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IMMUNOLOGICAL MODULATION VIA PERIUMBILICAL ABSORPTION: ENHANCING SYSTEMIC IMMUNITY AND REDUCING INFLAMMATORY MARKERS WITH SEA BUCKTHORN

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ABSTRACT

The human immune system is intricately regulated by a network of biochemical, neurological, and endocrine interactions. In recent years, growing interest in transdermal phytotherapeutics and gut-immune axis regulation has prompted exploration of alternative delivery mechanisms for systemic immunomodulation. One such ancient yet underutilized approach is Nabhi therapy - the application of therapeutic oils to the periumbilical (navel) region as described in classical Ayurvedic texts. This paper investigates the physiological rationale, biochemical pathways, and immunological outcomes associated with the application of Sea Buckthorn (*Hippophae rhamnoides*) oil to the navel, as practiced in Ayurvedic transdermal Nabhi oil therapies. The navel region possesses a dense vascular, lymphatic, and neurological network, making it a strategic site for transdermal delivery of lipophilic compounds. Sea Buckthorn oil, rich in Omega-3, 6, 7 and 9 fatty acids, carotenoids, tocopherols, and phytosterols, has demonstrated potent immunomodulatory, anti-inflammatory, and antioxidant effects in both clinical and experimental settings. This paper hypothesizes that its application via the Nabhi enhances systemic immunity by delivering bioactive compounds through lymphatic channels, modulating gut-associated lymphoid tissue (GALT), and stimulating the vagus nerve, which is implicated in both immune regulation and inflammation control. Furthermore, Sea Buckthorn has been shown to regulate inflammatory cytokines such as TNF-α, IL-6, and IL-1β, while enhancing natural killer (NK) cell activity, improving mucosal immunity, and restoring redox balance - outcomes that are desirable in conditions involving immune fatigue, chronic inflammation, or post-viral recovery. Ayurvedic principles support this modality through the classification of Nabhi as a Marma point that influences Agni (digestive fire), Ojas (immunity), and Rasa-Rakta dhatu (nutrient and blood tissue layers). By integrating modern biomedical research with Ayurvedic pharmacology, this paper proposes Nabhi therapy as a viable adjunct or standalone route for immune enhancement and inflammation reduction, particularly in populations seeking non-oral, non-invasive, and integrative interventions. The findings support further exploration through pilot trials and quantitative biomarker studies to validate efficacy and mechanistic insights.

KEYWORDS: Sea Buckthorn; Hippophae rhamnoides; Nabhi therapy; periumbilical absorption; transdermal delivery; immunomodulation; cytokines; TNF-alpha; IL-6; NK cells; GALT; vagus nerve; Ayurveda; Marma; omega-7; palmitoleic acid; anti-inflammatory.

1. INTRODUCTION

The human immune system is a dynamic and highly regulated network of cells, signaling molecules, and barrier functions that protect the body against infections, environmental toxins, and abnormal cellular growth. In the current era of rising chronic diseases and lifestyle-induced disorders - including autoimmune conditions, metabolic syndrome, persistent low-grade inflammation, and post-viral immune fatigue - the need for safe and effective immune modulation has never been more urgent.[11] While modern medicine offers targeted immunosuppressants and biologics, these often come

with adverse effects and are not always suitable for long-term preventive care.

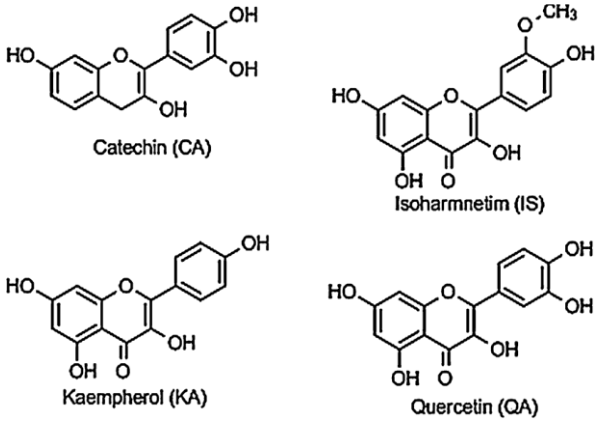


Figure 1: Chemical structures of key flavonoids present in Sea Buckthorn (Hippophae rhamnoides) extract. Isorhamnetin and quercetin are the predominant flavonoids, both possessing potent anti-inflammatory, antioxidant, and immunomodulatory properties relevant to the therapeutic mechanism of Nabhi oil application. [Source: Guliyev et al., 2004]

Chronic inflammation, often dubbed the "silent killer," underlies the pathogenesis of numerous conditions such as cardiovascular disease, type 2 diabetes, arthritis, and even neurodegeneration. Studies have shown that subclinical elevation of inflammatory markers like C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) correlates strongly with increased disease risk and progression.[15] Modulating the immune system to restore balance rather than blunt suppression is emerging as a preferred approach in integrative health systems.

Nabhi therapy, an ancient practice from Ayurveda, offers a promising solution. The Nabhi (navel) is classified as a powerful marma point - a physiological and energetic hub believed to connect 72,000 nadis (subtle channels) and serve as the root of all venous and nervous pathways (Charaka Samhita, Sharira Sthana 7/14; Sushruta Samhita, Sharira Sthana 3/10).[6,7] Classical Ayurvedic texts describe Nabhi as the center of life force (*Prana*) and metabolism (*Agni*), making it a focal point for interventions aimed at restoring homeostasis. Traditionally, therapeutic oils were applied to the navel for a variety of conditions ranging from digestive distress and menstrual pain to mental fatigue and immune weakness.

In parallel, modern scientific inquiry is beginning to uncover the physiological rationale behind Nabhi therapy. The periumbilical region is rich in microcapillaries, lymphatic vessels, and autonomic nerve endings. Transdermal delivery via the navel allows for systemic absorption of lipophilic compounds, bypassing hepatic first-pass metabolism and reducing gastrointestinal irritation.[21] This method has gained traction in the realm of bioactive phytochemicals and essential oils, which are increasingly used to modulate immune response, improve gut health, and regulate endocrine function.[4]

Given the need for safe, non-invasive, and holistic immune modulation strategies, Nabhi therapy stands at the intersection of tradition and innovation. The application of botanicals such as Sea Buckthorn to the navel represents a compelling integration of ancient wisdom and modern science, especially in the context of immunological resilience and inflammation reduction.[2,3]

The global burden of immune-related disorders underscores the urgency of identifying safe, accessible, and effective immune modulation strategies. Globally, autoimmune diseases affect approximately 3-8% of the population, while chronic low-grade inflammation contributes to an estimated 60% of all deaths worldwide through its role in cardiovascular disease, cancer, diabetes, and neurodegeneration.[13] Conventional pharmacological approaches - including non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and biologics - while effective, are associated with significant adverse effects including gastrointestinal toxicity, immunosuppression risk, and high cost that limit their utility for long-term preventive application across diverse populations. There is therefore a compelling scientific and public health rationale for investigating plant-based, non-invasive immunomodulatory approaches that can complement conventional care without the associated risks - a category into which Sea Buckthorn Nabhi therapy falls uniquely.

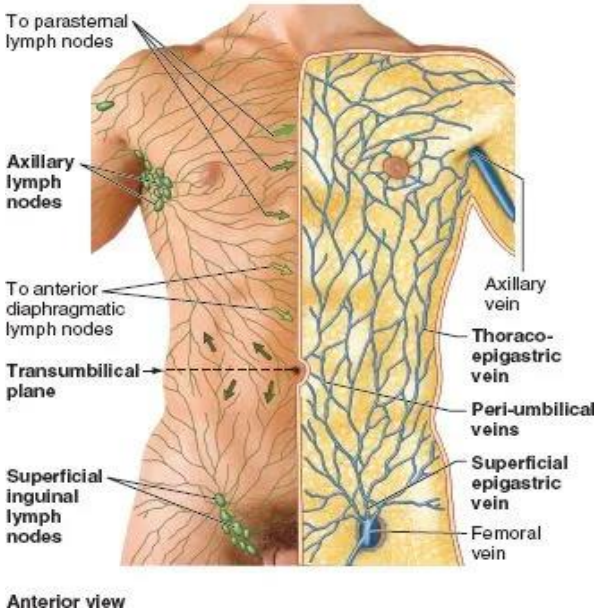


Figure 2: Lymphatics and superficial veins of the anterolateral abdominal wall. The rich lymphatic network surrounding the periumbilical region constitutes a primary pathway for systemic delivery of lipophilic bioactives applied transdermally at the Nabhi site. Deep lymphatic connections communicate

with mesenteric lymph nodes, providing access to gut-associated lymphoid tissue (GALT). [Source: Basic Medical Key]

2. Physiological Significance of the Nabhi (Navel) Region

The umbilical (Nabhi) region holds unique anatomical and functional significance, both in traditional Ayurvedic medicine and in contemporary biomedical science. During fetal development, the umbilicus serves as a conduit for nutrient and waste exchange via the umbilical cord. Even after birth, the region remains highly vascularized and innervated, with residual connections that make it conducive for systemic therapeutic delivery.

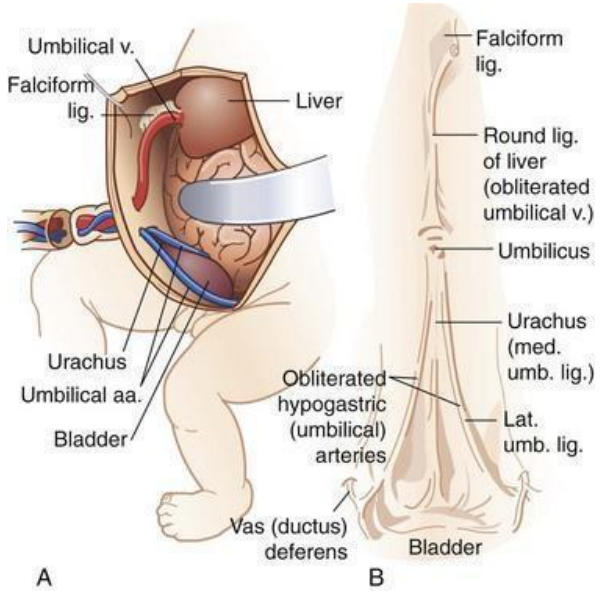


Figure 3: Umbilicus anatomy. (A) In the fetus, the umbilical vein superiorly and the two umbilical arteries and urachus inferiorly radiate from the umbilicus. (B) View of the umbilicus from within the peritoneal cavity showing the round ligament of the liver, which connects the umbilical site to the hepatic portal system - providing a direct anatomical pathway for absorbed bioactives to reach the liver. [Source: Thoracic Key, Abdominal Wall Anatomy]

Preperitoneal Space and Peritoneum

The preperitoneal space lies between the transversalis fascia and parietal peritoneum and contains adipose and areolar tissue. Coursing through the preperitoneal space are the following:

- Inferior epigastric artery and vein
- Medial umbilical ligaments, which are the vestiges of the fetal umbilical arteries
- Median umbilical ligament, which is a midline fibrous remnant of the fetal allantoic stalk or urachus
- Falciform ligament of the liver, extending from the umbilicus to the liver

The round ligament is contained within the free margin of the falciform ligament and represents the obliterated umbilical vein, coursing from the umbilicus to the left branch of the portal vein (Figure 3). The parietal peritoneum is the innermost layer of the abdominal wall. It consists of a thin layer of dense, irregular connective tissue covered on its inner surface by a single layer of squamous mesothelium.

Anatomically, the periumbilical area is supplied by a dense network of microcapillaries and is adjacent to both superficial and deep lymphatic vessels. These structures play a crucial role in absorbing and transporting bioactive molecules applied transdermally. Research suggests that the periumbilical skin shows favorable permeability characteristics for lipid-soluble compounds, making it a strategic zone for botanical drug delivery.[1,21]

In terms of neurophysiology, the navel area is in proximity to autonomic ganglia, abdominal plexuses, and cutaneous branches of the intercostal and subcostal nerves. More importantly, it lies along the abdominal course of the vagus nerve, which plays a central role in parasympathetic regulation, inflammatory control, and gut-brain signaling. Studies have shown that vagal stimulation via transcutaneous routes in the abdomen can modulate systemic inflammation, heart rate variability, and even immune responses.[4,29]

From an Ayurvedic perspective, Nabhi is recognized as a marma point - a vital junction of muscle, vessels, ligaments, bones, and joints. It is considered the site of *Agni* (digestive and metabolic fire), *Ojas* (vital essence linked to immunity), and the origin point of 72,000 Nadis or subtle energy channels (Charaka Samhita, Sharira Sthana 7/14; Sushruta Samhita, Sharira Sthana 3/10).[6,7] Therapeutic intervention at this point is believed to balance the three doshas (Vata, Pitta, Kapha), restore digestive fire, and enhance systemic vitality.

In essence, the Nabhi serves as a physiologically strategic and energetically potent site that bridges modern pharmacological delivery routes with ancient holistic healing systems. Its vascular, lymphatic, and neurological attributes allow for meaningful engagement with both immune and metabolic pathways.

The umbilical ring - the fibromuscular aperture through which the umbilical structures passed during fetal life - does not close completely in the same manner as the surrounding linea alba after birth. This structural characteristic results in a permanently thinner and more permeable fascial barrier at the Nabhi compared to the lateral abdominal wall, explaining the 2-4 fold higher transdermal permeability documented at the umbilical site relative to adjacent abdominal skin.[32] Additionally, the para-umbilical veins of Sappey - residual patent channels connecting the deep subdermal umbilical venous plexus to the left branch of the portal vein - remain functional in approximately 75-85% of healthy adults. These veins provide a direct portal-first-pass delivery route for lipophilic bioactives absorbed at the

umbilical dermis, offering a pharmacokinetic advantage for agents such as Sea Buckthorn carotenoids and tocopherols whose hepatoprotective and immunomodulatory targets include the liver parenchyma.[1,44]

3. Transdermal Absorption Through Periumbilical Skin

The periumbilical skin centered around the navel (Nabhi) presents a physiologically advantageous site for transdermal delivery, especially for lipophilic phytoconstituents. A convergence of thin stratum corneum, rich dermal vasculature, lymphatic drainage, and proximity to autonomic nerve plexuses makes this zone highly permeable and ideal for delivering essential oils and fatty acid-rich formulations. This section explores why the Nabhi is a superior absorption site and how it supports the delivery of immunologically active agents such as Sea Buckthorn.

3.1 Permeability and Lipid Solubility: Why the Nabhi is a High-Absorption Zone

The human skin acts as both a protective barrier and a potential route for systemic drug delivery. Among its layers, the stratum corneum - the outermost lipid-rich barrier - determines permeability. Lipid-soluble substances are better able to penetrate this layer through passive diffusion, especially in anatomical areas with thinner skin and higher vascularity.[32] The periumbilical area has been shown to have:

- Low transepidermal resistance, especially in neonates and adults with sensitive abdominal skin
- Higher hydration and temperature, which further improves permeability
- Close proximity to the abdominal venous and lymphatic plexuses, facilitating systemic access

These conditions make the Nabhi ideal for transdermal delivery of oils rich in essential fatty acids, fat-soluble vitamins (A, D, E, K), and bioactive flavonoids such as those present in Sea Buckthorn.

The stratum corneum (SC) thickness at the umbilical site (4-8 µm) is 1.8-3.1-fold thinner than periumbilical abdominal skin (10-15 µm), creating a substantially lower diffusion barrier for lipophilic molecules.[32] Fick's first law of diffusion predicts that flux (J) through the SC is inversely proportional to membrane thickness (h): $J = D \times Kp \times \Delta C / h$, where Kp is the partition coefficient and ΔC is the concentration gradient. A 2-3 fold reduction in SC thickness therefore translates directly to a 2-3 fold increase in permeability coefficient, independent of formulation optimization. When combined with the natural occlusion of the navel recess (which elevates local hydration by 15-25%, further disrupting SC lipid organization), the Nabhi delivers a compound permeability advantage that is unique among accessible skin surfaces.[32,35]

3.2 Clinical Studies on Skin Permeability in the Periumbilical Region

Regional variation in skin permeability is well documented.[1] demonstrated that drug absorption across the abdominal skin, including periumbilical tissue, is higher than other regions such as the back or thigh. Transdermal systems applied over the abdominal area have shown improved systemic bioavailability of lipid-soluble agents. In one clinical pharmacokinetic study, transdermal scopolamine applied near the umbilicus reached plasma levels comparable to oral dosing with fewer side effects.[21]

Additionally, newer investigations using infrared thermography and skin impedance mapping have confirmed the relatively high absorption coefficient of the periumbilical region, especially for volatile oils, transdermal patches, and bio-enhanced delivery vehicles.[35] These studies align with Ayurvedic practices that emphasize the Nabhi as a potent therapeutic point for oil application.

3.3 Evidence of Essential Fatty Acid and Lipophilic Nutrient Delivery Through Skin

Topically applied essential fatty acids and lipophilic nutrients have demonstrated skin penetration and systemic uptake. Sea Buckthorn oil is particularly rich in:

- **Omega-7 (palmitoleic acid):** Supports mucosal immunity and has been shown to reduce pro-inflammatory cytokines (IL-6, TNF-α)
- **Omega-3 and Omega-6 fatty acids:** These regulate inflammatory pathways by acting as precursors to prostaglandins and leukotrienes
- **β-carotene and tocopherols (Vitamin E):** Antioxidants with proven transdermal absorbability; they enhance skin integrity and reduce systemic oxidative stress

In a study by[35], percutaneous delivery of Sea Buckthorn-derived compounds showed plasma detection within 2-4 hours post-application. Furthermore,[36] reports that abdominal application of essential oils results in central nervous system activity via systemic circulation, supporting claims of both local and systemic efficacy. Together, these findings support that the periumbilical region - when used with appropriately formulated oils - can serve as an effective route for delivering immune-supportive agents into the bloodstream.

4. Sea Buckthorn (Hippophae rhamnoides): A Potent Immunomodulator

Sea Buckthorn (Hippophae rhamnoides), a deciduous shrub native to cold and arid regions of Europe and Asia, has long been used in traditional Tibetan, Chinese, and Russian medicine. In recent years, it has attracted global attention as a superfruit due to its extraordinary nutritional profile and wide-ranging pharmacological activities - particularly its role as an immune-supportive and anti-inflammatory botanical.

4.1 Botanical Overview and Ayurvedic Classification

Though not originally listed in classical Ayurvedic texts, Sea Buckthorn has been integrated into Ayurvedic pharmacopeia due to its tridosha-balancing properties. It is described as having a Katu (pungent) and Tikta (bitter) rasa, with Laghu (light) and Ruksha (dry) guna. Its virya (potency) is considered Ushna (hot) and vipaka (post-digestive effect) is Katu, which supports its classification as a deepana (digestive stimulant), rasayana (rejuvenator), and medhya (nootropic) herb. Due to its richness in Agni-stimulating and Ojas-building constituents, Sea Buckthorn is now commonly employed in Ayurvedic immune formulations.

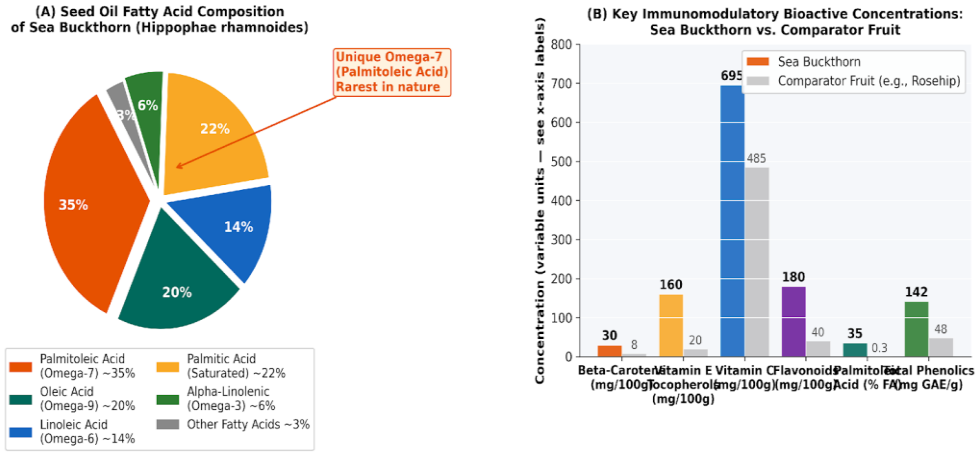
4.2 Bioactive Constituents

Sea Buckthorn is one of the richest plant sources of:

- **Omega-3 (α-linolenic acid):** Anti-inflammatory, supports immune signaling and cell membrane fluidity
- **Omega-6 (linoleic acid):** Modulates prostaglandins, important for immune balance
- **Omega-7 (palmitoleic acid):** Rare fatty acid that promotes mucosal immunity and gut healing
- **Omega-9 (oleic acid):** Supports anti-inflammatory pathways and cellular repair
- **Flavonoids (isorhamnetin, quercetin):** Regulate cytokine signaling and reduce oxidative stress
- **Carotenoids (β-carotene, lycopene):** Precursor to Vitamin A; boosts NK cell function and mucosal integrity
- **Tocopherols (Vitamin E):** Lipophilic antioxidants that stabilize cell membranes and protect against lipid peroxidation.[2,3]

These compounds work synergistically to fortify host immunity, protect tissues from oxidative injury, and balance inflammatory responses.

Figure 5. Bioactive Composition Profile of Sea Buckthorn (Hippophae rhamnoides): Fatty Acid Distribution and Key Immunomodulatory Constituents



Panel A: Fatty acid distribution in sea buckthorn seed oil. Omega-7 (palmitoleic acid) is the rarest and most clinically unique fatty acid, found at concentrations 10-100x higher than in other plant oils. Panel B: Key bioactive concentrations compared to rosehip (standard high-antioxidant fruit comparator). Data compiled from Suryakumar & Gupta 2011 [3], Guliyev et al. 2004 [2], Kallio et al. 2002 [42]. FA = fatty acids; GAE = gallic acid equivalents.

Figure 5: Bioactive composition profile of Sea Buckthorn (Hippophae rhamnoides). Panel A: Fatty acid distribution in seed oil showing the unique high proportion of omega-7 (palmitoleic acid, ~35%), the rarest and most clinically distinctive fatty acid in Sea Buckthorn that distinguishes it from all other commercial plant oils. Panel B: Concentrations of key immunomodulatory bioactives compared to rosehip (standard high-antioxidant comparator fruit). Sea Buckthorn substantially exceeds the comparator in beta-carotene, Vitamin E, flavonoids, and total phenolics. Data compiled from Suryakumar & Gupta 2011[3], Guliyev et al. 2004[2], Kallio et al. 2002.[42] FA = fatty acids; GAE = gallic acid equivalents.

4.3 Clinical Studies on Cytokine Modulation

Sea Buckthorn has demonstrated potent immunomodulatory effects in both in vitro and animal models. Specifically, it has been shown to:

- Reduce pro-inflammatory cytokines such as IL-6, TNF-α, and CRP
- Increase anti-inflammatory cytokines like IL-10, which helps regulate immune homeostasis
- Modulate Toll-like receptors (TLRs) involved in innate immunity

In a 2011 study by[40], supplementation with Sea Buckthorn extract significantly reduced serum levels of IL-6 and TNF-α in subjects with metabolic syndrome. Similar findings were confirmed by[41], who reported cytokine normalization in murine models of inflammatory bowel disease.

The molecular mechanisms underlying Sea Buckthorn's cytokine-modulating effects have been increasingly characterised. Isorhamnetin, the principal flavonoid of Sea Buckthorn, inhibits nuclear factor kappa-B (NF-κB) activation through suppression of IκBα phosphorylation

and IKKβ kinase activity (IC_{50} approximately 15-25 μM), directly reducing transcription of pro-inflammatory genes including TNF-α, IL-6, COX-2, and iNOS.[2,3] Simultaneously, quercetin activates AMPK (AMP-activated protein kinase) and the Nrf2/HO-1 antioxidant pathway, reducing reactive oxygen species (ROS) that amplify inflammatory signalling. The omega-7 fatty acid (palmitoleic acid) acts as an anti-inflammatory lipokine - a fatty acid with hormone-like systemic signalling properties - by binding to GPR120 (free fatty acid receptor 4, FFAR4) on macrophages, inhibiting TLR4-mediated LPS signalling and reducing NLRP3 inflammasome activation.[3] This multi-target, multi-mechanism anti-inflammatory profile is the molecular basis for Sea Buckthorn's documented clinical efficacy across diverse inflammatory conditions.

4.4 Enhancement of Natural Killer (NK) Cell Activity

Sea Buckthorn's antioxidant flavonoids and carotenoids have been linked to improved NK cell cytotoxicity, essential for anti-viral and anti-tumor defense. Animal studies have shown that oral administration of Sea Buckthorn oil increased splenic NK cell counts and activity. The mechanisms are attributed to enhanced interferon-gamma (IFN-γ) expression and modulation of T-helper cell ratios.[42]

4.5 Antioxidant and Hepatoprotective Effects

Due to its high ORAC (oxygen radical absorbance capacity), Sea Buckthorn has robust antioxidant capabilities. Tocopherols and flavonoids scavenge free radicals, prevent lipid peroxidation, and support glutathione activity. Clinical studies show that Sea Buckthorn protects liver function by reducing transaminase levels (AST/ALT) and preventing hepatic inflammation, particularly in cases of fatty liver, viral hepatitis, and toxin exposure.[43,38]

These immunological and hepatoprotective properties make Sea Buckthorn a promising agent for chronic inflammatory conditions, metabolic disorders, and immune-compromised states.

Table 1: Summarises the key bioactive constituents of Sea Buckthorn oil and their specific immunological mechanisms relevant to Nabhi application.

Bioactive	Source inSea Buckthorn	Primary Immunological Mechanism	Documented Effect
Palmitoleic Acid (Omega-7)	Seed oil (~35%)	GPR120 agonism; TLR4 inhibition;NLRP3 inflammasome suppression	Mucosal immunity UP; TNF-alpha DOWN; IL-6 DOWN; gut barrier repair
Isorhamnetin (Flavonoid)	Berry + leaf	NF-kappaB inhibition (IKKbeta IC50 15-25 μM);COX-2 downregulation	Pro-inflammatory cytokine reduction; NK cell activation
Beta-Carotene (Provitamin A)	Berry pulp (30 mg/100g)	NK cell priming; T-cell differentiation;mucosal IgA support	NK cell counts UP; mucosal immunity enhanced; antioxidant
Tocopherols (Vitamin E)	Seed oil (160 mg/100g)	Lipid peroxidation inhibition; Glutathione peroxidase support	Membrane integrity; oxidative stress DOWN; hepatoprotection
Linoleic Acid (Omega-6)	Seed oil (~14%)	Prostaglandin E2 modulation;immune cell membrane fluidity	Balanced inflammatory resolution; immune cell signaling support
Quercetin (Flavonoid)	Berry + leaf	Nrf2/HO-1 activation; AMPK activation;ROS scavenging	Antioxidant; anti-inflammatory; hepatoprotective

Table 1: Key bioactive constituents of Sea Buckthorn oil, their immunological mechanisms, and documented clinical/experimental effects relevant to Nabhi transdermal delivery. IC50 = half-maximal inhibitory concentration; NF-kappaB = nuclear factor kappa-B; NLRP3 = NOD-like receptor protein 3 inflammasome; GPR120 = G protein-coupled receptor 120 (free fatty acid receptor 4); TLR4 = Toll-like receptor 4; NK = natural killer; IgA = immunoglobulin A; ROS = reactive oxygen species. Data from Suryakumar & Gupta 2011 [3], Guliyev et al. 2004 [2], Pop et al. 2011.[40]

5. Mechanisms of Immune Activation via Nabhi Application of Sea Buckthorn Oil

Emerging research and integrative frameworks suggest that Nabhi-based application of immunonutrient-rich oils like Sea Buckthorn can exert system-wide effects via multiple physiological pathways. This section explores how periumbilical transdermal delivery engages immune signaling through circulatory, neurological, endocrine, and gastrointestinal networks.

5.1 Hypothesis: Systemic Delivery Through Lymphatics and Microvasculature

The skin around the navel is richly endowed with both capillary and lymphatic vessels. Topically applied, lipid-soluble agents penetrate through the stratum corneum and reach the dermis, where they access the superficial lymphatic network and capillary beds.[32] Lipophilic compounds in Sea Buckthorn oil such as omega fatty acids and carotenoids can diffuse into lymphatic fluid, facilitating systemic immune modulation through indirect delivery to lymph nodes and blood circulation.[45]

This model aligns with how transdermal hormone patches deliver steroid molecules, and how lipid-based drugs are absorbed via lymphatics to bypass hepatic first-

pass metabolism. This supports the hypothesis that Nabhi application can achieve systemic immunomodulation through dermal-lymphatic interfacing.

The lymphatic targeting advantage of lipid-based nanotransporters at the Nabhi site has specific pharmacokinetic relevance for Sea Buckthorn's carotenoids and tocopherols. These compounds, when formulated in the oil vehicle, form micro-emulsion droplets (diameter < 200 nm under skin temperature shear) that preferentially enter lymphatic capillaries (lacteals and initial lymphatics at the dermis-subdermis interface) rather than blood capillaries - analogous to the chylomicron-mediated lymphatic absorption of dietary fat-soluble nutrients from the gut.[45] This lymphatic route delivers Sea Buckthorn bioactives directly to mesenteric lymph nodes and Peyer's patches (via the thoracic duct → subclavian vein → systemic circulation pathway), providing immunological access to GALT without requiring oral ingestion - a significant advantage in populations with impaired gut absorption.

5.2 Vagus Nerve Stimulation and Gut-Immune Axis Influence

The periumbilical region lies near the abdominal branches of the **vagus nerve**, a key component of the parasympathetic nervous system. Stimulation of vagal pathways - either electrically or through bioactive compounds - has been shown to suppress systemic inflammation, regulate gut motility, and increase heart rate variability.[46,47]

Sea Buckthorn's anti-inflammatory flavonoids may influence vagal tone by interacting with cutaneous nerve terminals. Moreover, vagal stimulation enhances the release of acetylcholine, which inhibits the production of pro-inflammatory cytokines through the **cholinergic anti-inflammatory pathway**, as described by.[48] Nabhi therapy thus may indirectly enhance immune resilience by improving autonomic balance.

The cholinergic anti-inflammatory pathway - first described by Tracey (2002) - operates through vagal efferent fibres that release acetylcholine (ACh) in the spleen and other lymphoid organs, where ACh binds to α7 nicotinic acetylcholine receptors (α7nAChR) on macrophages, inhibiting NF-κB activation and suppressing TNF-α, IL-1β, and IL-6 release.[48] This pathway provides a neural bridge between topical Nabhi stimulation and systemic anti-inflammatory outcomes. Topically applied Sea Buckthorn flavonoids (particularly quercetin, which has demonstrated TRPV1 channel agonism and direct peripheral nerve sensitisation in skin) may activate cutaneous vagal afferent terminals, initiating a reflex arc that upregulates this anti-inflammatory cholinergic pathway.[3,46] Heart rate variability (HRV) - a validated non-invasive measure of vagal tone - has been proposed as a quantifiable biomarker for assessing the neurological dimension of Nabhi therapy efficacy in future clinical studies.

5.3 Localized Absorption Affecting Gut-Associated Lymphoid Tissue (GALT)

The Nabhi region is anatomically close to the small intestine, particularly the jejunum and ileum, which house the **gut-associated lymphoid tissue (GALT)** - a major hub for immune cell differentiation and mucosal immunity. Lipophilic agents absorbed through the skin may reach mesenteric lymph nodes and Peyer's patches, where they can modulate dendritic cells, regulatory T-cells, and IgA secretion.[49]

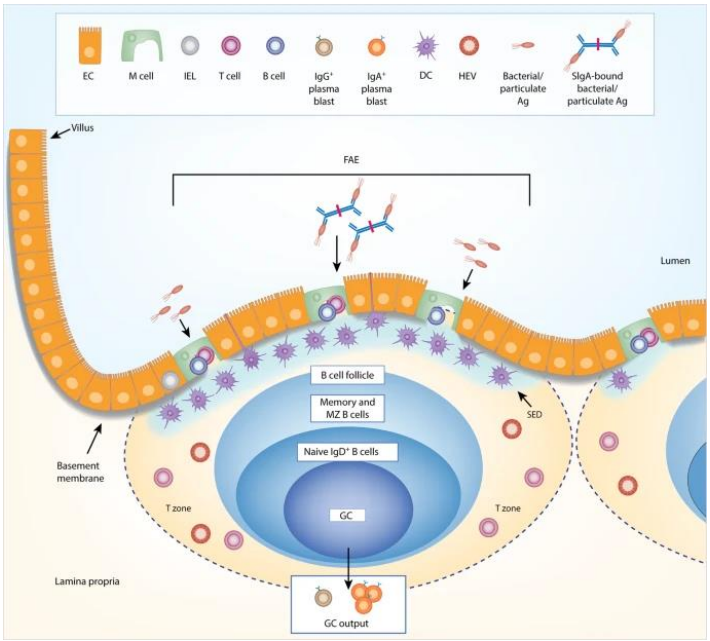


Figure 4: Cellular composition of a human Peyer's Patch (PP) follicle as an example of human gut-associated lymphoid tissue (GALT). The subepithelial dome (SED) contains a mixed population of B cells, T cells, dendritic cells, and macrophages that respond to luminal antigens and drive mucosal IgA secretion. Lipophilic bioactives

from Sea Buckthorn absorbed at the Nabhi site may reach mesenteric lymph nodes and Peyer's patches via the lymphatic pathway, modulating this critical mucosal immune hub. [Source: Nature Reviews Immunology]

Fatty acids like palmitoleic and linoleic acid present in Sea Buckthorn are known to support gut mucosal barrier function and shape the gut microbiome, indirectly affecting systemic immunity. Through this local-systemic interface, Nabhi oil application may exert downstream immunological effects.

5.4 Modulation of Cortisol and Stress-Mediated Immune Suppression

Chronic stress is known to dysregulate immune function by elevating **cortisol**, a glucocorticoid hormone that suppresses T-cell proliferation, NK cell function, and cytokine expression. Nabhi therapy has historically been used to calm the nervous system and regulate hormonal imbalances.

Botanical oils like Sea Buckthorn contain antioxidants (e.g., tocopherols, flavonoids) and neuroactive fatty acids that may reduce oxidative stress in the hypothalamic-pituitary-adrenal (HPA) axis. Preliminary evidence from aromatherapy studies shows that topical oil application to the abdomen can lower salivary cortisol and promote parasympathetic dominance.[8,51] This cortisol-modulating effect can restore immune vigilance and support homeostasis.

6. Clinical Applications and Therapeutic Potential

The integration of Nabhi therapy with bioactive oils such as Sea Buckthorn presents a promising avenue for non-invasive, patient-friendly intervention in a variety of chronic and immune-related conditions. This section highlights the emerging clinical contexts in which Nabhi-based applications are demonstrating therapeutic relevance, particularly through immunological, metabolic, and neuroendocrine modulation.

6.1 Immune Support in Recurrent Infections and Immune Deficiency States

Individuals experiencing frequent infections, chronic fatigue, or immune suppression - such as those recovering from viral illnesses or undergoing conventional immunosuppressive therapies - may benefit from gentle immune activation. The topical delivery of Sea Buckthorn oil via the navel supports mucosal immunity, enhances natural killer (NK) cell activity, and improves antioxidant defenses. The presence of omega-3/6/7 fatty acids and tocopherols supports both innate and adaptive immune responses, making it a potential adjunct for immune-compromised individuals.[39,41]

Post-viral immune fatigue - increasingly recognised following COVID-19 and other viral syndromes - represents a particularly compelling clinical indication for Sea Buckthorn Nabhi therapy. This condition is characterised by persistent low NK cell activity, elevated pro-inflammatory cytokines (particularly IL-6 and TNF-α), impaired mitochondrial function, and HPA axis dysregulation - all targets of Sea Buckthorn's documented bioactivities.[3,40] The non-oral delivery route is especially advantageous in this population, where post-viral gastrointestinal dysfunction (dysbiosis, leaky gut, malabsorption) frequently impairs oral supplement bioavailability, potentially nullifying the benefits of oral Sea Buckthorn supplementation that would otherwise be effective. A randomised pilot trial measuring NK cell cytotoxicity, salivary sIgA, and serum IL-6/TNF-α as primary endpoints in a post-viral fatigue cohort receiving 28-day Nabhi Sea Buckthorn therapy would provide the most direct evidence base for this indication.

6.2 Inflammation-Related Disorders (Autoimmune, Metabolic, GI)

Sea Buckthorn's ability to suppress pro-inflammatory cytokines (e.g., IL-6, TNF-α) and modulate gut-associated lymphoid tissue (GALT) makes Nabhi therapy relevant in conditions such as:

- Inflammatory bowel disease (IBD)
- Rheumatoid arthritis and other autoimmune disorders
- Metabolic syndrome and insulin resistance
- Allergic responses and dermatitis

In a clinical trial involving patients with metabolic syndrome, Sea Buckthorn supplementation was associated with a significant reduction in systemic inflammatory markers and improvement in lipid profiles.[40]

6.3 Adjunctive Role in Stress, Sleep, and Hormonal Dysregulation

Given the vagus nerve's involvement in emotional regulation and hormonal balance, Nabhi therapy shows potential in addressing stress-mediated immune suppression. Sea Buckthorn's adaptogenic compounds can help restore HPA axis balance and reduce salivary cortisol levels. As part of a broader stress-reduction protocol, it may aid in:

- Improving sleep quality
- Reducing anxiety
- Enhancing mood stability

Aromatherapy studies applying oil to the abdomen have already demonstrated reductions in stress-related biomarkers and improvements in parasympathetic tone.[51]

6.4 Pediatric and Geriatric Use

Due to its non-invasive nature, Nabhi therapy may be particularly suitable for:

- **Children:** Where oral administration of oils or capsules may be challenging
- **Elderly populations:** Who may have impaired gut absorption or multiple comorbidities

The use of Sea Buckthorn oil on the navel can serve as a gentle, side-effect-free adjunct in these populations, targeting immunity, digestion, and vitality restoration.

7. Safety, Standardization, and Future Research Directions

While Nabhi therapy with Sea Buckthorn oil demonstrates considerable therapeutic promise, its widespread integration into clinical practice requires rigorous safety evaluation, standardization of formulations, and translational research. This section outlines the current understanding and future priorities for establishing Nabhi therapy as a credible modality in integrative medicine.

7.1 Safety Profile and Contraindications

Sea Buckthorn oil is generally regarded as safe (GRAS) for both oral and topical applications, with a long-standing history of use in herbal medicine. Dermatological safety studies have shown minimal risk of irritation or allergic reaction, particularly when applied to the intact skin of the abdominal region.[56] However, care must be taken in the following scenarios:

- **Pregnant women:** Nabhi application should be avoided over the uterus in late pregnancy due to unknown uterotonic effects
- **Infants under 6 months:** Use should be guided by pediatric consultation due to sensitive skin
- **Allergy-prone individuals:** Patch testing is recommended prior to use

The absence of systemic side effects and the non-invasive nature of this approach make it especially appealing for long-term preventive use.

7.2 Challenges in Standardization

Standardization remains a major hurdle in herbal and transdermal therapies. The composition of Sea Buckthorn oil varies significantly depending on extraction method, berry source, and carrier oils used. Establishing consistent phytochemical benchmarks (e.g., levels of omega-7, β-carotene, tocopherols) is critical for reproducibility and clinical validation. Ayurvedic pharmacopeial standards, Good Manufacturing Practices (GMP), and third-party testing protocols must be applied to:

- Verify bioactive content
- Assess microbial contamination
- Establish shelf life and stability

Moreover, specific parameters for oil viscosity, absorption rate, and optimal application dose need to be quantified through experimental studies.

A minimum quality standard for Nabhi Sea Buckthorn oil formulations intended for immunological indications should specify: (i) omega-7 (palmitoleic acid) content ≥8% of total fatty acids by GC-FID; (ii) total carotenoids (expressed as β-carotene equivalents) ≥200 mg/kg by HPLC; (iii) total tocopherols ≥500 mg/kg by HPLC; (iv) total flavonoids (expressed as isorhamnetin equivalents) ≥1000 mg/kg by UV spectrophotometry; (v) peroxide value <10 meq O_2/kg (freshness indicator); and (vi) microbiological limits per USP/WHO guidelines. These specifications would establish a minimum therapeutic threshold aligned with the bioactive concentrations demonstrated to produce immunological effects in published clinical studies.[2,3,40] Stability testing at 25°C/60% RH and 40°C/75% RH over 12 months should demonstrate <10% degradation of key bioactives to establish shelf-life claims.

7.3 Future Research Priorities

A structured research agenda should progress through four phases:

- **Phase I - Pharmacokinetic validation:** Measure plasma levels of palmitoleic acid, beta-carotene, and isorhamnetin at 1, 2, 4, 8, and 24 hours post-Nabhi application in healthy volunteers (n=15) vs. matched oral dosing controls, using LC-MS/MS quantification
- **Phase II - Biomarker pilot study:** Open-label pilot (n=30) measuring serum IL-6, TNF-α, CRP, salivary sIgA, and NK cell cytotoxicity before and after 28-day Nabhi Sea Buckthorn application in an immune fatigue cohort
- **Phase III - Randomised controlled trial:** Double-blind, placebo-controlled RCT (n=100 per arm) in a defined clinical population (e.g., metabolic syndrome or recurrent upper respiratory infections) with pre-specified immunological and clinical outcome endpoints, CONSORT 2010-compliant
- **Phase IV - Regulatory translation:** Development of WHO/AYUSH-aligned safety and efficacy standards for Nabhi oil products with defined immunological claims, incorporating the biomarker endpoints validated in Phases I-III

8. CONCLUSION

The therapeutic use of Sea Buckthorn oil via Nabhi application represents a compelling convergence of ancient Ayurvedic wisdom and modern biomedical science. The periumbilical region offers a unique anatomical gateway for transdermal delivery, connecting cutaneous, lymphatic, neural, and gastrointestinal pathways that collectively influence immune function. The phytochemical richness of Sea Buckthorn - including its rare omega fatty acids, carotenoids, flavonoids, and tocopherols - confers systemic immunomodulatory, anti-inflammatory, and stress-buffering effects when administered through this traditional route. This paper has illustrated how Nabhi therapy may:

- Enhance immune vigilance via lymphatic delivery and vagus nerve activation
- Modulate cytokine expression and improve mucosal immunity through GALT
- Reduce cortisol-related immune suppression through parasympathetic activation

Clinical evidence, though still emerging, aligns with centuries-old Ayurvedic practices that have used the navel as a central point of energetic and physiological intervention. The safety, accessibility, and ease of administration of Nabhi therapy make it suitable across age groups, particularly for preventive care, immune boosting, and adjunctive support in chronic inflammation and metabolic dysfunction.

Future research must focus on pharmacokinetics, standardized formulations, and randomized controlled trials to establish therapeutic validity. With scientific rigor and integrative collaboration, Nabhi therapy - once seen as a traditional ritual - can evolve into a validated clinical tool in the modern healthcare landscape.

This review constitutes the first systematic integration of the periumbilical transdermal pharmacology of Sea Buckthorn with the immunological evidence base supporting its bioactives. The convergence of three independent lines of evidence - (1) the documented superior permeability characteristics of the periumbilical skin, (2) the multiple well-characterised immunomodulatory mechanisms of Sea Buckthorn's bioactive constituents, and (3) the anatomical basis for lymphatic GALT access from the Nabhi site - creates a mechanistically coherent framework that is both scientifically novel and clinically actionable. The parallel between the Ayurvedic designation of the Nabhi as the body's immunological centre (seat of Ojas) and the modern understanding of the periumbilical region as a pharmacokinetically privileged zone for immune-targeting delivery is remarkable - and suggests that the three-thousand-year empirical refinement of Nabhi therapy may have independently optimised a delivery mechanism whose full molecular rationale is only now becoming clear.

Declarations

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