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Review

Advanced Applications of Vitamin B Complex in Plastic and Cosmetic Surgery: Mechanisms and Therapeutic Benefits

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Abstract

The vitamin B complex, a group of water-soluble vitamins, is essential for various metabolic and cellular processes and critical for achieving optimal surgical outcomes in plastic and cosmetic procedures. This review examines the mechanistic contributions of this complex at the cellular level, including any roles in mitochondrial bioenergetics, redox balance, gene regulation, and cellular repair mechanisms. Niacinamide, as a precursor to NAD^+, enhances mitochondrial efficiency and facilitates energy production, supporting tissue regeneration. Pyridoxine functions as a cofactor in neurotransmitter biosynthesis and amino acid metabolism, contributing to nerve recovery post-surgery. Furthermore, cobalamin is crucial for maintaining the myelin sheath and facilitating axonal repair, thereby ensuring neuronal integrity and minimizing nerve damage. Additionally, pantothenic acid, through its role in coenzyme A synthesis, regulates fatty acid metabolism and accelerates cellular repair, aiding in wound healing. Biotin is fundamental for keratin synthesis and follicular cell proliferation, promoting skin integrity and hair regeneration, which are vital in aesthetic and reconstructive treatments. Meanwhile, thiamine ensures a sufficient energy supply for neuronal recovery and cellular resilience through modulating carbohydrate metabolism. Thus, by integrating these cellular mechanisms, the vitamin B complex enhances tissue repair, minimizes inflammation, and improves both aesthetic and functional outcomes. Advances in precision supplementation, innovative drug delivery methods, and regenerative medicine continue to expand the therapeutic potential of B vitamins in plastic and reconstructive surgery. This comprehensive overview underscores the clinical significance of these vitamins in optimizing surgical recovery and promoting long-term tissue health.

Keywords: vitamin B complex; skin; antiaging; wound healing; cellular metabolism

1. Introduction

Plastic and cosmetic surgery is a multifaceted and rapidly advancing discipline dedicated to the repair, reconstruction, and enhancement of the human body [1]. With the growing demand for procedures aimed at improving aesthetic appearance and functional outcomes, there is an increasing focus on optimizing perioperative care and outcomes. In recent years, the integration of nutritional science into surgical practice has opened new avenues for enhancing recovery, minimizing complications, and improving long-term results. Among various nutrients, the vitamin B complex has emerged as a metabolic and therapeutic agent, particularly in fields such as wound healing, scar modulation, nerve protection, and skin rejuvenation. Its biochemical versatility and systemic effects offer potential benefits that align with the physiological demands of plastic surgery [2]. The vitamin B complex comprises water-soluble vitamins, such as niacinamide (B3), pantothenic acid (B5), biotin (B7), thiamine (B1), pyridoxine (B6), and cobalamin (B12). Each of these vitamins has a unique and critical role in energy production, cellular metabolism, and neurological function [3,4]. Thiamine is crucial for carbohydrate metabolism, acting as a coenzyme in the Krebs cycle and the pentose phosphate pathway [5,6]. It facilitates the activity of key enzymes such as pyruvate dehydrogenase and α-ketoglutarate dehydrogenase, which are essential for ATP production [7,8]. In addition, thiamine is particularly important for nerve function, as it aids in neurotransmitter synthesis. A deficiency in thiamine leads to conditions such as beriberi, which affects the cardiovascular and nervous systems, and Wernicke-Korsakoff syndrome, which is often associated with chronic alcohol consumption and manifests as confusion, ataxia, and memory loss [5,9]. Niacin is a precursor for nicotinamide adenine dinucleotide (NAD) and its phosphate form (NADP), which are essential cofactors in metabolic reactions that produce cellular energy. These cofactors are involved in glycolysis, the citric acid cycle, and oxidative phosphorylation, making niacin crucial for ATP generation [10]. Additionally, niacin plays a role in DNA repair and cellular signaling. Niacin deficiency results in pellagra, a condition marked by the “three Ds”;

dermatitis, diarrhea, and dementia, which can be fatal if untreated [11,12]. Niacin has demonstrated benefits in plastic surgery by enhancing wound healing and improving tissue viability, particularly in preoperative flap preparation. Its role in collagen synthesis makes it a valuable supplement, although caution is warranted due to risks like thrombocytopenia and anemia with long-term use [13,14]. In addition, pantothenic acid is an essential component of coenzyme A (CoA), which is required for the metabolism of carbohydrates, proteins, and fats. It has a significant role in fatty acid synthesis and oxidation, as well as in the biosynthesis of acetylcholine, steroid hormones, and neurotransmitters. Since CoA is involved in numerous metabolic pathways, pantothenic acid deficiency is rare but can lead to symptoms such as fatigue, irritability, and metabolic imbalances [15,16]. Pantothenic acid supports wound healing in plastic surgery by promoting fibroblast proliferation and strengthening connective tissue, such as aponeurosis, at surgical sites. Supplementation, especially when combined with vitamin C, has been shown to improve scar strength postoperatively, suggesting its value in enhancing skin recovery and surgical outcomes [17,18]. Furthermore, vitamin B6, primarily in the form of pyridoxal phosphate (PLP), serves as a coenzyme in over 100 enzymatic reactions, particularly in amino acid metabolism. It is vital for neurotransmitter synthesis, including serotonin, dopamine, and gamma-aminobutyric acid (GABA), which regulate mood and cognitive function [13,19]. Additionally, pyridoxine is involved in hemoglobin production and immune function. A deficiency in B6 can lead to neurological symptoms such as depression, irritability, and seizures, as well as anemia due to impaired hemoglobin synthesis [20,21]. Nevertheless, biotin serves as a coenzyme in carboxylation reactions, playing a crucial role in gluconeogenesis, fatty acid metabolism, and amino acid catabolism [22]. Though rare, biotin deficiency can lead to symptoms like hair loss, dermatitis, and neurological disturbances, often caused by genetic mutations or excessive raw egg white consumption, which inhibits biotin absorption [23,24]. In cosmetic and plastic surgery applications, biotin could enhance skin and hair regeneration by supporting keratin infrastructure, promoting epithelial cell growth, and improving overall dermal health, thereby contributing to improved aesthetic outcomes and postoperative healing [25]. Nevertheless, Cobalamin contributes fundamentally to neurological function, red blood cell formation, and genomic stability through its role in homocysteine metabolism and methylation processes. These functions are particularly relevant in the surgical setting, where adequate B12 levels may support nerve recovery and reduce postoperative complications [26].

These B vitamins work synergistically to support mitochondrial function and energy production, playing vital roles in the electron transport chain, oxidative phosphorylation, and ATP synthesis [27]. Deficiencies in multiple B vitamins can severely impair mitochondrial function, leading to chronic fatigue and an increased risk of neurodegenerative diseases like Alzheimer's and Parkinson's disease [28]. Beyond metabolism, the vitamin B complex exhibits protective effects against oxidative stress, inflammation, and neurodegeneration, which are associated with plastic and cosmetic surgeries [29]. In our article, we explore the emerging significance of the vitamin B complex in plastic and cosmetic surgery, with a focus on its mechanistic roles in wound healing, nerve regeneration, skin restoration, and postoperative recovery. The review highlights how each B vitamin contributes to enhancing surgical outcomes and emphasizes their potential as supportive agents in improving both functional recovery and aesthetic results.

2. Specific Applications of the Vitamin B Complex in Plastic and Cosmetic Surgery

2.1 Niacinamide Related to Skin Restoration and Anti-Aging

The skin barrier serves as a protective layer against environmental stressors, pathogens, and moisture loss [30]. Niacinamide plays a crucial role in enhancing the integrity and function of the skin barrier by stimulating the production of ceramides, free fatty acids, and cholesterol, all of which are essential for maintaining skin hydration and preventing trans-epidermal water loss (Fig. 1) [31]. A clinical study found that topical niacinamide significantly improved skin hydration and barrier function within 12 to 24 weeks after application, leading to enhanced resilience against environmental damage and reduced sensitivity to irritants [26]. Furthermore, Gueniche *et al*. [32] investigated a dermocosmetic formulation (M89PF) containing niacinamide, hyaluronic acid, vitamin E, volcanic mineral water, and probiotic fractions. The study demonstrated that M89PF significantly improved skin hydration, accelerated barrier recovery, enhanced skin renewal, and reduced oxidative stress in both *in vivo* and *ex vivo* models. Clinical trials in women with stressed skin revealed that M89PF also rebalanced the microbiome, diminished fine lines, improved elasticity and radiance, and reduced pigmentation, especially in Asian populations [32]. Additionally, Lee *et al*. [33] found that topical application of niacinamide (2%) combined with human adipocyte-derived stem cell-conditioned media (ADSC-CM) significantly enhanced post-laser skin rejuvenation. Over a 3-week period following ablative fractional CO_2 laser treatment, participants showed marked reductions in wrinkles and pigmentation on the treated side, with greater patient satisfaction and improved global aesthetic scores compared to the control [33]. *In vitro* assays confirmed the combination's anti-inflammatory, antioxidant, and collagen-promoting effects, highlighting its synergistic potential in accelerating skin repair and remodeling after resurfacing procedures [33]. Additionally, a randomized, double-blind clinical study examined the synergistic effect of niacinamide and

4-hexylresorcinol, demonstrating superior skin tone correction and anti-aging benefits by enhancing tyrosinase inhibition, reducing fine lines, and improving skin firmness compared to niacinamide alone [34]. In addition, niacinamide is widely recognized for its depigmenting effects, particularly in reducing post-inflammatory hyperpigmentation (PIH) and melasma. It achieves this by inhibiting the transfer of melanosomes from melanocytes to keratinocytes, thereby decreasing visible skin pigmentation. This mechanism makes niacinamide an effective and safer alternative to hydroquinone for managing hyperpigmentation disorders [35,36]. A study comparing niacinamide to 4% hydroquinone found that it was equally effective in reducing melasma while exhibiting fewer side effects such as irritation and rebound pigmentation [37]. An emerging research has explored the role of niacinamide in combination with other depigmenting agents such as alpha-hydroxy acids (AHAs) and ascorbic acid. The synergistic effects of these compounds enhance skin brightening, reduce blotchiness, and even out skin tone, making niacinamide a critical component in comprehensive anti-pigmentation skincare regimens [38]. Hakozaki *et al*. [39] examined niacinamide and found that it does not inhibit tyrosinase or melanogenesis but significantly reduces melanosome transfer (35–68%) from melanocytes to keratinocytes. Clinical trials in Japanese women showed that a 5% niacinamide moisturizer decreased hyperpigmentation and increased skin lightness after four weeks, while 2% niacinamide with sunscreen further enhanced skin lightening [39]. A 12-week clinical study assessed the efficacy of a serum containing 5% niacinamide, 3% tranexamic acid (TXA), and 1% kojic acid in treating melasma and PIH in 55 Brazilian women with Fitzpatrick skin types I–IV, demonstrating significant improvements in pigmentation, skin tone homogeneity, and texture as early as week 2 with continued progress through week 12, highlighting niacinamide's role in inhibiting melanosome transfer and improving skin hydration [40]. Kimball *et al*. [41] reported that a topical formulation containing 4% niacinamide and 2% N-acetyl glucosamine significantly improved facial hyperpigmentation, enhanced skin tone uniformity, and supported epidermal turnover over 10 weeks. The observed effects were attributed to the inhibition of melanosome transfer and improved barrier function, offering a well-tolerated, non-hydroquinone-based strategy for addressing uneven pigmentation [41]. Furmanczyk *et al*. [42] evaluated a depigmenting gel serum containing niacinamide, tranexamic acid, 4-butylresorcinol, phytic acid, and hydroxy acids, showing a 67% reduction in melanin production and a 31% decrease in melanin index after 84 days, reinforcing niacinamide's depigmenting effects. Mi *et al*. [43] further confirmed niacinamide's environmental protection benefits, showing that 5 mmol/L niacinamide inhibited pollution-induced melanogenesis, preventing benzo(a)pyrene-induced pigmentation in a reconstructed human epidermis model, indicating its efficacy against environmental stressors. Chronic inflammation and oxidative stress contribute to skin aging, leading to fine lines, wrinkles, and loss of elasticity. In addition, niacinamide has been shown to counteract these effects by downregulating the production of pro-inflammatory cytokines, such as interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-α) [44,45]. This anti-inflammatory action is particularly beneficial in reducing redness, irritation, and photodamage associated with prolonged sun exposure [46]. Monfrecola *et al.* [45] study found that nicotinamide significantly downregulates UVB-induced pro-inflammatory cytokines IL-6, IL-10, MCP-1, and TNF-α in HaCaT keratinocytes, with the most effective reduction observed at 5 mM concentration. Nicotinamide exerts anti-inflammatory and immunomodulatory effects by inhibiting poly (ADP-ribose) polymerase (PARP)-1 and modulating NF-κB activity, reducing UV-induced skin inflammation and damage [45]. Another study showed that niacinamide significantly reduces UVB-, pollution-, and cigarette smoke-induced inflammation in keratinocytes by lowering IL-6, IL-8, and PGE2 levels while restoring Lamin B1. The study confirmed the ability of 5% niacinamide to reduce UV-induced erythema and skin inflammation markers (IL-1aRA/IL-1a) [47]. Zhou *et al*. [48] investigated the anti-inflammatory effects of niacin and its underlying mechanisms. The results showed that niacin reduces the production of pro-inflammatory cytokines in a dose-dependent manner while inhibiting NF-κB activation by blocking the phosphorylation of p65 and IκBα, thereby preventing inflammatory signaling [48]. Further analysis reveals that these effects are mediated through the HCA2 receptor, as silencing HCA2 or inhibiting G-protein signaling abolishes niacin's protective action [48]. A recent study demonstrated that niacinamide enhances dermal collagen synthesis, leading to improved skin elasticity and reduced wrinkle formation. By stimulating fibroblast activity and increasing ECM components, niacinamide contributes to skin firmness and structural integrity, making it a valuable ingredient in anti-aging skincare formulations [49]. In addition, a study explored the combined effects of niacinamide, vitamin C, and polydeoxyribonucleotide in mitigating melanogenesis by modulating nicotinamide nucleotide transhydrogenase, showing that this combination reduced oxidative stress, inhibited tyrosinase activity, and decreased melanin production in UV-B-irradiated animal skin [46]. Kim *et al*. [50] synthesized a niacinamide derivative (N-nicotinoyl dopamine, NND) with enhanced antioxidant properties, demonstrating that topical 0.1% NND reduced melanin production while neutralizing oxidative stress, reinforcing niacinamide's role as a potent free-radical scavenger.

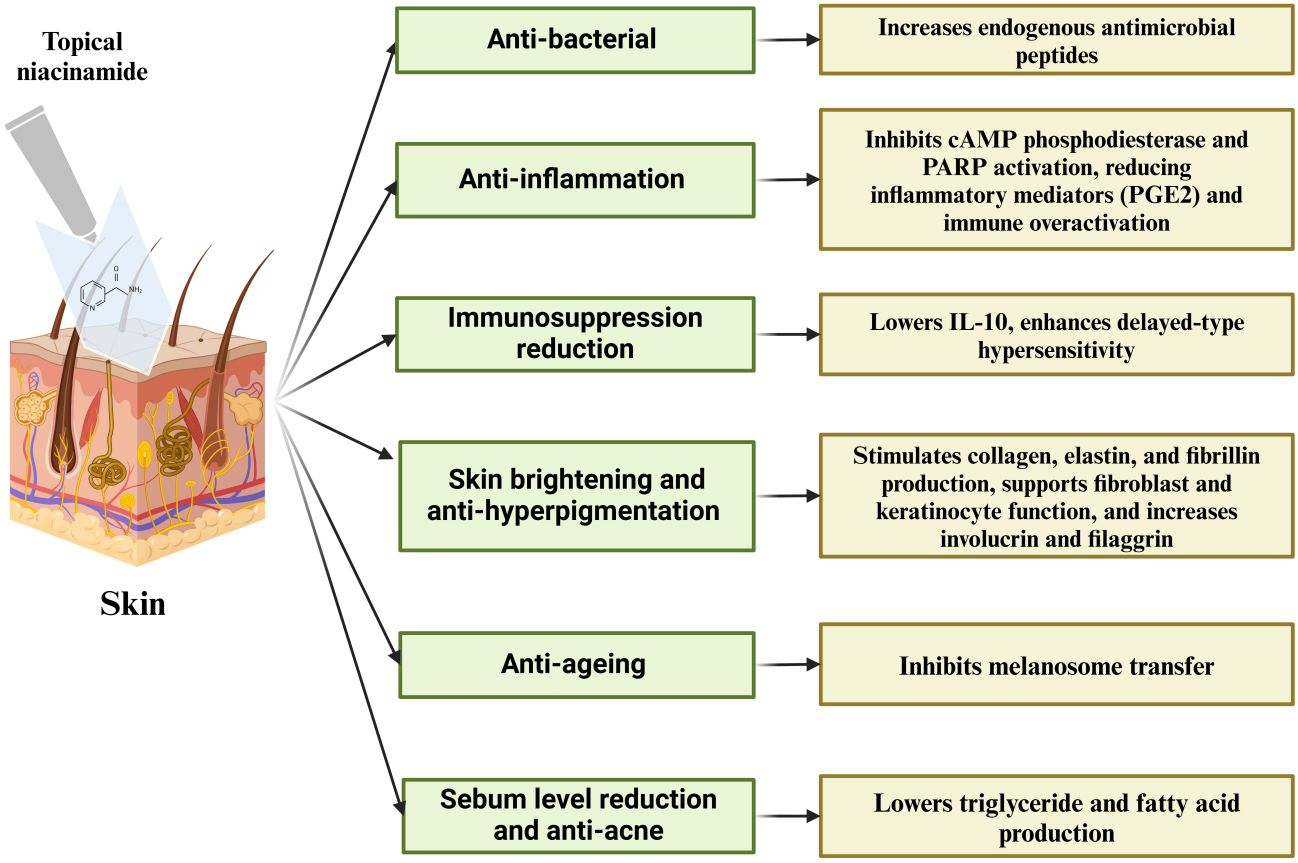

Fig. 1. Therapeutic benefits and biological effects of topical niacinamide in skin health.

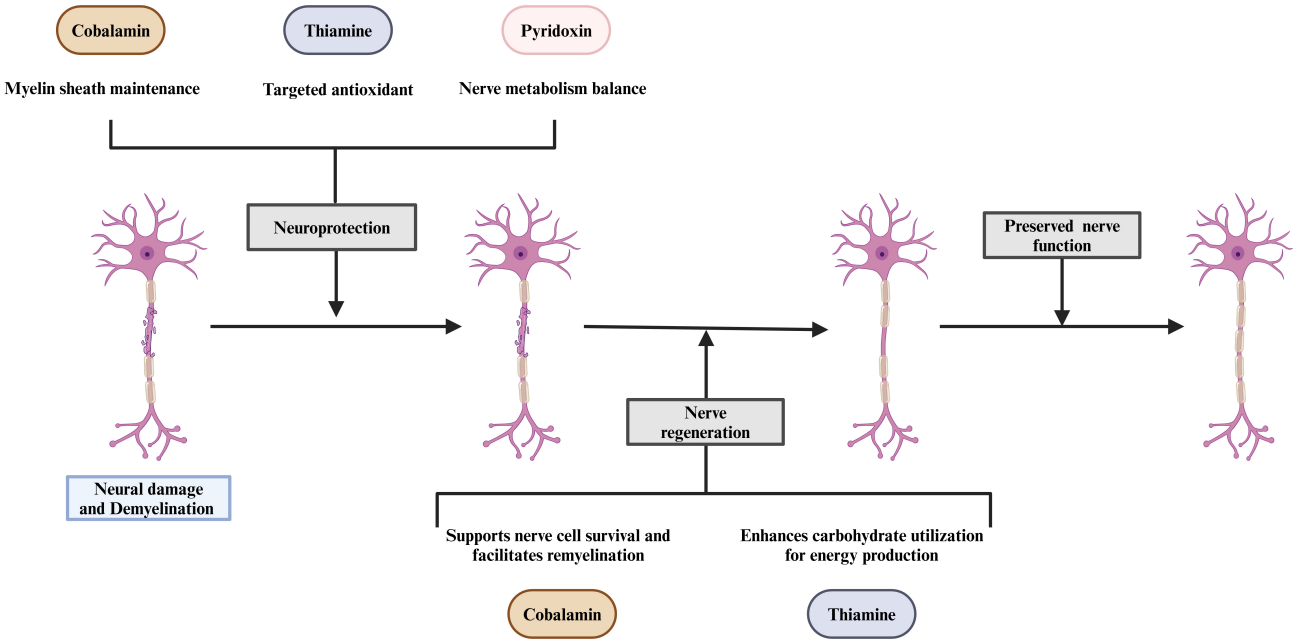

Fig. 2. The role of Cobalamin, Thiamine, and Pyridoxine in neuroprotection, nerve regeneration, and function preservation.

2.2 Pantothenic Acid: Wound Healing and Scar Management

Pantothenic acid and its derivatives, including dexpanthenol, have an essential role in wound healing through their involvement in cellular regeneration, inflammation, modulation, and collagen synthesis. Recent studies have demonstrated the efficacy of these compounds in promoting faster wound closure and improving healing outcomes.

A 5% dexpanthenol ointment significantly accelerates mucosal wound healing in a 3D nonkeratinized model with CO_2 laser-induced lesions. It enhances wound closure and upregulates key wound-healing genes (*CXCL10*, *MUC4*, *MUC16*, *MUC20*, *RARRES1*), promoting epithelialization and tissue repair, confirming its therapeutic potential [51]. Yildizhan *et al*. [52] and Küba *et al*. [53] found that dexpanthenol accelerates wound healing in animal models, with dexpanthenol showing comparable effects to sucralfate and superior results to other compounds in certain contexts. Heise *et al*. [54] further confirmed that a dexpanthenol-containing ointment significantly accelerated wound healing and improved cosmetic outcomes following fractional CO_2 laser resurfacing of photo-damaged skin. Compared to petroleum jelly, dexpanthenol-treated areas showed faster re-epithelialization, smaller lesion diameters, and higher patient and investigator satisfaction within the first 5 days post-treatment. These effects are attributed to dexpanthenol's ability to enhance hydration, stimulate epithelial repair, and support collagen remodeling [54]. Pantothenic acid has been shown to promote wound healing by enhancing the migration and proliferation of keratinocytes and fibroblasts, which are essential for epithelialization and collagen production [51,55]. Furthermore, the impact of pantothenic acid on the immune system, specifically its ability to modulate cytokine production. Pantothenic acid triggers immune cells to produce a range of cytokines, influencing both pro-inflammatory and anti-inflammatory responses, which is particularly beneficial in controlling excessive inflammation during wound healing [56]. The paradoxical nature of pantothenic acid's effects can shift the balance between proinflammatory and anti-inflammatory cytokines depending on the physiological context, thus enhancing its therapeutic potential in various inflammatory and immune-related conditions [57]. Etensel *et al*. [58] showed dexpanthenol significantly mitigated oxidative stress and tissue injury in a rat model of testicular ischemia-reperfusion injury. Administering dexpanthenol at 500 mg/kg reduced serum malondialdehyde levels and improved histopathological scores, indicating lower lipid peroxidation and structural damage. These protective effects are attributed to its role in boosting reduced glutathione, Coenzyme A, and ATP synthesis, thereby enhancing cellular resilience against ROS-induced injury [58]. Similarly, Heise *et al*. [59] revealed that dexpanthenol modulates gene expression to promote skin regeneration and improve wound healing at the molecular level. This regenerative effect is further supported by Proksch *et al*. [60], who reviewed dexpanthenol's long-established use in skin care, emphasizing its ability to restore the skin barrier and hydrate the skin, while Dell'Acqua and Schweikert [61] found that its derivative, panthenyl triacetate, activates metabolic pathways that stimulate skin healing. Furthermore, Ulger *et al*. [62] compared the wound healing efficacy of dexpanthenol and nebivolol in a rat model and found that both agents significantly enhanced healing compared to untreated controls. While wound closure rates were similar between the two treatment groups, dexpanthenol-treated wounds showed significantly lower inflammation and comparable levels of fibrosis and epithelialization [62]. This ability to improve healing was also seen in corneal wounds, as reported by Egger *et al*. [63], who found dexpanthenol effective in reducing pain and promoting recovery. Moreover, Li *et al*. [64] reported that a topical formulation containing 5% panthenol, madecassoside, and essential trace elements (copper, zinc, manganese) significantly improved skin recovery after fractional CO_2 laser resurfacing. The treatment reduced erythema, trans-epidermal water loss, pain, and postoperative edema, while promoting faster crust removal and delivering superior cosmetic outcomes compared to a standard hospital-prepared emollient [64]. Finally, Celebi *et al*. [65] showed that dexpanthenol significantly improved post-tonsillectomy recovery by alleviating pain and accelerating mucosal healing. Taken together, these studies emphasize the significant therapeutic potential of pantothenic acid in facilitating tissue repair, reducing inflammation, and promoting skin regeneration, making it a highly effective and versatile agent in medical, dermatological, and cosmetic surgery applications.

2.3 Biotin: Hair Transplantation and Management

Biotin has gained widespread use as a supplement for the management of hair loss, particularly in cases of biotin deficiency, which can manifest as alopecia, brittle nails, and other dermatologic issues [66]. Several studies have examined the efficacy of biotin in both clinical and experimental settings. El-Esawy *et al*. [67] demonstrated that male patients with androgenetic alopecia (AGA) had significantly lower serum levels of zinc and suboptimal levels of biotin, suggesting that biotin supplementation may improve hair quality and texture, although no correlation with disease severity was observed. Duchi *et al*. [68] introduced a novel encapsulated form of biotin, WS biotin, which significantly enhanced the water solubility of biotin and was shown to promote hair follicle keratin expression and the activation of hair growth-related genes *in vitro*. In a randomized controlled trial by Samadi *et al*. [69], the combination of biotin and dexpanthenol injections significantly improved hair density and reduced hair loss in patients with diffuse hair loss. Chavan [70] reported the successful reversal of premature graying in a 25-year-old female using a topical solution containing α-Melanocyte-Stimulating Hormone Agonist (Greyverse) along with oral biotin supplementation. After five months, the patient showed a $>$90% conversion of gray hair to black [70]. Another study compared the effectiveness of PRP therapy combined with biotin, redensyl, and saw palmetto in treating androgenetic alopecia. Results showed significant improvements in hair regrowth [71]. In addition to its therapeutic potential in hair regrowth, biotin's role in metabolic processes influencing

hair health has been explored. Güder and Eker [72] retrospectively analyzed biotin levels in dermatology patients, finding weak positive correlations between biotin levels and parameters such as basophil count and triglycerides. However, biotin did not show significant changes in hemogram parameters, suggesting that its effects may be more systemic than directly linked to hair growth [72]. Biotin's efficacy in enhancing hair follicle function was also explored in the context of scalp microbiome interventions. Jo *et al*. [73] identified biotin as one of the active compounds in *Staphylococcus epidermidis Cicaria*, a strain derived from the human scalp microbiome, which exhibited the ability to maintain the anagen phase in hair follicles and inhibit hair loss. Moreover, studies such as those by Benke *et al*. [74] have explored biotin's broader implications, specifically its use in patients with autism spectrum disorder and developmental delay, where biotin supplementation restored hair and nail growth in a patient with negligible growth in these areas. Biotin is also included in topical formulations for managing hair loss, such as in combination with other active ingredients like minoxidil or procapil, with studies indicating potential synergistic effects for promoting hair regrowth [75,76]. Sahay described a case of a young male with resistant alopecia areata who showed significant hair regrowth (>90%) after three months of treatment with tofacitinib, a Janus kinase inhibitor, combined with biotin supplementation. This approach led to a positive clinical response, marking biotin as a promising adjunct in resistant alopecia areata cases [77]. Nevertheless, Daulatabad *et al*. [78] investigated serum biotin levels in patients with premature graying (premature canities) and found that while biotin levels were slightly lower in affected individuals, the difference was not as substantial as deficiencies in vitamin B12 and folic acid. This suggests that biotin, though not the primary factor in premature graying, may still play a supportive role in hair pigmentation [78]. In a separate study, Grootens and Hartong [79] reported the successful use of biotin (10,000 µg daily) to treat valproate-induced telogen effluvium in a bipolar disorder patient. After three months of biotin supplementation, the patient's excessive hair loss was reversed, further demonstrating biotin's potential in managing drug-induced hair loss [79]. Furthermore, Weimann *et al*. [80] developed a sensitive assay for measuring biotin levels in plasma, which could improve diagnostic accuracy in clinical settings, particularly when evaluating the impact of high-dose biotin on hormone-related diagnostic tests; therefore, it underscores the importance of monitoring biotin levels in patients undergoing supplementation. However, despite the growing use of biotin supplements for hair management, studies such as those by Lipner and Almohanna *et al*. [81,82] highlight that biotin deficiency is relatively rare in healthy individuals, with biotin supplementation showing benefits primarily in cases of inherited biotinidase deficiency or other specific pathologies. Furthermore, biotin's efficacy in treating hair loss in patients without biotin deficiency remains unsupported by high-quality evidence. For example, a study by Şen and Türkçapar [83] on patients following sleeve gastrectomy found that although biotin supplementation was commonly used to manage post-surgical hair loss, it provided minimal improvement, particularly in patients without confirmed biotin deficiency.

2.4 Thiamine, Pyridoxine, and Cobalamin: Postoperative Nerve Protection

Postoperative nerve injuries represent a significant complication following various surgical procedures, potentially resulting in prolonged recovery, sensory deficits, and motor dysfunction. Optimal nerve recovery and regeneration post-surgery require effective neurometabolic support to maintain neuronal integrity and facilitate repair processes [84]. Recent scientific research highlights the importance of thiamine and cobalamin in enhancing neuronal metabolic efficiency and supporting myelin sheath regeneration, making them essential components of postoperative neurometabolic strategies (Fig. 2) [85,86]. Thiamine serves as a coenzyme for several enzymatic reactions essential for neuronal energy metabolism, particularly in the Krebs cycle and pentose phosphate pathway. These metabolic pathways support ATP production, essential for axonal transport, synaptic function, and neuronal repair [87,88]. Thiamine deficiency has been associated with demyelinating disorders and impaired nerve function. Studies suggest that adequate thiamine levels contribute to Schwann cell function and myelin maintenance, reducing the risk of postoperative neuropathy [89]. In addition, thiamine's role in modulating oxidative stress and inflammatory responses has been highlighted. It supports glutathione production, a key antioxidant, and reduces neuroinflammatory cytokine release, potentially mitigating neuropathic pain following surgery [90]. Experimental studies have demonstrated that thiamine supplementation enhances axonal regeneration following peripheral nerve injury. Research suggests that thiamine promotes the expression of nerve growth factors and accelerates functional recovery in nerve crush injury models. In clinical settings, patients receiving thiamine supplementation have shown improved nerve function and reduced neuropathic pain after surgery, supporting its potential role in postoperative nerve protection [91]. Alemanno *et al*. [92] reported that perineural administration of thiamine with levobupivacaine prolonged postoperative analgesia in patients undergoing interscalene block for shoulder surgery, extending pain relief without significant side effects. Thiamine enhances analgesia by increasing acetylcholine synthesis, which improves nociceptive inhibition at the spinal level, making it a potential adjunct for prolonged postoperative pain management [92]. In a chronic compression dorsal root ganglion model, thiamine administration leads to a dose-dependent reduction in pain sensitivity, stabilization of nerve ex-

citability, and restoration of tetrodotoxin-resistant (TTX-R) sodium currents [93]. Moreover, Benfotiamine (lipid-soluble thiamine) significantly improved nerve conduction velocity (NCV) and reduced advanced glycation end-products, including carboxymethyl-lysine (CML) and 3-deoxyglucosone (3DG)-type AGEs. Preventive administration of benfotiamine nearly normalized NCV and completely inhibited glycoxidation in nerve tissues [94].

Meanwhile, cobalamin is essential for myelin sheath maintenance and repair. It functions as a coenzyme in methylation reactions crucial for myelin production, ensuring nerve fibers' structural integrity and conductivity. Mekaj and Mekaj [95] reviewed the role of pharmacological agents in peripheral nerve regeneration and highlighted methylcobalamin as a key neuroregenerative compound. They explained that methylcobalamin supports nerve repair by promoting myelin sheath formation, increasing the number of Schwann cells and myelinated fibers, and enhancing axon diameter. It also helps restore axoplasmic flow and intracellular protein transport essential for nerve function. In addition, its antioxidant activity and brain-derived neurotrophic factor (BDNF) upregulation further strengthen its potential as a neuroprotective therapy in both systemic and local delivery strategies for peripheral nerve injury [95]. This is particularly relevant for postoperative patients with nerve damage, as myelin regeneration is key to restoring nerve function. High-dose methylcobalamin supplementation has been shown to significantly reduce neuropathic pain by suppressing pro-inflammatory cytokines, such as TNF-α and IL-6, which contribute to peripheral and central sensitization [96]. Zhang *et al.* [97] showed that methylcobalamin significantly reduces spontaneous pain episodes and hyperalgesia in patients with peripheral nerve injuries. These effects are attributed to its ability to promote remyelination, support axon regeneration, and modulate neuroinflammation [97]. Nevertheless, methylcobalamin has been found to play a significant role in axonal growth, as it facilitates the synthesis of methionine, an essential precursor for DNA and RNA synthesis in neuronal cells. This, in turn, promotes Schwann cell proliferation, enhances neurite outgrowth, and speeds up nerve fiber regeneration [98]. Abushukur and Knackstedt [99] reviewed preclinical evidence supporting the role of nutritional supplements in peripheral nerve injury recovery. They highlighted that methylcobalamin enhances nerve regeneration, remyelination, and functional recovery in animal models, particularly in injuries such as sciatic nerve crush and facial nerve damage. High-dose methylcobalamin was found to increase myelination, motor nerve conduction velocity, and reduce thermal hyperalgesia, positioning it as a promising adjunct in nerve repair strategies following reconstructive procedures or trauma [99]. Yoshimura *et al.* [100] investigated the neuroprotective effects of methylcobalamin incorporated into electrospun nanofiber sheets for preventing postoperative nerve adhesion and damage. In a rat sciatic nerve adhesion model, methylcobalamin sheets showed superior results compared to untreated groups and small intestinal submucosa (SIS) sheets, demonstrating reduced collagen deposition, decreased inflammatory cell infiltration, higher axon survival, and improved myelination [100]. On the other hand, Pyridoxine has a role in neurotransmitter synthesis, including GABA and serotonin, which contribute to reducing postoperative neuropathic pain and sensory disturbances. Yang and Wang [101] presented that pyridoxine inhibits depolarization-evoked glutamate release in rat cerebrocortical nerve terminals, suggesting a neuroprotective mechanism against excitotoxicity. The study found that pyridoxine suppresses glutamate release in a concentration-dependent manner by blocking voltage-dependent calcium (Ca^{2+}) influx through N- and P/Q-type Ca^{2+} channels, without altering synaptosomal membrane potential. Furthermore, pyridoxine inhibits protein kinase C (PKC) activation, reducing glutamate exocytosis [101]. Shabeeb *et al.* [102] showed that pyridoxine supplementation reduced hyperexcitability of sensory neurons, alleviating symptoms of numbness and neuropathic pain after surgical procedures.

3. Cellular Metabolism and Anti-Aging

Cellular aging is characterized by a progressive loss of cellular function driven by key molecular changes, including mitochondrial dysfunction, oxidative stress, DNA damage, and impaired repair mechanisms. These alterations lead to reduced energy production, accumulation of ROS, genomic instability, and eventual cellular senescence, contributing to tissue degeneration and diminished regenerative capacity. The vitamin B complex is deeply integrated into these processes through its role in supporting mitochondrial metabolism, maintaining redox balance, and facilitating DNA and RNA synthesis. By acting as cofactors in enzymatic reactions central to ATP production, antioxidant defense, and cellular repair, B vitamins help preserve cellular integrity and delay the onset of senescence. Their involvement in epigenetic regulation and modulation of pro-inflammatory pathways further strengthens their role in maintaining homeostasis during aging (Table 1, Ref. [5,9,86,103–111]) [112,113].

Cobalamin supports metabolic processes that regulate one-carbon metabolism and energy production, with its deficiency leading to systemic metabolic dysfunction and contributing to cellular aging. Studies have shown that cobalamin is essential for cellular reprogramming, with its depletion impairing cellular plasticity and tissue repair, while supplementation enhances regeneration through improved histone methylation and transcriptional fidelity [108,114]. Under normal conditions, cobalamin serves as a coenzyme for the enzyme methylmalonyl-CoA mutase, which catalyzes the conversion of methylmalonyl-CoA to succinyl-CoA. This reaction is essential for properly metabolizing certain fatty acids and amino acids. The resulting succinyl-CoA enters the Krebs cycle, which contributes to energy p-

Table 1. The role of B vitamins in cellular aging regulation.

Compound	Primary Function	Molecular Targets	Key Pathways Involved	Anti-Aging Mechanism	Clinical/Experimental Evidence
Thiamine (B1)	Coenzyme in carbohydrate metabolism	Pyruvate dehydrogenase, α-Ketoglutarate dehydrogenase	Krebs cycle, ATP synthesis	Maintains mitochondrial energy output, reduces ROS accumulation	Deficiency linked to neurodegeneration and mitochondrial dysfunction [5,9]
Niacin (B3)	NAD^+ precursor	SIRT1, PARP1	NAD^+/Sirtuin signaling, DNA repair, mTOR modulation	Promotes autophagy, genomic stability, and oxidative stress resistance	NAD^+ restoration reverses senescence in fibroblasts, protective against depression [103,104]
Pantothenic acid (B5)	Component of Coenzyme A	Fatty acid synthase, Acetyl-CoA synthase	Lipid metabolism, mitochondrial β-oxidation	Enhances mitochondrial dynamics and wound healing	Improves connective tissue strength in postoperative models [86]
Pyridoxine (B6)	Amino acid and neurotransmitter metabolism	PLP-dependent enzymes	One-carbon cycle, glutathione synthesis	Reduces inflammation, supports redox balance, collagen synthesis	Prevents LEV-induced behavioral symptoms; high doses linked to neuropathy [105,106]
Biotin (B7)	Coenzyme in carboxylation reactions	Pyruvate carboxylase, Acetyl-CoA carboxylase	Gluconeogenesis, lipid biosynthesis	Supports skin/hair renewal, epithelial turnover	Limited direct aging data; supports keratin infrastructure [107]
Cobalamin (B12)	One-carbon metabolism, DNA synthesis	Methionine synthase, Methylmalonyl-CoA mutase	DNA methylation, Krebs cycle	Regulates epigenetic stability, prevents MMA-induced mitochondrial damage	Increases Klotho expression, improves histone methylation in stem cells [108,109]
NMN	Direct NAD^+ precursor	SIRT1, SIRT3, PGC-1α	Mitochondrial biogenesis, autophagy, and neurovascular signaling	Restores mitochondrial function, improves cognitive and physical performance	Clinically shown to enhance NAD^+ levels and physical endurance [110,111]

NAD, nicotinamide adenine dinucleotide; CoA, coenzyme A; PLP, pyridoxal phosphate; MMA, methylmalonic acid; NMN, nicotinamide mononucleotide.

roduction and has a role in heme synthesis [115,116]. Additionally, cobalamin deficiency leads to the accumulation of methylmalonic acid (MMA), which disrupts mitochondrial function, increases oxidative stress, and triggers inflammation, accelerating the aging process (Fig. 3) [117]. Research further indicates that cobalamin contributes to longevity by increasing the expression of the anti-aging protein Klotho, potentially mitigating metabolic decline and age-related diseases [109]. Its role in modulating immune responses and maintaining gut microbiota balance has also been linked to reduced inflammaging, highlighting its systemic benefits in aging prevention [113]. Furthermore, studies on metabolic demands during cellular reprogramming reveal that B12 depletion impairs epigenetic modifications, leading to reduced reprogramming efficiency and limiting regenerative capacity, while supplementation restores these processes, reinforcing its potential in anti-aging therapies [108]. Song *et al*. [104] study demonstrates that the Nampt inhibitor FK866 mimics vitamin B3 deficiency by depleting intracellular NAD^+ levels, which in turn reduces SIRT1 activity and induces cellular senescence in human fibroblastic Hs68 cells. The senescence effect was reversed by nicotinic acid, nicotinamide, or NAD^+ supplementation, confirming that attenuated NAD^+-SIRT1 signaling is the primary mechanism [104]. The mTOR is a central regulator of cellular growth, metabolism, and survival. It functions through two distinct complexes, mTORC1 and mTORC2, with mTORC1 being particularly sensitive to nutrient availability and playing a critical role in aging by inhibiting autophagy and promoting anabolic processes. Chronic mTORC1 activation is associated with cellular senescence, stem cell exhaustion, and age-related tissue dysfunction [118]. Niacin and folate indirectly modulate mTOR signaling through their roles in NAD^+ metabolism, methylation cycles, and redox homeostasis. For instance, Tripathi *et al*. [119] demonstrated that vitamin B supplementation restores autophagic activity and suppresses aberrant mTOR signaling in hyperhomocysteinemia-induced cellular stress. Abdullah *et al*. [120] emphasize the interconnected roles of mTOR and sirtuins, particularly SIRT1, in regulating cellular aging, neurodegeneration, and proteostasis. They explain that mTOR inhibits autophagy, leading to the accumulation of misfolded proteins, while SIRT1 promotes autophagy and mitochondrial function via deacetylation of FOXO transcription factors and activation of PGC1α [120].

Nicotinamide mononucleotide (NMN), a derivative of niacinamide, plays an important role in mitochondrial energy metabolism by serving as a precursor to NAD+, a coenzyme essential for ATP production [121]. NMN supplementation has been shown to enhance mitochondrial function, improve oxidative phosphorylation, and boost cellular energy levels, all of which are crucial for maintaining skin vitality and delaying cellular senescence. By restoring NAD^+ levels, NMN counteracts age-related mitochondrial decline, which is a key factor in skin aging and reduced metabolic efficiency [122]. Wang *et al*. [123] explored NMN's role in rescuing mitochondrial dysfunction and delaying cellular senescence in mesenchymal stem cells (MSCs), emphasizing how its ability to restore NAD^+ levels and activate Sirt3 contributes to longevity and regenerative medicine. Similarly, Xu *et al*. [124] demonstrated NMN's ability to reverse hair follicle atrophy, enhance cell proliferation, and reduce oxidative stress, highlighting its therapeutic potential in androgenetic alopecia through the inhibition of the NF-κB p65 inflammatory pathway. The broader implications of NMN supplementation were reviewed by Soma and Lalam [125], who discussed its role in counteracting age-related metabolic decline, DNA damage, and immune dysregulation, establishing NMN as a potential therapeutic intervention in diabetes, cardiovascular diseases, and neurodegeneration. Clinical validation of NMN's efficacy was provided by Yi *et al*. [111], who conducted a randomized controlled trial in middle-aged adults, revealing that daily NMN supplementation significantly increased NAD^+ levels, improved physical performance, and enhanced overall health markers without adverse effects. NMN's neuroprotective properties were highlighted by Tarantini *et al*. [126], who demonstrated that it restores neurovascular function, reduces endothelial oxidative stress, and enhances cognitive performance in aging mice, suggesting its potential to prevent vascular cognitive impairment and neurodegenerative diseases. Furthermore, Mills *et al*. [110] confirmed NMN's long-term safety and efficacy in mitigating age-associated physiological decline, reporting significant improvements in energy metabolism, insulin sensitivity, and mitochondrial health over a 12-month study in aging mice. Moreover, Niacinamide facilitates DNA repair and genomic stability by enhancing the activity of poly (ADP-ribose) polymerase (PARP) enzymes, which detect and repair DNA strand breaks. This prevents the accumulation of genetic damage, a primary driver of cellular aging and skin deterioration. By activating PARP-dependent DNA repair mechanisms, niacinamide helps mitigate oxidative stress-induced mutations, reduce inflammation, and preserve skin integrity, making it a valuable anti-aging ingredient in dermatological and cosmeceutical formulations [127,128]. Cao *et al*. [129] explored nicotinamide's immunomodulatory role in autoimmune diseases, revealing that it suppresses dendritic cell hyperactivation through PARP-dependent NF-κB signaling, effectively reducing psoriasis severity and inflammation. Furthermore, Ziklo *et al*. [130] investigated niacinamide's antimicrobial properties, showing that it induces microbial cell cycle arrest, disrupts chromatin structure, and inhibits DNA replication, suggesting its potential as a natural preservative in skincare and cosmetic applications.

While the preceding sections have detailed the diverse physiological and therapeutic benefits of individual B vitamins in surgical and aesthetic contexts, it is equally im-

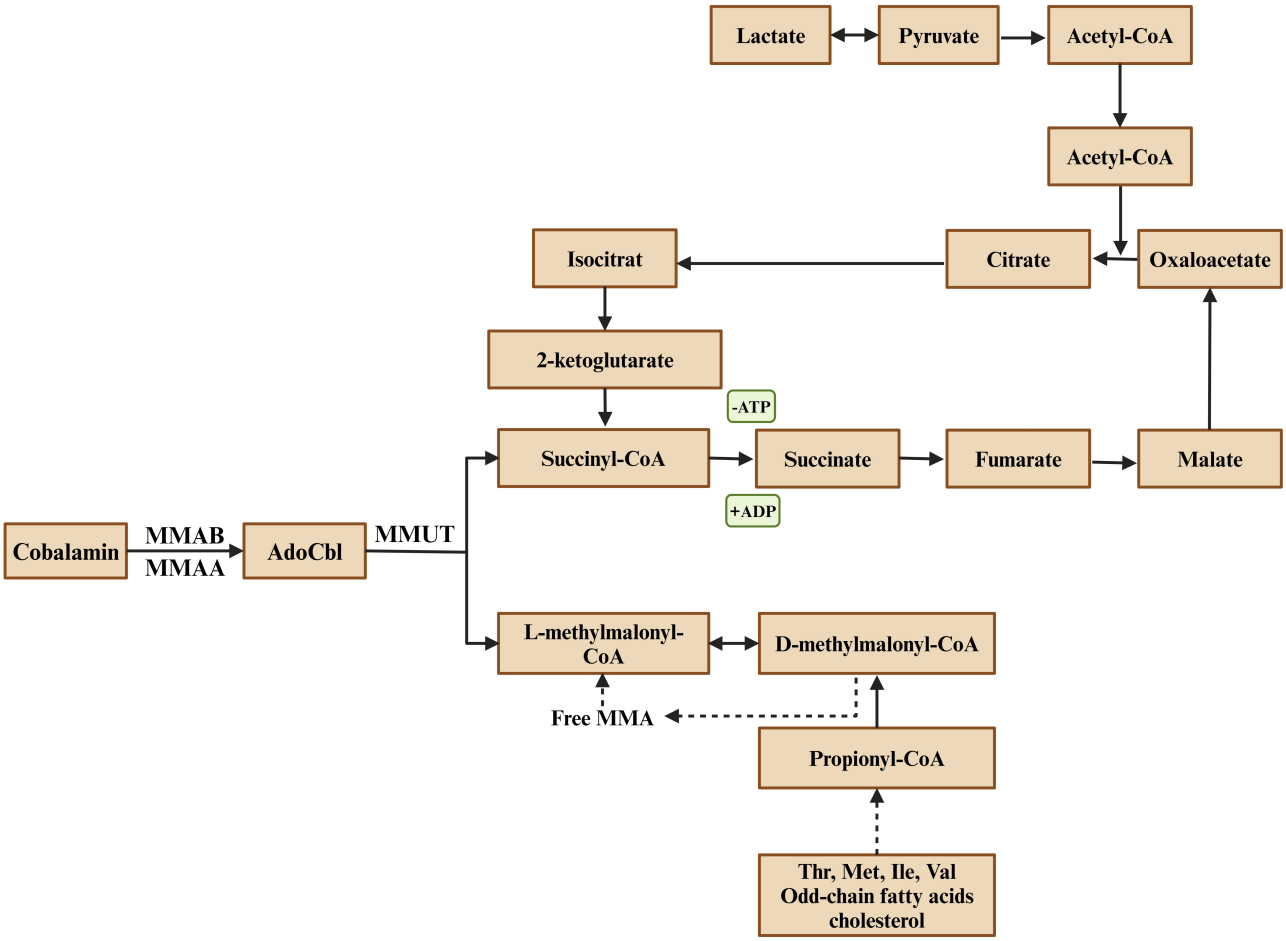

Fig. 3. The role of cobalamin (vitamin B12) in the conversion of propionyl-CoA to succinyl-CoA via methylmalonyl-CoA mutase (MMUT), linking odd-chain fatty acid and amino acid metabolism to the TCA cycle, with deficiencies leading to methylmalonic acid (MMA) accumulation. CoA, coenzyme A; MMAB, methylmalonic aciduria type B; MMAA, methylmalonic aciduria type A.

portant to contextualize these benefits within the broader framework of clinical safety. Understanding the potential adverse effects associated with high-dose or long-term supplementation provides essential guidance for integrating vitamin B complex into patient care. The following section addresses these safety considerations, ensuring a balanced approach that aligns therapeutic potential with evidence-based risk management.

4. Safety and Adverse Effects

Under normal physiological conditions, B vitamins are required for enzymatic functions that regulate metabolism, red blood cell production, and nervous system activity. Their widespread presence in food sources, including meats, dairy products, leafy greens, and fortified cereals, ensures adequate intake for most individuals [131]. Based on their water-soluble nature, excess amounts are typically excreted in urine, reducing the likelihood of toxicity [132]. Vitamin B supplementation is commonly used to prevent and manage deficiencies in high-risk groups, such as pregnant women, the elderly, vegetarians, and individuals with malabsorption disorders [4,133]. In elderly individuals, age-associated gastric atrophy, hypochlorhydria, and polypharmacy contribute to diminished absorption of cobalamin and folate, increasing the risk of neuropathy and cognitive decline [26]. Li *et al.* [134] concluded that vitamin B supplementation, particularly in individuals with mild cognitive impairment (MCI), may be a valuable preventative intervention against cognitive decline. They suggest that routine B vitamin supplementation could benefit elderly adults at risk of developing dementia. Furthermore, Vitagliano *et al.* [135] highlights that optimal preoperative nutritional status, including B vitamin adequacy, is crucial for favorable surgical and aesthetic outcomes. This is particularly important for elderly individuals undergoing cosmetic procedures, who are more prone to micronutrient deficiencies and impaired wound healing. Importantly, elderly individuals undergoing plastic surgery often present complex health profiles [135]. Broughton *et al.* [136] caution that vitamin supplements, including B complex, may interact with anesthesia and medications. Thus, surgeons should review all supplements

Table 2. RDAs and tolerable UL of B vitamins [4,148,149].

Vitamin	RDA (Adults 19–50 years)	Pregnant female	Tolerable UL
Thiamine (B1)	1.1–1.2 mg	1.4 mg	No established UL
Niacin (B3)	14–16 mg	18 mg	35 mg (nicotinic acid form)
Pantothenic Acid (B5)	5 mg	6 mg	No established UL
Pyridoxine (B6)	1.3–1.7 mg	1.9 mg	100 mg
Biotin (B7)	30 µg	30 µg	No established UL
DCobalamin (B12)	2.4 µg	2.6 µg	No established UL

RDAs, recommended daily allowance; UL, upper intake level.

during preoperative assessments [136]. Individuals with malabsorption disorders, such as celiac disease or Crohn's disease, often require higher doses of cobalamin and folic acid due to impaired intestinal absorption. Similarly, vegetarians and vegans are at higher risk of B12 deficiency since this vitamin is predominantly found in animal-based foods, making supplementation necessary to maintain optimal neurological and hematological function [137,138]. Pregnant and lactating women require increased levels of certain B vitamins to support fetal development and maternal health, where vitamin pyridoxine has been found to alleviate pregnancy-related nausea and vomiting, further emphasizing the importance of individualized nutrient planning during this period [139,140]. Athletes and individuals with high metabolic demands may require higher doses of B vitamins to support energy metabolism, muscle recovery, and endurance [141,142].

Furthermore, diabetes patients may benefit from additional thiamine, as diabetes-related complications are associated with thiamine depletion [143,144]. Toninello *et al.* [145] reported that glutathione and vitamins, including B-complex constituents, were reduced in diabetic wound tissue. Nutritional supplementation aimed at restoring these levels enhanced both tissue regeneration and cosmetic outcomes following surgery. Additionally, pyridoxine and cobalamin are critical in cardiovascular health, particularly in individuals with elevated homocysteine levels, which are linked to an increased risk of heart disease. Addressing these deficiencies through targeted supplementation can help mitigate disease progression and improve overall health outcomes [146,147]. The safe dosage of vitamin B complex varies based on physiological needs, dietary intake, and individual health conditions. The recommended daily allowances (RDAs) and tolerable upper intake levels (UL) for each B vitamin are established to ensure optimal health while preventing toxicity (Table 2, Ref. [4,148,149]) [150]. In burn patients, daily supplementation of B vitamins (B1 100 mg, B6 200 mg, cobalamin 2000 mcg) significantly reduced infection and sepsis rates, and shortened hospital stays. The high-dose cobalamin likely overcame issues of bioavailability, particularly in acute stress and catabolic states common in severe burns [151]. Gardiner and Hartzell [152] highlight the effect of thiamine in plastic surgery, presenting a case where postoperative hypotension and hypothermia were reversed only after intravenous thiamine. Furthermore, Sebastian *et al.* [153] reported that unrecognized thiamine deficiency in a post-bariatric patient caused acute neurological compromise following aesthetic procedures, reinforcing the necessity of vitamin B assessment in plastic surgery settings. In such high-risk cases, thiamine supplementation of 100–200 mg/day intravenously for 3–5 days, followed by oral maintenance doses of 10–20 mg/day, is typically recommended to prevent or treat deficiency-related complications [153]. The excessive pyridoxine supplementation, particularly in bariatric surgery patients, led to a significant rise in cases of pyridoxine toxicity, including sensory neuropathy, highlighting the need for stricter guidelines on pyridoxine dosing in clinical nutrition [109]. In addition, patients with a history of bariatric procedures, screening for cobalamin deficiency is warranted. In cases of confirmed deficiency, treatment typically involves intramuscular injections of 1000 micrograms weekly for four weeks, transitioning to monthly doses, or alternatively, daily oral supplementation of 1000 micrograms may be effective. Importantly, prophylactic supplementation in individuals with normal serum levels is not recommended, as it offers no added clinical benefit [154,155].

Most individuals tolerate B vitamins well when consumed through a balanced diet or in moderate supplement doses. They are frequently prescribed for deficiency-related conditions, including anemia, neuropathy, and cognitive decline [156,157]. However, certain health conditions, medication interactions, and long-term high-dose supplementation can lead to unintended effects. For instance, pyridoxine toxicity is well-documented, with prolonged intake of doses exceeding 200 mg per day leading to sensory neuropathy, causing symptoms such as numbness, tingling, and loss of coordination [158]. In extreme cases, these neurological impairments may become irreversible [158,159]. An investigation by Alsaadi *et al.* [106] explored the use of pyridoxine to manage behavioral side effects, such as agitation and irritability, in adult patients treated with levetiracetam. Among 51 patients, 66.6% showed significant improvement in symptoms with an average dose of 54.5 mg/day, suggesting pyridoxine as a potentially effective and well-tolerated adjunct for levetiracetam-induced behavioral disturbances.

Table 3. A general summary of the functional roles and mechanisms of B vitamins in plastic and cosmetic surgery.

B-Vitamin	Primary Role in Surgery	Mechanisms & Effects	Key Findings	References
Thiamine (B1)	Postoperative nerve function and cellular resilience	Supports carbohydrate metabolism, ATP production, and neuronal function; modulates oxidative stress and reduces neuropathic pain.	Enhances ATP synthesis for neuronal recovery, reduces oxidative stress, and improves nerve conduction and Schwann cell function.	[5,27,87,176]
Niacinamide (B3)	Skin restoration, anti-aging, and post-laser recovery	Enhances mitochondrial function, NAD^+ production, and DNA repair; improves skin barrier integrity, hydration, and pigmentation control.	Stimulates ceramide production for skin hydration, inhibits melanosome transfer to reduce hyperpigmentation, and enhances post-laser wound healing.	[30,31,175]
Pantothenic Acid (B5)	Wound healing and scar management	Essential for CoA synthesis, accelerating cellular repair, modulating inflammatory responses, and supporting collagen synthesis.	Dexpanthenol promotes keratinocyte proliferation and fibroblast activity, reduces oxidative stress, and improves healing outcomes in various wound models.	[51–53]
Pyridoxine (B6)	Neuroprotection and neurotransmitter synthesis	Functions as a coenzyme in neurotransmitter production; modulates excitotoxicity and supports pain modulation.	Regulates glutamate release to prevent excitotoxic damage, supports serotonin and dopamine synthesis, and alleviates postoperative neuropathic pain.	[101,102,177]
Biotin (B7)	Hair regeneration and follicular support	Supports keratin synthesis, enhances follicular proliferation, and contributes to scalp microbiome balance.	Applied in hair transplant recovery to improve follicular survival; enhances hair regrowth in alopecia and reduces drug-induced hair loss.	[66,68,70]
Cobalamin (B12)	Nerve regeneration and postoperative recovery	Essential for myelin sheath maintenance, axonal repair, and nerve impulse conduction; reduces nerve damage and facilitates recovery.	High-dose methylcobalamin accelerates nerve regeneration, reduces neuropathic pain by inhibiting pro-inflammatory cytokines, and enhances Schwann cell proliferation.	[96,98,100]

Table 4. Representative clinical human studies investigating the effects of vitamin B.

	Vitamin	Study Type & Sample	Intervention	Key Findings
Alemanno *et al*. [92]	Thiamine (B1)	Retrospective clinical study; 110 patients undergoing interscalene block for shoulder surgery	2 mg/kg thiamine hydrochloride added to 0.75% levobupivacaine *vs*. levobupivacaine alone	Prolonged postoperative analgesia duration (17.6 h *vs*. 11.4 h; $p < 0.001$).
Lee *et al*. [33]	Niacinamide	Randomized Controlled Trial (split-face); 25 patients	ADSC-CM combined with 2% niacinamide post-laser	Improved wrinkles, pigmentation, and collagen levels.
Hakozaki *et al*. [39]	Niacinamide	Randomized Controlled Trial; 18 Japanese women	5% niacinamide *vs*. vehicle	Reduced hyperpigmentation and increased skin brightness.
Navarrete-Solís *et al*. [37]	Niacinamide	Randomized Controlled Trial; 27 women	4% niacinamide *vs*. 4% hydroquinone	Effectively treated melasma with fewer side effects than hydroquinone.
Chiu *et al*. [175]	Niacinamide & Kinetin	Randomized Controlled Trial (split-face); 52 subjects	4% niacinamide combined with kinetin *vs*. placebo	Produced synergistic improvement in skin spots, pores, and wrinkles.
Heise *et al*. [54]	Panthenol	Randomized Controlled Trial; 38 patients	Dexpanthenol ointment *vs*. petroleum jelly	Accelerated wound healing and improved cosmetic outcomes.
Li *et al*. [64]	Panthenol, Madecassoside & Trace Elements	Randomized Controlled Trial (split-face); 43 women	Cream containing 5% panthenol, madecassoside, and trace elements	Improved healing post-laser treatment and reduced erythema and TEWL.
Samadi *et al*. [69]	Biotin & Dexpanthenol	Randomized Controlled Trial (double-blind); 50 patients	Intramuscular biotin combined with dexpanthenol	Increased hair density and improved terminal/vellus hair ratio; Bayer product was more effective.
El-Esawy *et al*. [67]	Biotin & Zinc	Observational study; 60 men with androgenetic alopecia	Serum biotin and zinc level comparison	Found lower biotin and zinc levels in AGA patients; suggested correlation with hair loss.
Stücker *et al*. [178]	Cobalamin (B12)	Randomized Controlled Trial (placebo-controlled); 49 patients with atopic dermatitis	Topical vitamin B12 cream *vs*. base cream	Significantly improved symptoms and showed excellent tolerability.
Elgharably *et al*. [179]	Cobalamin (B12)	Clinical supplementation report	1000 mcg sublingual vitamin B12 for dermatologic support	Improved skin and hair complaints associated with vitamin B12 deficiency.

ADSC-CM, adipocyte-derived stem cell-conditioned media; AGA, androgenetic alopecia.

Similarly, excessive niacin intake can cause flushing, gastrointestinal distress, and, at very high doses, hepatotoxicity. Sustained-release niacin formulations have been particularly associated with liver damage and metabolic disturbances, including insulin resistance and hyperglycemia [160,161]. Zhou and Han [162] identified a U-shaped relationship between dietary niacin intake and the risk of metabolic dysfunction-associated steatotic liver disease (MASLD), with the lowest risk observed at an intake of approximately 23.6 mg/day. The findings suggest that while moderate niacin consumption may be protective, excessive intake could increase MASLD risk. In addition, Li *et al*. [163] reported that excessive niacin intake was strongly associated with the rising prevalence of childhood obesity in the United States, with a 10-year lag correlation. Their study also showed that a 300 mg nicotinamide load induced insulin resistance, followed by reactive hypoglycemia in healthy individuals. Tian *et al*. [103] analyzed data from over 16,000 U.S. adults and found a U-shaped relationship between dietary niacin intake and depression risk, with the lowest risk observed at approximately 36 mg/day. Below this level, increased niacin intake was associated with reduced depression, while higher intakes were linked to elevated risk.

Other B vitamins, such as pantothenic acid, have an excellent safety profile, with minimal reported adverse effects. Scott *et al*. [107] found that panthenol, pantothenic acid, and related derivatives are safe for use in cosmetic products when formulated within currently accepted concentrations. The safety assessment, based on toxicological evidence and usage data, concluded that these ingredients do not pose significant health risks under intended conditions of use. Pantothenic acid toxicity is rare but may cause mild gastrointestinal symptoms such as diarrhea when taken in excessive amounts [164,165]. Biotin is generally safe; however, recent studies have shown that high doses may interfere with laboratory tests, particularly those assessing thyroid function and cardiac biomarkers, leading to potential misdiagnoses [166,167]. Furthermore, cobalamin is considered safe, even at high doses, due to its efficient storage and excretion mechanisms. However, hypersensitivity reactions and acne-like eruptions have been reported in some individuals taking high-dose cobalamin supplements [168,169]. Additionally, some studies have suggested that excessive cobalamin intake in individuals with kidney disease may be associated with adverse vascular effects [170,171]. The risk of vitamin B complex toxicity is further influenced by underlying health conditions and medication interactions. Individuals with liver disease should avoid excessive niacin intake due to its hepatotoxic effects, while those with kidney disease may be at risk of accumulating excess water-soluble vitamins, leading to unintended side effects [169,171]. Furthermore, certain medications can interact with B vitamins, altering their metabolism and effectiveness. For example, pyridoxine can reduce the efficacy of levodopa, a medication used for Parkinson's disease [172]. In addition, proton pump inhibitors and metformin can reduce cobalamin absorption, increasing the risk of deficiency in long-term users [173,174].

5. Future Directions

Despite the established role of the vitamin B complex in plastic and cosmetic surgery, several critical areas require further exploration to optimize its therapeutic applications (Table 3, Ref. [5,27,30,31,51–53,66,68,70,87,96,98,100–102,175–177] and Table 4 Ref. [33,37,39,54,64,67,69,92,175,178,179]). Research should focus on precision supplementation, innovative drug delivery systems, synergistic combinations with regenerative medicine, large-scale clinical trials, and the elucidation of epigenetic and anti-aging mechanisms. Addressing these research gaps will enable the development of more effective, personalized, and evidence-based strategies for enhancing surgical outcomes, promoting tissue regeneration, and improving post-surgical recovery.

The metabolic processing and physiological effects of B vitamins vary significantly among individuals due to genetic polymorphisms, enzymatic activity differences, dietary factors, and gut microbiota composition [180]. This variability necessitates a shift from generalized supplementation protocols toward precision medicine approaches that tailor B vitamin intake based on individual metabolic profiles and surgical requirements [180–182]. Investigating genomic markers such as MTHFR mutations, which affect folate and cobalamin metabolism, to determine optimal dosages for enhanced skin repair, nerve protection, and collagen synthesis [183]. Additionally, nutrigenomic and metabolomic studies should assess how gut microbiota influences the absorption and bioavailability of B vitamins, particularly biotin and pantothenic acid, which play key roles in wound healing and scar management [184,185]. Developing biomarker-based diagnostic tools for preoperative vitamin B screening can ensure patients receive adequate supplementation to enhance post-surgical recovery while preventing deficiencies that may lead to delayed wound healing, poor neural regeneration, and increased scar formation [186].

While the therapeutic benefits of B vitamins are well recognized, their rapid metabolism and excretion present challenges in maintaining sustained therapeutic efficacy. To overcome these limitations, further studies should explore the development of advanced drug delivery systems, including liposomal encapsulation, nanoemulsions, and polymeric microneedles, to enhance targeted delivery, sustained release, and localized action in plastic and cosmetic surgery applications [187,188]. Liposomal formulations, for instance, have shown improved penetration into dermal and neural tissues, making them valuable in postoperative wound healing, scar modulation, and skin rejuvenation [188,189]. Microneedle patches infused with niacinamide

and dexpanthenol offer a promising minimally invasive approach for enhancing skin barrier function and pigmentation control in post-laser treatments and hyperpigmentation disorders [190,191]. Additionally, hydrogel-based carriers loaded with cobalamin and pantothenic acid could serve as bioactive wound dressings, accelerating tissue regeneration by promoting fibroblast proliferation, extracellular matrix (ECM) remodeling, and angiogenesis [192,193]. More research should focus on transdermal and implantable formulations that ensure prolonged vitamin release, reducing the need for frequent supplementation and optimizing therapeutic outcomes in aesthetic and reconstructive procedures.

The integration of vitamin B complex with regenerative medicine techniques holds significant potential for advancing plastic and reconstructive surgery. Several studies suggest that niacinamide enhances mitochondrial function and stem cell viability, making it a valuable adjunct in MSC therapy for skin rejuvenation and hair follicle regeneration [127,194]. Additionally, vitamin B derivatives such as cobalamin and pyridoxine have an important role in Schwann cell proliferation and nerve regeneration, indicating their potential for incorporation into biodegradable nerve conduits for peripheral nerve repair [176,195]. Future research should investigate how vitamin B complex interacts with PRP and ECM scaffolds to synergistically promote tissue regeneration, modulate inflammatory responses, and accelerate post-surgical recovery. Furthermore, exploring the role of vitamin B-enriched bioinks in 3D bioprinting could pave the way for engineered skin grafts and customized reconstructive implants that optimize wound healing and aesthetic outcomes in plastic surgery. Nevertheless, current dosing recommendations for vitamin B supplementation are based primarily on nutritional requirements rather than the specific demands of perioperative care and tissue repair. Therefore, more researches need to focus on defining optimal dosages, duration of supplementation, and mode of administration for different surgical procedures, ensuring maximum efficacy with minimal risk [196,197]. Efforts should be made to elucidate the metabolic effects of chronic vitamin B supplementation and identify safe upper intake levels for patients undergoing prolonged reconstructive and cosmetic treatments [167,198]. Additionally, post-surgical clinical trials should evaluate objective measures of functional recovery, such as scar elasticity, skin hydration, and nerve conduction velocity, to determine the long-term benefits and risks of vitamin B complex therapy in plastic surgery patients [199,200]. Finally, future studies should explore how NAD^+ precursors modulate fibroblast lifespan, collagen biosynthesis, and dermal remodeling, particularly in post-surgical scar prevention and anti-aging therapies [201,202].

6. Conclusions

The vitamin B complex offers substantial therapeutic potential in enhancing the outcomes of plastic and cosmetic surgery. Its benefits extend beyond basic metabolic functions, aiding in skin restoration, wound healing, anti-aging therapies, and nerve protection. While the evidence supporting its role in these areas is promising, further research is needed to optimize dosing regimens, delivery methods, and the precise targeting of deficiencies based on individual patient profiles. Future studies should focus on integrating vitamin B complex into regenerative medicine and precision medicine frameworks, ensuring personalized care that maximizes therapeutic outcomes. Given its safety profile and multifaceted therapeutic roles, the vitamin B complex remains a critical element in advancing the clinical practice of plastic and cosmetic surgery.

Author Contributions

Conceptualization: HL, FD, and AA; Data collection & analysis: AA, XZ, and WZ; Supervision: HL, and AA; Writing original draft: FD, and AA; Writing - review & editing: XZ, HL, and WZ. All authors have contributed to the editorial changes made to the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Nguyen TT, Kilaru P. Plastic Surgery and Cosmetic Procedures: Augmentation and Reconstruction Procedures. FP Essentials. 2020; 497: 27–36.

[2] Shanmugasundaram Prema S, Ganapathy D, Shanmugamprema D. Prehabilitation Strategies: Enhancing Surgical Resilience with a Focus on Nutritional Optimization and Multimodal Interventions. Advances in Nutrition (Bethesda, Md.). 2025; 16: 100392. https://doi.org/10.1016/j.advnut.2025.100392.

[3] Hrubša M, Siatka T, Nejmanová I, Vopršalová M, Kujovská Krčmová L, Matoušová K, *et al*. Biological Properties of Vitamins of the B-Complex, Part 1: Vitamins B1, B2, B3, and B5. Nutrients. 2022; 14: 484. https://doi.org/10.3390/nu14030484.

[4] Hanna M, Jaqua E, Nguyen V, Clay J. B Vitamins: Functions and Uses in Medicine. The Permanente journal. 2022; 26: 89–97. https://doi.org/10.7812/TPP/21.204.

[5] Mrowicka M, Mrowicki J, Dragan G, Majsterek I. The importance of thiamine (vitamin B1) in humans. Bioscience reports. 2023; 43: BSR20230374. https://doi.org/10.1042/BSR20230374.

[6] Laliberté F, Bloom I, Alexander AJ. The Critical Role of Nutrition in Facial Plastic Surgery. Facial Plastic Surgery Clinics of North America. 2019; 27: 399–404. https://doi.org/10.1016/j.fsc.2019.04.005.
[7] Tylicki A, Łotowski Z, Siemieniuk M, Ratkiewicz A. Thiamine and selected thiamine antivitamins - biological activity and methods of synthesis. Bioscience Reports. 2018; 38: BSR20171148. https://doi.org/10.1042/BSR20171148.
[8] Mikkelsen K, Trapali M, Apostolopoulos V. Role of Vitamin B in Healthy Ageing and Disease. Sub-cellular Biochemistry. 2024; 107: 245–268. https://doi.org/10.1007/978-3-031-66768-8_12.
[9] Sambon M, Wins P, Bettendorff L. Neuroprotective Effects of Thiamine and Precursors with Higher Bioavailability: Focus on Benfotiamine and Dibenzoylthiamine. International Journal of Molecular Sciences. 2021; 22: 5418. https://doi.org/10.3390/ijms22115418.
[10] Kirkland JB, Meyer-Ficca ML. Niacin. Advances in Food and Nutrition Research. 2018; 83: 83–149. https://doi.org/10.1016/bs.afnr.2017.11.003.
[11] Hageman GJ, Stierum RH. Niacin, poly(ADP-ribose) polymerase-1 and genomic stability. Mutation Research. 2001; 475: 45–56. https://doi.org/10.1016/s0027-5107(01)00078-1.
[12] Surjana D, Halliday GM, Damian DL. Role of nicotinamide in DNA damage, mutagenesis, and DNA repair. Journal of Nucleic Acids. 2010; 2010: 157591. https://doi.org/10.4061/2010/157591.
[13] Gregory JF, DeRatt BN, Rios-Avila L, Ralat M, Stacpoole PW. Vitamin B6 nutritional status and cellular availability of pyridoxal 5'-phosphate govern the function of the transsulfuration pathway's canonical reactions and hydrogen sulfide production via side reactions. Biochimie. 2016; 126: 21–26. https://doi.org/10.1016/j.biochi.2015.12.020.
[14] Djadjo S, Bajaj T. Niacin. In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2023.
[15] Leonardi R, Jackowski S. Biosynthesis of Pantothenic Acid and Coenzyme A. EcoSal Plus. 2007; 2: 10.1128. https://doi.org/10.1128/ecosalplus.3.6.3.4.
[16] Ismail N, Kureishy N, Church SJ, Scholefield M, Unwin RD, Xu J, *et al*. Vitamin B5 (d-pantothenic acid) localizes in myelinated structures of the rat brain: Potential role for cerebral vitamin B5 stores in local myelin homeostasis. Biochemical and Biophysical Research Communications. 2020; 522: 220–225. https://doi.org/10.1016/j.bbrc.2019.11.052.
[17] Vaxman F, Olender S, Lambert A, Nisand G, Grenier JF. Can the wound healing process be improved by vitamin supplementation? Experimental study on humans. European Surgical Research. 1996; 28: 306–314. https://doi.org/10.1159/000129471.
[18] Aprahamian M, Dentinger A, Stock-Damgé C, Kouassi JC, Grenier JF. Effects of supplemental pantothenic acid on wound healing: experimental study in rabbit. The American Journal of Clinical Nutrition. 1985; 41: 578–589. https://doi.org/10.1093/ajcn/41.3.578.
[19] di Salvo ML, Safo MK, Contestabile R. Biomedical aspects of pyridoxal 5'-phosphate availability. Frontiers in Bioscience (Elite edition). 2012; 4: 897–913. https://doi.org/10.2741/E428.
[20] Brown MJ, Ameer MA, Daley SF, Beier K. Vitamin B6 Deficiency. In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2023.
[21] Qian B, Shen S, Zhang J, Jing P. Effects of Vitamin B6 Deficiency on the Composition and Functional Potential of T Cell Populations. Journal of Immunology Research. 2017; 2017: 2197975. https://doi.org/10.1155/2017/2197975.
[22] León-Del-Río A. Biotin in metabolism, gene expression, and human disease. Journal of Inherited Metabolic Disease. 2019; 42: 647–654. https://doi.org/10.1002/jimd.12073.
[23] Zempleni J, Hassan YI, Wijeratne SS. Biotin and biotinidase deficiency. Expert Review of Endocrinology & Metabolism. 2008; 3: 715–724. https://doi.org/10.1586/17446651.3.6.715.
[24] Cervantes A, Soos MP. Biotin Deficiency. In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2023.
[25] Kannan S, Balakrishnan J, Nagarajan P. Vitamin B7 (Biotin) and Its Role in Hair, Skin and Nail Health. In Shah AK, Tappia PS, Dhalla NS (eds.) Hydrophilic Vitamins in Health and Disease. Advances in Biochemistry in Health and Disease.Springer: Cham. 2024. https://doi.org/10.1007/978-3-031-55474-2_10.
[26] Pyrgioti EE, Karakousis ND. B12 levels and frailty syndrome. Journal of Frailty, Sarcopenia and Falls. 2022; 7: 32–37. https://doi.org/10.22540/JFSF-07-032.
[27] Depeint F, Bruce WR, Shangari N, Mehta R, O'Brien PJ. Mitochondrial function and toxicity: role of the B vitamin family on mitochondrial energy metabolism. Chemico-biological Interactions. 2006; 163: 94–112. https://doi.org/10.1016/j.cbi.2006.04.014.
[28] Lee MC, Hsu YJ, Shen SY, Ho CS, Huang CC. A functional evaluation of anti-fatigue and exercise performance improvement following vitamin B complex supplementation in healthy humans, a randomized double-blind trial. International Journal of Medical Sciences. 2023; 20: 1272–1281. https://doi.org/10.7150/ijms.86738.
[29] Ibrahim M, Khan S, Pathak S, Mazhar M, Singh H. Vitamin B-Complex and its Relationship with the Health of Vegetarian People. Natural Resources for Human Health. 2023. https://doi.org/10.53365/nrfhh/169824.
[30] Lim KM. Skin Epidermis and Barrier Function. International Journal of Molecular Sciences. 2021; 22: 3035. https://doi.org/10.3390/ijms22063035.
[31] Mohammed D, Crowther JM, Matts PJ, Hadgraft J, Lane ME. Influence of niacinamide containing formulations on the molecular and biophysical properties of the stratum corneum. International Journal of Pharmaceutics. 2013; 441: 192–201. https://doi.org/10.1016/j.ijpharm.2012.11.043.
[32] Gueniche A, Valois A, Salomao Calixto L, Sanchez Hevia O, Labatut F, Kerob D, *et al*. A dermocosmetic formulation containing Vichy volcanic mineralizing water, Vitreoscilla filiformis extract, niacinamide, hyaluronic acid, and vitamin E regenerates and repairs acutely stressed skin. Journal of the European Academy of Dermatology and Venereology. 2022; 36 Suppl 2: 26–34. https://doi.org/10.1111/jdv.17785.
[33] Lee YI, Kim S, Kim J, Kim J, Chung KB, Lee JH. Randomized controlled study for the anti-aging effect of human adipocyte-derived mesenchymal stem cell media combined with niacinamide after laser therapy. Journal of Cosmetic Dermatology. 2021; 20: 1774–1781. https://doi.org/10.1111/jocd.13767.
[34] Shariff R, Du Y, Dutta M, Kumar S 5th, Thimmaiah S, Doraiswamy C, *et al.* Superior even skin tone and anti-ageing benefit of a combination of 4-hexylresorcinol and niacinamide. International Journal of Cosmetic Science. 2022; 44: 103–117. https://doi.org/10.1111/ics.12759.
[35] Nair, NirmalaDutta, MaitreyeeKaru, JohnsonLim, Fei-LingDamodaran, AnitaLogt, Paul-Van-Der, *et al*. 26415 Regulation of postinflammatory hyperpigmentation by niacinamide through potential modulation of the protease inhibitor, SERPINB3. Journal of the American Academy of Dermatology. 2021; 85: AB99.
[36] Wohlrab J, Kreft D. Niacinamide - mechanisms of action and its topical use in dermatology. Skin Pharmacology and Physiology. 2014; 27: 311–315. https://doi.org/10.1159/000359974.
[37] Navarrete-Solís J, Castanedo-Cázares JP, Torres-Álvarez B, Oros-Ovalle C, Fuentes-Ahumada C, González FJ, *et al*. A Double-Blind, Randomized Clinical Trial of Niacinamide 4% versus Hydroquinone 4% in the Treatment of Melasma. Der-

matology Research and Practice. 2011; 2011: 379173. https://doi.org/10.1155/2011/379173.
[38] Resende DISP, Ferreira MS, Lobo JMS, Sousa E, Almeida IF. Skin Depigmenting Agents in Anti-Aging Cosmetics: A Medicinal Perspective on Emerging Ingredients. Applied Sciences. 2022; 12: 775. https://doi.org/10.3390/app12020775.
[39] Hakozaki T, Minwalla L, Zhuang J, Chhoa M, Matsubara A, Miyamoto K, *et al*. The effect of niacinamide on reducing cutaneous pigmentation and suppression of melanosome transfer. The British Journal of Dermatology. 2002; 147: 20–31. https://doi.org/10.1046/j.1365-2133.2002.04834.x.
[40] Desai S, Ayres E, Bak H, Manco M, Lynch S, Raab S, *et al*. Effect of a Tranexamic Acid, Kojic Acid, and Niacinamide Containing Serum on Facial Dyschromia: A Clinical Evaluation. Journal of Drugs in Dermatology. 2019; 18: 454–459.
[41] Kimball AB, Kaczvinsky JR, Li J, Robinson LR, Matts PJ, Berge CA, *et al*. Reduction in the appearance of facial hyperpigmentation after use of moisturizers with a combination of topical niacinamide and N-acetyl glucosamine: results of a randomized, double-blind, vehicle-controlled trial. The British Journal of Dermatology. 2010; 162: 435–441. https://doi.org/10.1111/j.1365-2133.2009.09477.x.
[42] Furmanczyk M, Brown A, Bustos J, de Henestrosa ARF, Trullas C, Granger C, *et al*. Efficacy and tolerability of a depigmenting gel serum comprising tranexamic acid, niacinamide, 4-butylresorcinol, phytic acid, and a mixture of hydroxy acids that targets the biological processes regulating skin melanogenesis. Journal of Cosmetic Dermatology. 2024; 23: 2058–2065. https://doi.org/10.1111/jocd.16148.
[43] Mi T, Dong Y, Santhanam U, Huang N. Niacinamide and 12-hydroxystearic acid prevented benzo(a)pyrene and squalene peroxides induced hyperpigmentation in skin equivalent. Experimental Dermatology. 2019; 28: 742–746. https://doi.org/10.1111/exd.13811.
[44] Papaccio F, D Arino A, Caputo S, Bellei B. Focus on the Contribution of Oxidative Stress in Skin Aging. Antioxidants (Basel). 2022; 11: 1121. https://doi.org/10.3390/antiox11061121.
[45] Monfrecola G, Gaudiello F, Cirillo T, Fabbrocini G, Balato A, Lembo S. Nicotinamide downregulates gene expression of interleukin-6, interleukin-10, monocyte chemoattractant protein-1, and tumour necrosis factor-α gene expression in HaCaT keratinocytes after ultraviolet B irradiation. Clinical and Experimental Dermatology. 2013; 38: 185–188. https://doi.org/10.1111/ced.12018.
[46] Boo YC. Mechanistic Basis and Clinical Evidence for the Applications of Nicotinamide (Niacinamide) to Control Skin Aging and Pigmentation. Antioxidants (Basel). 2021; 10: 1315. https://doi.org/10.3390/antiox10081315.
[47] Bierman JC, Laughlin T, Tamura M, Hulette BC, Mack CE, Sherrill JD, *et al*. Niacinamide mitigates SASP-related inflammation induced by environmental stressors in human epidermal keratinocytes and skin. International Journal of Cosmetic Science. 2020; 42: 501–511. https://doi.org/10.1111/ics.12651.
[48] Zhou E, Li Y, Yao M, Wei Z, Fu Y, Yang Z. Niacin attenuates the production of pro-inflammatory cytokines in LPS-induced mouse alveolar macrophages by HCA2 dependent mechanisms. International Immunopharmacology. 2014; 23: 121–126. https://doi.org/10.1016/j.intimp.2014.07.006.
[49] Marques C, Hadjab F, Porcello A, Lourenço K, Scaletta C, Abdel-Sayed P, *et al*. Mechanistic Insights into the Multiple Functions of Niacinamide: Therapeutic Implications and Cosmeceutical Applications in Functional Skincare Products. Antioxidants (Basel). 2024; 13: 425. https://doi.org/10.3390/antiox13040425.
[50] Kim B, Kim JE, Lee SM, Lee SH, Lee JW, Kim MK, *et al*. N-Nicotinoyl dopamine, a novel niacinamide derivative, retains high antioxidant activity and inhibits skin pigmentation. Experimental Dermatology. 2011; 20: 950–952. https://doi.org/10.1111/j.1600-0625.2011.01345.x.
[51] Grada A, Phillips TJ. Nutrition and cutaneous wound healing. Clinics in Dermatology. 2022; 40: 103–113. https://doi.org/10.1016/j.clindermatol.2021.10.002.
[52] Yildizhan E, Ulger BV, Akkus M, Akinci D, Basol O. Comparison of topical sucralfate with dexpanthenol in rat wound model. International Journal of Experimental Pathology. 2022; 103: 164–170. https://doi.org/10.1111/iep.12441.
[53] Küba MC, Türkoğlu A, Oğuz A, Tuncer MC, Kaya Ş, Başol Ö, *et al*. Comparison of local rosmarinic acid and topical dexpanthenol applications on wound healing in a rat experimental wound model. Folia Morphologica. 2021; 80: 618–624. https://doi.org/10.5603/FM.a2020.0097.
[54] Heise R, Schmitt L, Huth L, Krings L, Kluwig D, Katsoulari KV *et al*. Accelerated wound healing with a dexpanthenol-containing ointment after fractional ablative CO2 laser resurfacing of photo-damaged skin in a randomized prospective clinical trial. Cutaneous and Ocular Toxicology. 2019; 38: 274–278. https://doi.org/10.1080/15569527.2019.1597879.
[55] Kobayashi D, Kusama M, Onda M, Nakahata N. The effect of pantothenic acid deficiency on keratinocyte proliferation and the synthesis of keratinocyte growth factor and collagen in fibroblasts. Journal of Pharmacological Sciences. 2011; 115: 230–234. https://doi.org/10.1254/jphs.10224sc.
[56] Slyshenkov VS, Dymkowska D, Wojtczak L. Pantothenic acid and pantothenol increase biosynthesis of glutathione by boosting cell energetics. FEBS letters. 2004; 569: 169–172. https://doi.org/10.1016/j.febslet.2004.05.044.
[57] Gheita AA, Gheita TA, Kenawy SA. The potential role of B5: A stitch in time and switch in cytokine. Phytotherapy Research: PTR. 2020; 34: 306–314. https://doi.org/10.1002/ptr.6537.
[58] Etensel B, Ozkisacik S, Ozkara E, Karul A, Oztan O, Yazici M, *et al*. Dexpanthenol attenuates lipid peroxidation and testicular damage at experimental ischemia and reperfusion injury. Pediatric Surgery International. 2007; 23: 177–181. https://doi.org/10.1007/s00383-006-1781-x.
[59] Heise R, Skazik C, Marquardt Y, Czaja K, Sebastian K, Kurschat P, *et al*. Dexpanthenol modulates gene expression in skin wound healing in vivo. Skin Pharmacology and Physiology. 2012; 25: 241–248. https://doi.org/10.1159/000341144.
[60] Proksch E, de Bony R, Trapp S, Boudon S. Topical use of dexpanthenol: a 70th anniversary article. The Journal of Dermatological Treatment. 2017; 28: 766–773. https://doi.org/10.1080/09546634.2017.1325310.
[61] Dell'Acqua G, Schweikert K. Panthenyl triacetate transformation, stimulation of metabolic pathways, and wound-healing properties in the human skin. Journal of Cosmetic Science. 2012; 63: 1–13.
[62] Ulger BV, Kapan M, Uslukaya O, Bozdag Z, Turkoglu A, Alabalık U, *et al*. Comparing the effects of nebivolol and dexpanthenol on wound healing: an experimental study. International Wound Journal. 2016; 13: 367–371. https://doi.org/10.1111/iwj.12314.
[63] Egger SF, Huber-Spitzy V, Alzner E, Scholda C, Vecsei VP. Corneal wound healing after superficial foreign body injury: vitamin A and dexpanthenol versus a calf blood extract. A randomized double-blind study. Journal International D'ophtalmologie. 1999; 213: 246–249. https://doi.org/10.1159/000027429.
[64] Li W, Yu Q, Shen Z, Zhang Z, Li C, Li C, *et al*. Effects of a cream containing madecassoside, 5% panthenol, and copper-zinc-manganese on improving postlaser resurfacing wound healing: A split-face, randomized trial. Dermatologic Therapy. 2020; 33: e13533. https://doi.org/10.1111/dth.13533.
[65] Celebi S, Tepe C, Yelken K, Celik O. Efficacy of dexpanthenol

for pediatric post-tonsillectomy pain and wound healing. The Annals of otology, Rhinology, and Laryngology. 2013; 122: 464–467. https://doi.org/10.1177/000348941312200710.

[66] Yelich A, Jenkins H, Holt S, Miller R. Biotin for Hair Loss: Teasing Out the Evidence. The Journal of Clinical and Aesthetic Dermatology. 2024; 17: 56–61.

[67] El-Esawy FM, Hussein MS, Ibrahim Mansour A. Serum biotin and zinc in male androgenetic alopecia. Journal of Cosmetic Dermatology. 2019; 18: 1546–1549. https://doi.org/10.1111/jocd.12865.

[68] Duchi S, Rebollo Torregrosa P, Hajuj A, Molho D, Shkoor R, Saada NA, *et al*. The formulation and in vitro evaluation of WS Biotin, a novel encapsulated form of D-Biotin with improved water solubility for hair and skin treatment applications. International Journal of Cosmetic Science. 2024; 46: 119–129. https://doi.org/10.1111/ics.12914.

[69] Samadi A, Ketabi Y, Firooz R, Firooz A. Efficacy of intramuscular injections of biotin and dexpanthenol in the treatment of diffuse hair loss: A randomized, double-blind controlled study comparing two brands. Dermatologic Therapy. 2022; 35: e15695. https://doi.org/10.1111/dth.15695.

[70] Chavan D. Reversal of Premature Hair Graying Treated with a Topical Formulation Containing α-Melanocyte-Stimulating Hormone Agonist (Greyverse Solution 2%). International Journal of Trichology. 2022; 14: 207–209. https://doi.org/10.4103/ijt.ijt_85_22.

[71] Tr P, Ts R, K SK, Prasanna H. A Comparative Study of Topical Procapil With Platelet-Rich Plasma Therapy Versus Topical Redensyl, Saw Palmetto, and Biotin With Platelet-Rich Plasma Therapy in the Treatment of Androgenetic Alopecia. Cureus. 2023; 15: e38696. https://doi.org/10.7759/cureus.38696.

[72] Güder H, Eker P. A Retrospective Evaluation of the Laboratory Findings of Dermatology Patients Whose Biotin Levels Were Checked. Cureus. 2023; 15: e41482. https://doi.org/10.7759/cureus.41482.

[73] Jo H, Kim SY, Kang BH, Baek C, Kwon JE, Jeang JW *et al*. Staphylococcus epidermidis Cicaria, a Novel Strain Derived from the Human Microbiome, and Its Efficacy as a Treatment for Hair Loss. Molecules. 2022; 27: 5136. https://doi.org/10.3390/molecules27165136.

[74] Benke PJ, Duchowny M, McKnight D. Biotin and Acetazolamide for Treatment of an Unusual Child With Autism Plus Lack of Nail and Hair Growth. Pediatric Neurology. 2018; 79: 61–64. https://doi.org/10.1016/j.pediatrneurol.2017.10.013.

[75] Williams GR, Cervinski MA, Nerenz RD. Assessment of biotin interference with qualitative point-of-care hCG test devices. Clinical Biochemistry. 2018; 53: 168–170. https://doi.org/10.1016/j.clinbiochem.2018.01.018.

[76] Lin CC, Sun DS, Lin YL, Tsai TT, Cheng C, Sun WH, *et al*. A flexible and miniaturized hair dye based photodetector via chemiluminescence pathway. Biosensors & Bioelectronics. 2017; 90: 349–355. https://doi.org/10.1016/j.bios.2016.12.011.

[77] Sahay G. Resistant Alopecia Areata Treated with Tofacitinib. International Journal of Trichology. 2022; 14: 181–182. https://doi.org/10.4103/ijt.ijt_63_22.

[78] Daulatabad D, Singal A, Grover C, Chhillar N. Prospective Analytical Controlled Study Evaluating Serum Biotin, Vitamin B12, and Folic Acid in Patients with Premature Canities. International Journal of Trichology. 2017; 9: 19–24. https://doi.org/10.4103/ijt.ijt_79_16.

[79] Grootens KP, Hartong EGTM. A Case Report of Biotin Treatment for Valproate-Induced Hair Loss. The Journal of Clinical Psychiatry. 2017; 78: e838. https://doi.org/10.4088/JCP.17cr11469.

[80] Weimann A, Plomgaard P, Hilsted LM, Poulsen HE, Larsen EL. Quantification of biotin in plasma samples by column switching liquid chromatography - tandem mass spectrometry. Scandinavian Journal of Clinical and Laboratory Investigation. 2021; 81:127–136. https://doi.org/10.1080/00365513.2020.1871504.

[81] Lipner SR. Rethinking biotin therapy for hair, nail, and skin disorders. Journal of the American Academy of Dermatology. 2018; 78: 1236–1238. https://doi.org/10.1016/j.jaad.2018.02.018.

[82] Almohanna HM, Ahmed AA, Tsatalis JP, Tosti A. The Role of Vitamins and Minerals in Hair Loss: A Review. Dermatology and Therapy. 2019; 9: 51–70. https://doi.org/10.1007/s13555-018-0278-6.

[83] Şen O, Türkçapar AG. Hair Loss After Sleeve Gastrectomy and Effect of Biotin Supplements. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2021; 31: 296–300. https://doi.org/10.1089/lap.2020.0468.

[84] Godlewski CA, Kalagara H, Vazquez Do Campo R, Northern T, Kukreja P. Post-Surgical Inflammatory Neuropathy: An Underappreciated but Critical and Treatable Cause of Postoperative Neuropathy. Cureus. 2020; 12: e11927. https://doi.org/10.7759/cureus.11927.

[85] Kumar N. Nutrients and Neurology. Continuum (Minneapolis, Minn.). 2017; 23: 822–861. https://doi.org/10.1212/01.CON.0000520630.69195.90.

[86] Baranwal, N., Gong, J.H., Arnoff, T.E., Mehrzad, M. The role and management of vitamin supplementation in plastic surgery patients: A comprehensive review. European Journal of Plastic Surgery. 2024; 47: 22. https://doi.org/10.1007/s00238-024-02165-6.

[87] Leavell Y, Shin SC. Paraproteinemias and Peripheral Nerve Disease. Clinics in Geriatric Medicine. 2021; 37: 301–312. https://doi.org/10.1016/j.cger.2021.01.004.

[88] Velazquez-Arellano A, Hernandez-Vazquez AdJ. Chapter 35 - Vitamins as Cofactors for Energy Homeostasis and Their Genomic Control, With Special Reference to Biotin, Thiamine, and Pantothenic Acid. In Caterina RDE, Martinez JA, Kohlmeier M (eds.) Principles of Nutrigenetics and Nutrigenomics (pp. 271–277). Academic Press: New York. 2020.

[89] Kareem O, Nisar S, Tanvir M, Muzaffer U, Bader GN. Thiamine deficiency in pregnancy and lactation: implications and present perspectives. Frontiers in Nutrition. 2023; 10: 1080611. https://doi.org/10.3389/fnut.2023.1080611.

[90] Le Guennec L, Marois C, Demeret S, Wijdicks EFM, Weiss N. Toxic-metabolic encephalopathy in adults: Critical discussion and pragmatical diagnostic approach. Revue Neurologique. 2022; 178: 93–104. https://doi.org/10.1016/j.neurol.2021.11.007.

[91] Leuzzi V, Galosi S. Experimental pharmacology: Targeting metabolic pathways. International Review of Neurobiology. 2023; 169: 259–315. https://doi.org/10.1016/bs.irn.2023.05.005.

[92] Alemanno F, Ghisi D, Westermann B, Bettoni A, Fanelli A, La Colla L, *et al*. The use of vitamin B1 as a perineural adjuvant to middle interscalene block for postoperative analgesia after shoulder surgery. Acta Bio-medica. 2016; 87: 22–27.

[93] Song XS, Huang ZJ, Song XJ. Thiamine suppresses thermal hyperalgesia, inhibits hyperexcitability, and lessens alterations of sodium currents in injured, dorsal root ganglion neurons in rats. Anesthesiology. 2009; 110: 387–400. https://doi.org/10.1097/ALN.0b013e3181942f1e.

[94] Stracke H, Hammes HP, Werkmann D, Mavrakis K, Bitsch I, Netzel M *et al*. Efficacy of benfotiamine versus thiamine on function and glycation products of peripheral nerves in diabetic rats. Experimental and Clinical Endocrinology & Diabetes. 2001; 109: 330–336. https://doi.org/10.1055/s-2001-17399.

[95] Mekaj Y, Mekaj A. The Role of Pharmacological Agents in Nerve Regeneration after Peripheral Nerve Repair. In Maurício

AC (ed.) Peripheral Nerve Regeneration - From Surgery to New Therapeutic Approaches Including Biomaterials and Cell-Based Therapies Development. IntechOpen: Rijeka. 2017.

[96] Paez-Hurtado AM, Calderon-Ospina CA, Nava-Mesa MO. Mechanisms of action of vitamin B1 (thiamine), B6 (pyridoxine), and B12 (cobalamin) in pain: a narrative review. Nutritional Neuroscience. 2023; 26: 235–253. https://doi.org/10.1080/1028415X.2022.2034242.

[97] Zhang M, Han W, Hu S, Xu H. Methylcobalamin: a potential vitamin of pain killer. Neural Plasticity. 2013; 2013: 424651. https://doi.org/10.1155/2013/424651.

[98] Albay C, Akkalp AK. Alpha-Tocopherol and Cyanocobalamin Combination Accelerates Peripheral Nerve Healing: An Experimental Animal Study. Turkish neurosurgery. 2021; 31: 247–253. https://doi.org/10.5137/1019-5149.JTN.30784-20.3.

[99] Abushukur Y, Knackstedt R. The Impact of Supplements on Recovery After Peripheral Nerve Injury: A Review of the Literature. Cureus. 2022; 14: e25135. https://doi.org/10.7759/cureus.25135.

[100] Yoshimura Y, Iwahashi T, Kasuya T, Shimada T, Konishi K, Kamata A, *et al*. Methylcobalamin-containing nanofiber sheets have better neuroprotective effects than small intestinal submucosa sheets. Scientific Reports. 2025; 15: 950. https://doi.org/10.1038/s41598-024-78933-y.

[101] Yang TT, Wang SJ. Pyridoxine inhibits depolarization-evoked glutamate release in nerve terminals from rat cerebral cortex: a possible neuroprotective mechanism? The Journal of Pharmacology and Experimental Therapeutics. 2009; 331: 244–254. https://doi.org/10.1124/jpet.109.155176.

[102] Shabeeb D, Najafi M, Keshavarz M, Musa AE, Hassanzadeh G, Hadian MR, *et al*. Recent Finding in Repair of the Peripheral Nerve Lesions Using Pharmacological Agents: Common Methods for Evaluating the Repair Process. Central Nervous System Agents in Medicinal Chemistry. 2018; 18: 161–172. https://doi.org/10.2174/1871524918666180830101953.

[103] Tian S, Wu L, Zheng H, Zhong X, Liu M, Yu X, *et al*. Dietary niacin intake in relation to depression among adults: a population-based study. BMC Psychiatry. 2023; 23: 678. https://doi.org/10.1186/s12888-023-05188-8.

[104] Song TY, Yeh SL, Hu ML, Chen MY, Yang NC. A Nampt inhibitor FK866 mimics vitamin B3 deficiency by causing senescence of human fibroblastic Hs68 cells via attenuation of NAD(+)-SIRT1 signaling. Biogerontology. 2015; 16: 789–800. https://doi.org/10.1007/s10522-015-9605-9.

[105] Bossard V, Bourmeyster N, Pasini S, Dupuis P, El Balkhi S, Richard E, *et al*. Problematic rise of vitamin B6 supplementation overuse and potential risk to bariatric surgery patients. Nutrition. 2022; 102: 111738. https://doi.org/10.1016/j.nut.2022.111738.

[106] Alsaadi T, El Hammasi K, Shahrour TM. Does pyridoxine control behavioral symptoms in adult patients treated with levetiracetam? Case series from UAE. Epilepsy & Behavior Case Reports. 2015; 4: 94–95. https://doi.org/10.1016/j.ebcr.2015.08.003.

[107] Scott LN, Fiume M, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, *et al*. Safety Assessment of Panthenol, Pantothenic Acid, and Derivatives as Used in Cosmetics. International Journal of Toxicology. 2022; 41(3_suppl): 77–128. https://doi.org/10.1177/10915818221124809.

[108] Kovatcheva M, Melendez E, Chondronasiou D, Pietrocola F, Bernad R, Caballe A, *et al*. Vitamin B12 is a limiting factor for induced cellular plasticity and tissue repair. Nature Metabolism. 2023; 5: 1911–1930. https://doi.org/10.1038/s42255-023-00916-6.

[109] Choi JY, Min JY, Min KB. Anti-aging protein klotho was associated with vitamin B12 concentration in adults. Medicine (Baltimore). 2022; 101: e30710. https://doi.org/10.1097/MD.0000000000030710.

[110] Mills KF, Yoshida S, Stein LR, Grozio A, Kubota S, Sasaki Y, *et al*. Long-Term Administration of Nicotinamide Mononucleotide Mitigates Age-Associated Physiological Decline in Mice. Cell Metabolism. 2016; 24: 795–806. https://doi.org/10.1016/j.cmet.2016.09.013.

[111] Yi L, Maier AB, Tao R, Lin Z, Vaidya A, Pendse S, *et al*. The efficacy and safety of β-nicotinamide mononucleotide (NMN) supplementation in healthy middle-aged adults: a randomized, multicenter, double-blind, placebo-controlled, parallel-group, dose-dependent clinical trial. Geroscience. 2023; 45: 29–43. https://doi.org/10.1007/s11357-022-00705-1.

[112] Gonçalves AC, Portari GV. The B-complex vitamins related to energy metabolism and their role in exercise performance: A narrative review. Science & Sports. 2021; 36: 433–440. https://doi.org/10.1016/j.scispo.2020.11.007.

[113] Simonenko SY, Bogdanova DA, Kuldyushev NA. Emerging Roles of Vitamin B12 in Aging and Inflammation. International Journal of Molecular Sciences. 2024; 25: 5044. https://doi.org/10.3390/ijms25095044.

[114] Vílchez-Acosta A, Desdín-Micó G, Ocampo A. Vitamin B12 emerges as key player during cellular reprogramming. Nature Metabolism. 2023; 5: 1844–1845. https://doi.org/10.1038/s42255-023-00917-5.

[115] Takahashi-Iñiguez T, García-Hernandez E, Arreguín-Espinosa R, Flores ME. Role of vitamin B12 on methylmalonyl-CoA mutase activity. Journal of Zhejiang University. 2012; 13: 423–437. https://doi.org/10.1631/jzus.B1100329.

[116] Froese DS, Fowler B, Baumgartner MR. Vitamin B12, folate, and the methionine remethylation cycle-biochemistry, pathways, and regulation. Journal of Inherited Metabolic Disease. 2019; 42: 673–685. https://doi.org/10.1002/jimd.12009.

[117] Tejero J, Lazure F, Gomes AP. Methylmalonic acid in aging and disease. Trends in Endocrinology and Metabolism. 2024; 35: 188–200. https://doi.org/10.1016/j.tem.2023.11.001.

[118] Saxton RA, Sabatini DM. mTOR Signaling in Growth, Metabolism, and Disease. Cell. 2017; 169: 361–371. https://doi.org/10.1016/j.cell.2017.03.035. Erratum for: Cell. 2017; 168: 960–976. https://doi.org/10.1016/j.cell.2017.02.004.

[119] Tripathi M, Zhang CW, Singh BK, Sinha RA, Moe KT, DeSilva DA, *et al*. Hyperhomocysteinemia causes ER stress and impaired autophagy that is reversed by Vitamin B supplementation. Cell Death & Disease. 2016; 7: e2513. https://doi.org/10.1038/cddis.2016.374.

[120] Abdullah A, Mohd Murshid N, Makpol S. Antioxidant Modulation of mTOR and Sirtuin Pathways in Age-Related Neurodegenerative Diseases. Molecular Neurobiology. 2020; 57: 5193–5207. https://doi.org/10.1007/s12035-020-02083-1.

[121] Alegre GFS, Pastore GM. NAD+ Precursors Nicotinamide Mononucleotide (NMN) and Nicotinamide Riboside (NR): Potential Dietary Contribution to Health. Current Nutrition Reports. 2023; 12: 445–464. https://doi.org/10.1007/s13668-023-00475-y.

[122] Nadeeshani H, Li J, Ying T, Zhang B, Lu J. Nicotinamide mononucleotide (NMN) as an anti-aging health product - Promises and safety concerns. Journal of Advanced Research. 2021; 37: 267–278. https://doi.org/10.1016/j.jare.2021.08.003.

[123] Wang H, Sun Y, Pi C, Yu X, Gao X, Zhang C, *et al*. Nicotinamide Mononucleotide Supplementation Improves Mitochondrial Dysfunction and Rescues Cellular Senescence by NAD+/Sirt3 Pathway in Mesenchymal Stem Cells. International Journal of Molecular Sciences. 2022; 23: 14739. https://doi.org/10.3390/ijms232314739.

[124] Xu C, Dai J, Ai H, Du W, Ji H. β-Nicotinamide Mononucleotide Promotes Cell Proliferation and Hair Growth by Reducing Oxidative Stress. Molecules. 2024; 29: 798. https://doi.org/

10.3390/molecules29040798.
[125] Soma M, Lalam SK. The role of nicotinamide mononucleotide (NMN) in anti-aging, longevity, and its potential for treating chronic conditions. Molecular Biology Reports. 2022; 49: 9737–9748. https://doi.org/10.1007/s11033-022-07459-1.
[126] Tarantini S, Valcarcel-Ares MN, Toth P, Yabluchanskiy A, Tucsek Z, Kiss T, *et al*. Nicotinamide mononucleotide (NMN) supplementation rescues cerebromicrovascular endothelial function and neurovascular coupling responses and improves cognitive function in aged mice. Redox Biology. 2019; 24: 101192. https://doi.org/10.1016/j.redox.2019.101192.
[127] Camillo L, Zavattaro E, Savoia P. Nicotinamide: A Multifaceted Molecule in Skin Health and Beyond. Medicina (Kaunas, Lithuania). 2025; 61: 254. https://doi.org/10.3390/medicina61020254.
[128] Thompson BC, Surjana D, Halliday GM, Damian DL. Nicotinamide enhances repair of ultraviolet radiation-induced DNA damage in primary melanocytes. Experimental Dermatology. 2014; 23: 509–511. https://doi.org/10.1111/exd.12430.
[129] Cao AP, Wang YY, Shen YY, Liu YH, Liu JY, Wang Y, *et al*. Nicotinamide Suppresses Hyperactivation of Dendritic Cells to Control Autoimmune Disease through PARP Dependent Signaling. Nutrients. 2024; 16: 2665. https://doi.org/10.3390/nu16162665.
[130] Ziklo N, Bibi M, Sinai L, Salama P. Niacinamide Antimicrobial Efficacy and Its Mode of Action via Microbial Cell Cycle Arrest. Microorganisms. 2024; 12: 1581. https://doi.org/10.3390/microorganisms12081581.
[131] Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A. Vitamins and Minerals for Energy, Fatigue and Cognition: A Narrative Review of the Biochemical and Clinical Evidence. Nutrients. 2020; 12: 228. https://doi.org/10.3390/nu12010228.
[132] Tsuji T, Fukuwatari T, Sasaki S, Shibata K. Urinary excretion of vitamin B1, B2, B6, niacin, pantothenic acid, folate, and vitamin C correlates with dietary intakes of free-living elderly, female Japanese. Nutrition Research (New York, N.Y.). 2010; 30: 171–178. https://doi.org/10.1016/j.nutres.2010.02.001.
[133] Temova Rakuša Ž, Roškar R, Hickey N, Geremia S. Vitamin B12 in Foods, Food Supplements, and Medicines-A Review of Its Role and Properties with a Focus on Its Stability. Molecules. 2022; 28: 240. https://doi.org/10.3390/molecules28010240.
[134] Li S, Guo Y, Men J, Fu H, Xu T. The preventive efficacy of vitamin B supplements on the cognitive decline of elderly adults: a systematic review and meta-analysis. BMC Geriatrics. 2021; 21: 367. https://doi.org/10.1186/s12877-021-02253-3.
[135] Vitagliano T, Garieri P, Lascala L, Ferro Y, Doldo P, Pujia R, *et al*. Preparing Patients for Cosmetic Surgery and Aesthetic Procedures: Ensuring an Optimal Nutritional Status for Successful Results. Nutrients. 2023; 15: 352. https://doi.org/10.3390/nu15020352.
[136] Broughton G 2nd, Crosby MA, Coleman J, Rohrich RJ. Use of herbal supplements and vitamins in plastic surgery: a practical review. Plastic and Reconstructive Surgery. 2007; 119: 48e–66e. https://doi.org/10.1097/01.prs.0000252661.72071.8d.
[137] Alkalay MJ. Nutrition in Patients with Lactose Malabsorption, Celiac Disease, and Related Disorders. Nutrients. 2021; 14: 2. https://doi.org/10.3390/nu14010002.
[138] Giustina A, di Filippo L, Allora A, Bikle DD, Cavestro GM, Feldman D, *et al*. Vitamin D and malabsorptive gastrointestinal conditions: A bidirectional relationship?. Reviews in Endocrine & Metabolic Disorders. 2023; 24: 121–138. https://doi.org/10.1007/s11154-023-09792-7.
[139] Jouanne M, Oddoux S, Noël A, Voisin-Chiret AS. Nutrient Requirements during Pregnancy and Lactation. Nutrients. 2021; 13: 692. https://doi.org/10.3390/nu13020692.
[140] Esquivel MK. Nutrition for Pregnant and Lactating Women: The Latest Recommendations From the Dietary Guidelines for Americans 2020–2025 and Practice Implications. American Journal of Lifestyle Medicine. 2021; 15: 392–396. https://doi.org/10.1177/15598276211004082.
[141] Brancaccio M, Mennitti C, Cesaro A, Fimiani F, Vano M, Gargiulo B, *et al*. The Biological Role of Vitamins in Athletes' Muscle, Heart and Microbiota. International Journal of Environmental Research and Public Health. 2022; 19: 1249. https://doi.org/10.3390/ijerph19031249.
[142] Amawi A, AlKasasbeh W, Jaradat M, Almasri A, Alobaidi S, Hammad AA, *et al*. Athletes' nutritional demands: a narrative review of nutritional requirements. Frontiers in Nutrition. 2024; 10: 1331854. https://doi.org/10.3389/fnut.2023.1331854.
[143] Thornalley PJ. The potential role of thiamine (vitamin B1) in diabetic complications. Current Diabetes Reviews. 2005; 1: 287–298. https://doi.org/10.2174/157339905774574383.
[144] Ziegler D, Reiners K, Strom A, Obeid R. Association between diabetes and thiamine status - A systematic review and meta-analysis. Metabolism: Clinical and Experimental. 2023; 144: 155565. https://doi.org/10.1016/j.metabol.2023.155565.
[145] Toninello P, Montanari A, Bassetto F, Vindigni V, Paoli A. Nutritional Support for Bariatric Surgery Patients: The Skin beyond the Fat. Nutrients. 2021; 13: 1565. https://doi.org/10.3390/nu13051565.
[146] Miao Y, Guo Y, Chen Y, Lin Y, Lu Y, Guo Q. The effect of B-vitamins on the prevention and treatment of cardiovascular diseases: a systematic review and meta-analysis. Nutrition Reviews. 2024; 82: 1386–1401. https://doi.org/10.1093/nutrit/nuad127.
[147] Chen Q, Huang J, Shi X, Peng Y, Chen A, Huang L, *et al*. Associations between dietary B vitamin intakes and cognitive function among elderly individuals: An observational study. Nutrition. 2025; 134: 112716. https://doi.org/10.1016/j.nut.2025.112716.
[148] Ali MA, Hafez HA, Kamel MA, Ghamry HI, Shukry M, Farag MA. Dietary Vitamin B Complex: Orchestration in Human Nutrition throughout Life with Sex Differences. Nutrients. 2022; 14: 3940. https://doi.org/10.3390/nu14193940.
[149] Institute of Medicine (US) Standing Committee on the Scientific Evaluation of Dietary Reference Intakes and its Panel on Folate, Other B Vitamins, and Choline. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. National Academies Press (US): Washington (DC). 1998.
[150] Rana P, Roy V. Prescribing vitamin B complex: Need for reassessment. Indian Journal of Medical Research. 2021; 154: 781–785. https://doi.org/10.4103/ijmr.IJMR_1467_19.
[151] Chen LR, Yang BS, Chang CN, Yu CM, Chen KH. Additional Vitamin and Mineral Support for Patients with Severe Burns: A Nationwide Experience from a Catastrophic Color-Dust Explosion Event in Taiwan. Nutrients. 2018; 10: 1782. https://doi.org/10.3390/nu10111782.
[152] Gardiner S, Hartzell T. Thiamine deficiency: a cause of profound hypotension and hypothermia after plastic surgery. Aesthetic Surgery Journal. 2015; 35: NP1–NP3. https://doi.org/10.1093/asj/sju092.
[153] Sebastian JL, V JM, Tang LW, Rubin JP. Thiamine deficiency in a gastric bypass patient leading to acute neurologic compromise after plastic surgery. Surgery for obesity and related diseases: official journal of the American Society for Bariatric Surgery. 2010; 6: 105–106. https://doi.org/10.1016/j.soard.2009.04.017.
[154] Schijns W, Homan J, van der Meer L, Janssen IM, van Laarhoven CJ, Berends FJ, *et al*. Efficacy of oral compared with intramuscular vitamin B-12 supplementation after Roux-en-Y gastric bypass: a randomized controlled trial. The American

Journal of Clinical Nutrition. 2018; 108: 6–12. https://doi.org/10.1093/ajcn/nqy072.

[155] Ankar A, Kumar A. Vitamin B12 Deficiency. In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2024.

[156] Ford TC, Downey LA, Simpson T, McPhee G, Oliver C, Stough C. The Effect of a High-Dose Vitamin B Multivitamin Supplement on the Relationship between Brain Metabolism and Blood Biomarkers of Oxidative Stress: A Randomized Control Trial. Nutrients. 2018; 10: 1860. https://doi.org/10.3390/nu10121860.

[157] Gillies N, Cameron-Smith D, Pundir S, Wall CR, Milan AM. Exploring trajectories in dietary adequacy of the B vitamins folate, riboflavin, vitamins B6 and B12, with advancing older age: a systematic review. The British Journal of Nutrition. 2021; 126: 449–459. https://doi.org/10.1017/S0007114520004249.

[158] Paluszny A, Qiu S. Vitamin B6 Toxicity Secondary to Daily Multivitamin Use: A Case Report. Cureus. 2023; 15: e48792. https://doi.org/10.7759/cureus.48792.

[159] Hemminger A, Wills BK. Vitamin B6 Toxicity. In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2023.

[160] Javaid A, Mudavath SL. Niacin-induced flushing: Mechanism, pathophysiology, and future perspectives. Archives of Biochemistry and Biophysics. 2024; 761: 110163. https://doi.org/10.1016/j.abb.2024.110163.

[161] Kamanna VS, Ganji SH, Kashyap ML. The mechanism and mitigation of niacin-induced flushing. International Journal of Clinical Practice. 2009; 63: 1369–1377. https://doi.org/10.1111/j.1742-1241.2009.02099.x.

[162] Zhou J, Han J. Association of niacin intake and metabolic dysfunction-associated steatotic liver disease: findings from National Health and Nutrition Examination Survey. BMC Public Health. 2024; 24: 2742. https://doi.org/10.1186/s12889-024-20161-0.

[163] Li D, Sun WP, Zhou YM, Liu QG, Zhou SS, Luo N, *et al.* Chronic niacin overload may be involved in the increased prevalence of obesity in US children. World Journal of Gastroenterology. 2010; 16: 2378–2387. https://doi.org/10.3748/wjg.v16.i19.2378.

[164] Tahiliani AG, Beinlich CJ. Pantothenic acid in health and disease. Vitamins and Hormones. 1991; 46: 165–228. https://doi.org/10.1016/s0083-6729(08)60684-6.

[165] Sanvictores T, Chauhan S. Vitamin B5 (Pantothenic Acid). In StatPearls [Internet]. StatPearls Publishing: Treasure Island (FL). 2024.

[166] Gifford JL, Sadrzadeh SMH, Naugler C. Biotin interference: Underrecognized patient safety risk in laboratory testing. Canadian Family Physician Medecin de famille canadien. 2018; 64: 370.

[167] Li D, Ferguson A, Cervinski MA, Lynch KL, Kyle PB. AACC Guidance Document on Biotin Interference in Laboratory Tests. The Journal of Applied Laboratory Medicine. 2020; 5: 575–587. https://doi.org/10.1093/jalm/jfz010.

[168] Sobczyńska-Malefora A, Delvin E, McCaddon A, Ahmadi KR, Harrington DJ. Vitamin B12 status in health and disease: a critical review. Diagnosis of deficiency and insufficiency - clinical and laboratory pitfalls. Critical Reviews in Clinical Laboratory Sciences. 2021; 58: 399–429. https://doi.org/10.1080/10408363.2021.1885339.

[169] Calderon-Ospina CA, Nava-Mesa MO, Paez-Hurtado AM. Update on Safety Profiles of Vitamins B1, B6, and B12: A Narrative Review. Therapeutics and Clinical Risk Management. 2020; 16:1275–1288. https://doi.org/10.2147/TCRM.S274122.

[170] Doets EL, In 't Veld PH, Szczecińska A, Dhonukshe-Rutten RA, Cavelaars AE, van 't Veer P, *et al.* Systematic review on daily vitamin B12 losses and bioavailability for deriving recommendations on vitamin B12 intake with the factorial approach. Annals of Nutrition & Metabolism. 2013; 62: 311–322. https://doi.org/10.1159/000346968.

[171] Juszczak AB, Kupczak M, Konecki T. Does Vitamin Supplementation Play a Role in Chronic Kidney Disease? Nutrients. 2023; 15: 2847. https://doi.org/10.3390/nu15132847.

[172] Sato Y, Yasumiishi C, Chiba T, Umegaki K. [A Systematic Review to Identify Unacceptable Intake Levels of Vitamin B6 among Patients Taking Levodopa]. Shokuhin Eiseigaku Zasshi. Journal of the Food Hygienic Society of Japan. 2017; 58: 268–274. https://doi.org/10.3358/shokueishi.58.268. (In Japanese)

[173] Miller JW. Proton Pump Inhibitors, H2-Receptor Antagonists, Metformin, and Vitamin B-12 Deficiency: Clinical Implications. Advances in Nutrition (Bethesda, Md.). 2018; 9: 511S–518S. https://doi.org/10.1093/advances/nmy023.

[174] Mumtaz H, Ghafoor B, Saghir H, Tariq M, Dahar K, Ali SH, *et al*. Association of Vitamin B12 deficiency with long-term PPIs use: A cohort study. Annals of Medicine and Surgery. 2022; 82: 104762. https://doi.org/10.1016/j.amsu.2022.104762.

[175] Chiu PC, Chan CC, Lin HM, Chiu HC. The clinical anti-aging effects of topical kinetin and niacinamide in Asians: a randomized, double-blind, placebo-controlled, split-face comparative trial. Journal of Cosmetic Dermatology. 2007; 6: 243–249. https://doi.org/10.1111/j.1473-2165.2007.00342.x.

[176] Calderón-Ospina CA, Nava-Mesa MO. B Vitamins in the nervous system: Current knowledge of the biochemical modes of action and synergies of thiamine, pyridoxine, and cobalamin. CNS Neuroscience & Therapeutics. 2020; 26: 5–13. https://doi.org/10.1111/cns.13207.

[177] Mascarenhas R, Gouda H, Ruetz M, Banerjee R. Human B12-dependent enzymes: Methionine synthase and Methylmalonyl-CoA mutase. Methods in Enzymology. 2022; 668: 309–326. https://doi.org/10.1016/bs.mie.2021.12.012.

[178] Stücker M, Pieck C, Stoerb C, Niedner R, Hartung J, Altmeyer P. Topical vitamin B12–a new therapeutic approach in atopic dermatitis-evaluation of efficacy and tolerability in a randomized placebo-controlled multicentre clinical trial. The British Journal of Dermatology. 2004; 150: 977–983. https://doi.org/10.1111/j.1365-2133.2004.05866.x.

[179] Elgharably N, Al Abadie M, Al Abadie M, Ball PA, Morrissey H. Vitamin B group levels and supplementations in dermatology. Dermatology Reports. 2022; 15: 9511. https://doi.org/10.4081/dr.2022.9511.

[180] Hossain KS, Amarasena S, Mayengbam S. B Vitamins and Their Roles in Gut Health. Microorganisms. 2022; 10: 1168. https://doi.org/10.3390/microorganisms10061168.

[181] Yoshii K, Hosomi K, Sawane K, Kunisawa J. Metabolism of Dietary and Microbial Vitamin B Family in the Regulation of Host Immunity. Frontiers in Nutrition. 2019; 6: 48. https://doi.org/10.3389/fnut.2019.00048.

[182] Bösch ES, Spörri J, Scherr J. Vitamin Metabolism and Its Dependency on Genetic Variations Among Healthy Adults: A Systematic Review for Precision Nutrition Strategies. Nutrients. 2025; 17: 242. https://doi.org/10.3390/nu17020242.

[183] Costeira R, Evangelista L, Wilson R, Yan X, Hellbach F, Sinke L, *et al*. Metabolomic biomarkers of habitual B vitamin intakes unveil novel differentially methylated positions in the human epigenome. Clinical Epigenetics. 2023; 15: 166. https://doi.org/10.1186/s13148-023-01578-7.

[184] Wan Z, Zheng J, Zhu Z, Sang L, Zhu J, Luo S, *et al*. Intermediate role of gut microbiota in vitamin B nutrition and its influences on human health. Frontiers in Nutrition. 2022; 9: 1031502. https://doi.org/10.3389/fnut.2022.1031502.

[185] Uebanso T, Shimohata T, Mawatari K, Takahashi A. Functional Roles of B-Vitamins in the Gut and Gut Microbiome. Molecular Nutrition & Food Research. 2020; 64: e2000426. https://doi.org/10.1002/mnfr.202000426.

[186] Hannibal L, Lysne V, Bjørke-Monsen AL, Behringer S, Grünert SC, Spiekerkoetter U, *et al*. Biomarkers and Algorithms for the Diagnosis of Vitamin B12 Deficiency. Frontiers in Molecular Biosciences. 2016; 3: 27. https://doi.org/10.3389/fmolb.2016.00027. Erratum in: Front Mol Biosci. 2017; 4: 53. https://doi.org/10.3389/fmolb.2017.00053.

[187] Lindschinger M, Tatzber F, Schimetta W, Schmid I, Lindschinger B, Cvirn G, *et al.* A Randomized Pilot Trial to Evaluate the Bioavailability of Natural versus Synthetic Vitamin B Complexes in Healthy Humans and Their Effects on Homocysteine, Oxidative Stress, and Antioxidant Levels. Oxidative Medicine and Cellular Longevity. 2019; 2019: 6082613. https://doi.org/10.1155/2019/6082613.

[188] Chaves MA, Ferreira LS, Baldino L, Pinho SC, Reverchon E. Current Applications of Liposomes for the Delivery of Vitamins: A Systematic Review. Nanomaterials (Basel, Switzerland). 2023; 13: 1557. https://doi.org/10.3390/nano13091557.

[189] Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon. 2022; 8: e09394. https://doi.org/10.1016/j.heliyon.2022.e09394.

[190] Shin CI, Kim M, Kim YC. Delivery of Niacinamide to the Skin Using Microneedle-Like Particles. Pharmaceutics. 2019; 11: 326. https://doi.org/10.3390/pharmaceutics11070326.

[191] Nazary Abrbekoh F, Salimi L, Saghati S, Amini H, Fathi Karkan S, Moharamzadeh K, *et al.* Application of microneedle patches for drug delivery; doorstep to novel therapies. Journal of Tissue Engineering. 2022; 13: 20417314221085390. https://doi.org/10.1177/20417314221085390.

[192] Zhu K, Chen X, Yu D, He Y, Song G. Preparation and characterisation of a novel hydrogel based on Auricularia polytricha β-glucan and its bio-release property for vitamin B12 delivery. Journal of the Science of Food and Agriculture. 2018; 98: 2617–2623. https://doi.org/10.1002/jsfa.8754.

[193] Fernández-Villa D, Jiménez Gómez-Lavín M, Abradelo C, San Román J, Rojo L. Tissue Engineering Therapies Based on Folic Acid and Other Vitamin B Derivatives. Functional Mechanisms and Current Applications in Regenerative Medicine. International Journal of Molecular Sciences. 2018; 19: 4068. https://doi.org/10.3390/ijms19124068.

[194] Bissett DL, Oblong JE, Berge CA. Niacinamide: A B vitamin that improves aging facial skin appearance. Dermatologic Surgery: official publication for American Society for Dermatologic Surgery. 2005; 31: 860–865; discussion 865. https://doi.org/10.1111/j.1524-4725.2005.31732.

[195] Baltrusch S. The Role of Neurotropic B Vitamins in Nerve Regeneration. BioMed Research International. 2021; 2021: 9968228. https://doi.org/10.1155/2021/9968228.

[196] Hannibal L, Lederer AK, Storz MA, Huber R, Jacobsen DW. Vitamin B12 Status and Supplementation in Plant-Based Diets. Food and Nutrition Bulletin. 2024; 45 (1 suppl): S58–S66. https://doi.org/10.1177/03795721241227233.

[197] Zhang N, Wu Z, Bai X, Song Y, Li P, Lu X, *et al*. Dosage exploration of combined B-vitamin supplementation in stroke prevention: a meta-analysis and systematic review. The American Journal of Clinical Nutrition. 2024; 119: 821–828. https://doi.org/10.1016/j.ajcnut.2023.12.021.

[198] Barker T. Vitamins and Human Health: Systematic Reviews and Original Research. Nutrients. 2023; 15: 2888. https://doi.org/10.3390/nu15132888.

[199] Rask DMG, Puntel MR, Patzkowski JC, Patzkowski MS. Multivitamin Use in Enhanced Recovery After Surgery Protocols: A Cost Analysis. Military Medicine. 2021; 186: e1024–e1028. https://doi.org/10.1093/milmed/usaa505.

[200] Nunes R, Santos-Sousa H, Vieira S, Nogueiro J, Bouça-Machado R, Pereira A, *et al*. Vitamin B Complex Deficiency After Roux-en-Y Gastric Bypass and Sleeve Gastrectomy-a Systematic Review and Meta-Analysis. Obesity Surgery. 2022; 32: 873–891. https://doi.org/10.1007/s11695-021-05783-2.

[201] Reiten OK, Wilvang MA, Mitchell SJ, Hu Z, Fang EF. Preclinical and clinical evidence of NAD+ precursors in health, disease, and ageing. Mechanisms of Ageing and Development. 2021; 199: 111567. https://doi.org/10.1016/j.mad.2021.111567.

[202] Braidy N, Liu Y. NAD+ therapy in age-related degenerative disorders: A benefit/risk analysis. Experimental Gerontology. 2020; 132: 110831. https://doi.org/10.1016/j.exger.2020.110831.