

## A review of therapeutic and non-therapeutic properties of sea buckthorn

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### ABSTRACT

**Background and aims:** Sea buckthorn (*Hippophae rhamnoides* L.) is a deciduous plant and has highly variable type and size, from small shrubs to medium-sized trees, traditionally growing in Tibet and currently all over the world especially in Europe and Asia. This study aimed to overview some of therapeutic and non-therapeutic properties of SBT and its potential benefits and side effects in order to open up a clear understanding for further detailed study in this regard.

**Methods:** This review article was carried out by searching studies in Web of Science, Google Scholar, PubMed and ScienceDirect. The search terms were “Sea buckthorn”, “Sea buckthorn” and “hippophae”, “therapeutic”, “non-therapeutic”.

**Results:** Various studies have shown that sea buckthorn plays a role in the treatment of cardiovascular disease, liver fibrosis, skin diseases (eczema, acne.), arthritis, vaginal atrophy, dry eye. This herb has anti-inflammatory, anti-constipation, antioxidant, anti-aging, anti-cancer, anti-stress, antidepressant and antiproliferative effects. Besides, it enjoys some non-therapeutic properties including nutritive values (a good source of vitamin C, E, omega 3, 6, 7), oral and dental health care value and cosmetic value (in the industry of cosmetics: cream, shampoo, jellies, and etc.).

**Conclusion:** sea buckthorn is widely used for therapeutic and non-therapeutic purposes that trigger its significant value. Various combinations and numerous medicinal properties of its berries, fruits, extract, pulp, seed oil, leaves demand further and more studies about the other useful and unknown properties of this multifunctional plant.

**Keywords:** Medicinal plants, Sea buckthorn, *Hippophae*, Therapeutic effects, Non-therapeutic effects.

### INTRODUCTION

Sea buckthorn (SBT) or *Hippophae rhamnoides* L. from Elaeagnaceae family is of deciduous plants grown mostly in moderate climate and at high altitudes in many parts of the world including Europe and Asia.<sup>1, 2</sup> It is a herb that its leaves, flowers, and fruits are used to make medicine.<sup>3</sup> Different parts and forms of this plant was used for their different medicinal

properties such as its pulp, seed oil, its leaves, its berries, extract and juice.<sup>4</sup> This plant belongs to the Elaeagnaceae family.<sup>5</sup> This article presented therapeutic and non-therapeutic properties of this valuable medicinal plant. SBT involves in the anti-cancer therapy.<sup>6-8</sup> It was shown that it contributes in the treatment of vaginal atrophy.<sup>9</sup> Experimental studies report its

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usefulness in the treatment of dry eye.<sup>10</sup> SBT has a preventive activity for cardiovascular disease.<sup>11, 12</sup> Besides, it has an antioxidant, antibacterial and antiviral activities.<sup>12-19</sup> Its oil leads to anti-inflammation.<sup>20, 21</sup> SBT fruit and leaves have the property of wound healing,<sup>22-25</sup> gastric ulceration and erosions.<sup>26,27</sup> Besides, it has anti-depressant,<sup>28</sup> and anti-stress application.<sup>29</sup> In animal studies, it was shown that it is good for cardiovascular disease<sup>30,31</sup> and cerebral vascular injury.<sup>32</sup> It has also radio protective activity.<sup>33,34</sup> Its oil and leaf are anti-liver disease effect.<sup>35-37</sup> Its seed can be useful for the treatment of skin disease.<sup>35,36</sup> It has pharmacological effects<sup>37</sup> and anti-infection,<sup>38</sup> and it has inhibitory effects against platelet aggregation.<sup>38</sup> Given to non-therapeutic effects of this plant, it is noted that it has nutritive value,<sup>39-44</sup> hygienic oral and dental property<sup>45</sup> and ideal effect upon skin health.<sup>46-50</sup> This article presented the therapeutic and non-therapeutic properties of this valuable medicinal plant to contribute to further solutions in science.

There are wide varieties of phytochemical compounds for SBT that they change according to the origin, climate and technique of extraction. Generally, this plant consists of vitamins, mineral elements, monosaccharide, sugars, organic acids, free amino acids, large amount of carotenoids and vitamin E,<sup>14-16</sup> volatile compounds,<sup>17</sup> (Table 1) and different flavonoids (myricetin, quercetin, kaempferol, luteolin, and apigenin),<sup>18</sup> fatty acids,<sup>19</sup> triacylglycerol, glycerophospholipids, phytosterols, zeaxanthin esters, alpha-tocopherol and phenolic compounds. Compounds in its seed oil identified as campesterol, clerosterol, lanosterol, sitosterol, -amyrin, sitostanol, avenasterol, stigmasta-en-ol, -amyrin, stigmastadienol, lupeol, gramisterol, sitosterol, cycloartenol, cycloeucalenol, avenasterol, 28-methylbutusifoliol, 24-methylenecycloartanol,

erythrodiol, citrostadienol, uvaol, and oleanol aldehyde.<sup>28</sup>

**Table 1:** Main constituents of sea buckthorn oils after removal of juice

Ingredients	Seed oil	Pulp oil	Fruit residue oil
Vitamin E	+	+	+
Vitamin K	+	+	-
Carotenoids	+	+	+
Total acids	+	+	-
Total flavonoid	-	-	+
Total sterols	+	+	-
Unsaturated fatty acids	+	+	+
Saturated fatty acids	+	+	+

**Table 2:** Important compounds of sea buckthorn

Chemical constituents of sea buckthorn
Isorhamnetin-3-0-galactorhamnoside
Isorhamnetin-3-0-glucoside
Isorhamnetin-3-0-glucorhamnoside
Isorhamnetin-3-0-glucoarabinoside
Isorhamnetin-3-0-glucoglucoside
Isorhamnetin-7-0-rhamnoside
Isorhamnetin-3-0-gluco-7-orhamnoside
Myricetin
Quercetin-3-0-rutin
2,4-dihydroxy-chalcones-2-ogluconide
Quercetin
Isorhamnetin-3-0-galactoside
Isorhamnetin-3-0-gluco-(1-6) glucoside
Quercetin-3-0- glucoside
Quercetin-7-0- orhamnoside
Quercetin-3-0-methylether kaempferol

In a study, SBT has been scientifically analyzed and many of its traditional uses have been distinguished by means of some biochemical and pharmacological studies. Several pharmacological properties have been described for it including cytoprotective, anti-stress, Immuno-modulatory, hepatoprotective, radioprotective, anti-atherogenesis, anti-tumor, anti-microbial and tissue regeneration.<sup>1</sup>

A study by Carl Grey et al. has shown that the fruit of this plant has many bioactive compounds that inhibit the proliferation of cancer cells.<sup>6</sup> In their study, it is demonstrated that although the dose of the extract is in high importance in its antiproliferative effects, the existence of ursolic acid is of great importance in the treatment of cancer. In a laboratory study, the treatment of the liver cancer was investigated and its effect was confirmed.<sup>7</sup> In another study, the anti-carcinogenic potential of lipids from this plant was reviewed and it is found that its juice and oil was confirmed to have great amount of nutrients and bioactive substances such as vitamins, carotenoids, flavonoid, polyunsaturated fatty acids, free amino acids and elemental components that again emphasized on its anti-carcinogenic properties.<sup>8</sup>

In a randomized, double-blind, placebo-controlled study, it is demonstrated that the intake of SBT seed oil has a good effect in the treatment of vaginal atrophy in postmenopausal women. It is shown that it can improve in the integrity of vaginal epithelium and it can be an alternative for women who are not able to use estrogen.<sup>9</sup>

In a double-blind study of 100 women and men, it is illustrated that intake of the combination of SBT oil has a good effect on the symptoms of dry eye. It is demonstrated that it functions through decrease in inflammation and oxidative damage. It is shown that SBT oil reduces an

increase in tear film osmolarity during the cold season and positively affects the dry eye symptoms (redness and burning).<sup>10</sup>

Animal and human studies suggest that flavonoid in SBT may forage free radicals, reduce blood density, and boost function of heart. Flavanol aglycones of SBT trigger to prevent from cardiovascular disease.<sup>11</sup> In another study, it was mentioned that carotenoids and flavonoid derived from SBT could serve as a natural treatment for reducing the risk of cardiovascular disease (CVD).<sup>12</sup>

Fractions of SBT fruits were investigated for antioxidant activity and it was illustrated that the phenolic compounds play an important role in its antioxidant property.<sup>12</sup> Antioxidant and hepatoprotective activities of phenolic rich fraction (PRF) of SBT leaves were discussed. It was shown that PRF has potent antioxidant activity, prevent oxidative damage to major biomolecules and afford significant protection against CCL<sub>4</sub> induced oxidative damage in the liver.<sup>13</sup> Residue of SBT without seed is considered as an important resources of antioxidant for nutritional, pharmaceutical, cosmetic or food industries.<sup>14,15</sup> It was suggested that the alcoholic extracts of leaves and fruits of SBT have shown cytoprotective properties that prove its antioxidant activity.<sup>15</sup> the antioxidative properties of 10 genotypes of SBT were shown.<sup>16</sup> The cytoprotective and antioxidant properties of SBT against tertiary-butyl hydroperoxide was reported. It is revealed that retreating cells with SBT extracts prevent from cytotoxicity and keep antioxidants levels similar to that of control cells.<sup>17</sup> Besides, the berries of wild and cultivated SBT are rich in vitamin C and the combination of vitamin C and tocopherols and tocotrienols makes the fruit a very good source of antioxidant.<sup>18</sup> Administration of water soluble

polysaccharides from *Hippophae rhamnoides* leaf tea (WPHT) at 50 mg/kg d and 100 mg/kg d could increase the activities of plasma and liver superoxide dismutase and decrease the contents of plasma and liver homogenate malondialdehyde, with a significant difference from the model group ( $P < 0.05$ ). Thus, WPHT has a potential antioxidant property in vivo.<sup>19</sup>

The MeOH extract was confirmed to have maximum antibacterial activity.<sup>16</sup> SBT leaf extract has remarkable anti-inflammatory activity and it is able to treat inflammatory diseases due to its scavenging activity and/or its inhibitory effects on nitric oxide synthase activation.<sup>20</sup> A study shows that leaves of SBT have a preventive effect of immunosuppression and inflammation through modifying inflammatory pathway and restoring adaptive immune response.<sup>21</sup> In an animal study, Immuno-modulatory activity of SBT leaf extract was evaluated. These observations suggest that the SBT leaf extract has a significant anti-inflammatory activity and has the potential capability for the treatment of arthritis.<sup>51</sup>

Efficacy of topical administration of flavones of SBT on dermal wound healing in rats was investigated and it is suggested that SBT flavones improve the wound healing activity as indicated by promoting wound contraction, decreased time taken for epithelialization. It causes significant increase in reduced glutathione, vitamin C and catalase activities in wound granulation tissue and significant decrease in lipid peroxide levels, so it is demonstrated that flavones in SBT promotes wound healing activity.<sup>22</sup> In a study, patients receiving the dressing showed more obvious education reduction, pain relief and faster epithelial cell growth and wound healing, comparing the group treated with Vaseline gauze. It is found that SBT oil has definite effects on

the healing of burn wounds.<sup>23</sup> The SBT seed oil improve the wound healing process by increasing wound contraction, hydroxyproline, hexosamine, DNA and total protein contents comparing silver sulfadiazine (SS) ointment-treated group. Histopathological findings further confirmed the healing property of SBT seed oil.<sup>24</sup> SBT seed oil has also confirmed to possess remarkable effect in wound healing in the case of full-thickness burns and split-thickness harvested wounds.<sup>25</sup>

The CO<sub>2</sub> derived from SBT seed and pulp oils can both prevent and cure gastric ulcers.<sup>26</sup> In another study, prophylactic efficacies of SBT oil in comparison to other standard drugs for gastric ulceration and erosions were investigated.<sup>27</sup>

Anti-depressive effects of SBT fruits extract was examined and it is shown that it possess significant antidepressant-like effects in animal models of depression and may be served as a natural psychotherapeutic material against depression.<sup>28</sup>

The results in a study by Saggu et al. indicated that SBT leaf aqueous extract possesses potent adaptogenic activity with no toxicity even after sub-acute (30 days) maximal effective dose administration. Nicotine cause oxidative stress in rat brain to test the effects of SBT extract. It is demonstrated that vitamin E might have easily diffused to rat brain as a lipid soluble antioxidant, however, the plant extract, would not have sufficiently diffused to the brain to exert its antioxidant effect.<sup>52</sup> In another study, the results suggested that SBT extract can be used as a dietary supplement, especially by people who smoke in order to prevent nicotine-induced oxidative stress. Different sorts of vegetables, fruits and grains in daily diet protect the body against most of oxidative stress induced diseases, however, it is not necessarily mean that antioxidants cause not to suffer from diseases, especially when

they are used in artificial forms. It is worth-mentioning that most of the studies have been carried out in a short –time period and conducting on patients with existing diseases.<sup>53</sup> As far as SBT is a rich source of antioxidants both aqueous and lipophilic, as well as polyunsaturated fatty acids, it is a potential for treatment of coronary heart disease.<sup>30, 31</sup>

The studies showed that induced Hypoxia elevates free radical levels and as a result, malondialdehyde were significantly lowered after SBT pretreatment. The observations suggest that SBT seed oil possesses significant hypoxia protection activity and curtailed hypoxia induced enhanced vascular leakage in the brain.<sup>32</sup>

Radioprotective activity of this plant was investigated in a study and it is concluded that free radical scavenging, acceleration of stem cell proliferation and immunostimulation are the radioprotective attributes require further investigations.<sup>33</sup> It is also suggested that SBT possessed recovering effect and a short-term protective effect on the toxicity of oxidized cholesterol in rats. Taking all these data together, SBT may play an important role in diminishing the toxic effects of oxidized cholesterol in rats.<sup>34</sup>

It is demonstrated the positive effects of SBT on serum lipids, transaminase, and liver/spleen ratio and liver stiffness in patients with NAFLD, which may be further developed as a promising therapy for the treatment of nonalcoholic fatty liver disease.<sup>35</sup> Besides, it was found that SBT may be a hopeful drug for prevention and treatment of liver fibrosis.<sup>36</sup> Protective effects of SBT seed oil on carbon tetrachloride (CCl<sub>4</sub>)-induced hepatic damage in male ICR mice were examined<sup>37</sup> and it has shown that the treatment of SBT seed oil was also found to significantly increase the activities of superoxide

dismutase. Overall, the hepatoprotective effect of SBT seed oil at all tested doses was found to be comparable to that of Silymarin and have been supported by the evaluation of the liver histopathology in mice. In another study, it was found that pretreatment of leaf extract at a concentration of 100 and 200 mg kg<sup>-1</sup> body weight protected significantly the animals from CCl<sub>4</sub>-induced liver injury.<sup>38</sup>

In a placebo-controlled, double-blind study, the effect of seed and pulp oils of SBT on atopic dermatitis was investigated and it was shown that seed oil increased -linolenic acid and linolenic, -linolenic, and eicosapentaenoic acids in plasma. Thus, treatment by pulp oil increased the proportion of positive acids and decreased negative acids and it is really helpful in the treatment of atopic dermatitis.<sup>39</sup>

Flavones of SBT fruit can modulate the production and level of several signaling molecules related to function of immune system and inflammation in vitro, including several cytokines. The observations of these studies suggested that stimulation of IL-6 and TNF-alpha secretion had antimicrobial<sup>40</sup> and anti-virus infection property.<sup>41</sup>

Biological properties of the plant, its pharmacological effects and use in traditional medicine have been reviewed in a study by Guliyev.<sup>42</sup> Medicinal plants have been used for many years for different treatments.<sup>43</sup> However, therapy by medicinal plants and discovery should be focused more than before.<sup>44</sup>

A remarkable decrease in the maximum level of platelet aggregation was observed and also the positive effects of SBT on blood clotting were reported. However, further studies on the dose-response effects are required to examine the practical use of SBT supplements.<sup>45</sup>

SBT leaf extract can be used for food additives and for making useful natural

compounds.<sup>46</sup> Its leaves are used to make tea. Its juice can be used to make a nutritious beverage. Two main sources of valuable product are derived from the berries, juice from the fleshy tissue and seed as a single seed from each berry. The remained pulp after juice removal is used to extract “SBT yellow”, that is a food coloring material. Fruit juice contains great amount of sugar, organic acids, amino acids, essential fatty acids, phytosterol, flavonoid, vitamins and mineral elements. Phytosterol quantity in SBT is more than soybean oil. SBT oil is rich in oleic acid and omega-3 and omega-6 fatty acids.<sup>47</sup> Besides, it was shown that the nutritive value of SBT fruits and seeds is highly related to its origin.<sup>48</sup> Supplementation of diets with SBT fruits has a positive effect on everyday human food style.<sup>49</sup> The main vitamin in SBT fruit is vitamin C that contains 400 mg/100 g approximately.<sup>50</sup> It is suggested that SBT is useful for oral health and diseases. Although there are modern ways to treat oral and teeth diseases, many people still accustomed to utilize medicinal plants for dental disorders.<sup>54</sup>

Cosmetic purposes of SBT were reviewed that range from oil, juice, and food additives to candies, jellies, cosmetics, and shampoos.<sup>55</sup> The effects of topically applied water-in-oil emulsion (w/o) of SBT were examined. It was concluded that the topical antioxidant emulsion of *H. rhamnoides* significantly improved skin biomechanical parameters. The data obtained suggested that *H. rhamnoides* could be an alternative pharmacological tool for treating age-related loss of skin elasticity.<sup>56</sup> Its seed is found to be a source of seed oil, which is much unsaturated, because of its light absorption and emollient properties, as an ingredient in cosmetics, phytopharmaceuticals, or UV skin protectant preparations and the oil absorbs

ultraviolet light and promotes healthy skin.<sup>57</sup> The anti-sebum secretion effects of a topical skin-care cream emulsion (w/o) of SBT were investigated. The results showed formulation has good stability and anti-sebum secretion effects over 4 and 8 weeks, respectively.<sup>58</sup>

Skin health was shown that the consumption of SBT fruit had protective effect due to the high content of collagen that has potential as a protective and therapeutic drug candidate against skin aging that functions by regulating the moisture content, MMP expression levels and superoxide dismutase activity.<sup>59</sup> No scientifically confirmed side effects were reported.

## CONCLUSION

SBT is widely used for therapeutic and non-therapeutic purposes that trigger its significant value. Various combinations and numerous medicinal properties of its berries, fruits, extract, pulp, seed oil, leaves demand further and more studies about the other useful and unknown properties of this multipurpose plant.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

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