm the efficacy of the seed oil for this application[47,48]. Its functions may be to normalize output of gastric acid and reduce inflammation by controlling pro-inflammatory mediators. The antiulcerogenic effect of a hexane extract from *Hippophae rhamnoides* was tested on indomethacin-and stress-induced ulcer models. As a result hexane extract from *Hippophae* was found to be active in preventing gastric injury[49-52].

Liver diseases: A clinical trial demonstrated that sea buckthorn extracts helped normalize liver enzymes, serum bile acids and immune system markers involved in liver inflammation and degeneration[53]. In addition, sea buckthorn oil protects the liver from damaging effects of toxic chemicals, as revealed in laboratory studies[54]. Recent studies have shown that sea buckthorn contains lots of vitamin A precursors including $-carotene[14] and unsaturated fatty acids[4,12]. Zhao *et al*.[55] reported that sea buckthorn could protect the liver from damage induced by CCl_4. A combination of an antiviral drug and sea buckthorn in treating patients with chronic hepatitis-B could shorten the duration for the normalization of serum ALT[56].

Skin diseases: An ingredient of the oil, palmitoleic acid, is a component of skin. It is considered a valuable topical agent in treating burns and healing wounds. This fatty acid can also nourish the skin when taken orally if adequate quantities of sea buckthorn or its oil are consumed; this is a useful method for treating systemic skin diseases, such as atopic dermatitis. Sea buckthorn oil is already widely used alone or in various preparations topically applied for burns, scalds, ulcerations and infections. It is an ingredient in sun block. *Hippophae* oil has UV-blocking activity as well as emollient properties-and it is an aid in promoting regeneration of tissues[57,58].

In another study forty-nine patients received a daily dose of 5 g sea buckthorn seed oil, pulp oil or paraffin oil for four months. The fatty acid compositions of plasma phospholipids and neutral lipids of the patients were analyzed before, after one month and at the end of the treatment. Skin biopsies were taken from sixteen patients and the fatty acid compositions of skin glycerophospholipids were analyzed before and after the treatment. It was found that supplementation of the seed oil significantly increased the proportion of "-linolenic acid in plasma neutral lipids and total n-3 fatty acids in plasma phospholipids and neutral lipids. Increases in the proportion of "-linolenic acid, linoleic acid and eicosapentaenoic acid in plasma phospholipids by the seed oil treatment were close to significant. The pulp oil treatment increased the proportion of palmitoleic acid and lowered the proportion of pentadecanoic acid in both plasma phospholipids and neutral lipids. Seed oil treatment slightly increased the level of docosapentaenoic

acid (22:5 n-3) and decreased the level of palmitic acid (16:0) in skin glycerophospholipids. These results indicate a higher efficiency of incorporation and metabolism of "-linolenic acid than linoleic acid in form of sea buckthorn oil and a relatively stable fatty acid composition of skin glycerophospholipids[59-62].

In the next study, thirty-two cases were treated, among them 19 cases were males, 13 cases were females; the oldest was 78 years old, the youngest was 1 year and two months old. Twenty-eight cases of scalds were caused by various reasons and four cases were caused by gas burning; among them 12 cases were degree I burning, 18 cases were degree II light burning, 2 cases were degree II serious burning. In 14 cases, the burnt area were 5% and 10 cases were under 10%, 1 case was 15% and 4 case were above 20%. In 28 cases, they were treated with *Hippophae* seed oil directly after burning and in 4 cases, they were treated in other hospital first and then transferred and treated with *Hippophae* seed oil. It was established that *Hippophae* seed oil had functions like improve the human immunity, remove blood stasis and promote blood circulation, anti-inflammation and pain relieve, increase the tissue regeneration etc. and had magic effects in treating burns and scalds. This medicine is easy to use and reliable in the effectiveness without any side effect and could widely use in clinical treatment of burns and scalds[55,63,64].

Other properties: Sea buckthorn products are used for curing varieties of other diseases. Sea buckthorn oil act as strong antioxidant and used as for balancing the immune system[65,66]. Sea buckthorn flavonoid could significantly increase the anti-hyperlipemia condition[67]. The medicinal applications of sea buckthorn products are increasing regularly, with recent worldwide health applications and increasing popularity in the developing countries, however further detail summery can be found from[68-70] and Table 3.

Conclusion and future studies: The amount of experimental data evidencing important properties of many ingredients and bioactive substances from *Hippophae* is vast and continues to increase rapidly. It is possible to conclude that sea buckthorn is a promising plant containing many dietary as well as medicinal compounds with a potential beneficial role in human health. Thus, with the aim to establish whether these compounds from *Hippophae* are really capable to influence positively the incidence and progression of many chronic diseases in molecular and cellular level, a great deal of work in these areas is still necessary. This includes: (I) further studies on bioactive compounds from sea buckthorn and its metabolism in human beings, (II) analysis of factors affecting bioavailability, including interaction with other dietary compounds, (III) dietary variations within and between population and (IV) molecular or cellular mechanism involve during therapy.

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