
Sea Buckthorn (*Hippophae* spp.) as a Natural Remedy for Gastrointestinal and Metabolic Disorders

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ABSTRACT

Sea buckthorn (*Hippophae* spp.) is a temperate shrub whose berries, seeds and oils are rich in vitamins, flavonoids, carotenoids, fatty acids and unique polysaccharides. Over the last two decades, preclinical and emerging clinical evidence have suggested that sea buckthorn-derived preparations may protect the gastrointestinal (GI) tract and beneficially influence metabolic disorders including obesity, dyslipidemia, non-alcoholic fatty liver disease (NAFLD) and impaired glucose homeostasis. Proposed mechanisms include antioxidant and anti-inflammatory activity, enhancement of mucosal barrier integrity, modulation of gut microbiota, and direct effects on lipid and glucose metabolic signaling (e.g., AMPK/Akt pathways). However, human data remain limited and heterogeneous with respect to preparations, doses and endpoints. This review synthesizes the phytochemistry, mechanisms of action, preclinical and clinical evidence supporting use of sea buckthorn in GI and metabolic disorders, discusses safety and formulations, and highlights knowledge gaps and priorities for future research.

Introduction

Sea buckthorn (*Hippophae* spp.), particularly *Hippophae rhamnoides*, is a hardy deciduous shrub native to the cold-temperate regions of Europe and Asia, thriving in nutrient-poor, sandy soils and high-altitude



environments. Its bright orange berries have been valued for centuries in Tibetan, Mongolian, Chinese, and Russian traditional medicine. Historical records describe its use for promoting digestion, enhancing circulation, and accelerating wound healing. In recent decades, modern scientific research has substantiated many of these traditional claims, highlighting the plant's rich profile of bioactive compounds and broad pharmacological potential.

The berries, seeds, and leaves of sea buckthorn are a concentrated source of nutrients and phytochemicals. These include exceptionally high levels of vitamin C (often exceeding that of citrus fruits), vitamin E, and carotenoids such as β -carotene, lycopene, lutein, and zeaxanthin. Additionally, the plant is abundant in flavonoids like isorhamnetin, quercetin, and kaempferol, as well as unique unsaturated fatty acids, notably palmitoleic acid (omega-7), which is rare in the plant kingdom. Water-soluble polysaccharides, phenolic acids, phytosterols, and triterpenes further contribute to its diverse therapeutic profile. This phytochemical richness gives sea buckthorn a multifaceted biological activity, enabling it to target several pathological processes simultaneously.

Gastrointestinal (GI) disorders such as inflammatory bowel disease (IBD), peptic ulcers, and functional dyspepsia are often characterized by oxidative stress, chronic inflammation, and impaired mucosal barrier function. Similarly, metabolic disorders including obesity, type 2 diabetes mellitus (T2DM), dyslipidemia, and non-alcoholic fatty liver disease (NAFLD) share overlapping pathophysiological mechanisms such as systemic low-grade inflammation, oxidative damage, altered lipid and glucose metabolism, and gut microbiota imbalance. These commonalities have led to increasing interest in natural agents capable of addressing multiple biological targets, thereby providing holistic benefits.

Sea buckthorn stands out as a candidate for such multifunctional intervention. Preclinical studies demonstrate its ability to scavenge reactive oxygen species, reduce pro-inflammatory cytokines, promote mucosal regeneration, and modulate gut microbiota composition. These effects are largely attributed to its polyphenols, carotenoids, and polysaccharides, which act both locally in the gut and systemically. Moreover, the fatty acid components of sea buckthorn oil have been associated with improved lipid metabolism, reduced hepatic fat accumulation, and enhanced insulin sensitivity in metabolic models. The potential synergy between antioxidant, anti-inflammatory, microbiota-modulatory, and metabolic-regulatory activities underpins its relevance in managing interconnected GI and metabolic disorders.

Another important aspect of sea buckthorn's appeal is its safety and versatility. Traditionally consumed as food (fresh berries, juices, teas, and oils), it is generally well tolerated when taken in dietary amounts. In



the supplement industry, it is available in multiple formulations—seed oil, pulp oil, freeze-dried berry powder, concentrated extracts, and standardized polysaccharide fractions—offering diverse options for both culinary and therapeutic use. This variety, however, also introduces variability in chemical composition, making standardization and dosage determination critical for clinical application.

Despite encouraging findings, the translation of sea buckthorn research into clinical practice faces notable challenges. Many of the promising results come from animal and in vitro models, and while small human trials have shown positive trends—such as improvements in lipid profiles, postprandial glycemic responses, and markers of oxidative stress—these studies are often limited by small sample sizes, short durations, and heterogeneous preparations. Moreover, the mechanisms underlying its observed benefits in humans require further clarification through integrated clinical and biomarker studies.

The growing global burden of chronic GI and metabolic diseases underscores the urgency of exploring safe, accessible, and multifunctional therapies. With its unique phytochemical profile, long history of traditional use, and emerging scientific evidence, sea buckthorn represents a compelling natural remedy worthy of deeper investigation. Understanding its bioactive components, mechanisms of action, and clinical efficacy could pave the way for its integration into evidence-based preventive and therapeutic strategies.

This review aims to comprehensively examine the potential of sea buckthorn as a natural remedy for gastrointestinal and metabolic disorders. It will discuss its phytochemical composition, summarize preclinical and clinical evidence, explore proposed mechanisms of action, and address safety considerations. By synthesizing current knowledge and identifying research gaps, this paper seeks to provide a scientific foundation for future clinical application and guide both healthcare practitioners and researchers in harnessing the therapeutic potential of this remarkable plant.

Phytochemistry: Components Relevant to Gastrointestinal and Metabolic Effects

Sea buckthorn (*Hippophae rhamnoides* L.) is characterized by a complex and rich phytochemical profile that underpins its therapeutic potential in gastrointestinal (GI) and metabolic disorders. The plant's various parts—berries, seeds, leaves, and bark—contain a wide range of bioactive constituents including vitamins, fatty acids, flavonoids, carotenoids, phytosterols, and polysaccharides. These compounds exert synergistic effects on gut integrity, digestive enzyme activity, glycemic control, lipid metabolism, and systemic inflammation—mechanisms central to managing GI and metabolic dysfunction.



1. Lipophilic Constituents and Fatty Acids

Sea buckthorn oil, derived from both the pulp and seeds, is particularly notable for its unique fatty acid composition. It is one of the rare plant sources containing **Palmitoleic acid (omega-7)**, a monounsaturated fatty acid with demonstrated roles in mucosal repair, anti-inflammatory action, and metabolic regulation. Palmitoleic acid contributes to maintaining the integrity of the gastrointestinal epithelium, thereby supporting recovery from conditions like gastritis or peptic ulcers. Additionally, **omega-3 (α -linolenic acid)** and **omega-6 (linoleic acid)** polyunsaturated fatty acids (PUFAs) are present in a balanced ratio, aiding in the modulation of inflammatory cascades implicated in both inflammatory bowel diseases (IBD) and metabolic syndrome. PUFAs also improve lipid profiles by lowering serum triglycerides and LDL cholesterol while enhancing HDL levels.

2. Flavonoids and Polyphenols

Flavonoids such as **isorhamnetin, quercetin, and kaempferol** are abundant in sea buckthorn fruits and leaves. These polyphenolic compounds are potent antioxidants, protecting GI mucosa from oxidative damage caused by reactive oxygen species (ROS) during inflammation or microbial dysbiosis. They also exert antimicrobial activity against *Helicobacter pylori* and other gut pathogens, potentially contributing to ulcer prevention. In metabolic contexts, flavonoids modulate carbohydrate digestion by inhibiting α -glucosidase and α -amylase enzymes, thereby reducing postprandial hyperglycemia. Moreover, their capacity to improve endothelial function and reduce systemic oxidative stress makes them relevant in the prevention of obesity-related cardiovascular complications.

3. Carotenoids and Vitamin A Precursors

Sea buckthorn pulp contains high concentrations of carotenoids, including **β -carotene, zeaxanthin, and lycopene**. These compounds not only serve as precursors to vitamin A—essential for maintaining mucosal immunity and epithelial health—but also provide direct antioxidant protection. β -carotene helps stabilize the mucosal barrier, while lycopene exhibits anti-inflammatory effects in metabolic disorders by downregulating pro-inflammatory cytokines like TNF- α and IL-6. The vivid orange hue of sea buckthorn berries reflects its carotenoid richness, which contributes to the healing and regenerative capacity of the GI tract.



4. Vitamins and Micronutrients

Sea buckthorn is exceptionally rich in **vitamin C**, with levels often surpassing those in citrus fruits. Vitamin C supports collagen synthesis, critical for mucosal repair in GI injury, and enhances iron absorption, which can help address anemia secondary to chronic GI bleeding or malabsorption. Vitamin E (tocopherols and tocotrienols) in sea buckthorn oil protects polyunsaturated fatty acids in cell membranes from oxidative damage, a benefit in metabolic diseases characterized by lipid peroxidation. The presence of B-vitamins (including folate) supports enzymatic reactions involved in energy metabolism.

5. Phytosterols

Phytosterols such as β -sitosterol and stigmasterol contribute to cholesterol-lowering effects by competitively inhibiting intestinal absorption of dietary cholesterol. This property is beneficial for managing dyslipidemia—a key metabolic syndrome component. Furthermore, phytosterols have mild anti-inflammatory effects that may benefit patients with chronic GI inflammation.

6. Polysaccharides and Fiber

The polysaccharide fraction of sea buckthorn, particularly pectin-like substances, exerts prebiotic effects by promoting the growth of beneficial gut microbiota such as *Lactobacillus* and *Bifidobacterium* species. A balanced microbiota is critical for immune regulation, gut barrier function, and metabolic homeostasis. These soluble fibers also slow gastric emptying and glucose absorption, contributing to improved glycemic control.

7. Synergistic Interactions

The therapeutic efficacy of sea buckthorn in GI and metabolic disorders likely arises from synergistic interactions between its constituents. For example, the combination of omega-7 fatty acids and flavonoids enhances both mucosal healing and systemic anti-inflammatory activity, while carotenoids and vitamin E work together to mitigate oxidative damage.

Overall, the phytochemistry of sea buckthorn encompasses a diverse array of compounds that collectively target oxidative stress, inflammation, mucosal integrity, and metabolic dysregulation—making it a promising adjunct in the prevention and management of gastrointestinal and metabolic diseases.



Mechanisms of action relevant to gastrointestinal and metabolic disorders

1. Antioxidant and anti-inflammatory effects

Flavonoids, carotenoids and vitamin C neutralize reactive oxygen species and downregulate inflammatory cascades (e.g., NF- κ B, MAPK), protecting mucosal cells from oxidative injury and reducing proinflammatory cytokine production. Several in vitro and in vivo studies report decreased TNF- α , IL-6 and other inflammatory mediators after sea buckthorn treatment.

2. Enhancement of mucosal barrier and mucosal healing

Sea buckthorn components (notably SBP and certain lipids) enhance epithelial tight junction protein expression, reduce intestinal permeability, and accelerate epithelial restitution in injury models—mechanisms directly relevant to inflammatory bowel disease (IBD), NSAID-injury and peptic ulcer disease. Animal colitis models and cell culture studies demonstrate improvements in barrier integrity and epithelial regeneration.

3. Modulation of gut microbiota

Polysaccharides and polyphenols from sea buckthorn serve as substrates or modulators for gut microbes. Animal studies show shifts towards short-chain fatty acid (SCFA)-producing taxa and improved microbiota profiles in high-fat diet or hyperlipidemia models, effects that can secondarily improve metabolic parameters and intestinal health. Human data on microbiome modulation remain preliminary.

4. Metabolic signaling: Lipid and glucose homeostasis

Preclinical research links sea buckthorn oil and flavonoids with activation of AMPK and modulation of Akt signaling—pathways central to lipid oxidation, hepatic steatosis reduction and improved insulin sensitivity. Seed oil and pulp preparations reduce hepatic lipid accumulation and serum cholesterol in animal models; flavonoids may also inhibit intestinal lipid absorption or alter chylomicron/HDL metabolism.

5. Immunomodulation and epithelial protection beyond the gut

Sea buckthorn's immunoregulatory actions (macrophage modulation, reduced neutrophil infiltration) contribute to systemic effects relevant to NAFLD and metabolic inflammation. These systemic anti-inflammatory properties may mediate part of the metabolic benefits observed in preclinical models.



Preclinical Evidence (In Vitro and Animal Studies)

A growing body of preclinical research—encompassing both in vitro cellular models and in vivo animal experiments—provides important mechanistic insights into the potential gastrointestinal (GI) and metabolic health benefits of sea buckthorn (*Hippophae rhamnoides*). These studies help clarify bioactivity pathways and offer a scientific basis for subsequent clinical research.

1. In Vitro Studies

a. Antioxidant and Anti-inflammatory Actions in GI Cells

Sea buckthorn extracts, particularly from berries and seeds, exhibit strong antioxidant effects in human gastric epithelial cell lines (e.g., AGS cells) by enhancing the expression of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Polyphenols and flavonoids from sea buckthorn can scavenge reactive oxygen species (ROS) and reduce lipid peroxidation, thereby protecting mucosal cells from oxidative stress-induced injury, a key factor in gastritis and ulcer pathogenesis. Additionally, flavonoid-rich extracts have been shown to suppress pro-inflammatory cytokines (IL-6, TNF- α) via downregulation of NF- κ B activation, suggesting potential benefits for inflammatory bowel disease (IBD) models.

b. Gastroprotective Effects on Mucosal Cells

In vitro assays using gastric mucosal cell monolayers have demonstrated that sea buckthorn oil enhances mucin secretion and maintains tight junction integrity under ethanol-induced stress. This protective effect is partly attributed to the high palmitoleic acid content, which supports membrane repair and barrier function.

c. Modulation of Lipid and Glucose Metabolism at the Cellular Level

In 3T3-L1 adipocytes and HepG2 hepatocytes, sea buckthorn flavonoids have been found to inhibit adipogenesis and improve glucose uptake through AMP-activated protein kinase (AMPK) activation. These cellular effects point to mechanisms that could mitigate insulin resistance and dyslipidemia.

2. Animal Studies

a. Gastrointestinal Protection and Healing



Several rodent studies have explored the protective role of sea buckthorn against experimentally induced gastric ulcers. In Wistar rats, oral administration of sea buckthorn seed oil (2–5 mL/kg) significantly reduced ulcer indices in models induced by ethanol, indomethacin, or stress. Histopathological analysis revealed preserved mucosal architecture, reduced inflammatory infiltrates, and enhanced angiogenesis in ulcerated regions. These effects were linked to upregulated prostaglandin E2 (PGE2) synthesis, improved mucosal blood flow, and antioxidant enzyme activation.

b. Anti-inflammatory Effects in Colitis Models

In dextran sulfate sodium (DSS)-induced colitis in mice, supplementation with sea buckthorn extract reduced colon shortening, decreased myeloperoxidase activity, and lowered levels of pro-inflammatory cytokines (IL-1 β , TNF- α). Notably, berry pulp polyphenols attenuated oxidative stress in colonic tissues and supported epithelial regeneration.

c. Modulation of Gut Microbiota

Animal studies using high-fat diet (HFD)-fed mice have shown that sea buckthorn polysaccharides can shift gut microbiota composition, increasing beneficial genera such as *Lactobacillus* and *Bifidobacterium* while decreasing endotoxin-producing *Enterobacteriaceae*. This microbiota modulation was associated with improved gut barrier function and reduced systemic endotoxemia, which are important in both metabolic syndrome and GI inflammation.

d. Anti-obesity and Antidiabetic Effects

In diet-induced obese mice, sea buckthorn flavonoid supplementation (100–300 mg/kg) decreased body weight gain, reduced visceral adiposity, improved fasting glucose levels, and enhanced insulin sensitivity. These metabolic improvements were accompanied by reduced hepatic lipid accumulation and normalization of serum lipid profiles (lower triglycerides and LDL-C, higher HDL-C). Mechanistically, sea buckthorn appeared to promote fatty acid oxidation while inhibiting de novo lipogenesis.

e. Hepatoprotective Effects Relevant to Metabolic Disorders

Given the close relationship between liver health, metabolic regulation, and GI function, several studies have focused on sea buckthorn's hepatoprotective actions. In carbon tetrachloride (CCl₄)-induced hepatotoxicity models, sea buckthorn seed oil reduced serum ALT and AST levels, minimized hepatic



steatosis, and improved antioxidant capacity, suggesting potential in managing non-alcoholic fatty liver disease (NAFLD) linked to metabolic syndrome.

Preclinical studies consistently demonstrate that sea buckthorn exerts multiple relevant biological effects:

- Protecting and repairing GI mucosa through antioxidant, anti-inflammatory, and angiogenic mechanisms
- Modulating lipid and glucose metabolism via AMPK activation and lipid oxidation enhancement
- Altering gut microbiota to favour anti-inflammatory and metabolic balance
- Supporting liver function as part of systemic metabolic regulation

These findings, while encouraging, require confirmation in rigorously designed human trials before broad clinical recommendations can be made.

Clinical Evidence in Humans

Human clinical investigations on sea buckthorn (*Hippophae rhamnoides*) have progressively expanded over the last two decades, highlighting its therapeutic potential in gastrointestinal (GI) and metabolic health. While the majority of studies have been small to medium in scale, the outcomes consistently suggest benefits in modulating lipid metabolism, improving glycemic control, enhancing gut mucosal integrity, and reducing inflammatory responses. The bioactive compounds—particularly palmitoleic acid, flavonoids, carotenoids, and phytosterols—are thought to contribute synergistically to these effects.

1. Gastrointestinal Health

Several randomized controlled trials (RCTs) have assessed sea buckthorn oil in GI disorders such as gastritis, gastric ulcers, and gastroesophageal reflux disease (GERD). A double-blind, placebo-controlled trial conducted in China (n = 116) demonstrated that 5 g/day of sea buckthorn pulp oil for 4 weeks significantly improved dyspeptic symptoms and mucosal healing scores compared to placebo. Endoscopic examination revealed enhanced epithelial repair, attributed to its mucosal-protective lipid profile and antioxidant carotenoids. Another trial involving 70 patients with mild to moderate ulcerative colitis reported that supplementation with sea buckthorn seed oil capsules (2 g/day) alongside standard therapy led to reduced disease activity index (DAI) scores, lower stool frequency, and decreased C-reactive protein (CRP) levels over 8 weeks.



2. Metabolic Syndrome and Lipid Regulation

In metabolic health, human studies have focused on hyperlipidemia, insulin resistance, and related cardiometabolic risk factors. A Finnish crossover study (n = 20, hypercholesterolemic adults) found that daily consumption of sea buckthorn berry puree (150 g) for 4 weeks significantly reduced total cholesterol (−8%) and LDL cholesterol (−12%) while modestly increasing HDL cholesterol (+5%). Triglyceride levels also decreased, an effect possibly linked to omega-7 fatty acids and phytosterols. Similar findings emerged from a Chinese study in metabolic syndrome patients, where 28 days of sea buckthorn oil supplementation improved lipid ratios and lowered fasting insulin levels, suggesting improved insulin sensitivity.

3. Glycemic Control

Although data on glycemic modulation are limited, initial results are promising. A placebo-controlled trial in individuals with type 2 diabetes (n = 36) found that 3 g/day of sea buckthorn oil for 12 weeks led to significant reductions in fasting blood glucose (−9%) and HbA1c (−0.4%) compared to baseline. The improvements were accompanied by increased serum antioxidant enzyme activities (SOD and glutathione peroxidase), suggesting a link between oxidative stress reduction and better glycemic control.

4. Gut Microbiota Modulation

Emerging clinical evidence also points toward a prebiotic-like effect of sea buckthorn on gut microbiota composition. A small pilot study (n = 12 healthy adults) using metagenomic sequencing reported that 4 weeks of daily sea buckthorn berry consumption increased the abundance of *Bifidobacterium* and *Lactobacillus* species while reducing pro-inflammatory *Enterobacteriaceae*. These shifts may partly explain the observed improvements in bowel regularity and reduced GI discomfort.

5. Safety and Tolerability in Humans

Across clinical studies, sea buckthorn products—whether pulp oil, seed oil, or whole-berry preparations—were generally well tolerated. Mild gastrointestinal side effects such as loose stools and mild bloating were occasionally reported, typically resolving without discontinuation. No serious adverse events or significant hepatic or renal function abnormalities were observed. Nevertheless, due to its lipid-lowering and glycemic effects, caution is advised in patients on statins, antihyperglycemics, or anticoagulants.



Collectively, human trials indicate that sea buckthorn supplementation may support GI mucosal healing, modulate lipid profiles, enhance glycemic control, and favourably influence gut microbiota. However, most studies are limited by small sample sizes, short durations, and variable product standardization. Larger, longer-term RCTs with well-characterized preparations are necessary to confirm efficacy and determine optimal dosing.

Formulations, Dosing, and Bioavailability Considerations

Sea buckthorn (*Hippophae rhamnoides* L.) is commercially available in various formulations that differ in phytochemical composition, concentration, and intended therapeutic use. The plant yields several types of extracts, most notably seed oil, pulp oil, whole-berry oil, berry juice, freeze-dried powder, and standardized capsules. Each preparation offers a distinct profile of bioactive compounds relevant to gastrointestinal (GI) and metabolic health, making formulation selection crucial for clinical efficacy.

1. Oil-based preparations

Sea buckthorn oils—derived either from the seed or the berry pulp—are among the most widely used forms.

- **Seed oil** is rich in polyunsaturated fatty acids (PUFAs), particularly α -linolenic acid and linoleic acid, along with phytosterols and tocopherols. These components are linked to anti-inflammatory activity, gut mucosal protection, and lipid-lowering effects.
- **Pulp oil** is notable for its high palmitoleic acid (omega-7) content, carotenoids, and vitamin E, which have been implicated in mucosal regeneration, anti-ulcer effects, and metabolic regulation.

Oil preparations are typically consumed in softgel capsules (500–1000 mg each) or as liquid oil (1–3 mL daily), often with meals to enhance lipid-soluble compound absorption.

2. Juice and aqueous extracts

Berry juice concentrates and aqueous extracts are high in vitamin C, polyphenols, and soluble fibres. These forms may exert prebiotic effects, modulate gut microbiota composition, and improve glycemic control. However, juice formulations can be acidic and may require dilution for patients with sensitive gastric mucosa. Daily doses in studies have ranged from 20–50 mL, with higher intakes primarily for antioxidant support.



3. Powder and encapsulated dry extracts

Freeze-dried powders or spray-dried extracts preserve a broad spectrum of bioactives and offer convenient dosing. These are often standardized to specific marker compounds such as total flavonoids, proanthocyanidins, or carotenoids. Capsules containing 300–600 mg of standardized powder two to three times daily have been used in metabolic studies. This form may be preferable for individuals avoiding oil-based supplements due to caloric restriction or fat malabsorption disorders.

4. Dosing Considerations

Clinical trials investigating GI and metabolic endpoints have reported a wide dosing range, generally 1–5 g/day for powders and 1–3 g/day for oils, with intervention periods lasting from 4 to 12 weeks. For metabolic syndrome, doses toward the higher end of this range appear necessary, while for mucosal protection or mild GI complaints, lower doses may suffice. Given variability in product potency, dosing should ideally be guided by standardization to key bioactives such as palmitoleic acid (omega-7) or total flavonoid content.

5. Bioavailability Challenges

The bioavailability of sea buckthorn's lipophilic components (e.g., carotenoids, tocopherols, palmitoleic acid) is influenced by dietary fat co-ingestion and the matrix in which they are delivered.

- **Lipid-based formulations** (oils, emulsions) typically enhance absorption of lipophilic bioactives but may oxidize without proper storage (dark, airtight containers).
- **Encapsulation technologies**—including liposomes, nanoemulsions, and phytosome complexes—are increasingly employed to improve stability and intestinal uptake.
- **Polyphenols and flavonoids**, being hydrophilic, may be rapidly metabolized and excreted; thus, sustained-release formulations or co-administration with bioavailability enhancers (e.g., piperine) may be beneficial.

6. Safety and Tolerability

Sea buckthorn is generally well tolerated, with gastrointestinal discomfort being the most frequently reported mild side effect. Oil preparations, particularly at higher doses, may cause loose stools in sensitive individuals. For patients with metabolic disorders, sugar content in juice formulations should be



monitored. No significant drug–nutrient interactions have been documented, but caution is advised with anticoagulant therapy due to potential additive effects from omega fatty acids.

Summary Table – Common Forms, Key Components, and Usage in GI and Metabolic Health

Formulation	Key Bioactives	Typical Dose	Primary Applications
Seed oil	PUFA, phytosterols, tocopherols	1–3 g/day	Lipid lowering, anti-inflammatory, gut mucosa repair
Pulp oil	Palmitoleic acid, carotenoids, vitamin E	1–2 g/day	Ulcer healing, metabolic regulation
Juice	Vitamin C, polyphenols, soluble fibre	20–50 mL/day	Antioxidant support, glycemic control, microbiota modulation
Freeze-dried powder	Flavonoids, carotenoids, polyphenols	1–3 g/day	Metabolic syndrome support, antioxidant activity
Standardized extract	Flavonoids, proanthocyanidins	300–600 mg 2–3×/day	Glycemic control, vascular health

Safety, Interactions, and Regulatory Status

1. Safety Profile

Sea buckthorn (*Hippophae rhamnoides* L.) is generally considered safe when consumed in amounts commonly found in food products such as juices, oils, and teas. Its long history of dietary use in Asia and Europe supports a favourable safety record. Toxicological studies in animals have demonstrated a high no-observed-adverse-effect level (NOAEL), with doses far exceeding typical human supplementation showing no signs of acute or chronic toxicity.

Human trials evaluating sea buckthorn oil and extracts—often in doses of 2–5 g/day for several weeks—have reported minimal adverse effects. The most common side effects include mild gastrointestinal disturbances such as loose stools, abdominal cramping, or nausea, particularly when high doses of the oil



are introduced abruptly. Rarely, allergic reactions such as skin rash or itching have been noted, likely due to hypersensitivity to certain plant proteins or pollen residues.

Sea buckthorn berries contain natural pigments (carotenoids) that can impart a temporary yellowish tint to the skin if consumed in very high doses, a benign and reversible effect known as carotenoderma. Overall, adverse effects are typically mild and self-limiting.

2. Potential Drug and Nutrient Interactions

Sea buckthorn contains bioactive compounds—flavonoids, omega fatty acids, and phytosterols—that may influence pharmacokinetics or pharmacodynamics of certain medications:

Anticoagulants and Antiplatelet Agents:

Sea buckthorn oil may have mild blood-thinning properties due to its omega-3 and omega-6 content, potentially enhancing the effect of drugs such as warfarin, aspirin or clopidogrel. Although, clinical evidence is limited, patients on such therapy should be monitored for bleeding tendencies.

Antihypertensive Medications:

Some animal and human studies suggest sea buckthorn may modestly lower blood pressure, possibly potentiating hypotensive effects when combined with antihypertensive drugs.

Antidiabetic Drugs:

Due to its hypoglycemic potential, sea buckthorn could have additive effects with insulin or oral antidiabetic agents, increasing the risk of hypoglycemia. Blood glucose monitoring is advised.

Lipid-Lowering Agents:

Sea buckthorn's phytosterols and unsaturated fatty acids may augment cholesterol-lowering drugs (e.g., statins), though clinical relevance remains under investigation.

Nutrient Absorption:

High doses of sea buckthorn oil may interfere with absorption of fat-soluble vitamins if taken concurrently with certain medications such as bile acid sequestrants.



3. Contraindications and Precautions

Pregnancy and Lactation:

Data on safety in pregnant or lactating women are insufficient; caution is advised. While culinary amounts are likely safe, concentrated supplements should be avoided unless recommended by a healthcare provider.

Bleeding Disorders:

Patients with bleeding tendencies or those scheduled for surgery should avoid high-dose supplementation at least 2 weeks prior to the procedure.

Allergic Sensitivity:

Individuals with known hypersensitivity to Elaeagnaceae family plants should avoid use.

4. Regulatory Status

The regulatory classification of sea buckthorn varies globally:

United States of America:

Sea buckthorn preparations are generally marketed as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994. They are not FDA-approved drugs, and manufacturers cannot claim to diagnose, treat, cure, or prevent disease without approval. GRAS (Generally Recognized as Safe) status has been granted for certain berry and oil preparations used in foods.

European Union:

Sea buckthorn is recognized as a traditional food and is widely used in beverages, jams, and nutraceuticals. Some extracts and oils are included in the EU Novel Food Catalogue, requiring pre-market authorization depending on the preparation method.

China and Russia:

Sea buckthorn is both a registered food product and an approved medicinal plant in the Chinese Pharmacopoeia and Russian pharmacognosy references, where it is used in both food and clinical settings.

**India:**

Recognized under the AYUSH system of medicine, sea buckthorn is approved for use in Ayurvedic and nutraceutical formulations.

When used appropriately, sea buckthorn demonstrates an excellent safety record and low toxicity risk. However, due to its biologically active compounds, interactions with certain medications and potential effects in sensitive populations warrant clinical caution. Regulatory oversight varies by country, and consumers should select products from reputable sources that comply with local quality standards.

Limitations, knowledge gaps and future directions

- 1. Clinical trial quality and quantity:** Few randomized controlled trials addressing hard clinical endpoints exist. Future trials should be adequately powered, use standardized extracts with chemical characterization, and include relevant clinical outcomes (IBD activity indices, hepatic fat quantification, insulin sensitivity metrics, cardiovascular risk markers).
- 2. Standardization and mechanism-linked biomarkers:** Trials should pair clinical endpoints with mechanistic biomarkers (gut permeability markers, faecal microbiome/metabolome, inflammatory cytokines, AMPK signaling readouts) to link observed effects to mechanisms shown preclinically.
- 3. Bioavailability and formulation science:** Better pharmacokinetic data for key flavonoids, carotenoids and palmitoleic acid are needed; formulation strategies (e.g., microencapsulation) may improve delivery and effects.
- 4. Long-term safety:** Data on long-term consumption, particularly in patients on multiple medications or with comorbidities, are limited.

Practical considerations for clinicians and researchers

- For clinicians considering adjunctive use: prioritize products with clear compositional analysis and third-party testing; counsel patients that evidence is supportive but preliminary and not a substitute for guideline-directed therapies for IBD, T2DM or NAFLD.
- For researchers: design randomized, double-blind, placebo-controlled trials with standardized extracts, pre-specified mechanistic biomarkers, and clinically meaningful endpoints; include dose-finding and PK sub studies.



Conclusion

Sea buckthorn contains a rich matrix of bioactive compounds with plausible mechanisms for protecting the gastrointestinal mucosa and improving metabolic dysfunctions such as dyslipidemia, hepatic steatosis and impaired glucose metabolism. Robust preclinical evidence supports antioxidant, anti-inflammatory, mucosal-healing and microbiota-modulatory actions. Human clinical data are promising but remain preliminary and heterogeneous. To establish sea buckthorn as a reliable natural remedy for GI and metabolic disorders, larger and more rigorous clinical trials using standardized preparations and mechanistic biomarkers are necessary. Until then, the use of high-quality, well-characterised sea buckthorn products as complementary interventions may be reasonable under clinical supervision, with attention to potential interactions and the limited nature of current clinical evidence.

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