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# **TRENDING DIETARY SUPPLEMENTS**

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**Abstract:** Vitamins, minerals, herbs, amino acids, dietary fibers and the other so many chemicals are called as dietary supplements. They are widely used worldwide. Across all major categories overall dietary supplement use has increased year by year. By definition, they should maintain nutrients otherwise that may not be consumed in adequate amounts. So much dietary supplements are simply taken for healthy life, but some are used for reduce and modulate risk factors for chronic diseases, like cancer, cardiovascular diseases or birth defects. There are some other supplements which are used for benefits such as management of sleep, improving physical performance or weight management. They are not drugs and therefore they are not intended to diagnose, prevent, mitigate, treat or cure diseases. Nevertheless, there are so much dietary supplements selled as self-medication substances that promotes health related issues. But some of them may cause toxic reactions, interact with pharmaceuticals or other supplements and they may have been contaminated with heavy metals or do not contain the anticipated amount of ingredients. Also redundant of several nutrients may increase cancer risk. Generally, if there is no deficiencies or special conditions, there is no need to take supplements. In this review, we aimed to examine biological benefits of dietary supplements such as glutathione, pycnogenol, resveratrol, quercetin, chlorella pyrenoidosa, beta-glucan,  $\alpha$ -lipoic acid and bromelain. We called them as trending dietary supplements due to their improving effects on human health.

Keywords: Dietary, Health, Supplements, Nutrient, Disease

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# 1. Introduction

People have a hope that they can improve their health through diet or consumption of natural compounds. Accordingly, they have shown interest in herbal medicine (Zhang et al., 2018). Many people believe that natural remedies are harmless. However, recent publications have drawn attention to serious consequences arising from the side effects of herbal products, such as causing additional damage to patients who wants to solve the problems like obesity (Bent and Ko, 2004). Undesirable effects may occur due to the misuse of herbaceous, their contamination, and their interaction with other herbs and medicines. Therefore, they should be used carefully. However, all over the world, herbal products are not in a serious control and inspection since they are considered as food additives in the legal field and are not accepted as drugs (Sarışen and Çalışkan, 2005). In this review, the biological benefits of dietary supplements such as glutathione, pycnogenol, resveratrol, quercetin, chlorella pyrenoidosa, beta-glucan,  $\alpha$ -lipoic acid and bromelain was mentioned.

# 2. Dietary Supplements

### 2.1. Glutathione (GSH)

Glutathione (GSH) is a thiol-containing tripeptide, consisting of cysteine, glycine and glutamate (Grucza et

al., 2019). Higher glutathione levels, defend against cell damage and progression of disease (Gould and Pazdro, 2019). In one study, depletion of glutathione increases non alcholic steatohepatitis-related hepatic pathology in mices fed with a deficient diet in choline and methionine (diet MCD) examined. Wild type mices (wt) and genetically GSH deficient mices lacking of the modifier distinct component of Glutamate Cysteine Ligase (GCLmnull) mices (n=4-6, each group), were fed on the control (MCS), experimental (MCD) diet and standard chow diet (25% protein, 62% carbohydrates, 13% fat) for 21 days. MCD diet contained 17% protein, 65% carbohydrates, 10% fat. MCS diet was same + supplemented with 3g/kg DL-methionine and 2g/kg choline chloride. GCLm null mice were to a largely protected from MCD diet caused hepatocyte injury, high fat accumulation, tissue inflammation and fibrosis. GCLm null mice's livers have more capacity to metabolize exogenous and endogenous compounds and increased antioxidant activity than wt mice livers. The study determined the GSH effect on the development of liver steatohepatitis and severe GSH deficiency resulting from metabolic adaptations seem to defend them against the diet induced injury of liver (Haque et al., 2010). Oral supplementation of GSH isn't the most effective option for the enzymatic break down of ingested glutathione in the intestine by  $\gamma$ - glutamyltransferase (Gould and Pazdro, 2019). There may be no change in GSH levels or in parametres of oxidative stress despite acut or 4 weeks chronic oral GSH supplementation (Minich and Brown, 2019). But the amino acids components supplementation (glycineglutamine and cysteine) increases tissue glutathione synthesis. When orally administrated N-acetylcysteine (NAC) also converted into cysteine in liver, increases GSH levels in individuals with glutathione deficiency due to genetic defects, infections or metabolic problems (Gould and Pazdro, 2019). Vitamin E ( $\alpha$ -Tocopherol), vitamin B6 (pyridoxine), vitamin C (Ascorbate), selenium, magnesium and whey protein supports GSH biosynthesis. Also Mediterranean diet and the DASH diet improves GSH but western diet impaired GSH synthesis (Gould and Pazdro, 2019). Three weeks randomized crossover study of patients with metabolic syndrome, 450 mg/day oral GSH, 200 mg/day oral NAC and 450 mg/day sublingual form of GSH compared. Sublingual glutathione ended in an important increase in either plasma GSH or total plasma glutathione. Vitamin E levels of plasma also increased in this group (Schmitt et al., 2019). It is a major endogenous intracellular antioxidant to control oxidative stress level. Human plasma contains small amounts of reduced glutathione, which appears to increase after exercise. It is also the most popular supplement for athletes and physically active people. 2 weeks oral (1 g/day) GSH supplementation can relieve fatigue during and after cycling in healthy men. Mices received the different doses of GSH (500, 750, 1000 mg/kg) by intraperitoneal injection. By increasing the amount, swimming endurance increased (Grucza et al., 2019). Researching the skin-lightening effect of GSH in humans, three-arm study was conducted. Placebo group, GSH group (250 mg/d), GSSG group (250 mg/d oxidized form) taken supplements for 12 weeks orally. The index of melanin and all sites of ultraviolet spots inclinated to be lower than placebo in other 2 group. Subjects that supplemented glutathione showed more reduction in wrinkles and skin elasticity increased in both GSH and GSSG groups measured with placebo. No adverse effects were observed in the study (Weschawalit et al., 2017). Glutathione and Glutathione peroxidase (GPX) expression has been evaluated as an indicator of prognosis and response to cytotoxic therapies in tumor cells. GPX uses GSH for degradation of H<sub>2</sub>O<sub>2</sub> to H<sub>2</sub>O. 63 woman with breast cancer assessed in retrospective study. Glutathiones high expression characterized as an indicator of low response to chemotherapy in those analyzed patients, and contributed to the development of metastasis. As a result, GPX was highly expressed in these patients' breast cancer cells with a worse clinical outcome and reduced overall survival who underwent radiotherapy and chemotherapy (Jardim et al., 2013). Increased levels of glutathione is important for signal transduction, cellular functions homeostasis and protection from certain carcinogens. However, this high level can decelerate any cancer treatments that works by rising intracellular reactive oxygen species (ROS). It is important to find out these cells if there is a drug resisting mechanisms or not (Abdalla, 2011).

## 2.2. Pycnogenol

Pycnogenol is a dietary supplement used as a phytochemical remedy worldwide. It is in polyphenols class (Zhang et al., 2018). It is a flavonoid plant extract obtained from the grown *Pinus pinaster* (*Pinus maritima*) on the southwest coast of France (Becit et al., 2017). Standardized to 70±5% procyanidins; the other parts taxifolin, catechin and a range of phenolic acids, represented by benzoin acid and cinnamic acid derivatives (Zhang et al., 2018). Pine tree bark in ancient times as a cough syrup, treats inflammatory diseases, wound healing, prevent bleeding, and dental pain (Becit et al., 2017). In a meta-analysis which evaluates the effects of pycnogenol on blood pressure, from 148 articles about pycnogenol 9 case including 549 participants that received supplements from 150 mg/d to 200 mg/d, were examined. The estimate of change in systolic and diastolic blood pressure were -3.22 mmHg and -3.11 mmHg compared with the control respectively. Among hypertensive participants or those who have been intervened for more than 12 weeks, subgroup analyses showed higher blood pressure reduction. This meta-analysis from 9 cases provide better evidence of beneficial effects of pycnogenol on blood pressure (Zhang et al., 2018). In rats with cisplatin cytotoxicity, pycnogenol 200 mg/kg given orally for 5 days. Its antioxidant and antigenotoxic effects have been investigated. As a result of the research, the prooxidant enzymes (MPO, xanthine oxidase) induced by cisplatin, malondialdehyde and nitric oxide level, pycnogenol is normalized with, reduces chromosome errors and their mitotic index has been shown to be increased. In common results of clinical studies with a mean dose of 80 mg/day on 4665 subjects, it was concluded that the duration of use and dose were not associated with undesirable effects. It is predicted that 100-200 mg daily dose of pycnogenol may be safe in humans (Becit et al., 2017).

### 2.3. Resveratrol

Resveratrol (3,5,4-trihydroxystilbene) is found mainly in grape skins, peanuts, raspberries, mulberries, plums and some plants. Resveratrol is known to be a phytoallexin produced by plants, particularly as a result of pathogens attacking plants, injury or exposure to ultraviolet (UV) light. This substance is also believed to be protective in humans. According to researches, resveratrol, which has the ability to delay aging as an antioxidant and antimutagen, blocks the cellular changes leading to cancer formation and prevents the formation of unwanted tissues in the body (Bay Karabulut, 2008). A new process "browning", in white adipose tissue (WAT), similar properties to those of brown adipocytes. White adipose tissue browning could be a future altenative curative strategy for the prevention of obesity and its comorbidities. According to examine resveratrol (RSV)

and guercetin (0) combination whether would cause WAT browning effect, 36 rats were fed an obesogenic diet, 20% sucrose and 24% fat and divided to 4 groups: control, resveratrol group (15mg/kg daily RSV), Q group (30 mg/kg daily Q) and RSV+Q group. After 6 week of cure with combination of RSV + Q, a siginificant decrease occurred in adipose tissue mass but when administreted seperately no reduction occured in body fat. In one of study alone resveratrol (150 mg/kg/day), multilocular adipocytes in inguinal WAT appeared in high fat diet fed rats. But in this study there was no induced browning effect in WAT due to the difference in the dose. But in these study the results showed, for the first time RSV + Q combination has a brown-like modifying effect in rats fed an obesogenic diet (Arias et al., 2017). The protective effect of resveratrol can be utilized by consuming 375 mL of red wine per day, eating 50 red-black grape grains, or drinking commercially important resveratrol-containing extracts (Keskin et al., 2009).

# 2.4. Quercetin

Quercetin is the matchless biological elements of the flavonoids which founds in vegetables and fruits. It has benefits for mental and physical health. Flavonols in glycosides form primarily, founds in parts of so much plants edible parts including many fruits, vegetables, tubers and bulbs, spices, tea, herbs, wine (Chen et al., 2016). In plants it is originated from the phenylpropanoid pathway and reproduced from phenylalanine (Biancatelli, 2020). Evidence in various studies shows that connect with diabetes (type 2), abdominal obesity, and chronic low grade inflammation. Because of increasing antioxidative activities, the reduction of cytokine levels and the proinflammatory enzymes activity, quercetin has been act as a strong antiinflammation weapon. In both human and animal studies, these results have been found (Donath and Shoelson, 2011; Chen et al., 2016; Richmond and Yang, 2016). Quercetins immune activity includes macrophage phagocytosis, neutrophil chemotaxis increase, and activity of NK cell lytic and proliferation of mitogenstimulated lymphocyte (Aucoin et al., 2020). Animals with the diabetes (type 2) that received quercetin had been lower glucose plasma levels according to the control group. Receiving 0.08% portion of quercetin increases HDL cholesterol and plasma adinopectin, and decreases triacylglycerols and plasma total cholestereol. Assesments are needed to uncover the mechanisms by which quercetin functions to satisfactorily approach safety concerns (Chen et al., 2016). Three double-blind, placebo- controlled randomized clinical trials which two of them was athlete participants examined to asses prevention of immune disturbance, respiratory tract infection and preventing of COVID-19. Two studies used quercetin + vitamin C + nicotinamide combination; one study used 1000 mg/day quercetin, the other 500 mg/day and 1000 mg/day quercetin to placebo. The study three used only 1000 mg/day quercetin. In the two-week period following, the significant decrease

happened in the incidence of upper respiratory tract infection (URTI). Daily 1000 mg dose resulted in decreasing of upper respiratory tract infection when used in mono therapy or combined with vitamin C and nicotinamide. But a larger community clinical research repoted efficacy in athletic adults which are 40 years old or older. In COVID-19 treatment or prevention, the evidences are insufficient to recommend this supplement (Aucoin et al., 2020). The flavonoid Quercetin 7rhamnoside which is not related with antioxidant effects, was approved by the cytopathic effect inhibation assay (CPE) reduction test by its antiviral effect. The study showed this flavonoids antiviral activity against the swine diarrhea virus epidemic. Also quercetin can obstruct pneumolusin activity. The hemolysis tests used for confirming. It also inhibites a few respiratory viruses in cells cultured (Chojnacka et al., 2020). In one study when comparing receiving only vitamin B3 and C mice group has less prolonged time to death and improved survival than the quercetin (12.5 mg/kg weekly) + vitamin B3 + vitamin C mice group. Ascorbic acid and flavonoids (1:1 ratio) is useful for respiratory infections according to clinical trials. For 3 months 1 g/day oral supplementation has not outcomed in important adverse effects (Biancatelli et al., 2020). It can be a new potential medicine in a therapy of clinical pneumococcal infections. And it can be early therapy of respiratoy tract infections including COVID-19 with vitamin C (Biancatelli et al., 2020; Chojnacka et al., 2020).

# 2.5. Chlorella Pyrenoidosa

A single-cell marine microalga, Chlorella pyrenoidosa, is in the class Chlorophyceae and it has lots of special active biological ingredients. It contain chlophylls, β-carotene, polyunsaturated fatty acids and polysaccharides (Holmes et al., 2008). Most of the researches point on improving of functional peptides, such as chlorella pyrenoidosa protein (CCP), which as antimicrobial, antioxidant, lipidblood pressure-lowering, and immune lowering, regulatory functions (Hua et al., 2019). In this study, dried chlorella pyrenoidosa powders (CPE55) derived using ethanol 55% at 50°C in a ratio of 1:10 for 1hour. 32 male rats controlled 12 h day and night and 60% relative humidity with a standart diet. After 1 week rats divided into 4 groups: normal fat diet (NFD) (13.5% energy from fat), high fat diet (HFD) (67% normal diet, 20% sucrose, 3% cholesterol, 10% lard), HFD with CPE55 at 150 mg/kg daily (CPE55L) and HFD with 300 mg/kg daily (CPE55H). Throughout 8 weeks, different solutions of CPE55 groups were gavage feeding with 2 ml, normal fat diet and high fat diet groups were gavaged with 2 ml 0.9% saline solution. Administration orally with CPE55 significantly relieved dyslipidemia by increasing adverse blood lipid profile and limiting hepatic steatosis and lipid accumulation. There is no important difference in CPE55L and CPE55H groups for serum total cholesterol, serum triglyceride, serum LDL and serum HDL levels. It also improved Alloprevotella, Ruminococcus1, Alistipes and Prevotella bacterias and reduced the abundace of bacterias Lachnospira and Turicibacter which are in positive correlations of metabolic phenotypes (Wan et al., 2018). Metabolic phenotype maintain a read out an individual metabolic state. It is the product of genetic and environmental (lifestyle, gut microbial activity and diet) contributions under a particular set of conditions (Holmes et al., 2008). In the result of histopathological analysis, CPE55 could reduce the prevelance of ameliorate hepatocyte injury and hepatic steatosis (Wan et al., 2018). In order to investigate the effect of CPPH (chlorella pyrenoidosa protein hydrolysate) and chlorella pyrenoidosa protein hyrolysate-calcium chelate (CPPH-Ca) on gut microbiata and absorption of calcium in the rats fed with low calcium diet. In 10 groups, each 10 rats, (control: 5000mg/kg, model (1000mg/kg), HCaCO3 group, HGCa group, LCaCO<sub>3</sub> + LCPPH group, + MCaCO<sub>3</sub> + MCPPH group, HCaCO<sub>3</sub> + HCPPH group, LCPPH-Ca group, MCPPH-Ca group, HCPPH-Ca group) at the beginning there was no important difference in initial body weight. After 4 weeks, low calcium diet (model) group body weight was apparently lower than normal diet (control) group. The rats fed with HCPPH-Ca got weight more quickly than model group and HCaCO<sub>3</sub> group after 8 weeks. But there is no significant difference betwen control group and HCPPH-Ca group. The results specified that CPPH-Ca advanced body weight to a normal level, insomuch that in the middle dose. And HCPPH-Ca was better than HCaCO<sub>3</sub>, insomuch that in HGCa, and the calcium in CPPH-Ca absorbed more easily. It also improved the abundances of lactobacillus and firmicutes. Rothia, turicibacter, lactobacillus, streptococcus, showed positive corelation with anusual parameters like serum Ca and body weight while sutterella and bifidobacterium were both correlated with absorption of calcium positively (Hua et al., 2019).

# 2.6. Beta-glucan (β-glucan)

Beta-glucan ( $\beta$ -glucan) is a native polysaccharide occuring in the walls of plant cells (Ciecierska et al., 2019). This type of dietary fiber high in oats. In animal studies, β-glucan decrease energy intake and so body weight because of that it has been shown to be increase satiety related hormones. Increased viscosity retardates gastric emptying and decreases the absorption of nutrients. If carried in a whole food or take out from the food,  $\beta$ -glucans in the oat acts to have a positive effect on sense of satiety by hunger controlling and the desire to (Rebello al., 2016). In addition eat et to immunomodulatory, antioxidant and antitumor properties, beta-glucans have prebiotic properties also. It stimulates the growth of probiotic bacterial strains in the large intestine and inhibit pathogenic bacteria growth. Especially from grains, soluble beta-glucans fermented by microflora. Short-chain fatty acids like acetic acid, propionic acid and butyric acid produced by fermention of these compounds. And these fatty acids prevent obesity and colon cell proliferation thus inhibiting cancer cell growth (Ciecierska et al., 2019). To compare the effect of isolated β-glucan oat fractions of high and low

molecular weight on inlammatory markers in colitis model by taking as dietary supplementation. 27 rats with colitis (C) and 27 control healthy rats (H) were divided into 3 dietary groups (each n=9). First one was 1% of low molecular (1.7×10<sup>6</sup> supplemented with g/mol) mass oat beta-glucan, second one with 1% of high molecular (5.9×104 g/mol) mass oat beta-glucan, third group feed didnt have beta-glucan supplementation for 21 days. The molecular weight dependent curative effect of dietary beta-glucan in oat supplementation in TNBS (2,4,6-trinitrobenzenosulfinic acid) induced clitis demonstrated. By inhibation of submucosa and mucosa lymphocytes in filtration via its capacity to form a protective coat on intestinal wall, the study showed high molecular weight beta glucan has stronger sedative inflammation effects. Also low molecular weight β-glucan reduce the inflammatory signes such as the protein levels of cytokines and eicosanoids and modulate the cytokines and chemokines signaling pathways. One of interesting reason is the effectiveness of the oat beta-glukans supplementation is better preferably during ongoing inflammation than prevention of this colon disease in animals with TNBS-induced colitis (Zyla et al., 2019). In one of study to investigate efficacy of the oat (beta supplementation glucan) on immunological, physiological, metabolic and nutritional variants in 14 dogs, the dogs divided into two group and fed with control diet and 1% beta glucan supplementation during 71 days. There is no difference in peptid YY (PYY) and ghrelin between the groups. By decreasing the predominance of the response Th2, it can positively arrange the vaccine responce of dogs. It is resulted that oat beta glucan can be used at the 10 g/kg dose (food) is effective in decreasing total cholesterol, VLDL-c and LDLc (Ferreira et al., 2018). To see the efficacy of insoluble yeast beta-glucan on common cold symptoms double blind, placebo-controlled, randomized clinical trial study done. Over a period of 26 weeks 100 healthy but with a recurring infections, participants that receive either yeast beta-glucan or placebo (each n=50) documented each common infectious symptoms. When compared with the placebo group, the group with beta-glucan had importantly less infections during the most infection season. Also β-glucan importantly decreased the symptoms like sore throat, cough, runny nose in the betaglucan group (Graubaum et al., 2012). Termed trained immunity (TRIM), is the innation of immune community called the birth of the innate immune cells after exposure to an initial stimulus, metabolic, epigenetic and metabolic reprogramming? It is exposed in a memory and results in a memory phenotype of enhanced immune responses when exposed to a secondary, heterologous stimulus. βglucan has been shown to have a number of anti-viral properties, Trim's role as an inducer could possibly aid immune responses to SARS-CoV-2 and help prevent serious clinical complications. Clinical trials are required to confirm the effectiveness of this treatment in COVID-19 (Geller and Yan, 2020).

### 2.7. α-lipoic Acid (ALA)

For mitochondrial enzymes,  $\alpha$ -lipoic acid (ALA) is inherently occuring co-factor and antioxidant (Huerta et al., 2015). From cysteine and fatty acid in low quantities it synthesized de novo. Because of therapeutic effect it is important to eat exogenous sources of ALA (Mendoza-Nunez et al., 2019). In one study, 103 woman, aged 20-50 vears, between 27.5-40 BMI were recruited for parallel, short term randomized double blind placebo controlled trial. 4 groups of daily supplements occurred. 30 woman in group control (3 placebo-1 capsule (containing sunflower oil) and 3 placebo-2 capsules (containing same auxiliary as the lipoic acid capsules), 20 woman in EPA group (1300 mg/d of EPA distributed in 3 capsules of EPA 80 containing 433.3 mg of EPA and 13.8 mg of DHA as ethyl-esters and 3 placebo-2 capsules), 26 woman in  $\alpha$ -lipoic acid group (300 mg/d of  $\alpha$ -lipoic acid from 3 capsules containing 100 mg of  $\alpha$ -lipoic acid and 3 placebo-1 capsules) and 26 woman in EPA+  $\alpha$ -lipoic acid group ( daily 1300 mg of EPA and daily 300 mg of  $\alpha$ lipoic acid). After 10 weeks all groups showed important differences in the reducing body weight but the higher reduction is in  $\alpha$ -lipoic acid group. Important leptin decrease is also observed in this group. The group with EPA showed significant lower decline in leptine levels during weight loss (Huerta et al., 2015). One of the research, to define the efficacy of 600 mg/kg of  $\alpha$ -lipoic asid by the markers of oxidative stress (OxS), inflammation and AGE (advanced glycation end products) in older adults (60-74 years) with T2DM, 98 women and 37 men divided into 3 groups; EG (experimental group, n:50), PG (placebo group, n:50) and CG (control group, n:35). A guide were given to all participants about the amount and type of the daily food. After six months the important increment was seen in the blood HDL in the PG and EG group compared to the CG group. At HbA1c a reduction was seen in the EG and PG group compared to the CG but the difference was not significant. The antioxidant and anti-inflammatory efficacy of ALA at a dose 600 mg/kg do not support in this study. But the administration of doses daily 1200-1800 mg of ALA could be beneficial to decrease the inflammation, OxS and prevent the formation of AGEs that forms in diabetes (Type 2) in older adults must be confirmed through controlled clinical trials (Mendoza-Nunez, 2019).

### 2.8. Bromelain

Bromelain is a complex mixture of protease extracted from the stem or fruit of the pineapple. With the lack of side effects, it has anti-inflammatory, fibrinolytic, antithrombotic, immunomodulatory effects and anticancer activity (Rathnavelu et al., 2016). It can absorbed in intestine without losing out its biological activity and degredation (Kwatra, 2019). Through November 2017 in six databases an alectronic search was conducted. Non-randomized, randomized clinical trials and studies comparative examined that used bromelain after molar surgeries (lower third). The results showed the greater reduction of pain levels, trismus and edema in bromelain used groups (De Souza et al., 2019). Its analgesic properties that result in direct efficacy on pain mediators like bradykinin. It shows great potential in therapies for oncology patients. It has also significant role in arthritis pathogenesis. It is also effective fibrinolytic agent by stimulating the changing of plasminogen to plasmin effecting in increasing fibrinolysis. After giving daily 3000 FIP unit throughout 10 days to human no important changes in blood coagulation parameters. It has no significant side effects even after long-term use (Kwatra, 2019).

# 3. Conclusion

Dietary supplements should not be considered as drugs. It is known that such supplements affect the health of the individual positively only when recommended by experts and consumed correctly. Today, inadequate and unbalanced nutrition causes nutritional disorders. Efforts to reach healthy nutrition increase people's orientation to additional foods (vitamins, minerals, etc.). Today, the functional properties of foods (antioxidant, dietary fiber, amino acid, etc.) lead to the development of new products in the dietary supplements industry and can support individuals who need these supplements. Additionally their useful and supportive effects, dietary supplements can have many different side effects. These side effects can also cause serious problems. It should not be forgotten that dietary supplements consumed to benefit metabolism may interact with drugs used at the same time and negative effects may be seen. Problems arising from contamination, additives, toxicity, and incorrect dosing and labeling are among the reported problems with dietary supplements. There are supplements that have recently entered the literature such as glutathione, pycnogenol, resveratrol, quercetin, chlorella pyrenoidosa, beta-glucan,  $\alpha$ -lipoic acid and bromelain. Studies have shown that each supplement has different beneficial effects on the body. Glutathione is effective in tissue generation, cellular damage, disease progression. Pycnogenol has a role of decreasing the blood pressure. Resveratrol is an antioxidant and antimutagen which is naturallly found in wine. Quercetin is the biological element of flavonoids and has many positive effects on metabolism. Chlorella pyrenoidosa has antimicrobial, antioxidant, lipid lowering and immune functions. Beta-glucan is used mainly in respiratory system disease. The  $\alpha$ -lipoic acid especially in obesity, has so much benefits. Bromelain naturally found in has anti-inflammatory, fibrinolytic, pineapple antithrombotic, immunomodulatory effects and anticancer activities. Side effects have not been reported unless they are used in high amounts. Dietary supplements should be used in consultation with a healthcare professional.

### Author Contributions

All authors have equal contribution and all authors read

and approved the final manuscript.

#### **Conflict of Interest**

The authors declare that there is no conflict of interest.

#### References

- Abdalla MY. 2011. Glutathione as potential target for cancer therapy; More or less is good? (Mini-Review). Jordan J Bio Sci, 4(3): 119-124.
- Arias N, Pico C, Macarulla MT, Oliver P, Miranda J, Palou A. 2017. A combination of resveratrol and quercetin induces browning in white adipose tissue of rats fed an obesogenic diet. Obesity, 25: 111-121.
- Aucoin M, Cooley K, Saunders PR, Cardozo V, Remy D, Cramer H. 2020. The effect of quercetin on the prevention or treatment of COVID-19 and the other respiratory tract infections in humans: A rapid review. Adv in Integ Med, 7(4): 247-251. DOI: 10.1016/j.aimed.2020.07.007.
- Bay Karabulut A. 2008. Resveratrol ve etkileri. Türkiye KlinTıp Bil Derg, 28(6): 166-169.
- Becit M, Aydın S, Başaran N. 2017. İnsan sağlığında piknogenol: Bir genel derleme. FABAD | Pharm Sci, 42(2): 125-138.
- Bent S, Ko R. 2004. Commonly Used herbal medicines in the United States: A review. American J Med, 116: 478-485.
- Biancatelli RMLC, Berrill M, Catravas JD, Marik PE. 2020. Quercetin and vitamin C: An experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19). Frontiers in Immun, 11: 1451.
- Chen S, Jiang H, Wu X, Fang J. 2016. Therapeutic effects of quercetin on inflammation, obesity and type 2 diabetes. Mediators of Inflam, 2016: 9340637.
- Chojnacka K, Witek-Krowiak A, Skrzypczak D, Mikula, K. Mlynarz P. 2020. Phytochemicals containing biologically active polyphenols as an effective agent against Covid-19inducing coronavirus. J Func Foods, 73: 104146.
- Ciecierska A, Drywien ME, Hamulka J, Sadkowski T. 2019. Nutraceutical functions of beta-glucans. Rocz Panstw Zakl Hig, 70(4): 315-324.
- De Souza GM, Fernandes IA, Dos Santos CRR, Falci SGM. 2019. Is bromelain effective in controlling the inflammatory parameters of pain, edema, and trismus after lower third molar surgery? Asystematic review and meta-analysis. Phytot Res, 1-9. 33:473–481. DOI: 10.1002/ptr.6244.
- Donath MY, Shoelson SE. 2011. Type 2 diabetes as an inflammatory disease. Nature Rev Immun, 11(2): 98–107.
- Ferreira LG, Endrighi M, Lisenko KG, Duarte de Oliveira MR, Damasceno MR, Claudino JA. 2018. Oat beta-glucan as a dietary supplement for dogs. Plos One, 13(7): e0201133.
- Geller A, Yan J. 2020. Could the induction of trained immunity by  $\beta$ -Glucan serve as a defense against COVID-19? Hypot and Theory, 11: 1782.
- Gould RL, Pazdro R. 2019. Impact of supplementary amino acids, micronutrients and overall diet on glutathione homeostasis. Nutrients, 11(5): 1056.
- Graubaum HJ, Busch R, Stier H, Gruenwald J. 2012. A doubleblind, randomized, placebo-controlled nutritional study using an insoluble yeast beta-glucan to improve the immune defense system. Food and Nutr Sci, 3: 738-746.
- Grucza K, Cholbinski P, Kwiatkowska D, Szutowski M. 2019. Effects of supplementation with glutathione and its

precursors on athlete performance. Biomedical J Sci Tech Res, 12(4): 9434-9441. DOI: 10.26717/BJSTR.2019.12.002293.

- Haque JA, McMahan RS, Campbell JS, Shimizu-Albergine M, Wilson AM, Botta D. 2010. Attenuated progression of dietinduced steatohepatitis in glutathione-deficient mice. Lab Invest, 90: 1704-1717.
- Holmes E, Wilson ID, Nicholson JK. 2008. Metabolic phenotyping in health and disease. Cell, 134(5): 714-717.
- Hua P, Xiong Y, Yu Z, Liu B, Zhao L. 2019. Effect of chlorella pyrenoidosa protein hydrolysta-calcium chelate on calcium absorption metabolism and gut microbiota composition in low-calcium diet-fed rats. Marina Drugs, 17(6): 348.
- Huerta AE, Navas-Carretero S, Prieto-Hontoria PL, Martinez JA, Moreno-Aliaga MJ. 2015. Effects of  $\alpha$ -lipoic acid and eicosapentaenoic acid in overweight and obese woman during weight loss. Obesity, 23: 313-321.
- Jardim BV, Moschetta MG, Leonel C, Gelaleti GB, Regiani VR, Ferreira LC. 2013. Glutathione and glutathione peroxidase expression in breast cancer: An immunohistochemical and molecullar study. Oncology Rep, 30: 1119-1128.
- Keskin N, Noyan T, Kunter B. 2009. Resveratrol ile üzümden gelen sağlık. Türkiye Klin Tıp Bil Derg, 29(5): 1273-1279.
- Kwatra B. 2019. A review on potential properties and therapeutic applications of bromelain. World J Pharm Pharmac Sci, 8(11): 488-500.
- Mendoza-Nunez VM, Garcia-Martinez BI, Rosade-Perez J, Santiago-Osorio E, Pedraza-Chaverri J, Hernandez-Abad VJ. 2019. The effect of 600 mg alpha-lipoic acid supplementation on oxidative stress, inflammation and rage in older adults with type 2 diabetes mellitus. Oxidative Med and Cell Long, 2019: 3276958. DOI: 10.1155/2019/3276958.
- Minich DM, Brown BI. 2019. A review of dietary (phyto) nutrients for glutathione support. Nutrients, 11(9): 2073.
- Rathnavelu V, Alitheen NB, Sohila S, Kanagesan S, Ramesh R. 2016. Potential role of bromelain in clinical and therapeutic applications. Biomedical Rep, 5: 283-288.
- Rebello CJ, O'Neil CE, Greenway FL. 2016. Dietary fiber and satiety: the effects of oats on satiety. Nutri Rev, 74(2): 131-147.
- Richmond A, Yang J. 2016. The role of NF- $\kappa$ B in modulating antitumor immunity. Oncolmmunology, 5(1): e1005522.
- Sarışen Ö, Çalışkan D. 2005. Fitoterapi: Bitkilerle tedaviye dikkat. Sürekli Tıp Eğit Derg, 14(8): 182-187.
- Schmitt B, Vicenzi M, Garrel C, Denis FM. 2019. Effects of Nacetylcysteine, oral glutathione and novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. Redox Biol, 6: 198-205.
- Wan X, Li T, Liu D, Chen Y, Liu Y, Liu B. 2018. Effect of marine microalga chlorella pyrenoidosa ethanol extract on lipid metabolism and gut microbiata composition in high-fat diet-fed rats. Marine Drugs, 16(12): 498.
- Weschawalit S, Thongthip S, Phutrakool P, Asawanonda P. 2017. Glutathione and its antiaging and antimelanogenic effects. Clin Cosm Invest Dermatol, 10: 147-153.
- Zhang Z, Tong X, Wei YL, Zhao L, Xu JY, Qin LQ. 2018. Effect of pycnogenol supplementation on blood pressure: A systematic review and Meta-analysis. Iran J Pub Health, 47(6): 779-787.
- Zyla E, Dziendzikowska K, Gajewska M, Wilczak J, Harasym J, Gromadzka-Ostrowska J. 2019. Beneficial effects of oat betaglucan dietary supplementation in colitis depend on its molecular weight. Molecules, 24(19): 3591.