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Seabuckthorn Polyphenols and Human Health: Research Highlights and Future Scopes

Gargi Dey*

School of Biotechnology, KIIT Deemed to be University, Bhubaneswar, 751 024, India

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Abstract: Nutraceutical-rich functional foods have gained popularity in recent years as means of improving human health. Nearly 200 distinct kinds of nutritional and bioactive substances, such as phytosterols, polyunsaturated fatty acids, carotenoids, sugar alcohols, superoxide dismutase, and polyphenols, are found in seabuckthorn berries. A few seabuckthorn-based functional food products have been developed and clinically tested. Additionally, the author's lab has created two fruit-based, probiotic-fortified functional beverages (apple and seabuckthorn) that effectively guard against intestinal inflammation, particularly inflammatory bowel disease as tested in animal models. The author's team has also created a unique seabuckthorn wine by co-fermenting seabuckthorn with *Saccharomyces cerevisiae* and *Issatchenkia orientalis*, which was tested for hypercholesterolaemia effects in mice. Future applications require cutting-edge technologies to develop seabuckthorn-based formulations with enhanced functional properties. Innovations such as the use of non-thermal procedures like high pressure processing can help preserve the maximum content of phytonutrients and nutraceuticals in seabuckthorn-based ready-to-serve products. Furthermore, lack of sufficient in vivo models to definitively demonstrate that seabuckthorn preparations enhance hemostasis and cardiovascular or cancer diseases is another bottleneck that needs to be addressed. Little is known about how seabuckthorn preparations—especially commercial ones—affect human hemostasis, cardiovascular diseases, and other metabolic disorders in the scientific literature. Neither the prophylactic nor therapeutic dosages of seabuckthorn preparations are known at this time, nor are there any particular guidelines for their administration. In future, more large-scale, randomized clinical trials are required, particularly with both healthy and patient subjects.

Key words: Seabuckthorn, arid zones, functional food, nutraceuticals, metabolic disorders.

***Correspondence**
Gargi Dey
drgargi.dey@gmail.com, gargi.dey@kiitbiotech.ac.in

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Berries are a natural source of bioactive polyphenols that regulate metabolic processes and contribute to multiple health benefits. Among the major classes of polyphenols—flavonoids, phenolic acids, lignans, stilbenes, and phenolic polymers—flavonoids constitute the largest and most diverse group.

This class includes several subgroups, such as anthocyanins/anthocyanidins, flavonols, isoflavones, flavones, and chalcones (Panche *et al*., 2016). It is well established that berry polyphenols have wide range of biomedical applications which is attributed to their ability to trigger genetic signalling. Numerous studies have demonstrated a correlation between the consumption of berry polyphenols and the prevention or delay of chronic degenerative diseases (Kolehmainen *et al*., 2012; Saad *et al*., 2025). Emerging evidences have confirmed that a combination of polyphenols may exhibit additive or synergistic effects on enhancing the anti-inflammatory and antioxidant efficacy status in human subjects (Espinosa-Moncada *et al*., 2018; González-Gallego *et al*., 2010). These polyphenolic compounds provide protective effects through a variety of methods, such as interactions with cell receptors and enzymes, oxidative stress reduction, and prebiotic effects (Alves-Santos *et al*., 2020). When included in a regular diet, plasma concentrations of polyphenolics found in strawberries and blueberries have been linked to enhanced cognitive and executive performance in healthy older individuals (Rutledge *et al*., 2021). In prospective cohort studies, higher dietary intakes of flavonols have been linked to a lower incidence of dementia from Alzheimer's disease (Holland *et al*., 2020). High concentrations of polyphenols, such as anthocyanins, flavonols, phenolic acids, and proanthocyanidins, are found in black elderberries (Sambucus nigra). These polyphenols have the ability to alter the concentration of ROS in the intestinal luminal content and intestinal epithelium (Olejnik *et al*., 2016). Cloudberry, alpine bearberry, and lingonberry polyphenolic extracts have shown potential in protecting diet-induced obese mice against hepatic steatosis and metabolic syndrome by preventing hyperinsulinemia, lowering liver triacylglycerol accumulation, lowering blood endotoxins, and lowering intestinal and hepatic inflammation (Anhê *et al*., 2018).

As general population turn to preventative medicine to augment their medical needs, interest in wild berries for their medicinal benefits has grown over time, despite the fact that commercial dark berries like blueberries, cranberries, and lingonberries have been the subject of much research.

Among the berries, seabuckthorn has drawn a lot of interest because of the wide variety of phytochemicals found in the berries and leaves, including polyphenols, carotenoids, and vitamin E (Guo *et al*., 2017 a,b,c).

Current status on seabuckthorn berries for biomedical applications: This plant is a native of cold, arid regions in Asia and Europe, seabuckthorn (*Hippophae rhamnoides* L.). It has also been brought to North and South America (Kaushik *et al*., 2025; Gaur, *et al*., 2025). Seabuckthorn berries contains almost 200 different types of nutritive and bioactive compounds, including phytosterols, polyunsaturated fatty acids, carotenoids, sugar alcohols, and superoxide dismutase and polyphenols (Wang *et al*., 2022). Majority of sea buckthorn's polyphenols are flavonoids and phenolic acids compounds (Ma *et al*., 2019). The primary flavonoids found in seabuckthorn are isorhamnetin, kaempferol, catechin, and epicatechin (Fan *et al*., 2012). The most prevalent aglycone among the flavonols is isorhamnetin, (which is normally present in 60% of all flavonol aglycones) present in 2 forms viz., isorhamnetin-3-O-rutinoside (30%) and isorhamnetin-3-O-glucoside-7-O-rhamnoside (10%) (Ma *et al*., 2016; Pop *et al*., 2013). Seabuckthorn berries contain phenolic acids among which caffeic acid, gallic acid, and *p*-coumaric acid, salicylic acid are the main ingredients (Bittova, *et al*., 2014). Seabuckthorn berries also contain proanthocyanadins (Ma *et al*., 2024).

China's National Health Commission has classified seabuckthorn (*Hippophae rhamnoides* L.) as a "medicine food homology" fruit. Several research groups worldwide have confirmed the significant bioactivity of seabuckthorn flavoniods, which includes cardiovascular improvement, antidiabetic, anti-obesity activity, antibacterial, cytoprotective, antitumor, immunomodulatory, antifatigue, anti-inflammatory, antioxidative and anticholinergic activities (Ja´sniewska and Diowksz, 2021; Ciesarová *et al*., 2020; Olas *et al*., 2018; Zhao *et al*., 2020; Tian *et al*., 2018; Tkacz *et al*., 2020). The most prominent flavonol in seabuckthorn, isorhamnetin, demonstrated the strongest anti-proliferative effect against the human liver cancer cell HepG2 (Guo *et al*., 2017b,c). Similarly, isorhamnetin and isorhamnetin-3-O-glucuronide show significant cytotoxic affect against human breast cancer MCF-7 cells through a ROS-dependent apoptotic pathway (Wu *et al*., 2018). Additionally, in apolipoprotein E knockout mice (apoE -/-), isorhamnetin has shown to prevent the development of atherosclerotic plaque (Luo *et al*., 2015). The biological activities of two isorhamnetin derivatives that were separated from the phenolic fraction of the seabuckthorn berries: viz., (isorhamnetin 3-O-beta-glucoside-7-O-alfa-rhamnoside) and (isorhamnetin 3-O-beta-glucoside-7-O-alfa-(3′′′-isovaleryl)-rhamnoside) were investigated in *in vitro* utilizing assays based on human blood platelets and plasma to observe its protective qualities against oxidative damage to the plasma's lipid and protein components (Skalski and colleagues, 2019). They established that isorhamnetin derivatives of seabuckthorn showed anti-coagulant, anti-platelet aggregation and antioxidant activities. In a study by Zhou *et al.* (2020) on the impact of seabuckthorn puree on cardiovascular disease risk factors in individuals with hypercholesterolemia, patients (n=56) were given 30 g of the frozen seeded fruit puree before meals three times a day. The findings imply that seabuckthorn puree (especially the phenolics) decreased blood pressure and inflammatory C-reactive protein.

There is currently a lot of interest in developing sea buckthorn-based products that could improve cardiovascular health. A few functional food products containing fractions of seabuckthorn have been formulated and tested clinically. For example, a Chinese formulation containing seabuckthorn flavonoids, hydroxypropyl derivatives, and linoleic acid was evaluated in 160 patients with coronary heart disease. Following three months of administration, the formulation demonstrated significantly improved therapeutic efficacy compared with the placebo group (Cui and Jia, 2014a). Another Chinese formulation containing isorhamnetin, quercetin, and kaempferol when administered to a group of 200 patients could reduce angina pectoris (Cui and Jia, 2014b). According to Tkacz *et al*. (2020), phenolic acids derived from seabuckthorn berries were more effective than flavonols at free radicals scavenging potential. The phenolic fraction (0.5-50 g mL^{-1}) from seabuckthorn fruits appears to have anti-adhesive qualities, according to Olas *et al* (2017). Guo and colleagues (2017a), reported that among the phenolic acids found in berries, gallic acid was found to have more potent anti-proliferative effect against the human liver cancer cell Hep G2 than protocatechuic acid and ferulic acid.

Synergistic role of polyphenols and probiotics in seabuckthorn-based functional foods: Dietary polyphenols and probiotic microorganisms represent two major classes of bioactive components known to positively influence human health. Increasing evidence suggests that interactions between probiotic strains and dietary polyphenols exert additive or synergistic effects on host physiology. The integration of polyphenol-rich substrates with probiotic bacteria therefore represents a promising strategy for the management of gastrointestinal disorders. Several studies have evaluated probiotic products based on seabuckthorn juice and demonstrated enhanced functional efficacy attributable to synergistic bioactivity (Terpou *et al*., 2017, 2019).

The authors' laboratory has developed two probiotic-fortified fruit-based functional beverages prepared from seabuckthorn and apple matrices with potential protective effects against intestinal inflammation, particularly inflammatory bowel disease (IBD) (Sireswar *et al*., 2017, 2019, 2020, 2021). The effects of two fruit matrices—malt-supplemented apple juice (APJ+M) and malt-supplemented seabuckthorn juice (SBT+M)—on the protective and in vivo anti-inflammatory activity of *Lacticaseibacillus rhamnosus* GG (LR) were investigated using a dextran sulfate sodium (DSS)-induced colitis model in zebrafish (*Danio rerio*).

Zebrafish were fed standard pellets coated with the experimental beverages twice daily for 30 days, followed by induction of experimental colitis through exposure to 1% DSS for three days. Intestinal tissues were subsequently collected for physiological, biochemical, and molecular analyses. Administration of the functional beverages significantly attenuated DSS-induced pathological alterations, including disruption of intestinal barrier integrity, oxidative stress imbalance, and elevated expression of pro-inflammatory markers.

The magnitude of protection varied among treatment groups. Probiotic-fortified seabuckthorn juice (SBT+M+LR) exhibited greater protective efficacy than probiotic-fortified apple juice (APJ+M+LR), as evidenced by reduced mucosal damage and lower histopathological scores. SBT+M+LR markedly enhanced antioxidant defence mechanisms by increasing the activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and reduced glutathione (GSH), which were compromised following DSS administration.

Furthermore, expression levels of inflammatory mediators—including NF-κB, TNF-α, IL-1β, IL-6, IL-8, CCL20, MPO, and MMP9—were significantly reduced, while anti-inflammatory cytokine IL-10 expression increased following treatment with the functional beverages. The superior protective performance of SBT+M+LR compared with APJ+M+LR indicates that seabuckthorn phenolic compounds enhance the in vivo immunomodulatory activity of *L. rhamnosus* GG. Collectively, these findings demonstrate that combining probiotics with polyphenol-rich seabuckthorn matrices exerts synergistic effects that may alleviate immune dysfunction and protect against colitis, suggesting their potential as alternative dietary interventions for IBD management.

An important corollary emerging from these studies is that seabuckthorn phenolics possess stronger anti-inflammatory activity than apple-derived phenolics. This knowledge provides a scientific basis for the development of targeted therapeutic functional foods aimed at managing inflammation-related human disorders.

Development of novel seabuckthorn wine through co-fermentation technology: In addition to probiotic beverages, the authors' laboratory has developed a novel seabuckthorn wine through co-fermentation of seabuckthorn (*Hippophae rhamnoides* L.) juice using *Saccharomyces cerevisiae* and *Issatchenkia orientalis* (Negi and Dey, 2013).

Seabuckthorn juice is characterized by low pH and high concentrations of organic acids, particularly malic and ascorbic acids, resulting in a highly sour, astringent, and bitter sensory profile (Tang *et al.*, 2001; Tiitinen *et al.*, 2005). Despite its recognized health benefits, these sensory limitations restrict its wider utilization in food applications (Laaksonen *et al.*, 2016; Ma *et al.*, 2017). To overcome these constraints, an optimized production technology incorporating efficient malolactic fermentation was developed to improve organoleptic quality while preserving bioactive compounds.

The production parameters were standardized to maximize retention of total phenolic content (TPC) alongside malic acid degradation. Co-fermentation resulted in approximately 55% reduction in malic acid content, significantly improving product palatability. The final seabuckthorn wine contained a TPC of 2.18 g gallic acid equivalents (GAE)/L and demonstrated strong antioxidant capacity, including a 2.63 mmol/L Trolox equivalent scavenging activity against DPPH radicals. Ferric-reducing antioxidant power and ABTS assays indicated antioxidant performance comparable to commercial wines such as Cabernet Shiraz and Beaujolais.

High-performance liquid chromatography analysis revealed elevated levels of rutin, myricetin, and quercetin relative to Cabernet Shiraz wine. Biological evaluation further demonstrated significant physiological benefits. In male LACA mice, oral administration of seabuckthorn wine improved redox balance, reduced oxidized glutathione levels, and attenuated phorone-induced oxidative stress. Supplementation also decreased hepatic lipid peroxidation and enhanced superoxide dismutase activity, indicating improved resistance to oxidative damage. Moreover, mice fed a high-cholesterol diet exhibited a 197% increase in the HDL-C/LDL-C ratio following seabuckthorn wine administration compared with untreated controls (Negi *et al.*, 2013).

This study provides the first scientific evidence demonstrating that seabuckthorn wine exerts protective effects against oxidative stress and diet-induced hypercholesterolemia, highlighting its potential as a functional fermented nutraceutical product.

Future scopes in seabuckthorn polyphenols research: Sea buckthorn (*Hippopheae L*) plants in India have proven useful in rehabilitation and conservation of Himalayan ecosystem after large scale mass cultivation. In near future, the challenge of mass cultivation of seabuckthorn varieties would be the utilization of this bioresource especially the large quantities of berries. Diverse phytonutrient contents in seabuckthorn berries and leaves make it therapeuticallypotent and very lucrative for pharmaceutical and food industries. Existing gaps in current processing techniques reduces the phytonutrient content of the formulations by several folds. This necessitates novel technologies which can deliver sea buckthorn-based formulations with maximum retention of functional phytonutrients. Non-thermal processing such as high-pressure processing offers an alternative to conventional thermal processing to meet these demands.

Sea buckthorn research has panned out in diverse areas ranging from optimizing agronomic conditions to genetic engineering for elite varieties to phytochemical analysis of fruits and leaves, to extraction of nutraceuticals from pulp and leaves, to development of therapeutic formulations and herbal adjuvants. However, sea buckthorn industry is still a collection of small and medium enterprises, applying conventional processing technologies of thermal processing, solvent extraction, drying.

Current consumer demand for functional nutrition have compelled global food industry to focus on not just clean-label technologies to improve energy expenditure, microbial inactivation, shelf stability, but also on maximum retention of phytonutrients. Several commercial products are available in global market. Seabuckthorn-based commercial products have specially made market presence in China, India, USA, Germany and Finland. Products can be broadly classified into lipid-fraction products like oil from peel, seeds, and pulp, and aqueous-fraction, for example, clarified juice (Puganen *et al*., 2018). Seabuckthorn pulp oil has been formulated into number of cosmaceutical and nutraceuticals products as they contain palmitoleic, oleic, linoleic and linolenic acids (Yang and Kallio, 2001). Additionally, lyophilized sea buckthorn powder is a common ingredient in meals including cheese, yogurt, chocolate, and baked goods (Nilova and Malyutenkova, 2018).

However, the absence of connections among the numerous studies on sea buckthorn's health impacts makes it difficult to investigate particular mechanism of action (Liu *et al*. 2017). Future innovations in food sector should be directed to designing novel food matrices and products which are healthier than the existing formats. In this context, sea buckthorn industry needs to head toward a "technological convergence" with the goal of establishing highly efficient processing technologies for safe, shelf-stable functional products. However, one of the greatest challenges faced by the sea buckthorn industry in India is the existing inefficiencies in sea buckthorn production pipeline. Technological innovation in seabuckthorn value chains should enhance the up-keep of safety and quality of the products and increase its availability throughout global market. Innovations, like use of non-thermal techniques like High pressure processing can not only provide an alternative pasteurization strategy but also aid in retaining maximum nutraceutical and phytonutrient properties of the seabuckthorn-based ready-to-serve products.

Another issue that needs to be addressed is that there are not enough of *in vivo* models to conclusively show that seabuckthorn preparations improve hemostasis and cardiovascular conditions, or cancer conditions. Furthermore, there is a dearth of information in the scientific literature regarding the impact of seabuckthorn preparations, particularly commercial goods, on human hemostasis, CVDs and other metabolic disorders. In addition, there are currently no specific guidelines for the use of seabuckthorn preparations, nor are the prophylactic and therapeutic dosages of these preparations known. In future more randomized clinical trials with larger groups are needed, especially with healthy volunteers and diseased subjects. In order to get reliable data supporting the effectiveness of seabuckthorn phenolics in humans, it is also crucial to investigate the role of various sea buckthorn products in the prevention and treatment of metabolic disorders.

Conclusions

Sea buckthorn juices need to be designed into therapeutic food products as they can serve as excellent natural delivery matrices for nutraceuticals. One of functional food product which definitely needs to be taken up by local seabuckthorn processors is the seabuckthorn-based probiotic products which is completely absent in Indian markets. Considering the synergistic benefits that can be delivered through one product, it definitely demands research attention and commercialization.

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Competing Interests

The authors declare no competing interests.

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About the Author

Gargi Dey is proficient researcher and teaching professor with postdoctoral experience from Germany and France in projects of molecular nutrition, microbial biotechnology, biochemistry with specialization

in food safety and functional foods. She is also one of the Founder Members of Gut Leben Inc, San Diego (GUT LEBEN | Naturally Multifunctional Beverages – "Live Well. Live Healthy" (gutlebenhealth.com). Contributed in the cutting-edge research platform of the company as Research Director from 2017 in developing nutrient based solutions for chronic disorders like diabetes, CVD, psychological and cognitive functions and inflammation. She has guided several PhD and M.Tech research students. She has also been secured financial support for research projects from DBT-BIRAC, DST, ICMR and TRIFED. She has received the National Award for Outstanding Research from the Seabuckthorn Association of India on 5th March, 2025.

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