## Sea buckthorn (*Hippophae rhamnoides* L.) as a potential source of nutraceutics and its therapeutic possibilities - a review

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#### Abstract

Sea buckthorn (*Hippophae rhamnoides* L.) is in the focus of interest mainly for its positive effects on health of both human and animal organisms. The whole plant of sea buckthorn and especially its berries are a source of a large number of different bioactive compounds. The greatest attention has been drawn to its high content of vitamins, minerals, natural antioxidants, n-3 and n-6 fatty acids, and proteins. Sea buckthorn is valued for its antioxidant, cardioprotective, antiatherogenic, antidiabetic, hepatoprotective, anti-carcinogenic, immunomodulatory, antiviral, antibacterial, anti-inflammatory and vasorelaxant effects. Due to these and other positive effects, the plant is included in both human and animal nutrition, in the latter case to increase the biological value of animal products. This review summarises the botanical characteristics of sea buckthorn, lists the bio-active substances contained in individual parts of the plant, their effects in the prevention of a number of different diseases and their possible utilisation in human and animal nutrition.

Bioactive substances, therapeutic effects, functional food, nutrients

For humankind, vegetation is a source of basic nutrients, raw materials for industrial use as well as many bioactive substances. Plants with exceptional properties and a wide range of application include, beside others, the sea buckthorn (*Hippophae rhamnoides* L.). Its Latin name is derived from the words "hippo", meaning horse, and "phaos", which is gloss or flare (Michel et al. 2012). Thus the compound may be translated as a shining horse (Li and Beveridge 2003), or more freely as a glossy coat (Valíček and Havelka 2008).

## **Botanical characteristics**

Sea buckthorn (Hippophae rhamnoides L.) is included in the Elaeagnaceae family (Řezníček and Plšek 2008). It is a family of eudicots of the Rosales order. The family includes around 100 species in three genera mostly found in the moderate geographical latitudes of the Northern hemisphere. Seaberries are classified in the plant taxonomy into six species and 12 subspecies (Bal et al. 2011). Sea buckthorn is native to Central Asia (Řezníček and Plšek 2008) and North-Western Europe. At present, it is also grown in Canada and the USA (Yang and Kallio 2001). Seaberries grown in the Czech Republic mainly include sea buckthorn and Russian silverberry.

Seaberries are shrubs or small trees mostly no more than 3 to 4 m high (Michel et al. 2012). They are trees with alternate, often silver-gray, simple leaves and blossom without crown. Seaberry branches are often covered with numerous rigid thorns (Řezníček and Plšek 2008). Seaberries are dioecious and anemophilous. Male plants have flower buds × 2–3 bigger than female plants. Flowers do not produce nectar and therefore, pollination by insects is not possible; the only possibility is wind pollination (Li and Beveridge 2003).

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Phone: +420 541 562 673 E-mail: karaskovak@vfu.cz http://actavet.vfu.cz/ Sea buckthorn has narrow lanceolate alternate leaves (Řezníček and Plšek 2008; Michel et al. 2012). The top of the leaf is dark green. The bottom of the leaf is green with silver-gray tone. The silver-gray colouring is caused by the presence of trichomes that are only found on the bottom of leaves (Li and Beveridge 2003).

Seaberries naturally grow in higher altitudes at about 2000 to 3600 metres above sea level. They are highly resistant to temperature extremes, well tolerating temperatures in the range of -45 to +43 °C. They typically grow on riverbanks and on the sunny side of steep slopes (Dhyani et al. 2007). Seaberries well tolerate drought, high levels of soil salinity, and acid soils (Khan et al. 2010). Their root system is well organised. The roots bear bulbils of dove egg size containing bacteria binding nitrogen in soil (Valíček and Havelka 2008), as well as other essential components (Li and Beveridge 2003). The roots are strong and that is why seaberries are often used to protect the soil against erosion or in recultivation processes (Kumar and Sagar 2007).

Berries as well as other parts of sea buckthorn represent a rich source of biologically active compounds. For this reason the plant has been in the centre of attention virtually world-wide. The chemical and nutritional composition of sea buckhorn berries as well as the content of bioactive compounds depend on many factors. The most important factors include different subspecies, origin, climate conditions, time of harvesting, and methods of processing (Bal et al. 2011).

#### Berries and seed of sea buckthorn

The numerous fruits are dark yellow, orange or red when ripe, oval shaped and 6–9 mm long. The fruit consists of a seed wrapped in soft, juicy and fleshy tissue – the pulp. The seed is 2.8 to 4.2 mm long, dark brown, ellipse-shaped and glossy on the surface (Michel et al. 2012).

The chemical composition of berries depends on the variety, climate conditions, fruit size, ripeness and the processing method (Leskinen et al. 2010). Sea buckthorn and especially its berries provide a rich source of many minerals, including, but not limited to Ca, P, Fe, and K. Sea buckthorn has a large content of vitamin C, several-fold compared to other fruits (Christaki 2012). The vitamin C content in sea buckthorn ranges between 360 and 2500 mg/100 g (Ba1 et al. 2011). The plant is a valuable source of the vitamin B group, mainly B1 (thiamine) and B2 (riboflavin) (Christaki 2012). Other vitamins rich in sea buckthorn include, for example, vitamin E (Michel et al. 2012), vitamins A and K (Bekker and Glushenkova 2001; Fatima et al. 2012). The berries provide a good source of carotenoids, mainly  $\beta$ -caroten, lycopene, lutein, and zeaxantin (Michel et al. 2012). The saccharide content is also high. The most common carbohydrates are glucose, fructose, and xylose. All parts of the plant contain many different proteins, mainly albumins and globulins (Li and Beveridge 2003). Sea buckthorn is a source of organic acids, mainly malic acid, guinic acid, oxalic acid, citric acid, and tartaric acid. Sea buckthorn is a good source of flavonoids too, mainly quercetin, kaempferol, myricetin, and isorhamnetin, and an important source of tocopherols (Fatima et al. 2012).

#### The pulp

The pulp of sea buckthorn contains mainly  $\alpha$ -,  $\beta$ - and  $\gamma$ -carotens, glycopene, and zeaxantin. Vitamin B group is mainly represented by B1 (thiamine), B2 (riboflavin), B6 (pyridoxine), vitamin PP (nicotinamine, niacin, vitamin B3), and folic acid necessary for nucleic acid synthesis. The vitamin C content depends on the variety and natural conditions. Plants growing in Central Asia contain 150–200 mg/100 g, and Alpine plants contain around 800 mg/100 g. The berries do not contain ascorbinase for ascorbic acidolysis, thus vitamin C is well preserved in dry fruit and in products (Valíček and Havelka 2008). The peel of the stem and fruits contains 5-hydroxytryptamine, which is found rarely in plants (K um ar

et al. 2011). This substance (5-hydroxytryptamine) is used for treatment of post-shock depression.

#### Sea buckthorn leaves

The leaves contain a remarkable quantity of nutrients and bioactive substances, mainly phenolic. They contain on average 3.8% of saccharides, 0.2% of protopectin, 1% of organic acids, 170 mg/100 g of catechin, polyphenols, carotenoid lycopene, bioflavonoids, and coumarins. The leaves also contain a significant concentration of vitamin C (up to 370 mg/100 g) and tannins (8%) (Valíček and Havelka 2008).

#### Sea buckthorn oils

Two oil types may be extracted from the sea buckthorn, either from the pulp or from the seeds. The pulp contains 4–13% of oil, and dry pulp contains about 20–25% of oil (Zeb 2006; Valíček and Havelka 2008). Sea buckthorn is a good source of mainly unsaturated fatty acids (Christaki 2012). The pulp oil contains 180–240 mg of carotenoids in 100 g, of them 40–100 mg in form of caroten, 110–330 mg of vitamin E and unsaturated fatty acids, mainly linoleic and linolenic acids. Specific types of acids include ursolic acid and oleanolic acid, with anti-inflammatory, wound healing, toning and blood pressure reducing effects (Valíček and Havelka 2008). The pulp oil contains the highest concentration of palmitoleic acid (16:1, n-7), up to 43% (Fatima et al. 2012).

Sea buckthorn seeds contain 8–20% oil (Kumar et al. 2011). The oil content is mainly affected by the harvest time, size, and colour of berries (Yang and Kallio 2002). Seed oil mainly includes unsaturated fatty acids – 90% (linoleic 47 mg, linolenic 18 mg, oleic 16 mg) and saturated palmitic acid (Valíček and Havelka 2008). Seed oil is the only oil with the linoleic acid to linolenic acid ratio of 1:1 (Yang and Kallio 2002; Cenkowski et al. 2006; Kumar et al. 2011).

Oil pressed from sea buckthorn seeds is mainly rich in essential fatty acids such as linoleic acid (18:2, n-6), making up to 42% of the total fatty acid, and  $\alpha$ -linolenic acid (18:3, n-3), up to nearly 39% of the total fatty acid content. Sea buckthorn is also a good source of oleic acid (18:1) (Christaki 2012). In addition to the above, the oil also contains other n-3 and n-6 as well as n-7 and n-9 fatty acids, which are present in lower quantities (Solcan et al. 2013).

#### Selected major effects on health of organisms

The sea buckthorn berries have been used for centuries by inhabitants of Europe, Central and South-Eastern Asia in traditional medicine for treatment of different diseases as well as for disease prevention (Li and Beveridge 2003; Michel et al. 2012). In China sea berries have been used in traditional medicine for centuries (Li and Beveridge 2003).

At present, sea buckthorn has become popular especially for its positive effects on the human organism. Sea buckthorn is valued for its antioxidant, cardioprotective, antiatherogenic, antidiabetic, hepatoprotective, anti-carcinogenic, immunomodulating, antiviral, antibacterial, anti-inflammatory and vasodilating effects (Table 1). It also reduces occurrence of stomach ulcers, supports wound healing, accelerates treatment of skin disorders and reduces pain (Suryakumar and Gupta 2011; Christaki 2012; Michel et al. 2012). Other important properties of sea buckthorn include its cytoprotective effects. Sea buckthorn acts positively against asthma and pulmonary diseases (Upadhyay et al. 2010), against increased sebum secretion and affects platelet aggregation (Khan et al. 2010). Its antistress and adaptogenic activities have been confirmed (Michel et al. 2012).

Sea buckthorn also positively affects metabolic diseases (Bal et al. 2011), with the ability to slow down ageing and protect against radiation-induced damage, accelerate the healing of burns and frostbites, and reduce hair loss. Sea buckthorn also positively affects

Antioxidant activity     Tocopherols   Minimisiation of lipid oxidisation     Pain alleviation   Antioxidant activity     Carotenoids   Contribution to collagen synthesis     Contribution to collagen synthesis   Contribution to epithelium growth     Haemorrhage prevention   Haemorrhage prevention     Vitamin K   Wound healing support     Positive effect against ulceration   Antioxidant activity     Vitamin C   Antioxidant activity     Vitamin B complex   Cellular renewal stimulation     Nerve tissue regeneration   Improvement of micro-circulation in the skin     Anti-carcinogenic effect   Prevention of ulceration     Phytosterols   Antioxidant activity     Cytoprotective effect   Prevention of ulceration     Regulation of inflammatory processes   Antioxidant activity     Polyphenolic components   Cytoprotective effect     Wound healing support   Immunomodulating effect     Polyunsaturated fatty acids (PUFA)   Neuroprotective effect     Reduction of risk of myocardial infarction and stroke   Wound healing support     Granic acids   Anti-carcinogenic effect     Reduction of risk of arthritis   Coumarins and triterpens   Suppor	Component	Therapeutic effect
Tocopherols   Minimisation of lipid oxidisation     Pain alleviation   Pain alleviation     Carotenoids   Contribution to collagen synthesis     Contribution to collagen synthesis   Contribution to collagen synthesis     Contribution to collagen synthesis   Contribution to collagen synthesis     Vitamin K   Wound healing support     Positive effect against ulceration   Positive effect against ulceration     Vitamin C   Antioxidant activity     Vitamin B complex   Cellular renewal stimulation     Nerve tissue regeneration   Improvement of micro-circulation in the skin     Anti-carcinogenic effect   Prevention of ulceration     Phytosterols   Antioxidant activity     Polyphenolic components   Cytoprotective effect     Cardio protective effect   Wound healing support     Polyunsaturated fatty acids (PUFA)   Neuroprotective effect     Reduction of risk of myocardial infarction and stroke   Wound healing support     Organic acids   Support for appetite, sleep, memory and learning     Blood circulation increase   Zinc     Enzyme cofactor function   Increased utilisation of vitamin A	Tocopherols	Antioxidant activity
Pain alleviation       Antioxidant activity       Carotenoids     Contribution to collagen synthesis       Contribution to cpithelium growth       Haemorrhage prevention       Vitamin K     Wound healing support       Positive effect against ulceration       Vitamin C     Antioxidant activity       Vitamin B complex     Cellular renewal stimulation       Nerve tissue regeneration     Improvement of micro-circulation in the skin       Anti-carcinogenic effect     Prevention of ulceration       Phytosterols     Antioxidant activity       Polyphenolic components     Cytoprotective effect       Polyphenolic components     Cytoprotective effect       Polyunsaturated fatty acids (PUFA)     Neuroprotective effect       Reduction of risk of myocardial infarction and stroke     Wound healing support       Organic acids     Support for appetite, sleep, memory and learning       Blood circulation increase     Zinculation or insk of arthritis		Minimisation of lipid oxidisation
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Phytosterols   Antiatherogenic effect     Prevention of ulceration   Regulation of inflammatory processes     Antioxidant activity   Cytoprotective effect     Polyphenolic components   Cardio protective effect     Wound healing support   Immunomodulating effect     Polyunsaturated fatty acids (PUFA)   Neuroprotective effect     Organic acids   Reduction of risk of myocardial infarction and stroke     Wound healing support   Anti-carcinogenic effect     Corganic acids   Wound healing support     Zinc   Support for appetite, sleep, memory and learning     Blood circulation increase   Zinc     Zinc   Enzyme cofactor function		Anti-carcinogenic effect
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Organic acids   Reduction of risk of myocardial infarction and stroke     Organic acids   Wound healing support     Anti-carcinogenic effect   Reduction of risk of arthritis     Coumarins and triterpens   Support for appetite, sleep, memory and learning     Blood circulation increase   Blood circulation increase     Zinc   Enzyme cofactor function     Increased utilisation of vitamin A		Anti-carcinogenic effect
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Anti-carcinogenic effect     Reduction of risk of arthritis     Coumarins and triterpens   Support for appetite, sleep, memory and learning     Blood circulation increase     Zinc   Enzyme cofactor function     Increased utilisation of vitamin A		Wound healing support
Reduction of risk of arthritis     Coumarins and triterpens   Support for appetite, sleep, memory and learning     Blood circulation increase   Blood circulation increase     Zinc   Enzyme cofactor function     Increased utilisation of vitamin A		Anti-carcinogenic effect
Coumarins and triterpens Support for appetite, sleep, memory and learning   Blood circulation increase   Zinc   Enzyme cofactor function   Increased utilisation of vitamin A		Reduction of risk of arthritis
Blood circulation increase       Zinc     Enzyme cofactor function       Increased utilisation of vitamin A	Coumarins and triterpens	Support for appetite, sleep, memory and learning
Zinc Enzyme cofactor function Increased utilisation of vitamin A	Zinc	Blood circulation increase
Increased utilisation of vitamin A		Enzyme cofactor function
		Increased utilisation of vitamin A

Table 1. Major components of sea buckthorn and their principal therapeutic effects (Michel et al. 2012)

mental functions, in particular reducing memory loss in elderly people. Its positive effects have been utilised for acceleration of wound healing, especially in people after ear, nose and throat operations where seaberry oil has been part of the treatment. The oil has also been used for protection against solar radiation (Li and Beveridge 2003). Sea berry products may be used in various drug forms from liquids via powder, patches, pastes, films, ointments and aerosols to suppositories (Li and Beveridge 2003).

# Antioxidant effects and immunomodulating properties

Sea buckthorn contains many natural antioxidants in all of its parts. Its leaves, stems, tubers, roots as well as blossom contain a high content of ascorbic acid (vitamin C), and also carotenoids, polyphenols, flavonoids, tocopherols, alkaloids, chlorophyll derivates, amino acids and amines (Bal et al. 2011; Christaki 2012). Other natural antioxidants

present in sea buckthorn include sterols, tannins, vitamins, and minerals (Kumar et al. 2013).

Natural antioxidants inhibit or delay the oxidation of other molecules by inhibiting the initiation or propagation of oxidizing chain reactions (Bal et al. 2011). Free radicals, a product of cellular metabolism, can cause a number of diseases by exogenous chemical or stress effects (cancer, diabetes mellitus, cardiovascular and nerve system disorders) (Upadhyay et al. 2010; Kumar et al. 2013). Kim et al. (2011) evaluated the antioxidant and alpha-glycosidase inhibitory effects from the extract, fractions, and isolated compounds of sea buckthorn leaves The butanol fraction, which contained the highest amount of phenolic compounds, showed higher radical-scavenging activity and also the most powerful alpha-glycosidase inhibitory effect.

Flavonoids of sea buckthorn also provide antioxidant and anticarcinogenic effects. They protect cells against oxidative damage, subsequent genetic mutations, and cancer (Gao et al. 2000; Zeb 2006; Suryakumar and Gupta 2011). A potential chemopreventive effect of sea buckthorn berries in mice was observed by Suryakumar and Gupta (2011). In high-fat diet-induced obese mice sea buckthorn leaf tea proved their antioxidant effect and effect of visceral obesity reduction (Lee et al. 2011).

#### **Cardioprotective effects**

Flavonoids contained in sea buckthorn as well as the unsaturated fatty acids contained in sea berry oil are able to improve the function of the cardiovascular system (Zeb 2006; Suryakumar and Gupta 2011) and to prevent heart diseases (Christaki 2012). Flavonoids show a favourable effect on the strength of heart muscle contraction and the cardiac rhythm (Li and Beveridge 2003; Kumar et al. 2013). The effect of sea buckthorn on cardiovascular functions and coronary microvessels in spontaneously hypertensive stroke-prone rats was studied by Koyama et al. (2009). Experimental rats were fed a feed enriched with sea buckthorn powder at the amount of 0.7 g/kg of feed for 60 days. The effects included a significant decrease of the mean arterial blood pressure, heart rate, total plasma cholesterol, triglycerides and glycated haemoglobin in the rats. The arteriolar capillary portions of microvessels expressing alkaline phosphatase decreased, but there was a trend for an increase in the total capillary density. It was concluded that sea buckthorn fruits improved the metabolic processes and reduced hypertensive stress on the ventricular microvessels.

Another study focusing on the antihypertensive effect of total flavonoids from sea buckthorn seeds and mechanism of their action in long-term sucrose-fed rats by evaluating its ability to regulate insulin and angiotensin II concentrations was done by Pang et al. (2008). Feeding a high sucrose diet (HS: 77% kJ from carbohydrates, 16% from proteins, 6% from lipids) for 6 weeks resulted in a significant increase of the systolic blood pressure by 25.6%, plasmatic insulin concentrations by 114.24%, triglyceride contents by 82.14%, and activated angiotensin II contents in the heart and the kidneys. Administration of a diet enriched with sea buckthorn flavonoids significantly reduced the increased hypertension, hyperinsulinaemia and dyslipidaemia. In addition, this diet (mainly at 150 mg/kg/day) increased the blood concentration of circulating angiotensin II. The results showed that the antihypertensive effect of the sea buckthorn enriched diet at least in part improved insulin sensitivity and blocked the angiotensin II signal path. The study proved that a diet with total flavonoids extracted from sea buckthorn seed residues may be used for treatment of hyperinsulinaemia in the non-diabetic state with cardiovascular diseases (Pang et al. 2008).

The most important flavonoids are quercetin and isorhamnetin (Suryakumar and Gupta 2011). The abovementioned effects are probably achieved by reduced blood glucose concentrations, absorption of free radicals (Suomela et al. 2006), reduced susceptibility of

low-density lipoproteins to oxidation (Eccleston et al. 2002) and anti-hypertensive effect (Wang et al. 2011).

## Antiatherogenic effects

Sea buckthorn food supplementation has been proved to be able to reduce total cholesterol, triglycerides and LDL-cholesterol, and increase HDL-cholesterol levels in comparison to sea buckthorn-free diet (Yang and Kallio 2002; Suryakumar and Gupta 2011). Seed oil is the most effective in this area (Christaki 2012). Basu et al. (2007) found that seed oil of seaberries showed significant antiatherogenic and cardioprotective effects in rabbits.

## Antibacterial and antiviral effects

Antibiotic treatment of bacterial diseases is in many cases less effective and leaves residues in animal products (e.g., bee products, etc.). It is therefore necessary to find an alternative, especially using natural ingredients (Kuzyšinová et al. 2014). The phenolic compounds of sea buckthorn represent the main group of phytochemicals which exhibit antibacterial and also antiviral effects. These compounds both suppress gram-negative bacteria (Khan et al. 2010) and reduce gram-positive bacteria (Kumar and Sagar 2007). A recent study involves a new phytochemical substance called hipporamin. It is a phenolic compound from a nature source (Michel et al. 2012). Hipporamin positively suppresses a wide spectrum of bacterial as well as viral diseases (Suryakumar and Gupta 2011). Antimicrobial activities have also been reported for sea buckthorn berries (Puupponen-Pimia et al. 2001), seeds (Chauhan et al. 2007) and leaves (Upadhyay et al. 2010).

Michel et al. (2012) report that the active agents contained in sea buckthorn manly inhibit *Bacillus cereus, Pseudomonas aeruginosa, Staphylococcus aureus, Yersinia enterocolitica* and *Enterococus faecalis* bacteria. These effects are mainly shown by extracts from sea buckthorn leaves. Oil obtained by pressing is a very effective inhibitor of bacterial growth, especially of *Escherichia coli* (Christaki 2012). Also Kaushal and Sharma (2011) confirmed that sea buckthorn seed oil showed good antimicrobial properties (growth inhibition zone diam. 4.0 mm) against *Escherichia coli*.

Sea buckthorn has also shown unique biological properties against viral diseases, antiviral activity against the influenza virus and herpes virus. The suppressing effect on the influenza virus is provided by inhibition of viral neuraminidase present in the virus. Sea buckthorn also positively inhibits HIV infections in cellular cultures (Shipulina et al. 2005; Michel et al. 2012). Jain et al. (2008) suggest that the sea buckthorn leaf extract has a significant anti-Dengue activity and has a potential for the treatment of Dengue fever.

## Anti-inflammatory effects

In traditional medicine sea buckthorn has been used for treatment of stomach ulcers for its effect on anti-inflammatory mediators (Xing 2002). Oil and leaves support regeneration of skin wounds and support treatment of skin disorders (Upadhyay et al. 2009). Palmitoleic acid contained in sea buckthorn is a component of skin fat and thus represents a valuable component of topical treatment of cellular tissue and wounds (Bal et al. 2011; Kumar et al. 2011). Sea buckthorn leaves are able to protect irradiated mice against inflammation (Tiwari and Bala 2011). Li and Beveridge (2003) report that Russian cosmonauts used sea buckthorn berries in their diet and oils in creams for protection against solar radiation.

#### Antidiabetic effects

Other positives of sea buckthorn include mitigation of the symptoms of diabetes mellitus. This effect is caused by achieving reduced blood glucose concentrations by dietary supplementation with sea buckthorn (Christaki 2012).

In diabetes, sea buckthorn not only affected the lowering of blood sugar including fasting blood glucose and two h postprandial blood glucose, but also the treating of complications. Sea buckthorn has been shown to be effective in cell cultures, animal studies, and clinical practice. Although sea buckthorn has been shown to have positive effects in relieving symptoms such as fatigue, dry mouth, and dry eye in non-diabetic diseases, it is still unclear whether it has a therapeutic effect on the symptoms of diabetes. Studies have to be conducted to test and verify the effect of sea buckthorn on symptoms in diabetic patients. On the whole, sea buckthorn is a candidate for complementary therapy of diabetes (Wang et al. 2011).

## Anticarcinogenic activity

Favourable effects of sea buckthorn also include the anticarcinogenic activity (Michel et al. 2012). Anticarcinogenic effects have mainly been reported for substances extracted from sea buckthorn berries (Christaki 2012). One of the main components contributing to this effect is quercetin that induces apoptosis in cancer cells. The best effect has been reported in relation to the treatment of patients with colon cancer, leukaemia, and prostatic carcinoma (Patel et al. 2012). Other studies suggest that sea buckthorn oil alleviates haematological damage caused by chemotherapy, such as part of treatment of leukaemia (Yang and Kallio 2002). Therapeutic effects are ascribed to substances such as catechin, gallocatechin, and epigallocatechin (Khan et al. 2010). Sea buckthorn has also been reported to favourably affect the inhibition of certain factors causing stomach cancer in humans (Li and Beveridge 2003).

Yasukawa et al. (2009) isolated and identified three phenolic compounds, (+)-catechin, (+)-gallocatechin, and (-)-epigallocatechin and a tritepenoid, ursolic acid from the active fraction of the 70% ethanol extract of sea buckthorn which exhibited a remarkable anti-tumour activity.

Induction of the apoptotic activity and apoptotic morphological changes of the nucleus including chromatin condensation were also observed in the HL-60 cells treated with some of the flavonols isolated from sea buckthorn such as quercetin, kaempherol, and myricetin (Hibasami et al. 2005).

## Hepatoprotective effects

The liver is often affected by a multitude of environmental pollutants and drugs, all of which place a burden on this vital organ which can damage and weaken the liver and eventually lead to hepatitis or cirrhosis (Zimmerman and Ishak 1994). Sea buckthorn has shown numerous positive effects on liver protection and treatment of liver diseases (Bark at et al. 2010). Hepatotoxins such as ethanol, carbon tetrachloride, and acetaminophen cause various degrees of hepatocyte damage, degeneration, and subsequent death of hepatic cells (Ramesbabu et al. 2011; Michel et al. 2012; Solcan et al. 2013). Substances contained in sea buckthorn such as unsaturated fatty acids,  $\alpha$ -tocopherol or  $\beta$ -caroten protect hepatic cells against damage by hepatotoxins (Ramesbabu et al. 2011). Flavonoids are mainly responsible for protection against liver fattening (Li and Beveridge 2003). Sea buckthorn might also contribute to prevention of liver fibrosis in the future (Suryakumar and Gupta 2011).

A trial focused on the effect of sea buckthorn on the toxicity of oxidized cholesterol proved that sea buckthorn administered in the diet reduced plasma concentrations of alanine transaminase (ALT), aspartate transaminase (AST), and alkalic phosphatase (ALP), which indicates that the plant may have a protective effect against hepatotoxicity induced by oxidized cholesterol (Yeh et al. 2012).

The hepatoprotective activity of sea buckthorn leaves and seed oil was evaluated using carbon tetrachloride  $(CCl_4)$  induced hepatic damage in animals (Geetha et al. 2008; Hsu

et al. 2009). The results showed that sea buckthorn leaf alcoholic extract as well as seed oil ameliorated  $\text{CCl}_4$ -induced liver injury as evidenced by both histological and biochemical findings.

In a study by Maheshwari et al. (2011), some of the phenolic constituents of sea buckthorn leaves, such as gallic acid, myricetin, quercetin, kaempferol, and isorhamnetin were identified in the phenol rich fraction by reverse-phase high-performance liquid chromatography (RP-HPLC). Oral administration of the phenol rich fraction at dose of 25–75 mg/kg body weight significantly protected from  $CCl_4$  induced elevation in aspartate aminotransferase, alanine aminotransferase,  $\gamma$ -glutamyl transpeptidase and bilirubin in serum, enhancing hepatic antioxidants. These observations suggest that the phenol rich fraction has a potent antioxidant activity and prevents against  $CCl_4$  induced oxidative damage in the liver.

## Immunomodulating effects

Sea buckthorn strengthens and accelerates the immune response of the organism (Michel et al. 2012). It accelerates regeneration of mucous membranes in the gastrointestinal tract, such as in the stomach, the large intestine, the urinary tract, and the oral cavity (Christaki 2012). The sea buckthorn components most contributing to the immunomodulating effect include flavonoids such as leucocyanidin and catechin in the first place and then also isorhamnetin, quercetin, and quassin. These substances strengthen the immune system of the organism and increase resistance to illnesses (Li and Beveridge 2003).

The immunoprotective effect of sea buckthorn fruit against immunodepression caused by T-2 toxin was tested in broiler chicks (R am as a my et al. 2010). The immunoprotective effect of sea buckthorn and glucomanane was evaluated with the help of humoral immune reaction against NCD (Newcastle disease virus), LaSota strain vaccine (haemoagglutination test), immunoglobulin concentrations, phagocyte index and DTH (delayed-type hypersensitivity) reaction against 2, 4-dinitroflurobenzene (DNFB) between days 25 and 28 of the trial. A significant decrease of non-specific immunity was observed in the group receiving T-2 toxin, shown by the phagocyte index, DTH reaction, haemagglutination inhibition (HI) titre and total serum Ig, in comparison with the healthy control group. The group fed sea buckthorn and glucomanane showed a significant increase of the HI titre and total serum Ig. These birds also showed a significant increase of the DTH reaction and non-specific immune response. Sea buckthorn itself protected against the immunosuppressive effect of T-2 toxin, but sea buckthorn in combination with glucomanane showed an additional protective effect against T-2 toxicity.

According to Lavinia et al. (2009) essential oils extracted from sea buckthorn berries improve the immune response in broilers. The skin of broiler chicks fed sea buckthorn showed a higher degree of lymph-follicular reaction (Lonare et al. 2009). Sea buckthorn oil supports tissue regeneration, with consequent positive effects on mucous membranes such as in the stomach (Erkkola and Yang 2003), the duodenum (Lavinia et al. 2009), the urogenital tract, and the oral cavity (Erkkola and Yang 2003).

## Effects suppressing the occurrence of gastric and duodenal ulcers

Hexane extract from sea buckthorn acts positively against indomethacin, stress, and ethanol which contribute to the development of gastric ulcers (Khan et al. 2010). The extract also shows positive effects in the treatment of duodenal ulcers (Li and Beveridge 2003).

Huff et al. (2012) studied the efficacy of a commercial product containing the berries and pulp of sea buckthorn in the therapy and prevention of gastric ulcers in horses. The mean score of non-glandular gastric ulcers significantly (P < 0.05) increased in all the horses after an intermittent feed deprivation. The number of glandular ulcers and their severity were significantly lower in horses fed sea buckthorn enriched feed compared to the control group. Sea buckthorn was not effective in the therapy/prevention of natural equine non-glandular ulcers, however, the glandular ulcer score was significantly lower in the sea buckthorn fed group after feed deprivation. Sea buckthorn may therefore be used in the prevention of glandular ulcers in horses in case of intermittent feeding.

## **Dermatological effects**

Substances contained in sea buckthorn prevent dermatological diseases such as atopic eczema (Khan et al. 2010). Creams containing sea buckthorn extracts support treatment of skin disorders such as melanosis, chloasma, xeroderma, and recurrent dermatitis (Li and Beveridge 2003; Barkat et al. 2010).

Burnt sheep were administered sea buckthorn seed oil and in 6, 14 and 21 days after the injury, the wound blood flow and epithelization were determined. After 14 days the percentage of epithelization in the areas treated with sea buckthorn was higher than in the untreated areas. The epithelization time was significantly shorter compared to the untreated areas (Ito et al. 2014).

#### Platelet aggregation

Positive effects on platelets are mainly shown by flavonoids and fatty acids. Their main function is suppression of platelet aggregation induced by collagen, probably by inhibition of the thyrosine kinase activity (Patel et al. 2012). Another substance significantly contributing to platelet aggregation is sitosterol (Johansson et al. 2000).

Thanks to the abovementioned favourable effects on the health of organisms, in the future sea buckthorn and its products may be expected to be widely used in therapy and prevention both in humans and animals.

## Role of sea buckthorn in human and animal nutrition

Interest in utilisation of sea buckthorn products has been increasing recently in the area of human as well as animal nutrition. Thanks to the functional properties and unique taste of the berries they can be used for production of juice, bonbons, jelly, jam, alcoholic and non-alcoholic beverages or dairy product flavours (Gao et al. 2000; Bal et al. 2011). Oils from the seeds and pulp may be used as ingredients in food supplements such as jelly, plant capsules, or oral fluids (Yang and Kalilo 2002). They are also used in cosmetic products such as shampoo (Bal et al. 2011). Leaves are used for production of extracts, teas or cosmetics (Guan et al. 2005).

Stobdan et al. (2013) report that sea buckthorn is a rich source of nutrients and bioactive substances. Juice made from the berries is rich in sugar, organic acids, amino acids, essential fatty acids, phytosterol, flavonoids, vitamins, and minerals. The juice contains 24 minerals and 18 different amino acids. Total phytosterol content is  $\times$  4–20 higher than in soybean oil. Seeds represent a valuable source of oil with high level of oleic acid and the 1 : 1 ratio of n-3 and n-6 fatty acids. The oil absorbs ultraviolet light and promotes healthy skin. The leaves contain many nutrients and bioactive substances such as carotenoids, free and esterified sterols, triterpenols, and isoprenols.

Sea buckthorn has long been used in animal nutrition as an additive to feed mixtures for its favourable effects on animal health. A positive effect on the quality of farm animal products has been observed. Ancient Greeks used leaves and twigs of sea buckthorn for feeding animals, with a positive effect on the weight gain and shinning coat, especially in horses (Suryakumar and Gupta 2011).

Kaushal and Sharma (2011) report that seed cakes and sea buckthorn leaves are rich in proteins and minerals and represent a beneficial animal feed. Similarly Biswas et al. (2010) consider sea buckthorn leaves, seed and berry residues a suitable feed for farm animals and poultry, mainly in dry and cold regions. In poultry, sea buckthorn positively affected the egg production and body weight of laying hens (Wang 1997).

Although information about potential applications of sea buckthorn and its products in animal nutrition and its potential positive impact on animal product quality is available, further research studies and knowledge in this area may significantly contribute to the extension of the sea buckthorn application area.

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