Review Article

Functional nutrition in postoperative plastic surgery: focus on seroma and fibrosis prevention

Nutrição funcional no pós-operatório de cirurgia plástica: enfoque na prevenção de seroma e fibrose

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ABSTRACT

Introduction: Based on the wide range of possible consequences and complications of plastic surgery and the role of nutrition in the recovery process of these, we see the need for therapeutic practices to ensure effectiveness of the final aesthetic result. **Method:** This study is characterized as a non-systematic review of the possible associated nutrients, bioactive compounds and herbal medicines to prevent seroma and fibrosis. Thus, we used scientific journal articles from electronic media, national laws and textbooks published between 2002 and 2012. **Results:** We demonstrated that the main causes of seroma and fibrosis are changed healing, inflammation, oxidative stress and edema. Thus, we designed a practical guide with nutrients, bioactive compounds and herbal medicines that can be used to prevent, control or mitigate the complications after plastic surgery. **Conclusion:** It was emphasized that for the treatment of covered conditions is essential that there is a multidisciplinary approach, emphasizing a medical, nutritional and therapeutic monitoring covering the known changes in the pathophysiology of seroma and fibrosis.

Keywords: Seroma; Fibrosis; Nutrition; Functional food; Phytotherapy.

RESUMO

Introdução: Com base na grande variedade de possíveis sequelas e intercorrências de cirurgias estéticas e no papel da nutrição no processo de recuperação dessas, percebe-se a necessidade de práticas terapêuticas que garantam eficácia do resultado estético final. **Método:** O presente estudo caracteriza-se como uma revisão não sistemática que associou possíveis nutrientes, compostos bioativos e fitoterápicos que previnam ou amenizem seroma e fibrose no pós operatório. Para tanto, foram utilizados artigos de revistas científicas do meio eletrônico, legislações nacionais e livros didáticos, publicados entre os anos de 2002 e 2012. **Resultados:** Demonstrou-se que as principais causas de seroma e fibrose são cicatrização alterada, inflamação, estresse oxidativo e edema. Dessa forma, foi elaborado um guia prático com os nutrientes, compostos bioativos e fitoterápicos que podem ser utilizados a fim de prevenir, controlar ou amenizar as complicações no pós-cirúrgico de procedimentos estéticos. **Conclusão:** Salientou-se que para o tratamento das condições abordadas é fundamental que haja um traba-

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lho multiprofissional, enfatizando um acompanhamento médico, nutricional e fisioterápico que abranja as alterações conhecidas na fisiopatologia de seroma e fibrose.

Descritores: Seroma; Fibrose; Nutrição; Alimento funcional; Fitoterapia.

INTRODUCTION

The Brazilian Society of Plastic Surgery showed that a substantial number of plastic surgeries, both aesthetic and reparative, were performed in the last years. The number of interventions positions the country in the second place in plastic surgery, next only to the United States, where approximately 800,000 procedures are done every year[1].

In Brazil, every 3 years, >1,000,000 aesthetic surgeries are performed. However, the efficiency of plastic surgery does not depend solely on the surgical planning. Both pre- and postoperative care have been highlighted as important factors in preventing complications and promoting a more satisfactory aesthetic result[1,2].

Concerning complications, the local ones, such as edema, seroma, bruising, hematoma, fibrosis, and necrosis of the dermofat flap, are the most frequent; however, although rare, systemic complications such as deep vein thrombosis and pulmonary embolism also occur[3].

Despite the popularity of aesthetic surgery, there is a need for technical improvements in order to enhance the postoperative physical aspect and reduce complications. A number of risk factors have been proposed, including previous abdominal surgery, smoking, hypertension, and obesity[4].

The risk factors mentioned above could lead to nutritional deficits, which, in turn, could more easily be reverted to reduce the susceptibility to complications and impaired healing. Furthermore, the expectations from the patients may exceed the goals and experience of the surgeon, increasing the need to optimize aesthetic results with the help of practices alternative to surgery[5].

For this reason and with the goal of improving the effects of the surgical intervention, it is essential to evaluate the nutritional status of the patient and plan the intake of macro- and micronutrients in the interval between the perioperative and postoperative periods[6].

On the basis of the growing number of aesthetic surgeries in Brazil; the wide variety of possible consequences and complications from these operations; the role of nutrition in the healing process, inflammation, and immunity; the need for multidisciplinary work; and, primarily, the lack of studies addressing these topics, the present study is important in order to improve the recovery, quality of life, and self-esteem of patients, in addition to the effectiveness of the final aesthetic result[1,3].

Therefore, in this study, we aimed to perform a literature review on the causes of seroma and fibrosis, including the possible nutrients, bioactive compounds, and phytotherapeutics that can prevent or mitigate these complications after plastic surgery, and to organize the knowledge acquired in a practical guide to assist in its clinical application.

METHODS

This study is a nonsystematic review of the literature with data from electronically available scientific journal articles, national legislation, and textbooks at the Universidade do Vale do Itajaí (UNIVALI) that have been published between 2002 and 2012.

In searching for scientific articles, the following databases were consulted: Google Scholar, Medline (United States National Library of Medicine), Latin American and Caribbean Health Sciences (LILACS), Science Direct, PubMed, and Scielo. The following Portuguese keywords and their English equivalents were searched: “complicações” (complications), “pós-operatório” (postoperative), “fibrose” (fibrosis), “seroma” (seroma), “cicatrização” (healing), “colágeno” (collagen), “inflamação” (inflammation), “sistema imune” (immune system), “estresse oxidativo” (oxidative stress), “edema” (edema), “alimentação” (food), “nutrientes” (nutrients), and “nutrição funcional” (functional nutrition).

Seroma and Fibrosis

Seroma has a prevalence of between 1% and 57%, with the most frequent values being between 10% and 15% after an abdominoplasty[3,7]. In Brazil, studies on this surgical procedure indicate highly variable percentages, ranging from 1.8% to 30%[8-11].

Seroma is characterized by an accumulation of serous fluid due to leakage of plasma and lymph deep in the dermofat flap, displacement of the abdominal flap, section of blood and lymph vessels, disruption of lymphatic channels, an augmented inflammatory and healing process, and an increase in fibrinolytic activity[3,7,12].

The primary physiopathology of seroma is poorly elucidated and remains controversial. Nevertheless, it is known to cause bulging and fluctuation of the site, leading to discomfort, dissatisfaction, predisposition to morbidities (necrosis, dehiscence, and sepsis), and delayed healing, recovery, adjuvant therapy, and hospital discharge. The treatment consists in puncture, drainage, and medication[13,14].

The patient’s age, arterial hypertension, use of heparin, high body mass index, low concentration of protein and albumin, and high serum concentration of interleukin (IL)-1-RA have been recently reported to be linked to a higher risk of postoperative seroma formation[15]. The treatment

strategies are based on medication, including antibiotics, anti-inflammatory drugs, analgesics, and diuretics, as well as on aspiration, puncture, and drainage, and reconstructive surgery[16].

On the other hand, fibrosis occurs in the lipoaspirated tissue as a repair mechanism; however, it is characterized by the formation or abnormal development of excess fibrous connective tissue composed of elastin and collagen, resulting in hard or nodular lesions[17]. In a retrospective analysis covering 25 years in the databases of 26,259 health-care services of four surgeons, the prevalence of fibrosis was of 2.3%[18].

It should be emphasized that this complication, which may occur especially after liposuction, has a genetic cause induced by enzymatic deficiencies or pathological processes, and that the blood and lymph circulation efficiency is an important factor in the healing process, in acute trauma, or in chronic inflammation[19]. Furthermore, fibrosis formation is mediated by the interaction between growth factors and pro-fibrotic cytokines, as well as by the influence of these mechanisms on the extracellular matrix, mechanical tension, and oxidative stress[20].

Treatment of the condition is important to avoid future deformities. Treatment needs to be initiated early in collagen synthesis, which increases between the 6th and 17th day; after the 42nd day, this process ceases and remodeling of the accumulated collagen occurs[21].

In view of the possible causes of seroma and fibrosis, which include healing, collagen formation, inflammation, immune dysfunction, oxidative stress, and edema, it becomes necessary to understand the reactions involved in the above conditions and correlate them with functional nutrition. Figure 1 shows the metabolic network of the interrelation of the factors contributing to the formation of seroma and fibrosis.

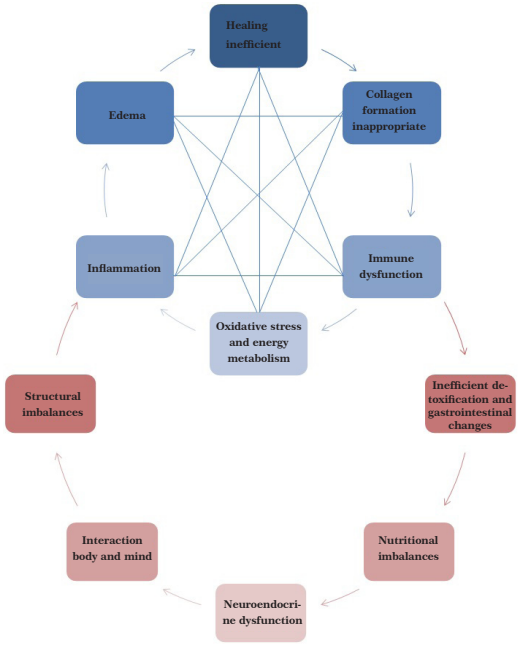

Figure 1 – Metabolic network of the interrelation between seroma and fibrosis. Adapted from Vasquez[22].

FACTORS CONTRIBUTING TO SEROMA AND FIBROSIS FORMATION

Healing and collagen formation

Healing is a dynamic and immediate process of tissue repair in response to an injury, with the aim of restoring the anatomical, structural, and functional characteristics of the patient. This recovery comprises three phases that occur simultaneously. The inflammatory phase, which is dependent on vitamin K, has a duration of 4–6 days and includes hemostasis, phagocytosis, and cell migration. From the third day up to weeks after, the phase known as proliferative, granulation, or fibroplasia phase occurs, where the requirements for carbohydrates, protein, lipids, vitamins A, C, and B complex, iron, zinc, and magnesium increase to promote cell proliferation, collagen synthesis, and neovascularization. Finally, the maturation phase or remodeling can extend up to 2 years, which involves stabilization of collagen and an increase in the resistance of the scar[23]. Figure 2 shows the healing phases, predominant cell types, and vascular response[24].

Under this system, nutrition is considered a major factor as many nutrients can influence the healing phases because

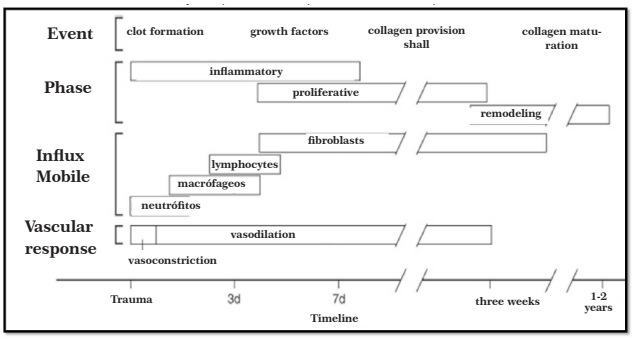

Figure 2 – Healing phases, predominant cell types, and vascular response.
Source: Mathes[24].

of their involvement in the synthesis of new tissues, suppression of oxidation, healing optimization, and also in immunocompetence[25].

Concerning the nutritional factors, it is observed that decreases in amino acids, nucleic acids, or any cofactors involved in the repair process is significantly harmful. Preoperative malnutrition and especially protein deficiency and DNA dysfunctions interfere with collagen synthesis, fibroblast proliferation, decrease in angiogenesis, and reduction in proteoglycans. Furthermore, carbohydrate deficiency leads to protein catabolism and, together with the deficit in vitamins and minerals, such as vitamin A, thiamine, vitamin C, and zinc, worsens the clinical condition[26].

Inflammation and immune system

Inflammation is the first stage of the healing process, and is closely linked to oxidative stress and reduced antioxidant capacity. However, when inflammation becomes chronic, it is characterized by a prolonged inflammatory response and tissue destruction. Many inflammatory cells secrete cytokines such as TGF-1 and IL-13, which are fibrinogenic[20].

The inflammatory phase comprises the influx of neutrophils, macrophages, and lymphocytes to the lesion site, as well as vasoconstriction, platelet aggregation, and increase in vascular permeability; the proliferative phase involves granulation, the influx of fibroblasts and keratinocytes, re-epithelialization, capillary formation, and extracellular matrix production; and the final stage (or remodeling) is dependent on the balance between the synthesis and degradation of collagen[27].

Thus, age, nutritional status, chronic diseases, caloric intake, cortisol release, stress, pain, and anesthesia affect the body's immune function, and can negatively interfere in the defense mechanism of the patient. Deficiencies in nutrients such as zinc, selenium, and vitamin B6 alter the immunity and protection of the host, increasing the risk for infections in the postoperative period[28].

In addition to those nutrients, Mitchell et al.[29] cite vitamins A, C, and E as important owing to their antioxidant functions and their role in cellular metabolism; however, only vitamin E has been proven to strengthen the immune system, as the scientific proof is poor or inconsistent for the other nutrients. However, the authors emphasize that high doses of vitamins B1, B2, B6, folate, and niacin may impair immunology; moreover, supplementation of >800 mg/day of vitamin E seems to have no benefits, whereas that of >100 mg/day of zinc has an effect on lymphocyte proliferation.

Oxidative stress

The process of ischemia-reperfusion during plastic surgery creates a state of oxidative stress, which is characterized by an increase in reactive oxygen species (ROS) released by damaged tissues and inflammatory cells, and is interrelated with the formation of fibrosis. Excess ROS damages cellular components such as proteins, lipids, and nucleic acids, creating an oxidant-antioxidant imbalance, which is represented by an increase in NADPH oxidase, activation of cytochrome *c* and xanthine oxidase, dysfunctions in mitochondrial respiration, and suppression of superoxide dismutase[20].

Anesthetic agents are a considerable source of oxidation, causing the formation of reactive oxygen, which inflicts damage to tissues and the healing process. The excess of free radicals, as mentioned, has several harmful effects, such as immunity suppression, altered cellular function, increase in lipid peroxidation, and inadequate interaction of the nutrients that form collagen, which, in turn, causes loss of tissue flexibility[30].

In parallel, oxidative stress during and after the surgical procedure involves inflammatory, endocrine, and immunological activation, characterized by the massive production of cytokines (such as IL-1, IL-2, IL-6, and IL-8) that are responsible for the progression and amplification of the immune response, and the activation of macrophages, platelets, and mast cells, which form free radicals, becoming a vicious cycle[31].

Top part of the form

According to Ratnam and colleagues[32], the human antioxidant defense system is not complete without the dietary antioxidants, which confirms the importance of the daily intake of these compounds.

In this context, antioxidants (carotenoids, vitamins A and C, selenium, and phenolic compounds) can neutralize the free radicals resulting from the surgical procedure, playing an important role in the prevention of additional damage. Some enzymes also have an antioxidant function, such as catalase, superoxide dismutase, and glutathione peroxidase, although there are nutrients that act as cofactors for their proper functioning. Even though there is a clear need for supplementation of antioxidant nutrients and enzyme cofactors, this is not yet clearly elucidated in the literature. Commonly, a combination of nutrients in low doses is prescribed instead of mega-doses, solely to supplement the blood and tissue losses after the surgery[28,33].

Edema

Edema is generated by inflammation through the increase in vascular permeability of a noninfectious exudate that leaks into the interstitial space, providing a humid layer that contains growth factors crucial for wound healing and facilitating the infiltration of inflammatory cells in the lesion; however, when the edema is excessive, it allows the development of fibrosis and seroma[26].

Other contributing factors

On the basis of the metabolic network of interrelations shown in Figure 1, it can be stated that several organic imbalances contribute to the formation of seroma and/or fibrosis; this is based on the concept that functional nutrition has a multidisciplinary coverage focused on gene expression and biochemical individuality[34]. In this context, it is easy to understand that structural dysfunctions may contribute to inflammation and oxidative stress. Problems of the body/mind interaction, such as depression, anxiety, and psycho-emotional stress, lead to inflammation and a decline in immune system functions, in addition to intestinal hyperpermeability and urinary excretion of nutrients. Problems in detoxification, in turn, overload the body, initiating a pro-inflammatory process; finally, intestinal dysbiosis impairs food digestion and absorption, producing algogenic and inflammatory substances capable of activating the immune system[22].

Role of functional nutrition

Functional nutrition has the goal of improving the quality of life, health, and well-being of patients, beyond the basic nutritional functions of food. For this purpose, initially

the mediators of the symptoms presented by the patient and corresponding to each system of the metabolic interrelation network are identified. Then, strategies to inhibit or modulate the triggers are then chosen in order to reestablish the balance of the systems, allowing a multidimensional approach and a higher therapeutic efficacy[34,35].

As there is an increase in nutritional needs in hypermetabolism and organic disorders, the nutrient requirements are often not satisfied with traditional food, and supplements and/or fortified food become necessary. Therefore, a wide variety of nutritional supplements are available to improve the triggers of seroma and fibrosis[25].

According to Rahm[30], nutritional supplementation during the pre- and postoperative periods can have a significant impact on the surgical outcome, reducing hematomas, edema, and inflammation, and promoting proper wound healing, besides increasing immunity and reducing oxidative stress. In this way, when addressing the nutritional status and providing guidance focused on supplementation, the aesthetic surgeon or nutritionist can positively influence the prevention of postoperative complications.

However, supplementation should be specific to the nutritional deficiency, with the main source being food intake and avoiding administering a supplementation amount that surpasses pharmacological values and generates adverse effects. In this context, the use of supplements that cause prolonged bleeding, drug or anesthetic interaction, and cardiovascular disturbances should be suspended for 2 weeks before and 1 week after the surgical procedure[27].

The necessary nutrients, as well as their daily doses and functions for the regulation of processes linked to prevention of seroma and fibrosis, are described in Charts 1 to 4.

Chart 1- Daily doses, functions, and observations of macronutrients that can prevent, mitigate, or treat seroma and fibrosis.

Macronutrients	Oral daily dose	Functions
Water	30ml/kg 1ml/kcal Minimum 1500 mL	Adequate tissue perfusion Prevents the increase in glucose levels that impairs the healing process Prevents hypovolemia Removal of catabolism products
Carbohydrates	55–60% of total energy value (TEV) from complex carbohydrates Do not exceed 5 mg/kg	Activation of hexokinase and citrate synthase used in tissue repair Activation of gene expression Cooperation with macrophages and fibroblasts in angiogenesis Energy for lymphocytes and fibroblasts Energy supply, preventing protein catabolism and mobilization of fatty acids Hormonal Inflammatory Lactate metabolism contributes to collagen synthesis Regulation of adhesion, proliferation, and migration of cells Regulation of leukocytes, epithelial cells, and endothelial cells Transport
Proteins	1.5–1.8 g/kg	Anabolism Source of energy Growth and tissue repair Controls the inflammatory phase Cellular proliferation, mainly fibroblasts Synthesis and deposition of collagen and proteoglycans Revascularization and angiogenesis Improves the humoral and cellular immunity Formation of lymphocytes Phagocytic capacity of leukocytes Prevents infection

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Arginine	5–15 g 30 g arginine aspartate (17g free arginine) Up to 60 g can be tolerated	Deposition of proteins in the scar Decreases nitrogen loss Anabolic hormonal stimuli in the wound Generation of nitric oxide Induction of healing mediators such as insulin, HGH, and IGF-1 Enhances lymphocyte immune function Improves perfusion, microvascularization, and angiogenesis Improves monocytic response and restores macrophages Precursor of nitric oxide, which is a vasodilator with antibacterial and angiogenic properties Precursor of nitric oxide Collagen production, by being a precursor of proline, and facilitates the connection between the two components Cellular proliferation Secretion of growth hormone Synthesis and deposition of collagen by being a precursor of proline * In hepatic and renal failure, the electrolyte levels should be carefully analyzed
Carnitine	-	Helps in the enzymatic antioxidant defenses
Cysteine	-	Synthesis of connective tissue and collagen
	300–600 mg	Cofactor of enzymatic systems of collagen synthesis
Glutamine	0.3–0.6 g/kg 20–40 g in catabolic state Do not exceed 10 g in the normal state	Anabolism and anticatabolism Anabolism and anticatabolism Antioxidant, by being a component of glutathione Increases the synthesis of muscle proteins Fuel for rapidly dividing cells Stimulates the release of growth hormones Source of energy after stress and for epithelialization of cells through gluconeogenesis Intestinal integrity Precursor of purines, pyrimidines, and phospholipids Proliferation of lymphocytes Proliferation of lymphocytes, stimulating the inflammatory response Reduction of infection Fibroblast and macrophage synthesis Synthesis of purine and pyrimidine Transports and decreases nitrogen loss * Contraindicated in hyperammonemia, hepatic failure, and renal failure
Glycine	250 mg	Collagen formation
Lysine	250mg	Collagen formation
Methionine	-	Synthesis of collagen and connective tissue
Proline	250mg	Collagen formation
Lipids	20–25% of TEV Do not exceed 2 g/kg	Assist in the remodeling phase Energy source Formation of extracellular matrix Supply of cell membrane phospholipids and prostaglandins Metabolic, inflammatory, and vascular functions of cells Signaling molecules, through eicosanoids and other mediators Synthesis of prostaglandins

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Fatty acids mono-unsaturated and polyunsaturated	ω6/ω3 ratio of 5:1	Alteration in free radical production Anti-inflammatory, anticoagulant, vasodilator, and antiplatelet actions Activation of protein kinase C and specific genes Composition and fluidity of the cell membrane Controls vascular permeability Lipase control Energy source and storage Inflammation Inhibition of eicosapentaenoic (attenuation of immune and inflammatory responses), tumor necrosis factor, interleukin-1, and of platelet activation generating attenuation Maintenance of the tissue microperfusion Cell proliferation, apoptosis, and angiogenesis Remodeling of collagen and cellular matrix Molecular signaling *High doses: delay healing due to negative effects on coagulation

Legend: (*) represents observations; (-) unspecified amounts in the postoperative period.
Sources: Badwal[6], Gantwerker[26], Wild[27], Mitchell[28], Rahm[30], Kücükakin[33], Brioschi[34], Collins[35], Nunes[36], Shetyy[41], Pitzer[42].

Chart 2 - Daily doses, functions, and observations of micronutrients that can prevent, mitigate, or treat seroma and fibrosis.

Micronutrients	**Oral daily dose**	**Functions**
Vitamin A b-Carotene Lycopene Lutein Zeaxanthin	Maximum 5.000–25.000 UI	Accelerates epithelialization and wound closure Antioxidant Attenuates the ischemia-reperfusion process Activation of macrophages, natural killer cells, and lymphocytes Helps in glycoprotein synthesis Controls the anti-inflammatory effects of corticosteroids Collagen cross-linking Fibroblasts differentiation Stimulates phagocytosis Cytokine expression Induces inflammatory response Lymphopoiesis Maintenance of the immune system by promoting the influx of monocytes and macrophages Modulates collagenases activity Antibody production Reverses the effects of glucocorticoids in the inflammatory phase Collagen synthesis and re-epithelialization *High doses: toxicity

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Vitamin B complex	B2: 10 mg B3: 150 mg B5: 2.5–10 mg B6: 10–50 mg B7: 50–150 μg B9: 0.4–1 mg B12: 250–1000 μg B1: 10–100 mg	Angiogenesis Activation of protein, tissue, and DNA synthesis Increase in collagen Increase in growth hormone Cofactors in the production of energy and antibodies Collagen cross-linking Ensures leukocyte function Precursor of proline Regulates oxidative stress Removal of necrotic tissue
Vitamin C	60 mg–2 g	Accelerates tissue regeneration Adhesion of endothelial cells Angiogenesis and capillary force Antioxidant in hydrophilic medium Attenuates the ischemia-reperfusion process Decreases susceptibility to infections Decreases capillary permeability and endothelial reactivity Balance of the extracellular matrix Stability of the collagen triple helix Promotes healing and scar resistance Proline and lysine hydroxylation Induces cell mitosis and monocyte migration Antioxidant cooperative interaction with vitamin E, regenerating it Improves leukocyte action Improves phagocytosis Prevents dehiscence Protection from the damage caused by medication Chemotaxis Carnitine synthesis Complement system support * In the presence of transition metals such as iron, vitamin C becomes pro-oxidant
Vitamin D	-	Regulates the synthesis of structural proteins, including type 1 collagen Controls growth and cellular differentiation Improves epithelialization Stimulates fibronectin synthesis and activation of macrophages maturation
Vitamin E	200–800 mg	Antioxidant Attenuates the ischemia-reperfusion process Maintains cell membrane integrity Anti-inflammatory Improves the immune system Anti-inflammatory function identical to corticosteroids Improves coagulation Antioxidant cooperative interaction with vitamin C * High doses: reduce collagen production and scar resistance

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Vitamin K	5 – 10 mg	Anti-bleeding Homeostatic capacity Carboxylation of glutamate in coagulation Prevents prolonged bleeding and nutrient loss, hematoma and infection
Calcium	-	Action of collagenases in degradation, blood coagulation and collagen remodeling
Cobalt	-	Antibody cofactors Guarantee leukocyte function
Copper	1–2 mg	Angiogenesis Antioxidant cofactor and from cytochrome *c* in energy formation Cofactor of healing enzymes Cross-linking of collagen and elastin Formation of hemoglobin, erythrocytes, and bones Function in cytochrome oxidase and superoxide dismutase Synthesis of collagen and elastin Synthesis of proteins and connective tissue * Associates with vitamin C for collagen formation
Iron	-	Activation of natural killer cells Cofactor of healing enzymes Ensures phagocytic capacity of neutrophils Hydroxylation of proline and lysine Cytokine production Proliferation, differentiation, and number of T cells Oxygen transport, preventing tissue hypoxia * In the presence of transition metals such as iron, vitamin C and quercetin become pro-oxidant
Magnesium	0,3-5mg	Cofactor of enzymes of protein synthesis, collagen, superoxide dismutase, and metalloproteins Structural stability of ATP
Manganese	0,3-0,5mg	Antioxidant – superoxide dismutase Cofactor of healing enzymes Function in metalloproteinases Hydroxylation of collagen Protein synthesis and energy
Selenium	100-210μg	Antioxidant (glutathione system) Cofactor of lipid metabolism Management of inflammation Prevents infection Vitamin E protector Regulates the generation of by-products of lymphocytes

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Zinc	15–400 mg 200 mg zinc sulfate (50 g free zinc) for 14 days maximum	Antioxidant – superoxide dismutase and glutathione Apoptosis of myeloid and lymphoid cells Protein kinase C Activity of helper T cells, development and proliferation of lymphocytes and interleukin production Increases the immune function through the development and activation of lymphocytes Cofactor of enzyme synthesis, RNA polymerase, DNA, metalloproteins, and collagen Erythropoiesis Maintenance of the intestinal mucosa Proliferation of cells and fibroblasts Re-epithelialization Protein synthesis and cell replication Vitamin A transport * High doses: inhibit macrophage migration, negatively interfere with collagen production, copper and iron absorption, and can cause gastrointestinal problems

Legend: (*) represents observations; (-) unspecified amounts in the postoperative period.
Sources: Badwal[6], Gantwerker[26], Wild[27], Mitchell[28], Rahm[30], Kücükakin[33], Brioschi[34], Collins[35], Nunes[36], Shetyy[41], Pitzer[42].

Chart 3 – Daily doses, functions, and observations of bioactive compounds that can prevent, mitigate, or treat seroma and fibrosis.

Bioactive compounds	**Oral daily dose**	**Functions**
Lipoic acid	30–75 mg	Antioxidant ATP production Regeneration of other antioxidants such as coenzyme Q10, vitamin C, and vitamin E
Bromelain	1500 mg	Accelerates healing and reabsorption of the hematoma Anti-inflammatory action Reduces edema, inflammation, and pain
Coenzyme Q10	10–50 mg	Antioxidant Improves the immune system ATP production Protects the stability of cellular membranes Protects DNA Regeneration of other antioxidants, such as ascorbic acid and a-tocopherol Gene regulation
Flavonoids	600–1500 mg 30–50 mg	Anti-inflammatory Antioxidant in hydrophilic and lipophilic medium Support to the immune system * In the presence of transition metals such as iron, quercetin becomes a pro-oxidant
Hesperidin	15–30 mg	Antioxidant Anti-inflammatory

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Isothiocyanates and indoles	-	Help in body detoxification Inhibit DNA mutation Reduce the production of 16-a-hydroxyestrone (pro-inflammatory and immuno-deregulatory)
Melatonin	-	Antioxidant Stimulates gene expression and activity of antioxidant enzymes Immunostimulant
Proanthocyanidin	-	Antioxidant Anti-inflammatory Vasodilator
Resveratrol	-	Antioxidant Anti-inflammatory
Rutin	15–30 mg	Antioxidant Improves the lymphatic and venous circulation * Synergy with vitamin C
Probiotics and prebiotics	-	Calcium absorption Increase the levels of vitamin B complex and amino acids, such as methionine, lysine, and tryptophan Improves macrophage production and stimulates suppressor cells Prevents the adhesion and activation of pathogens Immune modulation

Legend: (*) represents observations; (-) unspecified amounts in the postoperative period.
Sources: Badwal[6], Gantwerker[26], Wild[27], Mitchell[28], Rahm[30], Kücükakin[33], Brioschi[34], Collins[35], Nunes[36], Shetyy[41], Pitzer[42].

Chart 4 – Common name, scientific name, daily doses, functions, and observations of phytotherapeutics that can prevent, mitigate, or treat seroma and fibrosis.

Common name	Scientific name	Oral daily dose	Functions
Turmeric	Curcuma longa	1.5–3 g	Anticoagulant Anti-inflammatory Antioxidant Glycemic control Prevents fibrosis
Artichoke	Cynara scolymus	20g	Antioxidant Increases glutathione activity Diuretic
Liquorice	Glycyrrhiza glabra	-	Anti-inflammatory Antioxidant Immunomodulatory Neutralizes immunosuppressors (except glucocorticoids)
Caraway	Carum carvi	-	Antioxidant
Rosemary	Rosmarinus officinalis	3-6g	Antioxidant Anti-inflammatory Healing

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Garlic	Allium sativum L.	0,5-1g	Anti-inflammatory Antioxidant (increase in glutathione) Antiplatelet Increases immunity Hypoglycemic Vasodilator * Contraindicated in the preoperative period
Aloe vera	Aloe barbadensis BC	-	Anti-inflammatory Antioxidant Healing Glycemic control Stimulates macrophages
Arnica	Arnica montana	3g	Anti-inflammatory Antiseptic Vasodilator Reduction of edema, bruising, and pain
Brazilian pepper	Schinus terebenthifolius	1g	Anti-inflammatory Healing
Greater burdock	Arcticum lappa L.	2,3g	Anti-inflammatory Diuretic
Boldo	Peumus boldus	-	Antioxidant Acute anti-inflammatory
Indian olibanum	Boswellia serrata	-	Anti-inflammatory
Cashew	Anacardium occidentale	4,5g	Healing
Pot marigold	Calendula officinalis L.	1.6–5 mg flavonoids	Anti-inflammatory Healing
Chamomile	Matricaria chamomilla L.	0.009–0.03 mg apigenin	Antioxidant Anti-inflammatory
Small cardamom	Cinnamomum verum Cinnamomum cássia	-	Anti-inflammatory Antioxidant Glycemic control Improves blood circulation
Cardamomo	Elettaria cardamomum	-	Antioxidant Anti-inflammatory Assists apoptosis
Cardus marianus	Silybum marianum L.	70-300mg	Antifibrotic Anti-inflammatory of the membrane Antioxidant Acts in phase 2 of detoxification Increases glutathione Blocks toxins uptake Prevents injury by xenobiotics Facilitates the action of proteins Regulates the permeability of the membrane
Field horsetail	Equisetum arvense	3g	Edema control
Green tea	Camellia sinensis	-	Antioxidant
Chapéu de couro	Echinodorus macrophyllus	1g	Anti-inflammatory Mild diuretic

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Shell ginger	Alpinia zerumbet	20g	Diuretic
Cumin	Cuminum cyminum L.	-	Antioxidant
Comfrey	Symphytum officinale L.	0.03–0.16 mg allantoin	Healing
Common dandelion	Taraxacum officinale	3–12 g	Anti-inflammatory Antioxidant (increases glutathione and superoxide dismutase) Glycemic control Diuretic Prebiotic
Blacksamson echinacea	Echinacea angustifólia DC	-	Anti-inflammatory Healing Immunostimulant * Contraindicated in the preoperative period
Black sage	Varronia curassavica Jacq.	3g	Anti-inflammatory
St. John's wort	Hypericum perforatum	-	* Contraindicated in the preoperative period
Anise	Pimpinella anisum L.	-	Antioxidant Cytoprotective
Espinheira santa	Maytenus ilicifolia Maytenus aquifolia Mart	2-6g	Analgesic Anti-inflammatory Antioxidant Antiulcerogenic Healing Detoxification
Devil's claw	Harpagophytum procumbens D.C.	600–6000 mg	Anti-inflammatory Antioxidant
Ginger	Zingiber officinale Roscoe	1-2g	Anti-inflammatory Antioxidant Spasmodic
Ginkgo biloba	Ginkgo biloba	-	* Contraindicated in the preoperative period
True ginseng	Panax ginseng	-	Antioxidant Pharmacological effects on the immune, endocrine, and nervous systems Improves chemical stress Improves the functions of the cellular membrane Reduces muscle damage and inflammation * Contraindicated in the preoperative period
Siberian ginseng	Acanthopanax senticosus	-	Anti-inflammatory
American witch-hazel	Hamamelis virginiana	3-6g	Skin and mucous membranes anti-inflammatory

Continue...

Continuation...

Peppermint	Mentha piperita	-	Antimutagenic Antioxidant Anti-inflammatory DNA repair
Macela	Achyrocline satureioides	1,5g	Anti-inflammatory
Yarrow	Achillea millefolium	1-2g	Anti-inflammatory
Bitter melon	Mormodica charantia L.	-	Healing
Pau-ferro	Caesalpinia ferrea	7,5g	Healing
Black pepper	Piper nigrum	-	Antioxidant Anti-inflammatory
Stonebreaker	Phyllanthus niruri L.	10g	Diuretic
Golden root	Rodhiola rosea	-	Antioxidante
Pomegranate	Punica granatum L.	6g	Anti-inflammatory
White willow	Salix alba	400 mg–3 g 60–120 mg salicin	Anti-inflammatory
Sage	Salvia officinalis	-	Anti-inflammatory
Broadleaf plantain	Platago major L	6-9g	Anti-inflammatory
Cat's claw	Uncaria tomentosa	600-900mg	Anti-inflammatory Antioxidant Immune regulation Vasodilator
Sweet broom	Scoparia dulcis	1–3 mL dye	Antioxidant Anti-inflammatory Glycemic control * Synergy with Silybum marianus L.

Legend: (*) represents observations; (-) unspecified amounts in the postoperative period.
Sources: Marques[43], Brasil[44], Brasil[45], Brasil[46].

CONCLUSION

The results of the research performed show that seroma and fibrosis are caused by exacerbated and interrelated physiological alterations, such as the healing process, collagen formation, inflammation, immune system changes, oxidative stress, and edema, and that there are several components of functional food, such as nutrient, bioactive, and phytotherapeutic compounds, that are well documented and can be used to prevent, control, or mitigate complications in the postoperative period after plastic surgery. In this sense, it is essential that the nutritional and metabolic imbalances are recognized and corrected by the professional, who is ethically committed to maintain the functional and aesthetic well-being of the patient. This correction is primarily based on food ingestion and secondarily on supplementation, taking into account, however, the contraindications and possible adverse effects. It is important to highlight that for the treatment seroma and fibrosis, a multidisciplinary approach is crucial, with emphasis on a clinical, nutritional, and physiotherapeutic monitoring that covers all changes known to be related to the physiopathology of these conditions.

In addition, taking into account the complexity of the topic, more studies are required concerning the influence of food consumption with the goal of improving the surgical results, quality of life, and aesthetic outcomes. We suggest the use of other scientifically valid methods for the assessment of the complications mentioned in this work, aiming at results that include all the variables involved in the diagnosis, prevention, and treatment of seroma and fibrosis.

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