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A narrative review on safety and efficacy of egg white peptide formulation enriched with dietary fiber in the critical set up

Nidhi Singh[1*], Dr. Pavan Hanchanale[2], Dr. Abhijeet Deshmukh[3], Ipsita Chakravarti[4], Arpita Ghosh Deb[5]

[1] Clinical Dietitian, Oncoheal, Pune, Maharashtra, India

[2] Consultant Gastroenterologist and Hepatologist, Jupiter Hospital, Pune, Maharashtra, India

[3] Consultant, Neuro Intensive Care Unit, Ruby Hall Clinic, Pune, Maharashtra, India

[4] Department of Head Dietetics, The Calcutta Medical Research Institute, CK Birla Hospitals, Kolkata, West Bengal, India

[5] Clinical Dietitian, Bellevue Clinic, Kolkata, West Bengal, India

Abstract

Protein seems to be the most crucial macronutrient for wound healing, enhancing immune system performance, and preserving lean body mass in the critical care situation. The majority of critically sick patients have high protein needs due to high catabolic stress. High-quality proteins, vitamins, and minerals are found in eggs, a nutrient-dense food. Eggs whites are recognized as a source of high-quality proteins with an amino acid score of 100.It is important to pay more attention to the role that eggs and egg components play in the prevention and treatment of disease. Eggs are used in a wide range of industrial processes in addition to being renowned as a "functional food" that helps prevent illness and promote wellness. Egg white is broken down by enzymes, producing hydrolysates that are quickly absorbed and have a variety of physiological effects. The egg white peptide's potential pharmacological actions, such as antibacterial, anti-cancer, anti-inflammatory, and ACE (angiotensin-converting enzyme) inhibition as well as immunomodulatory effects, have been documented. Unfortunately, the scientific evidence supporting the advantages of egg white powder supplementation over conventional additive proteins like whey protein or casein in the context of severe illness is still lacking. Thus, we performed a narrative review concentrating on the effect of egg white supplementation in critically ill patients. We used search engines like PubMed and Google Scholar for this purpose. However, this is a narrative review, we would recommend more systemic reviews and interventional studies to highlight the effect of egg whitepedtide supplementation in critically ill patients.

Keywords: Safety and efficacy, dietary fiber, enhancing immune system

Introduction

Patients witha critical illness often experience a catabolic stress state that causes a systemic inflammatory response. This response is accompanied by disproportionately high rates of mortality, prolonged hospitalization, and increased infectious morbidity [1].

Protein seems to be the most crucial macronutrient for wound healing, enhancing immune system performance, and preserving lean body mass in a critical care situation [2, 3]. The American Society for Parenteral and Enteral Nutrition (ASPEN) recommends that a critically ill adult patient consumes between 1.2 and 2.0 g of protein per kilogram of body weight per day, or that the presumed non-protein calories to nitrogen ratio (NPC: N ratio) be between 70 and 100:1. Unfortunately, the NPC: N ratio in the most widely used enteral formulae is high. As a result, it is advised to take additional protein supplements to supply enough protein. According to the recommendations of the European Society of Parenteral and Enteral Nutrition (ESPEN), whole-protein formulas, such as milk protein, egg white protein, and soy protein, are among the most suitable supplements for critically ill patients [4, 5].

For a number of years, casein protein, or cow's milk protein, was the clear choice protein supplement in hospitals, but its cost is exorbitant and its supply is scarce. On the other hand, compared to other kinds of protein supplements, egg white protein powder is more widely available and less expensive [6].

Unfortunately, scientific evidence supporting the advantages of egg white powder supplementation over conventional additive proteins like whey protein or casein in the context of severe illness is still lacking. In this narrative review, we concentrated on understanding the effect of egg white supplementation in critically ill patients where protein loss and catabolism are frequently observed.

Aim and Objective

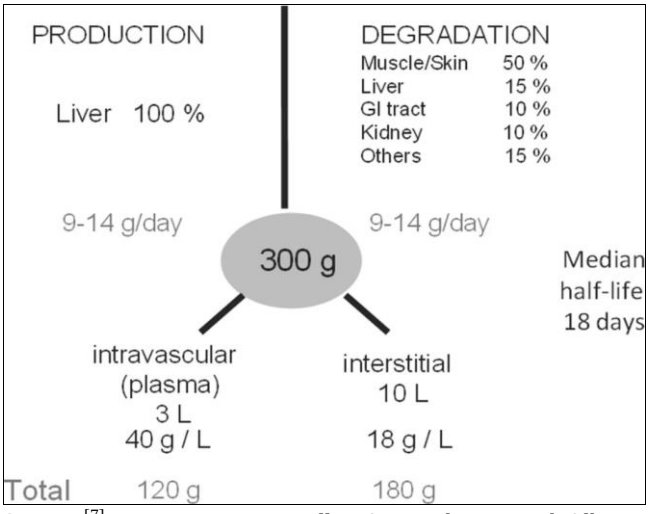
To examine the most recent medical research on safety and efficacy of egg white or egg white peptide supplementation in critically ill patients, with a particular emphasis on the biological effects of egg white in critically ill patients.

Methodology

We performed a narrative review of the current literature. We used PubMed and Google Scholar and other relevant sites for this purpose. The search terms were albumin supplementation, egg white powder, critically ill patient, hypoalbuminemia, and other relevant terms related to the topic discussed. Duplicate articles were removed we only considered articles written in English, with no restrictions on the date of publication.

Background

Role of Albumin in critically ill patients



Source [7]**:** Vincent, JL., Russell, J.A., Jacob, M. *et al*. Albumin administration in the acutely ill: what is new and where next? Crit Care 18, 231 (2014)

Fig 1: Metabolism of Albumin

Albumin's relevance in human physiology seems to be reflected in the way it is metabolized as depicted in Figure 1. The rate of synthesis and degradation may be controlled on several levels per se. Intravascular oncotic pressure is one of the most basic regulatory mechanisms. It is important to keep in mind that trauma, infections, or any other clinical factors that cause inflammation may inhibit albumin synthesis in critically ill patients [8].

Consequence of low albumin levels in the body

Hypoalbuminemia is generally defined as a serum albumin concentration ≤3.0 g/dl

Specific clinical conditions where hypoalbuminemia is commonly seen are: Elderly malnourished patients, Malignancy, Surgical Interventions, Chronic obstructive pulmonary disease, Pancreatitis, Coronary Artery Disease, Inflammatory Bowel Disease, Liver Disease, Patients with severe sepsis or septic shock, Burns, Renal Disease, Peripheral Vascular Disease, Community-acquired pneumonia [9].

The primary contributing factors for albumin losses in the body likely include increased albumin losses from gastrointestinal bleeding and other sources, increased capillary permeability that causes a redistribution of albumin from the intravascular to the interstitial space (previously known as third-spacing), and dilution from intravenous fluid administration. Additionally, due to poor nutritional status or abnormal liver function, some patients' baseline albumin levels may already be below normal, especially in elderly patients. Importantly, hypoalbuminemia is linked to poor outcomes, including an increase in complications, regardless of the underlying processes, also reduced short-term and long-term survival in critical patients [9].

Discussion

Egg and egg white protein

With an amino acid score of 100, which is equal to that of milk and soybeans, egg whites are recognized as a source of high-quality proteins. They exhibit biological activity like antibacterial, antioxidant, metal-chelating, antihypertensive, anticancer, and immunomodulatory ones, egg white and yolk proteins in particular are regarded as functional dietary ingredients [10, 11].

The net protein utilisation (NPU) value for egg white proteins, whether cooked or uncooked, is higher than that of whey and soybean proteins, despite equal amino acid scores, according to a prior study [12]. Egg white proteins are characterised by their abundance of branched-chain and sulfur-containing amino acids. Previous research has shown that taking egg white proteins increases the body's protein levels. Proteins from egg whites can also increase muscle mass and strength after exercise. Reduced blood LDL-cholesterol and visceral fat are two additional benefits of egg white proteins [13].

Antinutritional factors

Eggs' major proteins contain protease inhibitors, which can prevent digestive enzymes like pepsin, trypsin, and chymotrypsin from properly degrading egg proteins. Ovoinhibitor, ovomucoid, and cystatin are a few of these molecules that include many disulfide bonds, which are thought to give them some modest resistance to denaturation by proteases and stomach acids. Heat may partially denature some of these antinutritional substances. The tight complex that forms between avidin and the bound vitamin B8 may reduce the bioavailability of biotin for consumers [11].

Egg white peptide

The production of hydrolysates with antioxidant characteristics, which have been found to have antifatigue measures that are stronger than those of egg white proteins. The sequence, composition, and length of amino acids have a substantial influence on peptide activity. It enables quick absorption in the gut [12, 14].

Egg White Peptides EP-1, which have good heat resistance, are created by hydrolysing fresh chicken egg white with enzymes. Peptides from egg whites exhibit a variety of characteristics not seen in amino acids or proteins.

Matsuoka and colleagues found in an animal investigation that egg white hydrolysates maintain the nutritional value of egg whites and are quickly absorbed by the body [12].

Biological benefits of Egg White Peptide

Antioxidant effect

The functional features, physical activities, and applications as dietary ingredients are all strongly impacted by changes in hydrolysate characteristics of a protein source. Different protein sources' hydrolysates have been shown to have antioxidant activity, including whey, soy, egg yolk, prawn, tuna, etc. have been known to possess antioxidant activity.

When compared to the original protein or amino acid mixture, it was discovered that the egg-yolk protein hydrolysates displayed stronger antioxidant activity in a linoleic acid oxidation system. The antioxidant efficacy of peptides made from pepsin-treated crude egg white was also 7found in different studies [15, 16, 17].

Improved Insulin Sensitivity

Insulin is necessary for the body's tissues to perform their various metabolic processes normally. Insulin primarily targets adipose tissue, which plays a significant role in the metabolism of lipids and glucose. Pre-adipocyte

development into mature adipocytes is aided by insulin, which also causes the overexpression of immunomodulatory proteins like peroxisome proliferator-associated receptor gamma (PPAR) and the inclusion of lipid droplets [18].

In a study, it was observed that EWH could promote adipocyte differentiation by increased lipid accumulation, increased release of adiponectin and upregulation of peroxisome proliferator associated receptor gamma (PPARγ) and CCAAT/ enhancer binding protein alpha (C/EBP-α). EWH treatment increases extracellular signal regulated kinase 1/2 (ERK1/2) phosphorylation to a level similar to that of insulin, indicating insulin sensitizing and mimetic properties of the EWH. EWH further attenuated cytokine induced inflammatory marker; cyclooxygenase -2 (COX-2) by 48.78%, possibly through the AP-1 pathway. Given the critical role of adipose in the pathogenesis of insulin resistance and metabolic syndrome, EWH may have potential applications in the prevention and management of metabolic syndrome and its complications [18].

Antihypertensive activity

Cardiovascular diseases (CVDs) and their accompanying consequences, such as atherosclerosis and stroke, have been linked to hypertension as a risk factor [19]. The renin-angiotensin system (RAS), oxidative stress, inflammation, and decreased nitric oxide (NO) synthesis are only a few of the pathways and elements that contribute to the underlying processes of hypertension [20].

A great source of affordable, high-quality proteins is egg white. It has been found that the hydrolysate of egg white protein (EWP) produced by different proteases exhibits a number of bioactivities, including ACE inhibition, vasodilation, and antioxidant activity, which prevent cardiovascular disease [16, 18, 21]. Egg white protein (EWP) hydrolysate (EWH) was studied in an animal experiment to determine whether it had a hypotensive impact on spontaneously hypertensive rats (SHRs), with the aim to develop EWH as a functional food as a blood pressure modulator. According to the study's conclusions, during the 28-day experimental period, the systolic and diastolic blood pressures of the SHRs given the EWH diet were shown to be considerably or quantitatively lower than those of the other groups. Additionally, when compared to the control, EWH treatment significantly ($p<0.05$) increased the levels of nitric oxide in both the plasma of the SHRs and hCMEC/D3 cells.Moreover, when compared to the control, EWH consumption significantly ($p<0.01$) decreased the plasma angiotensin II level in the SHRs. Thus, it was established that EWH has benefits for managing and preventing hypertension in addition to its basic nutritional value, making it a valuable resource for the development of functional foods [22].

Antifatigue effect

Sarcopenia is characterized by a decrease in muscle and bone mass. It is commonly known that eating enough protein significantly aids in the development of muscles. It might be challenging for the elderly to get enough protein, therefore they require sources of high-quality protein. Intense activity damages or exhausts muscles in addition to producing an excess of free radicals in the muscle tissues [23]. This can lead to reduced physical activity, which might cause muscle mass to decline as a result. In earlier studies involving human subjects, EWH has been shown to reduce muscular injury in long-distance runners [24]. Egg white contains significant amounts of branched-chain amino acids (BCAAs) and amino acids containing sulphur [25]. Because glutathione is produced *in vivo* from sulfur-containing amino acids, egg white is expected to have antioxidant effects that are linked to antifatigue effects and the prevention of various diseases like arteriosclerosis [26].

BCAAs have also been demonstrated to lessen muscle weariness. Their blood concentration increases after ingesting an EWP preparation, and it decreases after exercise [27, 28].

As a result, it is also likely to anticipate a BCAA-mediated antifatigue benefit. Further investigation into the effect of the EWH preparation on the mice's swimming endurance revealed that the EWH group's improved swimming duration through day 14 was significantly greater than that of the casein group ($p = 0.049$). These findings offer more proof that ingesting EWH lengthened swimming sessions and offers mechanistic backing for an anti-fatigue benefit mediated by its antioxidant activity [29].

Controlling Obesity and the Gut Microbiota

The gut microbiota and EW pepsin hydrolysates may work together to reduce short-chain fatty acids, which would therefore reduce the likelihood of obesity-related disorders and dyslipidemia. Short-chain fatty acids (SCFA), lactate, fecal lactate, and ammonium concentrations were higher in obese rats given 750 mg/kg body weight of EW pepsin hydrolysate in drinking water for 12 days compared to controls, and the microbial load was lower in the feces. The reduction in microbial load (which included Lactobacillus, Enterococcus, and Clostridium leptum) in turn lowered microbial metabolism as seen by a decrease in SCFA levels. This was because of EW's antioxidant and anti-inflammatory properties during lipogenesis [30].

Anti-Cancer Effects of Egg white peptides

Lysozyme was the first protein from hen eggs whose sequence was discovered. It can enhance the effectiveness of anti-cancer medications, stop the development of bacterial carcinogenesis, and speed up the healing process after immune suppression [31]. Breast cancer cell migration was inhibited after the administration of a preparation comprising self-assembled nanostructured lysozyme particles [32]. Following the administration of EW hydrolysates, the onset of apoptosis reduced the viability of cancer cells Ovotransferrin (OVT), which has antioxidant, antibacterial, anti-cancer, and potent metal chelation characteristics, protects the developing embryo [33]. Functional peptides produced by OVT hydrolysis have potent anti-cancer properties against breast and colon cancer cells [34]. In human stomach adenocarcinoma cells, egg peptides exhibited anti-cancer behaviour, with a 20% cytotoxicity [35]. Bioactive peptides derived from OVT and lysozyme can be used to treat cancer, including colon and breast cancer because they have inhibited the growth of cancer cells and reduced cytotoxicity against normal cells [36].

Effect of egg albumin on the nutritional status of CAPD patients

Clinicians have specific concerns about hypoalbuminemia in Peritoneal dialysis (PD) patients who continue to lose protein into the effluent. Numerous non-nutritional factors,

including comorbidities, volume status, and inflammation, may have an impact on serum albumin. Most of the time, albumin synthesis in the liver outweighs albumin losses in the urine or effluent [37].

28 patients undergoing continuous ambulatory peritoneal dialysis (CAPD) were randomly assigned to one of two groups: the study (n = 13) or the control (n = 15) in a randomised, open-label, controlled clinical trial. Both groups received standard nutritional advising; the study group also received an oral supplement made of egg albumin. All patients underwent monthly clinical and biochemical tests during the 6-month follow-up period, as well as quarterly reviews of how well their nutrition and dialysis were working. Serum albumin levels were similar between the groups; however, the study group saw a considerable rise (baseline vs. final) but the control group did not. At the end of the follow-up period, the proportion of patients who had moderate or severe malnutrition dropped by 28% in the trial group compared to the control group, or 6%. When compared to controls, oral administration of the egg albumin-based supplement in the study group significantly increasedserum albumin, and calorie and protein intake. Additionally, this action was linked to a trend toward increased anthropometric parameters and improved Subjective Global Assessment evaluation. The oral supplement can be a simple, affordable, and secure way to help peritoneal dialysis patients' nutritional status [9].

Need of dietary fiber in Critically ill patients

In critically ill patients, Gastrointestinal complications have various complications and harmful consequences. Dietary fiber is an important component of the human dietas ithelps in maintaining the optimum balance of the gut microbiota by providing the needed substrate to produce small-chain fatty acids (SCFAs). SCFAs are recognized for maintaining intestinal barrier integrity, decreasing the inflammatory response in the intestinal epithelium, and playing a role in immunomodulation and local gut homeostasis by suppressing pathogenic bacteria overgrowth and promoting the growth of commensal microflora, like lactobacillus and bifidobacterial which together comprise more than 90% of microflora [38, 39].

Diarrhea is one of the most frequent complications in tube-fed patients and is a complicating factor for enteral nutrition management. Dietary fiber improves diarrhea, preserves microbiota by increasing SCFA levels, and decreases hospital length of stay in certain populations. Studies have stated that initiating enteral nutrition with fiber-enriched formulas helps in avoiding frequent feeding interruptions that cause protein energy malnutrition in ICU patients. Studies have also reported that dietary fiber supplementation in critically ill patients appears to be safe, without detrimental impact on gastrointestinal symptoms like diarrhea, constipation, gastric intolerance, and vomiting [39, 40, 41].

Conclusion

Over the past few decades, research on bioactive peptides produced from egg protein has advanced. The main method for making bioactive peptides from egg protein is enzymatic hydrolysis. Studies have concluded that peptides produced from egg proteins possess higher functional activities compared to undigested proteins. Proteins must be converted into peptides in order for them to operate more effectively and absorb more nutrients in the gastrointestinal system. Nonetheless, there has not been good research into the reasons for the functional activity of peptides, in terms of their purification and characterization. There is therefore a definite need for more such studies. Proteins containing several bioactive peptides have been studied for their anti-inflammatory, immunomodulatory, anti-hypertensive, anti-diabetic, anticancer, and antibacterial properties [9, 10].

Also, even though serum albumin may not be an appropriate serum protein marker to determine the benefits of protein supplementation. However, studies have shown that consuming enough egg white protein may help critically ill patients maintain their level of certain serum protein markers [6, 9].

Over time, enteral formulas have evolved to meet the needs of patients. They didn't contain fiber at first out of concern that it would lead to intestinal obstruction. Fortunately, growing evidence regarding the benefits of fiber, such as enhanced immunomodulatory gut function, positive effect in serum lipid and glucose regulation, and others, have allowed its introduction in modern available form. In all hemodynamically stable, critically sick patients, the use of soluble fibre has been shown to be safe and may even be thought to be helpful for lowering gastrointestinal symptoms, particularly diarrhoea. Thus, using soluble fibre to treat critically ill individuals may be beneficial [41].

Limitations

This is a Narrative review. We need more systematic reviews, observational cohort studies, and RCTs that focuses on specific patient groups and mechanism to further explain the molecular and physiologic rationale for the beneficial effects of albumin supplementation in specific groups of critically ill patients.

References

1. Mahanna E, Crimi E, White P, Mann DS, Fahy BG. Nutrition and metabolic support for critically ill patients. *CurrOpinAnaesthesiol.*2015:28(2):131–138
2. Griffiths RD. Nutrition support in critically ill septic patients. *CurrOpin Clin NutrMetab Care*,2003:6(2):203–210.
3. Weijs PJ, Cynober L, DeLegge M, Kreymann G, Wernerman J, Wolfe RR. Proteins and amino acids are fundamental to optimal nutrition support in critically ill patients. *Crit Care*,2014:18(6):591.
4. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, *et al*. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) *JPEN J Parenter Enteral Nutr*,2016:40(2):159–211.
5. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, *et al*. ESPEN guidelines on enteral nutrition: intensive care. *Clin Nutr*,2006:25(2):210–223. doi: 10.1016/j.clnu.2006.01.021.
6. Bhurayanontachai R, Sa-Nguansai S. Change of serum prealbumin levels and serum protein markers between egg white powder and casein protein additives in standard enteral feeding formulas in critically ill patients with acute respiratory failure. J Intensive Care,2016:27:4-32.

7. Vincent JL, Russell JA, Jacob M, *et al*. Albumin administration in the acutely ill: what is new and where next? Crit Care,2014:18:231.
8. Caironi P, GattinoniL.The clinical use of albumin: the point of view of a specialist in intensive care. Blood Transfus,2009:7:259-67. DOI 10.2450/2009.0002-09
9. Dharmsena A, BSD W, Gandhi J, Nair A. Schematic Review of Oral Egg Albumin Protein – An Overview In Critically Ill Patient. European Journal of Molecular & Clinical Medicine, 2022, 9(3). ISSN 2515-8260.
10. Lee JH, Paik HD. Anticancer and immunomodulatory activity of egg proteins and peptides: a review. Poult Sci,2019:98(12):6505-6516
11. Réhault-Godbert S, Guyot N, Nys Y. The Golden Egg: Nutritional Value, Bioactivities, and Emerging Benefits for Human Health. Nutrients,2019:11(3):684
12. Matsuoka R, Kurihara H, Nishijima N, Oda Y, Handa A. Egg White Hydrolysate Retains the Nutritional Value of Proteins and Is Quickly Absorbed in Rats. Scientific World Journal,2019:2019:5475302.
13. Matsuoka R, Shirouchi B, Umegatani M, Fukuda M, Muto A, Masuda Y, Kunou M, Sato M. Dietary egg-white protein increases body protein mass and reduces body fat mass through an acceleration of hepatic β-oxidation in rats. Br J Nutr,2017:118(6):423-430
14. Kato Y, Sawada A, Numao S, and Suzuki M, "Chronic effect of light resistance exercise after ingestion of a high-protein snack on increase of skeletal muscle mass and strength in young adults," Journal of Nutritional Science and Vitaminology,2011:57(3):233–238.
15. Cho DY, Jo K, Cho SY, Kim JM, Lim K, Suh HJ, *et al*. Antioxidant Effect and Functional Properties of Hydrolysates Derived from Egg-White Protein. Korean J Food Sci Anim Resour,2014:34(3):362-71. doi: 10.5851/kosfa.2014.34.3.362. Epub 2014 Jun 30. PMID: 26761178; PMCID: PMC4597870.
16. Davalos A, Miguel M, Bartolome B, Lopez-Fandino R. Antioxidant activity of peptides derived from egg white proteins by enzymatic hydrolysis. J Food Prot,2004:67:1939-1944.
17. Sakanaka S, Tachibana Y, Ishihara N, Juneja LR. Antioxidant activity of egg-yolk protein hydrolysates in a linoleic acid oxidation system. Food Chem,2004:86:99-103
18. Jahandideh F, Chakrabarti S, Davidge ST, Wu J. Egg white hydrolysate shows insulin mimetic and sensitizing effects in 3T3-F442A pre-adipocytes. PLoS One, 2017, 12(10).
19. Danaei G, Singh GM, Paciorek CJ, Lin JK, Cowan MJ, Finucane MM, *et al*. The global cardiovascular risk transition: Associations of four metabolic risk factors with national income, urbanization, and western diet in 1980 and 2008. Circulation,2013:127:1493-1502.
20. Jahandideh F, Chakrabarti S, Majumder K, Li Q, Panahi S, *et al*. Egg white protein hydrolysate reduces blood pressure, improves vascular relaxation and modifies aortic angiotensin II receptors expression in spontaneously hypertensive rats. J Funct Foods,2016:27:667-673.
21. Grootaert C, Matthijs B, Voorspoels S, Possemiers S, Smagghe G, Van Camp J. Egg-derived bioactive peptides with ACE-inhibitory properties: A literature update. Food Funct,2017:8:3847-3855
22. Lee DE, Jung TH, Jo YN, Yun SS, Han KS. Enzymatic Hydrolysis of Egg White Protein Exerts a Hypotensive Effect in Spontaneously Hypertensive Rats. Food Sci Anim Resour,2019:39(6):980-987.
23. Murakic-Sposta S, Gussioni M, Moretti S, Pratail L, Giardini G, Tacchini P, *et al*. Effects of mountain ultra-marathon running on ROS production and oxidative damage by micro-invasive analytic techniques, 2015.
24. Sugiyama K, Kawada C, Uno S, Yoshida H, Kishimoto Y, Taguchi C, *et al*. The Effects of egg white peptides ingestion for long-distance runners on antifatigue in endurance training. Research Quarterly for Athletics,2016:106:10–18. in Japanese
25. WHO, Energy and protein requirements (WHO technical report series, 1985, 724. Report of a joint FAO/WHO/UNU expert consultation. World Health Organization, Geneva
26. Steinberg D, Parthasarathy S, Carew TE, Khoo JC, Witztum JL. Beyond cholesterol. Modifications of low-density lipoprotein that increase its atherogenicity. New England Journal of Medicine,1989:320:915–924.
27. Matsumoto K, Koba T, Hamada K, Sakurai M, Higuchi T, Miyata H. Branched-chain amino acid supplementation attenuates muscle soreness, muscle damage, and inflammation during an intensive training program. Journal of Sports Medicine and Physical Fitness,2009:49:424–431.
28. Kato Y, Numao S, Miyauchi R, Suzuki M. Effect of intermittent blood volume fluctuation of light resistance exercise after ingestion of the high-protein snacks on plasma branched-chain amino acid concentrations in young adults. Journal of Nutritional Science and Vitaminology,2010:56:255–259.
29. Matsuoka R, Kimura M, Uno S, Shidara H, Kunou M. Egg white hydrolysate improves fatigue due to short-term swimming load test in mice. Food Sci Nutr,2018:6(8):2314-2320
30. Requena T, Miguel M, Garcés-Rimón M, Martínez-Cuesta MC, LópezFandiño R, Peláez C. Pepsin Egg white Hydrolysate Modulates Gut Microbiota in Zucker Obese Rats. Food Funct,2017:8(1):437–443.
31. Zheng K, Lu M, Liu Y, Chen Q, Taccardi N, Hüser N, *et al*. Monodispersed Lysozyme-Functionalized Bioactive Glass Nanoparticles with Antibacterial and Anticancer Activities. Biomed. Mater, 2016, 11(3).
32. Mahanta S, Paul S, Srivastava A, Pastor A, Kundu B, Chaudhuri TK. Stable Self-Assembled Nanostructured Hen Egg white Lysozyme Exhibits strong Anti-proliferative Activity against Breast Cancer Cells. Colloids Surf. B: Biointerfaces,2015:130:237–245
33. Valenti L, Dongiovanni P, Fargion S. Diagnostic and Therapeutic Implications of the Association between Ferritin Level and Severity of Nonalcoholic Fatty Liver Disease. Wjg,2012:18(29):3782–3786.
34. Ibrahim HR, Kiyono T. Novel Anticancer Activity of the Autocleaved Ovotransferrin against Human colon and Breast Cancer Cells. J. Agric. Food Chem,2009:57(23):11383–11390
35. Lee JH, Moon SH, Kim HS, Park E, Ahn DU, Paik HD. Antioxidant and Anticancer Effects of Functional Peptides from Ovotransferrin Hydrolysates. J. Sci. Food Agric,2017:97(14):4857–4864

36. Zhang X, Chelliappan B SR, Antonysamy M. Recent Advances in Applications of Bioactive Egg Compounds in Nonfood Sectors. Front Bioeng Biotechnol,2021, 16.
37. Guest S. Hypoalbuminemia in peritoneal dialysis patients. Adv Perit Dial,2013:29:55-60. PMID: 2434449
38. Frazier TH, DiBaise JK, McClain CJ. Gut microbiota, intestinal permeability, obesity-induced inflammation, and liver injury. JPEN J Parenter Enteral Nutr,2011:35(5):14s–20s. https://doi.org/ 10.1177/0148607111413772. 3.
39. Venegas-Borsellino C, Kwon M. Impact of Soluble Fiber in the Microbiome and Outcomes in Critically Ill Patients. CurrNutr Rep,2019:8(4):347-355.
40. Yagmurdur H, Leblebici F. Enteral nutrition preference in critical care: fibre enriched or fibre-free. Asia Pac J Clin Nutr,2016:25(4):740-6.
41. Reis AMD, Fruchtenicht AV, Loss SH, Moreira LF. Use of dietary fibers in enteral nutrition of critically ill patients: a systematic review. Rev Bras Ter Intensiva,2018:30(3):358-365.