A Review on Dietary Supplements: Health Benefits, Market Trends, and Challenges

[1]Abubakar Ahmad Aliyu, [2]Singh Karishma, [3]Muhammad Isa Abdurrahman, [4]Adamu Usman Tsoho

[1,2]Research Scholar, Department of Life Sciences, Sharda University, Greater Noida, India.
[3]Research Scholar, Department of Civil Engineering, Sharda University, Greater Noida, India.
[4]Kano University of Science and Technology, Wudil.

***Abstract*: Food is one of the basic needs of life, which supplies various nutrients that the body utilizes to give energy, repair outworn tissues, and sustain life and development. Since nutrients can support life and growth, every individual needs to maintain adequate nutrition for better health and productivity, keeping in mind that various nutrients have various functions and differ according to their need in the body. As a result, many countries like India, Nigeria, America, England, and others formulate dietary guidelines such as RDA and DRI to achieve optimum nutrition. People who cannot meet their nutritional requirements directly through daily food intake due to physiological factors, age, or work usually use food supplements. For this work, literature on food and dietary supplements published and indexed in Science Direct and Scopus were searched and comprehensively analyzed. The study majorly focused on health claims of food supplements such as their use in the management of Diabetes, Cancer, CVDs, Cognitive function, Obesity-induced erectile dysfunction, Bone mineral density, and their use in athletes. The risk associated with food supplements, constraints, market trends, and future perspectives were also presented. Among all the supplements studied during this review, Omega 3 fatty acid was generally accepted and highly efficient dietary supplement with no or little critics. It is recommended that more regulations should be imposed on such products to protect human life as dietary supplements are not always safe. It should only be used when prescribed or suggested by a physician or qualified health care professional with related experience.**

***Keywords:* Supplements, Health, Dietary, Food, Benefit.**

1.0 INTRODUCTION

Food supplements, as defined by European Food Safety Authority (EFSA), "are concentrated sources of nutrients or other substances with a nutritional or physiological effect intended to supplement a normal diet" [1]. When consumed, dietary supplements are intended to provide health benefits such as prevention of diseases, improvement of mental and general health, enhancement of athletic performance, and compensation for dietary shortcomings [2]. Dietary supplements are neither drugs nor conventional foods; they are intended to supplements food in providing added nutrients and improve general wellbeing. It should be noted they are not intended to replace food or serve as a medicine to cure chronic diseases. At early genesis in food supplements, these products are not regulated for their safety and standard. Manufacturers of supplements, especially in the USA, were not required to provide sufficient health claims or adverse health effects relating to their products as they are considered natural food ingredients. These products remain unregulated until, in the year 1994 that congress passed the Dietary Supplement Health and Education Act (DSHEA) to regulate dietary supplements. Under this act, the Federal Drug Agency (FDA) has the power to recall a supplement from the market when it is scientifically proved to be unsafe [3]. The FDA's responsibility extended through multiple years with some minor changes until, in 2006 the congress passed by Dietary Supplement and Nonprescription Drug Consumer Protection Act (NDCPA), which requires the manufacturers to report any adverse health issue to the FDA to determine the safety of the products. The needs for dietary supplements is always increasing due to the increase in health issues (i.e., diseases related to metabolic syndrome), changing food habits, physical inactivity, desk bound employments, and tight job scheduled, which paves a way to the increasing consumption of junk foods that are nutrient deficient accompanied with high energy content resulting to improper dieting. People consider the beneficial effects of food supplements to make up the deficiencies that may occur by such improper dieting. Some of the beneficial effects of these supplements are shown in figure1.

Dietary supplements have a vast advantage in promoting health and wellbeing when taken according to their intended use. The question is, are these supplements safe to be taken simultaneously with drugs to speed up recovery from diseases? According to a systematic review of 433 cancer patients that simultaneously took drugs and supplements, the authors identified 167 potential drugs–supplements interactions in which 13.9% of the patients fall into the at-risk group of such interactions. The review further elucidated drugs that frequently interact with supplements such as; warfarin, cyclophosphamide, paclitaxel non-steroidal anti-inflammatory drugs, and vinorelbine, among others. Whereas garlic, Green tea, Mistletoe, Iron, St John's wort, Ginger, potassium, and magnesium, etc., are among the most frequently used supplements that interact with drugs [4]. The identified reactions given above were not backed with full clinical trials, but they were theoretically presented. So taking dietary supplements accompanied by drugs simultaneously should only be considered when directed by a qualified physician. However, many people are engaged in taking dietary supplements without adequate knowledge of the risk associated with such supplements. For example; the result of a study carried out on the knowledge concerning dietary supplements among general public in southeastern Poland reveals that the majority of the respondents used one or more form of dietary supplements, in which a higher number of the respondents had little subjective knowledge on such supplements [5]. This finding clearly shows a need to increase public awareness of the use, function, and risk of dietary supplements.

Some example of dietary supplements includes; vitamin D, vitamin A, creatine, Terrestris, caffeine, bicarbonate, Nicotinamide, amino acids, chromium, chrysin, omega 3-fatty acid, colostrum, creatine, hydroxymethyl butyrate (HMB), ornithine alpha ketoglutarate, protein, boron, Tribulus vanadium, zinc, and others. Dietary supplements are available in various forms, such as capsules tablets, soft caps, soft gels, liquids, and powders. According to various researches, the demand for dietary supplements is always increasing due to the increase in healthcare costs, sports activities, geriatric population, pregnancy related abnormalities, and concerns over health care prevention rather than conventional treatment.

A study by the National Diet and Nutrition Surveys (NDNS) in the United Kingdom for adults aged 19-64 and older > = 65 years in 2012/13-2013/14 using a one year recall reported that 15% of men and 24% of women use at least one or more forms of the supplement within the range of 19-64 years, while in older adults, it was found to be 30% of men and 41% of women respectively [6]. It should not be a surprise to have such a large percentage of food supplements users because some studies have proven the efficacy of various food supplements.

For example, Calcium supplementation in a various prospective randomized clinical trials have shown potentials to increase bone acquisition in adolescence [7, 8], early adulthood, as well as in the third decade of life [9, 10]. But when calcium supplementation ceased, the beneficial effect achieved in the studies on bone mineral density (BMD) disappeared unless calcium intakes were maintained [11]. Among the reasons for the use of supplements include: to improve immunity, to compensate for an inadequate diet, to meet abnormal demands of hard training or frequent competition, to improve performance, to keep up with team-mates or opponents for athletes, recommended by coach, mentor, parent, friend or other influential people.

Vitamins, minerals, and plant products are the most commonly used dietary supplements in the USA, while vitamins and minerals derived products are most widely used in the EU countries as they account for 50% of total sales, energy drinks account for 7% market share, and other forms of Dietary supplements account for the remaining 43% [12].

Dietary supplements have vast physiological functions, especially vitamin supplements, which serve as antioxidants in the body. Figure 1 shows the various functions of dietary supplements in the human body. It is believed that antioxidant supplements reduce the level of free radicals in the body in addition to the improvement of both eye health and cognitive functions. While calcium and vitamin D supplements have a greater positive impact on bone density and reduce bone demineralization at a later age. Furthermore, folic acid and omega 3 fatty acids prevent birth defects and reduce the risk of developing heart related diseases, respectively.

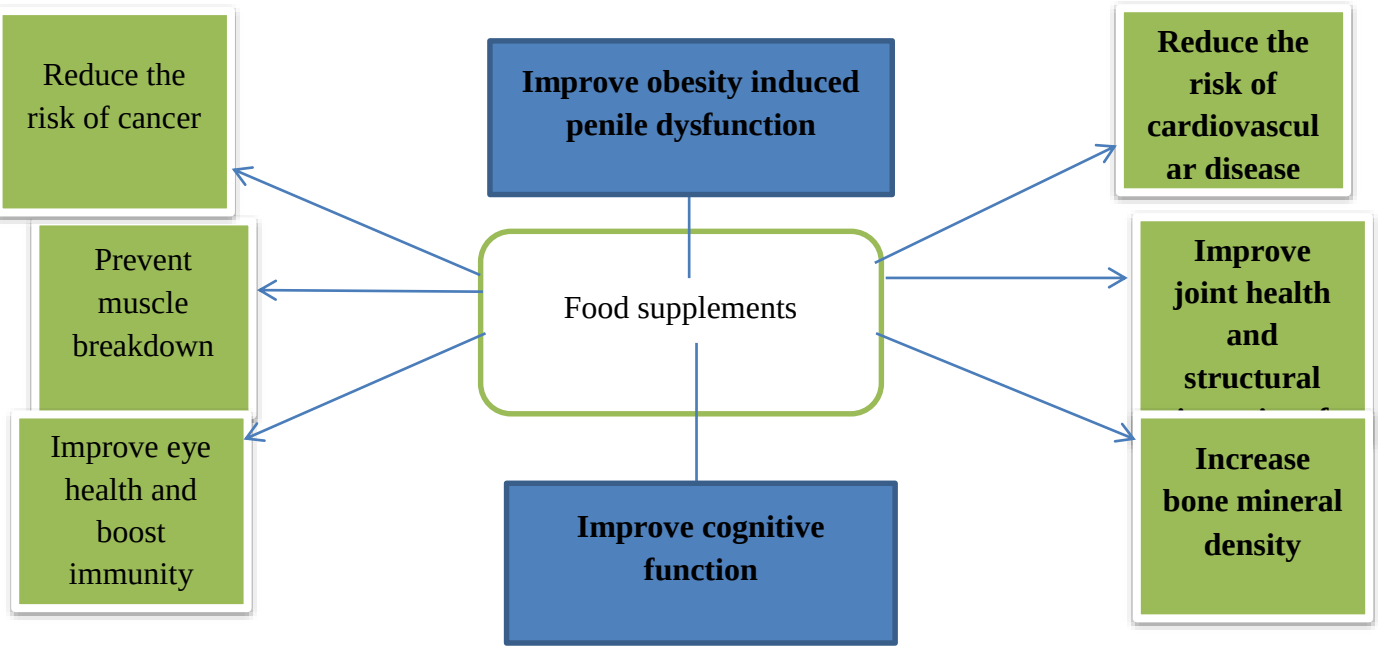

Figure 1: Health benefits of dietary supplements

2.0 Classification of Food Supplements

Dietary supplements are divided into two categories depending on their intended use, according to the National Agency of Medicines; European food information council [13].

1. Food supplements as food products. They are intended to supplement the normal/usual diet.
2. Foodstuffs for special nutritional uses as a beverage, it is made up with special composition as a special diet for certain population group e.g. for nutrition during life cycle such as healthy infants, toddlers, elderly, and people suffering from metabolism disorder or for categories of persons in a special physiological condition e.g pregnant and lactating mothers. Apart from above classification, Food supplements can be grouped based on various aspects, such as their origin, natural sources, chemical composition,

physiological function, and lots more. Since we are dealing with the health benefit of food supplements, we look into their physiological groups. Figure 2 shows the major groups of food supplements based on their physiological function.

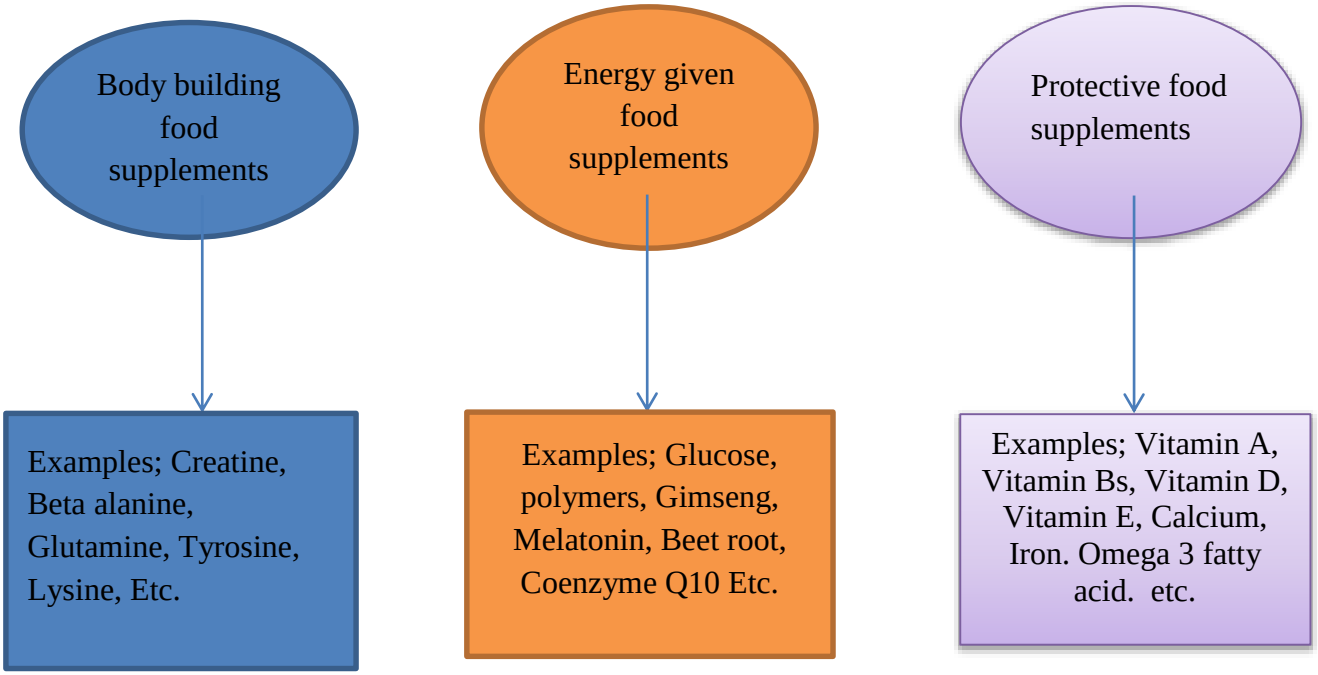

Figure 2. Groups of food supplements based on physiological function

3.0 HEALTH CLAIMS

3.1 Supplements in Cognitive Function

Cognitive function is an intellectual process that deals with awareness, alertness, learning capacity, ability to recall and comprehend ideas within an individual. One study carried out in Australia assessed the effect of vitamin supplementation, i.e., folate, cobalamin, and pyridoxine, on cognitive function in 56 healthy young women with no external stressors. They were administered high doses of B vitamins (750 g folate, 15 g cobalamin, 75 mg pyridoxine) in tablets or capsules for five weeks [14]. Based on the measured Information processing speed, memory, attention, and executive function, the result shows a supplementation group with folate, vitamin B6, and vitamin B12 enhance memory performance compared to the placebo group.

Presley et al. [15] Show that Nitric oxide from nitrate supplements optimizes brain function through modulation in the cerebral blood flow. It is believed that the beneficial effect of nitrate supplement on cognition appears to be linked with its nitric oxide conversion. Nitrate supplementation in older adults improves cerebral blood flow around areas associated with brain executive functioning. Pomeroy et al., [16] also depicted plentiful evidence related to the positive effects of some dietary supplements, including tyrosine studies assessed by Stroop task, caffeine, Ginko Biloba, and gimseng in the enhancement of memory and cognitive functions among the different study population.

3.2 Supplement in Cardiovascular Diseases

Cardiovascular diseases are those diseases that are related to the reduced efficiency or malfunction of the heart. A series of 11 studies on the association of Omega 3 fatty acid supplements and CVD death risk were reviewed, with total patients of 39,044 participants divided in to 2 groups (i.e. high risk and low risk group). The participants were supplemented with an average dose of omega 3 fatty acid containing Eicosa Pentaenoic Acid / Docosa Hexaenoic of 1.8 g/day with a mean follow up duration of 2.2 years. The result depicted that the risk of cardiovascular deaths and sudden cardiac death was significantly reduced at 0.87 95% confidence interval each, while non-fatal cardiovascular issues and all-cause mortality were also reduced at 0.92 95% confidence interval each. The reduced mortality advantage was mainly attributed to the studies that included patients at high risk. The relationship between the daily intake of omega-3 fatty acid supplements and clinical outcomes failed to be proved in a Meta-regression; this brings the scientists to the conclusion that omega-3 fatty acids supplements should be considered in the secondary prevention of CVD [17].

Another important dietary supplement to look into is resveratrol, which is believed to have an anti-oxidative capacity. Various studies showed its significant protective effect against pathophysiological factors related to CVD issues and its ability to reduce oxidative stress within endoplasmic reticulum. Resveratrol, combined with omega 3 fatty acid derived from fish oil, when consumed as supplements, was associated with the reduction of hypertension, stroke, and coronary heart diseases reported by many research projects [18].

Chen et al. [19.] Reported that adequate intake of vitamins and minerals such as vitamin A, vitamin K, zinc, copper, and magnesium (at or above the Adequate Intake level) was associated with reduced fundamental causes of CVD mortality, but the associations only linked to nutrient intake via foods.

3.3 Dietary Supplement in Diabetes

Diabetes is a metabolic disorder characterized by high blood sugar level above the normal range, resulting from lack of insulin, insufficient insulin production, or insensitivity of insulin, thus affecting major nutrients, especially carbohydrates. Diabetes is a deadly disorder that can result in several health issues such as retinopathy, neuropathy, nephropathy, and other organ related failures. Researches have been done to ascertain whether dietary supplements affect to promote health condition in diabetic patients. Some of the dietary supplements tested in clinical trials include chromium, omega 3 fatty acid, and alpha lipoic acid [20]. Among the 3 supplements above, only alpha lipoic acid positive effect on diabetes escaped controversies, while some studies on chromium and omega 3 fatty acid found little or no efficacy on diabetic patients [21, 22]. The alpha lipoic acid sources include liver, potatoes, Brussels, spinach, sprouts, peas, broccoli, and yeast.

Supplements such as vitamins, minerals, botanicals, and amino acids have provided healthier and safer replacements for traditional and costly medicines. These supplements are usually free from significant side effects, readily available, and inexpensive. The use of dietary supplements is anticipated to encourage good health and improve diabetic Patients [4].
However, chromium supplements in a trial on diabetes and non diabetic Patients.
Diabetes patients, other studies on chromium deficient patients showed some benefit on the same markers above [23].

Khan el at. [24]. Report similar published studies in which participants received 1, 3, or 6 g cinnamon daily for 40 days, their blood glucose levels were lowered from 18% to 29%. The glucose level was further reduced for up to 20 days for the participants who ingested the least amount (1 g) of the supplement even after its cessation. Also, bitter melon as a dietary supplement is found to contain hypoglycemic effect which lower blood glucose level, its
possible modes of action include increased tissue absorption of glucose, increased glycogen synthesis in the muscles and liver, an d increased glucose oxidation [25].

According to the Science daily, it shows the works of different researchers on the use and mode of action of bitter melon, as researchers have isolated four bitter melon compounds that activate an enzyme called Activated protein kinase (AMPK). AMPK controls fuel metabolism and facilitates the absorption of glucose in a way similar to exercise. Nicotinamide is another supplement that is known to delay the onset of diabetes in low risk people. It has been shown that this compound has a beneficial effect on animal models. In a study that looked at non-obese rats, a dose of 0.5 mg / g body weight of subcutaneous Nicotinamide treatment has proven promising. The treated rats had better glucose tolerability and no glycosuria [26]. Another study on Curcumin reveals that curcumin provides strong evidence in beta cell functionality. In a double blind randomized placebo controlled trial comprising 240 pre diabetic patients, the treatment group was given 250 mg / capsule of curcumin supplement six times daily. After nine months, the result shows that no one in the treatment group developed type 2 diabetes mellitus when compared with the 16.4% in the placebo group, which eventually developed type 2 diabetes mellitus [27]. This finding believes that curcumin may be beneficial for the prediabetic patient to prevent the occurrence of diabetes mellitus.

3.4 Supplement in Athletes

Athletics is a sport, including ranges of games such as races, football, swimming, jumping, and throwing, etc. while an athlete is a person who is proficient in sports and other forms of physical exercise. Athletes need energy and body building food for their various respective sport requirements; they have an increased demand for nutrient dense food than average adults; this is to cover up for what has been lost during training or competition. But due to the insufficient time for most athletes, preparing nutrient dense food that will provide all requirements to their body may not be achieved. Coincidently, available dietary supplements seem to be a better option.

For the athlete undergoing hard training, nutritional supplements are also seen as encouraging adaptations to train, allowing more regular and rigorous training by facilitating rehabilitation between training sessions, minimizing disease or injury induced interruptions to train, and helps to improve competitive performance [28]. According to various Surveys, the prevalence of supplement use is common among sportsmen and women, but a robust research basis supports only a few of these supplements, and some may even be detrimental to the athlete. Energy bars and drinks are some of the Special sports foods that play a real role in athletes. In some instances, certain nutritional supplements like protein and meal replacements may also be beneficial. An increased intake of specific nutrients from food or supplementation may help to correct identified essential nutrient deficiency in the athlete [29].

Recently, dietary supplements among athletes have increased as they aim to improve overall performance and meet their dietary requirements, such as assisting athletes in consuming the appropriate amount of calories, proteins, and carbohydrates. However, inappropriate use of food supplements might lead to health complications. Additionally, athletes are also tightened by anti-doping regulations to prevent such practices [30, 31].

According to Omar [28] food supplements plays a vital role in the life of athletes with some examples of their health benefit given, the work shows that Antioxidants such as Vitamins C, selenium, beta carotene, and vitamin E helps to prevent tissue damage in

athletes and facilitate proper utilization of oxygen in the muscle for flexible contraction. Amino acid supplements that serve as nitrogen sources such as; lysine, tryptophan, arginine, and tyrosine prevent muscle breakdown caused due to the increased nitrogen loss due to heavy exercise. Glucosamine supplements help athletes, especially soccer players (who suffer frequent knee and joint injuries), by promoting joint health and boosting cartilage's structural integrity and durability. Caffeine (1-2mg/body kg) can improve the response rate, processing time and increase alertness during a match. The benefits mentioned above are sufficient to prove the efficacy of dietary supplements in athletes. But care should be taken to ensure the practice of doping and supplement abuse were averted.

In recent years, the use of dietary supplements among athletes has been in an increasing trend as they help both in improving the overall performance and in meeting dietary requirements such as helping athletes to consume the appropriate amount of calories, proteins, and carbohydrate. Although, inappropriate use of food supplements might lead to health complications. Additionally, athletes are also tight up by anti-doping regulations to prevent such practices [3; 4].

3.5 Dietary Supplement in Cancer

Cancer is a generic name for abnormal cells with an abnormally rapid growth rate. It can be either malignant or benign cells, thus affecting health. Its significance makes it one of the most leading causes of mortality because of its rapid ability to spread to different parts of the body. Cancer patients are always looking obsessed with effective medications, weather from modern functional foods, or traditional medicines. It is believed that cancer patients commonly used Herbal medicines and dietary supplements, but there is concerned over interaction with conventional medicine [32]. It is not strange that the use of complementary and alternative medicines (CAM) such as herbal and dietary supplements is well documented and is common in patients, particularly those suffering from chronic diseases, i.e., cancer, among others [33].

A pigment “lycopene” in the carotenoid, responsible for a tomato's red color, effectively controlled cancer reported by a group of researchers at Harvard University in the mid-50s and attributed that lycopene effectiveness is as a result of its powerful anti-oxidative properties. This result's announcement by the research group caused a massive impact worldwide and paved the way for further studies in this field [34].

Calcium is another supplement widely used in several health issues. An observational study using meta-analysis supports an association between higher calcium intake and reduced risk of breast cancer [35]. Higher calcium intake in a meta-analysis was associated with reduced risk of colorectal cancer [36].

Another meta-analysis study result shows that supplemental antioxidants [37, 38]. Calcium and folic acid [39] did not substantially impact the risk of colorectal cancer. Katta and brown [40] In their study reported that dietary antioxidant supplements via food have a promising effect on non-melanoma skin cancer (NMSC), while oral antioxidant supplements have not shown promising result. The study recommended that upcoming researches related to this field should focus on antioxidant supplements taken through food consumption.

3.6 Dietary Supplement in Obesity induced Erectile Dysfunction

Erectile dysfunction, also known as impotence, is a sexual dysfunction characterized by the inability to develop or maintain an erection of the penis during sexual intercourse [41], ED is the most common symptomatic manifestation of multiple diseases of sexual dysfunction that affect men after 40 years of age, It was estimated that over 150 million men were affected with one or more erectile related dysfunction worldwide, and by 2025 it was forecasted to affect around 250 million men [42, 43]. Dietary supplements play an important role in ameliorating this condition, with several researches shed light on their efficacy on erectile dysfunction.

A recent study has shown that S. platensis, when supplemented in food, provides benefits in healthy rats by promoting a positive effect on the NO signaling pathway in their aorta [44], it reduces both body adiposity in obese rats ileo and oxidative stress, and it also prevents damage on the erectile function that can be caused by a hypercaloric diet [45, 46].

Recently in an in vivo study carried out by Diniz et al. [47], it was observed that a diet supplemented with spirulina platensis helps improve erectile dysfunction in a rat. The result shows that the group of rats fed on a hypercaloric diet with S. platensis supplementation has an increased number of penile erections accompanied with reduced latency for the erection (averagedh 13.8 ± 2.3) when compared with the standard group that were fed with a hypercaloric diet only (26.7 ± 2:2 min)

3.7 Dietary Supplement in Bone Mineral Density (BMD)

The amount of bone mineral contained in bone tissue is called bone mineral density. It reflects the strength of bones in an individual represented by the availability of calcium of such an individual. Insufficient bone mineral density is associated with bone fragility at a later stage in life, which leads to a high risk of developing bone related diseases such as osteoporosis. To cater to this risk, individuals need to ingest food containing sufficient calcium at the early and mid-stage of life as a means of primary prevention. Intake food containing adequate calcium should extend through the elderly stage.

Several studies have proved the efficacy of calcium supplement in bone mineral density, one of which was conducted among adolescent girls aged 15-16 in New Zealand by Merrilees et al. [48], which aims to determine the effect of calcium on bone mineral density for 3 years (2 years supplementation and one year follow up). The result shows that the group of girls who ingested a supplement of dairy products containing mean calcium 1160mg/day had an increase in BMD at trochanter, lumbar spine and femoral neck compare to those in the control group. The study further shows that the supplementation does not cause adverse health issues on body weight, blood lipid profile, fat, and lean mass. But, during the follow up period (a year after the supplementation period), it was found that the majority of the girls returned to their regular diet, which signifies their selection of the supplemented dairy product is hard to maintain.

4.0 MARKET TREND

Maughan et al., [29] reported that "The global market of food supplements was estimated to be around USD 46 billion in 2001, with the US food supplements market being estimated at USD 16.7 billion in 2000 (Financial Times, Apr 19, 2002)". Globally, in 2013 the food supplements market was estimated at around USD104 billion, while the dietary supplements market in the U.S.A was estimated to be at approximately USD 27.2 billion by 2015. Moreover, the market was projected to maintain its strong momentum in the next couple of years, with an expected increase of 5-6% compound growth rate per year [49].

Some of the major brands of food supplements available in the market nowadays include; Himalaya, Longrich, Amway, Forever, Herbalife, etc. According to Zion market research [50], the market value for dietary supplements worldwide has been estimated to be around 132.8 billion USD in 2016, with projections to hit approximately 220.3 billion USD in 2022. Figure 3 gives a clear presentation of Zion market research. Another study by Research and Market [51] pointed out that the global market for dietary supplements was valued at around 163.1 billion USD in 2019. A report from FMI [52] predicted that the dietary supplement market would continue to grow rapidly due to the increasing awareness of healthy living through a good diet. It was projected that by 2025 global dietary supplements market will hit a significant value of around 252,100 USD with a compound annual growth rate of 7.4%. The report further elaborates the forecasted global market value into different regions; the summary of the predicted areas is given in table 1.

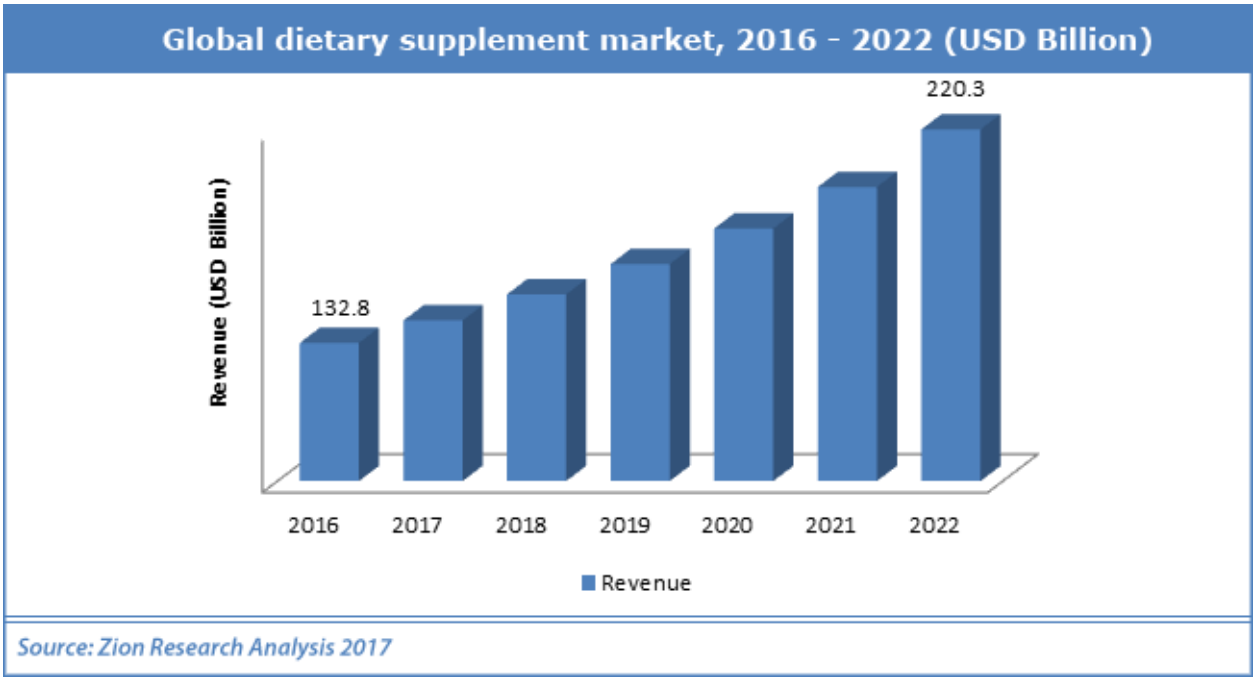

Figure 3: Global dietary supplement (2016-2022)

Table 1. Forecasted global dietary supplements market value by 2025 according to regions

S/N	Region	Market value (billions)	CAGR (%)
1	APEJ	USD 57,789.5	9.2
2	Japan	USD 20,392.5	6.4
3	North America	USD 78,894.7	7.2
4	Western Europe	USD 60,146.9	7.2
5	Latin America	USD 14,272.4	8.5
6	Eastern Europe	USD 60,146.9	7.0
7	MEA	USD 6,007.7	5.4

Source: Future Market Insight (2015)

MEA = Middle East

APEJ = Asia Pacific excluding Japan

5.0 CONSTRAINS

Many studies depicted that dietary supplements are not always consumed at average doses, but rather consumed at high doses to supplement the body's deficient nutrients with or without knowing what type of nutrients the body needs, at what particular situation, and in what quantity. This behavior puts people at risk of overconsumption of dietary supplements, which eventually leads to the development of life-threatening diseases such as cancer and cardiovascular diseases in the near future. Despite the fact that supplements are considered and regulated as food, more standards of manufacture, storage, marketing, and use should be implemented, as some labels on the package of supplements may contain errors, overages, it may be expired, or it may have been stored poorly in a manner that may adversely affect human health when consuming rather than its stipulated health benefits.

Recently, Kołodziej et al. [5], in their study on "Knowledge Concerning Dietary Supplements among General Public" conducted in southeastern Poland involving 410 participants, reported a high prevalence of dietary supplement use among the study population. However, still, a substantial proportion of the study community lacks accurate information about these products. Therefore, there is need to provide both education to the community and to have access to empirically credible research outcomes.
Another setback of food supplements is that some studies reported that food supplements have no efficacy to promote human health but instead confer adverse effects. Some of the studies include; A clinical trial found that there is an increase in the risk of prostate cancer when capsulated omega -3 fatty acid was taking as "food fortification" [53]. Another result of clinical trials depicted that enriched bromelain from pineapple when taking in capsule triggers gastritis, reflux, and ulcer severity; hence, It was recommended not to be used in the case of such aforementioned health issues [54, 55].Therefore, there is a need for solid scientific research based evidence to clear the dispute between the studies that are "for or against" the efficacy of food supplements to human health.

6.0 FUTURE PERSPECTIVE

Food supplement industries usually make supplements as a concentrated isolate or, in combination with another bioactive element; this practice is termed as a potential mistake that can lead to deviation of the bioactive agent from its expected health benefit; this is because bioactive agents tend to exhibit many differential physical and chemical properties when they are isolated from their natural environment, so it may not be possible to calculate and measure those properties in an isolated form. For example, genistein from soya beans in its natural environment has Cross Linking Former (CLF) feature, but when it is isolated from its natural environment, this feature may not be possible to be determined analytically. Thujone" from *Salvia officinalis* is one of the major substances that trigger cancer proliferation. Does this mean we should not consume tea prepared from this plant? The answer is "No" because It shows a carcinogenic effect only when it is in an isolated form. Observably, when taken as tea in its natural environment containing more than 6,000 metabolites, thujone shows antibacterial and antiviral properties; these properties are entirely different compared to an isolated form of it [34]. Furthermore, two studies reported that the efficacy of dietary supplements could be only achieved when taking through food consumption; both studies depicted dietary supplements in their natural environments have greater influence to confer health benefit than in an isolated form [40, 19]. We are likely to experience greater changes in dietary supplements' modulations and presentation through different techniques to achieve optimum health benefits and clear existing ambiguities on food supplements in the future.

In the near future, food supplements industries that produce isolates of concentrated bioactive agents (food supplements) may need to adjust the production mode and presentation of these supplements. In the other hand, the market trend of dietary supplements will push higher through the next decade as there is an apparent high demand for such products as a result of multiple reasons we had stated earlier in this article. Some surveys have already forecasted the previous statement, one of which is Zion market research [50] which stated that the market value for dietary supplements worldwide had been estimated to be around 132.8 billion USD in 2016, with projections to hit approximately 220.3 billion USD in 2022

As food supplements' market share is always trending higher, scientific critics, including knowledge and awareness, are continuously increasing simultaneously. Therefore, we should anticipate more researches concerning many aspects of food supplements in the near future

7.0 CONCLUSION

The use of dietary supplements should be monitored by caution and should not be taken to manage or treat a health condition unless recommended by a health care provider. People misinterpreted the term "natural" as a substance that is safe and free from harm. In fact, been "Natural" does not mean safe at all times. However, food supplements' safety depends on many factors, such as its chemical makeup, its preparation, its mechanism of action, the quantity of the dose been used, etc. Certain natural herbs may be dangerous; for example, kava and comfrey negatively affect the liver. Many supplements can contain one or more active ingredients, which can have powerful effects in the body. Consumers of dietary supplements should always be alerted to unexpected side effects, especially when taking a new supplement.

Some supplements may affect the body's response to anesthesia when taking before or after surgery. Furthermore, the activity of blood thinners (i.e., antiplatelets and anticoagulants) can be reduced by vitamin K supplement, vitamin A toxicity is strongly

associated with liver damage; likewise, iron toxicity may adversely affect the liver, excess calcium is associated with increased risk of kidney stone, excess protein supplements intake damages kidneys and liver, and antioxidant vitamins supplements may interfere with cancer chemotherapy.

Despite the health benefits of these products, overconsumption can lead to the toxicity of the affected nutrients, as some studies yielded negative effects on their efficacy. Even though food supplements are considered food, they are not strictly monitored by regulation as in drugs. Therefore, it is advisable to use caution and seek consultation from physicians, registered dieticians, and other qualified related health care providers. In addition, to spare you oneself from uncertainties (expiration and false claims) related to isolated food supplements, it will be essential to consider taking dietary supplements via food consumption rather than taking it as an isolated form.

More regulations to monitor the production, marketing, research, and development should be provided to explore the additional evidence concerning their safety and health claims. It is also recommended that their interaction with drugs and precise doses should be clearly identified with credible scientific evidence that will convince the scientific world regarding their future safety and acceptability.

REFERENCES

[1] European food safety authority "Food supplements" https://www.efsa.europa.eu/en/topics/topic/food-supplements 2017.
[2] I. Frey, Hoffmann, and T. Heuer, "Characterization of vitamin and mineral supplement users differentiated according to their motives for using supplements; results of the German National Nutrition Monitoring (NEMONIT)", Public Health Nutr, vol. 20, no. 12, pp. 2173–2182. 2017.
[3]Dietary supplement Health and Education Act. Public law 103 – 417. Available at http://www/fda.gov/opacom/laws/dshwa/html. 1994 Accessed on 18-6-2020.
[4] A. Afolayan, & O. Wintola, "Dietary Supplements in the Management of Hypertension and Diabetes- A Review". Afr. J. Tradit. Complement. Altern. Med, 11(3), 248. https://doi.org/10.4314/ajtcam.v11i3.35 2014.
[5] G. Kołodziej, B. Cyran-Grzebyk, J. Majewska, & K. Kołodziej, "Knowledge Concerning Dietary Supplements among General Public". BioMed Research International, 2019, 1–12. https://doi.org/10.1155/2019/9629531 2019.
[6] NatCen SR, MRC EWL & University College London MS. National Diet and Nutrition Survey Years 1-6, 2008/09-2013/14. 8th ed. Colchester, Essex: UK Data Archive; 2017.
[7] M.G. Chan, K. Hoffman M. McMurry, "Effects of dairy products on bone and body composition in pubertal girls". J Paediatr 126:551–556. 1995.
[8] J, Cadogan, R. Eastell, N. Jones, M. Barker, "A study of bone growth in adolescent girls: the effects of an 18 month milk-based dietary intervention". J Bone Miner Res 10 (Suppl 1): S350. 1995. (Abstract)
[9] V. Matkovic, D. Fontana, C. Tominac, P. Goel, C.H. Chesnut, "Factors that influence peak bone mass formation: a study of calcium balance and the inheritance of bone mass in adolescent females". Am J Clin Nutr 52:878–888 1990
[10] R.R. Recker, K.M. Davies, S.M. Hinders, R.P. Heaney, M.R. Stegman, D.B. Kimmel, "Bone gain in young adult women". JAMA 268:2403–2408. 1992,
[11] C.W. Slemenda, T.K. Reister, M, Peacock, C.C. Johnson, "Bone growth in children following the cessation of calcium supplementation". J Bone Miner Res 8 (Suppl): S154. 1993. (abstract)
[12] F. Sirico, S. Miressi, C. Castaldo et al. "Habits and beliefs related to food supplements: results of a survey among Italian students of different education fields and levels," *PLoS ONE*, vol. 13, no. 1, Article ID e0191424, 2018.
[13] European food information council (EUFIC). " Analysis on dietary guidelines based food in Europe" 2009.
[14] J. Bryan, E. Calvaresi, D. Hughes, "Short-term folate, vitamin B-12, or vitamin B-6 supplementation slightly a_ects memory performance but not mood in women of various ages". J. Nutr.132, 1345–1356. 2002.
[15] T.D. Presley, A.R. Morgan, E. Bechtold, W. Clodfelter, R.W. Dove, J.M. Jennings, R.A. Kraft, S.B. King, P.J Laurienti, W. Jack, "Acute effect of a high nitrate diet on brain perfusion in older adults. Nitric Oxide", 24, 34–42. 2011.
[16] D.E. Pomeroy, K.L. Tooley, B. Probert, A. Wilson, E. Kemps, "A Systematic Review of the Effect of Dietary Supplements on Cognitive Performance in Healthy Young Adults and Military Personnel". Nutrients, 12(2):545. Published 2020 Feb 20. DOI:10.3390/nu12020545
[17] P.E. Marik, J. Varon, "Omega-3 dietary supplements and the risk of cardiovascular events: A systematic review", Clinical Cardiology 32(7), 365-372. 2009
[19] F. Chen, M. Du, J.B. Blumberg, K. H. Chui, M. Ruan, G. Rogers, Z. Shan, L. Zeng, F. F. Zhang. "Association between dietary supplement use, nutrient intake, and mortality among US adults: a cohort study". Ann. Intern. Med. doi: 10.7326/M18-2478 2019
[19] B.B. Kakoti, D.G. Hernandez-Ontiveros, M.S. Kataki, K, Shah, Y. Pathak, S.K. Panguluri, "Resveratrol and omega-3 fatty acid: Its implications in cardiovascular diseases". *Front Cardiovasc Med* Dec 11:2:38. doi : 10.3389/fcvm.2015.00038. eCollection 2015.
[20] J. Martin, Z.Q. Wang, X.H. Zhang, D. Wachtel, J. Volaufova, D.E. Mathews, and W.T. Cefalu, "Chromium picolinate supplementation attenuates" 2006
[21] W.T. Cefalu, and F.B. Hu, "Role of chromium in human health and in diabetes. Diabetes Care", 27:2741-2751. 2004
[22] D.A. De Luis, R. Conde, R. Aller, O. Izaola, M. Gonzalez Sagrado, J.L. Perez Castrillon, A. Duenas and E. Romero, "Effect of omega-3 fatty acids on cardiovascular risk factors in patients with type 2 diabetes mellitus and hypertriglyceridemia": an open study. Eur. Rev. Med. Pharmacol. Sci., 13: 51-55. 2009

[23] M.D. Althuis, N.E. Jordan, E.A. Ludington, and J.T. Wittes, "Glucose and insulin responses to dietary chromium supplements: A meta-analysis". Am.J. Clin. Nutr. 76(1):148-155. 2002
[24] A. Khan, M. Safdar, M.M. Ali Khan, K.N. Khattak, and R.A. Anderson, "Cinnamon improves glucose and lipids of people with type 2 diabetes". Diabetes Care 26:3215,- 3218. 2003
[25] L. Shane-McWhorter, "Complementary & Alternative Medicine (CAM) Supplement Use in People with Diabetes: A Clinician's Guide". Alexandria, Va., American Diabetes Association. 2007
[26] S. Yeung, J. Soliternik, & N. Mazzola, "Nutritional supplements for the prevention of diabetes mellitus and its complications". Journal of Nutrition & Intermediary Metabolism, 14, 16–21. https://doi.org/10.1016/j.jnim.2018.07.003 (2018).
[27] S. Chuengsamarn, S. Rattanamongkolgul, R. Luechapudiporn, C. Phisalaphong, S. Jirawatnotai, "Curcumin extract for prevention of type 2 diabetes". Diabetes Care. ;35(11):2121-2127. doi:10.2337/dc12-0116. 2012
[29] R. J. Maughan, D. S. King, & T. Lea, "Dietary supplements". J. Sports Sci, 22(1), 95–113. https://doi.org/10.1080/0264041031000140581 2004
[29] O. S. Aljaloud, "Dietary Supplements for Professional Athletes: A Great Potential for Saudi Arabia". J. nutri. *health* food eng.3(1). https://doi.org/10.15406/jnhfe.2015.03.00097 2015.
[30] M. Dunford, "Fundamentals of sport and exercise nutrition", Human Kinetics, Champaign, Ill, USA. 2010
[31] H.H. Tian, W.S. Ong, C.L. Tan, "Nutritional supplement use among university athletes Singapore". Singapore Med J 50(2): 165-172. 2009
[32] S. M. Alsanad, E. M. Williamson, R.L. Howard, "Cancer patients at risk of herb/food supplement drug interactions: a systematic review", Phytotherapy research 28 (12), 1749-1755. 2014
[33] A.K. Goey, K.D. Mooiman, J.H. Beijnen, J.H. Schellens, I. Meijerman, "The relevance of in vitro and clinical data for predicting CYP3A4-mediated herb-drug interactions in cancer patients". Cancer Treat Rev 39(7): 773–783. 2013
[34] İ. A. Saraçoğlu, (n.d). Background, Present, and Future of Food Supplements. 8. 2018
[35] P. Chen, P. Hu, D., Xie, Y. Qin, Fudi H.W. Wang, "Meta-analysis of vitamin D, calcium and the prevention of breast cancer" Breast cancer research and treatment 121 (2), 469-477, 2010
[36] M. Huncharek, J. Muscat, B. Kupelnick, M. Huncharek, J. Muscat, and B. Kupelnick, 2009
[37] G, Bjelakovic, D. Nikolova, R.G, Simonetti, C. Gluud "Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis". Lancet. 2004 Oct 2-8; 364(9441):1219-28. doi: 10.1016/S0140-6736(04)17138-9. PMID: 15464182
[38] N.D. Pecollo, P.L. Martel, T. Norat, E. Barrandon, S. Bertrais, P.Galan, S. Hercberg, "Beta-carotene supplementation and cancer risk: a systematic review and metaanalysis of randomized controlled trials" 21 April 2010 https://doi.org/10.1002/ijc.25008.
[39] C. Carroll, K. Cooper D. Papaioannou. D. Hind, P. Tappenden, H. Pilgrim, A. Booth, "Meta-analysis: folic acid in the chemoprevention of colorectal adenomas and colorectal cancer" 01 March 2010 https://doi.org/10.1111/j.1365-2036.2010.04238.x
[40] R. Katta, D.N. Brown, "Diet and skin cancer: The potential role of dietary antioxidants in nonmelanoma skin cancer prevention" Journal of skin cancer 2015,
[41] M,P. McCabe, I.D. Sharlip, E. Atalla, R. Balon, A,D. Fisher, E. Laumann, S,W. Lee, R. Lewis, R.T. Segraves, "Definitions of Sexual Dysfunctions in Women and Men: A Consensus Statement From the Fourth International Consultation on Sexual Medicine" 2015. J Sex Med. 2016 Feb;13(2):135-43. doi: 10.1016/j.jsxm.2015.12.019. PMID: 26953828.
[42] M. Wyllie, C. Page, M. Curtis, and. M. Sutter, "As drogas e o Sistema genitourinário," in Farmacologia integrada, Eds., 2014 pp. 495–501, Manole, Barueri, 2a edition.
[43] C. E. Riedner, "Evaluation of the effect of obesity on the association between ischemic heart disease and erectile dysfunction," Postgraduate Program in Medicine - Medical Sciences, Federal University of Rio Grande do Sul (UFRS), Porto Alegre. 2017
[44] A.D. Brito, A,S, Silva, A.A. de Souza, P.B. Ferreira, I.L.L.de Souza, L.C.D. Araujo, et al., (2019). "Supplementation with Spirulina platensis modulates aortic vascular reactivity through nitric oxide and antioxidant activity," Oxidative Medicine and Cellular Longevity, vol. 2019, Article ID 7838149, 12 pages.
[45] I L. L. de Souza, C. Bárbara, Barros, G.A. de Oliveira, R. Fernando, Queiroga, T, Lydiane. Toscano, et al., "Hypercaloric diet establishes erectile dysfunction in the rat: mechanisms underlying the endothelial damage," Frontiers in Physiology, vol. 8, p. 760. 2017
[46] L. L. De Souza, "Food supplementation with Spirulina platensis prevents the development of obesity and erectile dysfunction in Wistar rats by modulating endothelium-derived factors and oxidative stress" [Ph.D. Thesis], Federal University of Paraiba, João Pessoa. 2018.
[47] A. F. A., Diniz, I. L. L., de Souza, D, E, Ferreira, D. Carvalho, M. T. Barros, B. C., Ferreira, P. B., da Silva, M. Júnior, F. F. L., de Lima, T. L. Toscano, A. S., Silva, D, F. Cavalcante, & B. A. da Silva, "Potential Therapeutic Role of Dietary Supplementation with *Spirulina platensis* on the Erectile Function of Obese Rats Fed a Hypercaloric Diet". Oxidative Medicine and Cellular Longevity, 2020, 1–14. https://doi.org/10.1155/2020/3293065
[48] M. J. Merrilees, E. J. Smart, N. L. Gilchrist, C. Frampton, J. G. Turner, E. Hooke, R. L. March, & P. Maguire, "Effects of dairy food supplements on bone mineral density in teenage girls". Eur. J. Nutr, *39*(6), 256–262. https://doi.org/10.1007/s003940070004 2000
[49] McKinsey & Company. Consumer and Shopping Insights. Cashing in on the booming market for dietary supplements. Dec. (2013) [https://www.mckinseyonmarketingandsales.com/ sites/default/ files/pdf/CSI_VMHS_FNL_0.pdf] (accessed July 2020).
[50] Zion Market Research. Dietary supplements market by Ingredients (Botanicals, Vitamins, Minerals, Amino Acids, Enzymes) for additional supplements, medicinal supplements, and sports nutrition applications - Global Industry Perspective, Comprehensive analysis and forecast, 2016-2022. Available online: https: //www.zionmarketresearch.com/report/dietary-supplements-market. (Accessed on Jun 23, 2020).

[51] Research and market (2020) "global dietary supplement market (2020-2025): consumer behavior analysis by countries, buying pattern analysis, demographic, trend analysis, survey finding, and results, leading companies, and their market strategies" http://www.reseachandmarkets.com/r/r4h6fl
[52] Future Market Insights (FMI). Dietary supplements market – Driven by increasing demand for health products: Global industry analysis and opportunity Assessement 2015-2025.
[53] T. M. Brasky, A. K. Darke, X. Song, C. M. Tangen, P. J. Goodman, I. M. Thompson, F. L. Jr.Meyskens, G. E. Goodman, L. M. Minasian, H. L. Parnes, E. A. Klein, A. R. Kristal, "Plasma Phospholipid Fatty Acids and Prostate Cancer Risk in the Select Trial" J. Natl. Cancer Inst. 15 1132-1141. 2013
[54] H. R. Maurer, "Cellular and Molecular Life Sciences" CMLS, 9 1234-1245. 2001
[55] J. R. Jamison, "Clinical guide to nutrition and dietary supplements in disease management," ISBN 0-443-07193-4. 2009