ACTA SCIENTIFIC NUTRITIONAL HEALTH

Volume 3 Issue 9 September 2019

Research Article

Designer Foods, Dietary Supplements, for Better Cardiovascular Health

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Received: July 09, 2019; **Published:** August 16, 2019

Abstract

Metabolic diseases, such as hypertension, excess weight, obesity, type-2 diabetes, and vascular diseases, have increased in the both incidence and prevalence, to epidemic proportions worldwide, in the last three decades. During this period, obesity has increased by two-folds, and diabetes by four folds. Cardiovascular diseases are the number one killers and have retained this position for over 100 years. No country has reduced, reversed, or prevented the increase in the incidence of these diseases. Modern medicine has failed, to prevent the increase of these chronic diseases and has instead, opted for drug discovery and management of such risks. These diseases are basically lifestyle diseases. In view of this fact, we would like to encourage holistic lifestyle, emphasize the need for robust physical activity, wellness, and heart healthy diet. In an earlier article, we discussed changing concepts of healthcare, which includes, heavy emphasis on physical fitness and wellness. In this article, we would discuss heart healthy diet, designer foods, dietary supplements, and complementary therapies for reduction, reversal, and prevention of metabolic risks, such as oxidative stress, chronic inflammation, altered blood flow, endothelial dysfunction, and subclinical atherosclerosis. Examples of designer foods include, designer eggs, with enhanced omega-3 fatty acids, improved variety of staple grains, such as white rice, wheat, and corn. Improved animal diet, for the development of high-quality tissues. We have discussed the importance of genomic studies of animals and plants, for selective breeding and genetic engineering. Use of stem cells for synthetic meat. Since we are interested in the early interventions of metabolic risks, as a major strategy for prevention of CVDs, we also discussed development of dietary supplements and complementary therapies, using indigenous phytochemicals. Since the basic cause for developing metabolic risks is altered lifestyle, we emphasize the importance of healthy life style including physical fitness, heart healthy diet and wellness.

Keywords: Foods; Dietary Supplements; Cardiovascular Health

Introduction

Chronic metabolic diseases such as hypertension, excess weight, obesity, type-2 diabetes, and vascular diseases, have increased to epidemic proportions, worldwide in the last three decades [1]. The high incidence of hypertension is a major global public health challenge, as it increases morbidity and mortality through cardiovascular and kidney diseases. Published studies indicate, that close to 31% of the population (1.4 billion individuals) had hypertension in 2010 [2]. Currently, 2.1 billion people, nearly one third of the world's population, are either obese or overweight, according to a new, first of a kind analysis of trend data, from 188 countries. An analysis of 45 countries, representing 90% of the population, estimates that in 2018, there were more than 500 million type-2 diabetes worldwide. Noncommunicable (NCD) Risk Factor Collaboration Group used data from 751 studies, from 146 of the 200 countries for their estimate. Based on the report, if post -2000 trends in the increased incidence of diabetes continue, the probability of meeting the global target of halting the rise in the prevalence of diabetes by 2025, to the level of 2010 level worldwide is lower than 1%. During the same period (1980-2010), in China, 7- national diabetes mellitus surveys were conducted; and result revealed that the prevalence of diabetes had increased by 17-fold [2]. Potential risk factors which contributed include, social and economic development, urbanization, dietary pattern and Westernized lifestyle. Cardiovascular disease (CVD), remains a major cause of health loss for all regions of the world [2].

Framingham Heart Study (FHS) was initiated in 1948, by the National Heart Institute (NIH) in the town of Framingham, Massachusetts [3]. Investigators sampled 2 of every three adults aged 30-59 years. That study is now considered one of the longest, most important epidemiological studies in the medical history. The study demonstrated link between the modifiable risk factors such as cigarette smoking, hypertension, low-density lipoproteins, and individual's risk for developing heart disease. During the same period, Professor Ancel Keys at the University of Minnesota, initiated Seven Countries Study (SCS), the first major study to investigate diet and

lifestyle, along with other risk factors for cardiovascular disease. The main hypothesis of this study was, that the rate of coronary artery disease in populations and individuals, vary in relation to their physical characteristics and lifestyle, particularly in the fat composition of the diet and serum cholesterol. Exploratory studies began in Italy, Spain, South Africa and Japan. During the first phase of the study, standardized lifestyle and risk factor surveys were conducted at 5 and 10 years of follow-up. Early on in the study, Professor Keys and colleagues observed, that across cultures in the Seven Countries, cultures differed in their diets and corresponding differences were seen in saturated fat, serum cholesterol, and coronary artery disease incidence, after 5-and 10-years follow-up [4].

As a continuation of the population-based CVD epidemiology and prevention project, the North Karelia project was launched in 1972, to carry out a comprehensive community-based CVD prevention program [5,6]. By 1972, North Karelian men had earned the dubious distinction of having the highest rate of heart disease in the world. By the early 2000s, the number of deaths of Finnish men ages 35-64 from coronary artery disease had plunged down to 75%. Much of this reduction, came from dramatic reduction in risk factors such as high cholesterol and smoking. Cholesterol lowering was the strongest contributor [6]. Professor Pekka Puska the principal investigator of this probably unrepeatable successful project, summarizes his effort in the following way: "The experiences and results of the North Karelia Project in Finland supports the idea, that a well-planned and determined community-based Programme, can have major impact on lifestyles and risk factors, and such a development really leads quite rapidly, to reduced cardiovascular rates in the community. Furthermore, they demonstrate, the strength of community-based approach in changing the people's risk factors as well as give practical experience in organizing such activities." Since then, several clinical studies have demonstrated the beneficial effects of robust management of modifiable risk factors, in the reduction of premature mortality [1,2].

Altered metabolism, leads to the development of metabolic risks such as oxidative stress, chronic inflammation, excess weight, changes in the flow dynamics of circulating blood, endothelial dysfunction, hardening of the arteries, and subclinical atherosclerosis. Metabolic diseases such as hypertension, excess weight, obesity and diabetes are basically lifestyle diseases. The progression of these diseases leads to various clinical complications including the precipitation of acute vascular events, such as heart attacks and stroke. No country has reduced, reversed, or prevented these chronic metabolic diseases [2]. Modern medicine has failed, to prevent the increase in the incidence and prevalence of these diseases. Instead, has opted for drug discovery and management of observed risk factors. Just management of risk factors will not reduce the serious health care burden imposed by these diseases. We and others have articulated this dilemma, and called for immediate action, by all the stakeholders. In an earlier article, we have articulated about a novel way of using the cohorts from Fitness and Wellness participants, who are motivated about their health, to develop an early diagnosis and prevention program. In this review, we will describe, some novel approaches to develop healthy diets, designer foods, and phytochemical-based dietary supplements, for use as complimentary therapies.

Discussion

Some of the dietary components, that contribute to the development of metabolic risks, include excess salt, excess sugar, excess carbohydrates, and type of fats. Following large-scale studies showing, that a high salt intake leads to high blood pressure (BP), the Dietary Guidelines for Americans set the recommended sodium intake at 2300 milligrams per day. Historically, salt consumption is in use for several thousands of years. At about 1000 years ago, the salt consumption already had risen to 5g / day. International Study on Macro/Micronutrients and Blood Pressure (INTERMAP), in 17 populations in China, Japan, the UK and the USA concluded, that "The adversary association of dietary sodium with BP, is minimally attenuated by other dietary constituents; these findings underscore the importance of reducing salt intake for the prevention and control of prehypertension and hypertension [7]. The DASH-(Dietary Approaches to Stop Hypertension)-like diet, with increase in nutrient-dense intakes of vegetables, fruits, whole grains, fat-free and low-fat dairy products, legumes, unsalted nuts and seeds, seafoods and unsaturated vegetable oils- is effective in lowering BP [8]. When it comes to dietary salt, the first thing to know is that the salt that is used at the dinner table is not the biggest sodium contributor in the American diet, in fact, the majority of the sodium Americans consume, (more than 70%) is found in processed foods and restaurant meals.

Sugar consumption doesnot cause diabetes. A diet high in calories from any source (including sugar) contributes, to weight gain and weight gain which increases the risk for type-2 diabetes. In people with diabetes, cells are resistant to insulin thus causing sugar to accumulate in the blood. Excess sugar and fat then contribute to weight gain, thus reducing insulin sensitivity in the body. Highly processed foods, are the major source of excess sodium, added sugars and unhealthy fats. Such foods contribute to about 60% of calories and 90% of the added sugars in the American diet (Added Sugars: The American Heart Association). Globally, policies are shifting towards mandatory reformulation of processed foods in terms of added salt, sugar, and types of fats. According to a recent article in the British Medical Journal, 'Consensus on Salt and Health (CASH)', - only one out of the 28 food categories surveyed, is on track to meet Public Health England's (PHE) 2017 salt reduction targets. The food industry will also fail, to hit a PHE target to achieve 20% reduction in added sugar. Out of the three nutrients, proteins, carbs and fats, only carbohydrates (carbs) have the greatest impact on blood sugar control as the body breaks them down to glucose. The rise of ultra-processed foods has coincided with growing rates of obesity and diabetes [9].

Dariush Mozaffarian, dean of Tufts University's School of Nutrition, agrees with the findings of a land mark study by the NIH, which claims that it is not the salt, sugar, or fat; but ultra-processed foods that drive weight gain. However, it was suggested that much of the real food should be eaten alongside with processed foods that are healthy. The rise in obesity and type-2 diabetes prevalence, occurred in parallel with an increasingly industrialized food system, characterized by large scale production of high-yield, inexpensive, agricultural products (corn, soy, wheat and rice), which were processed to generate an abundance of 'added value' foods. NCD Risk Factor Collaborator Group observed that from 1975 to 2016, the number of girls with obesity increased from 5 million to 50 million, and boys from 6 million to 74 million. In other words, childhood obesity increased 10-fold worldwide since 1975 [10]. Reducing excess weight, will require modifying both energy intake and energy expenditure and not necessarily focusing on either alone. Americans Consume on an average 250-300 grams of carbohydrate a day, accounting for 55% of their daily intake. Several studies including the Seven Countries Study, have demonstrated the beneficial effects of a Mediterranean diet and low carb diets, compared to the low-fat diets. Dr. Walter Willet, Chairman of the Department of Nutrition, Harvard School of Public Health says, "Fat is not the problem." "If the Americans could eliminate sugary beverages, potatoes, white bread, pasta, white rice and sugary snacks, we would wipe out almost all the problems we have with excess weight, diabetes, and other metabolic diseases."

What really is the healthy diet? Harvard Heart Healthy plate consists of 50% fruits and vegetables, 25% of whole grains, 25% of protein with vegetable oils or monosaturated fats. The United States Department of Agriculture (USDA), recommends a similar combination of nutrients and includes dairy products (Fiure 1). In most countries, people cannot afford this type of heart healthy food plate. Major source of daily diet consists of staple grains such as, corn, wheat and rice, supplemented with a minimum of vegetables, meat, fish, poultry and dairy products, depending on the availability and affordability. According to the Food Agriculture Organization (FAO), maize, rice and wheat, provide more than half of caloric intake. Worldwide, rice wheat, maize and to a lesser extent, sorghum and millets, are important staple foods, critical to the survival of billions of people. In 2018, corn production was 1100 metric tons (MT), wheat was 735 MT, and Rice 500 MT (www.statistica.com/Agriculture/Farming). Rice is the staple food for half of the world's population. Most staple foods are inexpensive and plant-based. In recent years, there is a growing trend to develop organically grown products. Similarly, we assume that there will also be a growing interest in developing designer, 'value added' healthy foods such as designer eggs, designer milk, designer grain, probiotics, designer foods enriched with micro and macro nutrients, designer fats, proteins and amino acids. In China, more than 3,000 varieties of health foods are available for use, in their traditional medicine practice. In this overview, we will briefly discuss some aspects of this novel approach with special reference to our area of interest: cardiometabolic diseases.

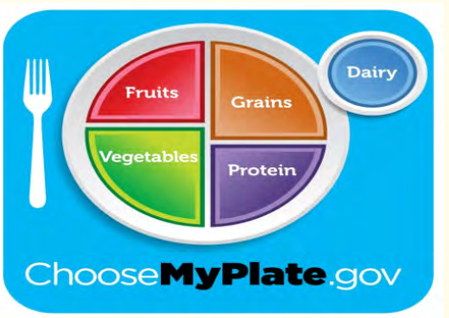

Figure 1: Healthy Diet Plate: Source: US Department of Agriculture (www.ChooseMyPlate.gov).

Excess weight, obesity and type-2 diabetes are major health problems worldwide. The Danish Diet study demonstrated, that higher whole-grain intake is associated with lower risk for type-2 diabetes, among middle-aged men and women [11]. In this study, however, wheat, rye, and oats were used as sources for whole grains. Results showed a consistent association between high-whole grain intake and lower risk of type-2 diabetes, irrespective of the type of cereal consumed. With participants between the ages 50-65, (n=55,645) researchers observed that, high whole grain intake among men was associated with a 34% decrease in risk of diabetes. Whole grains are rich in fibers, which are not easily metabolized and thus, help with insulin sensitivity. Researchers at Kawasaki University, Japan, have also demonstrated that eating glutinous brown rice twice daily for 8 weeks, improves glycemic control in Japanese patients with diabetes [12]. Can intake of brown rice help to slow the spread of type-2 diabetes? To tackle this issue the researchers from Harvard School of Public Health (HSPH), launched a Global Nutritional and Epidemiological Transition (GNET) Working Group, a collaborative initiative, between researchers from the Departments of Epidemiology at HSPH and their colleagues in Asia, Latin America and Africa with the aim to prevent the global diabetes epidemic by improving the carbohydrate quality of staple foods in the diets of people from around the world.

About half a century ago, researchers at the Central Food Technological Research Institute, Mysore, India, developed deodorized fish flour and yogurt from peanut milk as a good source of protein. Although these products received an initial welcome, they did not gain acceptance and as such failed to get into the main stream market. Though brown rice revolution may pay a big dividend in the areas, where people are used to consuming brown rice, it will fail in the countries, where white rice is preferred. White rice, a common Indian staple grain, has a high glycemic index and low fiber content. High-Fiber White Rice (HFWR) was developed in India, using bio-

chemical screening approaches and classical breeding techniques. Mohan and associates from Madras Diabetes Research Foundation (MDRF), conducted a randomized control trial on HFWR and observed that the dietary fiber content was five-fold higher and glycemic index of HFWR was 23% lower than the conventional white rice. The study concluded, that the new HFWR variety may be considered as a potentially healthier alternative, to commercial white rice, in rice-eating populations, since it has lower glycemic index and high fiber content [13]. Similar breeding and selection processes are in progress, for other staple grains in different countries, to improve their nutritional quality.

Wahab and associates from Pakistan reported a study in which they selected eight different varieties of wheat for nutritional qualities and concluded that, it is possible to select and cultivate new varieties of wheat with better nutritional qualities, enriched with the preferred micronutrients [14]. Out of the ten genotypes validated, RSP-561 possessed maximum levels of starch protein, iron, zinc, soluble protein, gluten, calcium, carotenoids, and antioxidant compositions [15,16]. Several studies worldwide have demonstrated, that improved crops can be developed by classical breeding, mutagenesis, and transgenesis [16]. Similar studies have been carried out on corn breeding in order to improve the nutritional quality and suitability for health benefits. Among various corn varieties, high amylose corn (HACS) has attracted the most research interest with emphasis on the impacts of high-amylose corn flour/starch (HACF/HACS), on postprandial glycemic/insulinemic responses, insulin sensitivity, satiety/appetite, lipid metabolism/obesity, colon/gut health and mineral absorption [17]. In view of the fact, that these have components with slow digestive rate, HACS/HACF have been incorporated into various types of food products for feeding studies, and their effect on the postprandial glucose/insulinemic responses validated.

The principal phytochemicals present in corn seed and corn silk include polyphenols, phenolic acids, flavonoids, anthocyanins, glycosides, carotenoids and polysaccharides of biological importance [18]. The presence of these chemicals makes corn a medicinal plant, which shows various biological activities particularly the antioxidant, antimicrobial, antidiabetic, anti-obesity, antiproliferative, hepatoprotective, cardioprotective, and renal protective activities. In Vietnam, 32 percent of corn grown, are genetically modified, to prevent diabetes and obesity. Global Nutrition Epidemiologic Transition Initiative has been working with 11 countries to reduce diabetes by improving the quality of staple foods, through culturally-appropriate interventions [19]. Great progress has been made in the past decade, with respect to application of biotechnology to generate nutritionally improved crops. Biofortified staple crops such as rice, maize, and wheat harboring essential micro-nutrients (to benefit the malnourished individuals as well as new varieties of crops, which have the ability to combat chronic metabolic diseases) have been developed. Recently, a new line of biotechnology, based on gene editing has come to the forefront. Genome editing focuses on nuclease- based forms of engineering, such as the TALENS (transcription activator like effector nucleases) or the CRISPR associated systems. These and other similar technologies, will revolutionize the way we think about enhancing food crops, to improve global nutrition and health [20,21].

Now that we have briefly discussed the role of dietary salt, sugar, carbohydrates, and some recent studies related to the improvement of dietary components, let us turn our attention to what is being done to modulate the dietary fats. Framingham heart studies and many other studies have reported the ill effects of unhealthy fat in developing excess weight, obesity, diabetes and vascular diseases, including their role in the precipitation of acute vascular events such as heart attacks and stroke. Since the time Bang and Dyerberg, studied the Greenland Eskimo diet and published their observations, about the rarity of ischemic heart disease in Greenland Eskimos, there is a great interest in the modifications of certain diets by enriching with Omega-3 fatty acids [22]. These investigators also analyzed the plasma lipids of Eskimos and observed that they had low lipid concentrations, in spite of high fat diet (Omega 3-fatty acids: Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA). Based on these observations the study concluded, that coronary atherosclerosis, and diabetes mellitus, are very rare among Eskimos. This revolutionary discovery at that time, inspired several leading researchers worldwide, to concentrate their work on demonstrating the health benefits of dietary Omega-3 fatty acids. In blood platelets, upon activation, arachidonic acid is released from membrane lipids and converted to a proactive prostaglandins G_2 and H_2, which are further converted to thromboxane A_2 (Figure 2). On the other hand, in the vessel wall, anti-aggregatory, vasoactive, prostacyclin (PGI_2) is produced. Following the work of Bang and Dyerberg, there was a concerted effort, to show that Omega -3 fatty acids are converted to their respective prostaglandins and Thromboxanes A_3 and A_4, seemed to be less.

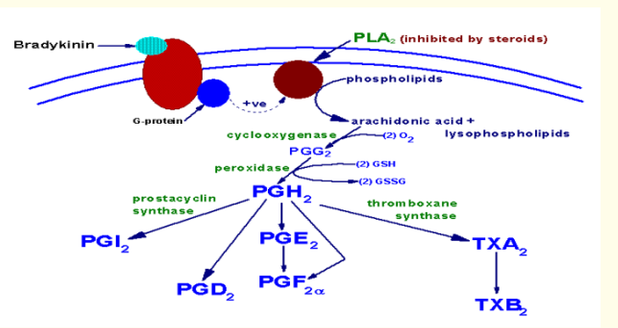

Figure 2: Arachidonic acid Metabolism via Cyclooxygenase (COX) and Prostacyclin Synthetase. (Public Domain).

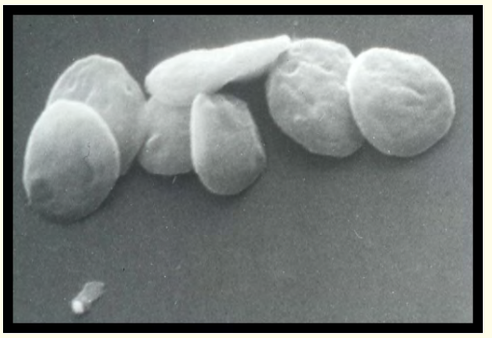

Figure 3: Unactivated Platelets.

Figure 4: Activated Platelets on Vessel Wall.
Courtesy: (Late) Professor, James G White.

Aggregatory than the Thromboxane A2. During the same period, it was demonstrated that the antiplatelet drug, aspirin (acetyl salicylic acid) inhibited irreversibly the key enzyme of (COX) PG synthesis. In view of this observation, various professional societies, public health policies promoted these ideas, and as such, there was a shift in the way the dietary fats were modified to meet these health guidelines. Omega -3 fatty acids have received a lot of attention in recent years, due to the growing body of evidence that, they help to combat range of medical conditions, such as cardiovascular disease and thrombotic episodes. We have articulated in our earlier articles, the mechanisms involved in platelet activation, and the meta-analysis results of multiple clinical trials on Fish oil [22]. Naturally omega 3-fatty acid enriched foods include, mackerel, salmon, cod liver oil, herring, oysters, sardines, anchovies, and caviar.

Many Governments consider WHO dietary guidelines, to the state-of-the-art scientific evidence, translating them to regional and national dietary guidelines [23]. The 2018 WHO draft guidelines (which relies on 84 randomized control trials), on dietary fatty acids and trans fatty acids, recommend reducing total intake of saturated fat, and replacing it with polyunsaturated and monounsaturated fatty acids. The recommendation failed to consider evidence that the health effects of saturated fat varieties depends on the specific fatty acid and on the specific food source. A food-based transition of the recommendation for saturated fat intake, would avoid unnecessary reduction or exclusion of foods that are key source of important nutrients. In view of such observations and recommendations, we feel that it would be a better approach, to enrich the food with appropriate healthy fats. Having said that, it is not easy to incorporate Omega-3 three fatty acids into processed foods. Highly unsaturated fats tend to oxidize fast and are not good for incorporation into the processed foods. The expert committee strongly recommends, a more food-based translation of how to achieve a healthy diet, than consideration of the draft guidelines on the reduction in the total intake of saturated fatty acids.

By changing the diet of hens, egg producers have succeeded in improving upon the quality of already nutritious egg. Most 'designer eggs' are enriched with omega-3 fatty acids, a heart-healthy nutrient that is otherwise found in seafood (salmon), flaxseed and walnuts [24]. Russian researchers have demonstrated, that selenium-enriched chicken, pork, and meat can also be produced by using organic selenium in the diets of such animals [25]. French researchers have developed, a new natural multi-enriched egg (Benefic eggs) with omega-3 fatty acids, vitamins D and E, carotenoids, iodine, and selenium [26]. The same research group demonstrated, that by feeding the animals with fish extracts or algae (oils), the level of DHA could be increased by 20-folds in fish, 7-folds in chicken, and less than 2- folds in beef [27]. Some studies have shown, that it is not necessary to feed animals with linseed-supplemented diets for a long period, to have the highest increase in poly unsaturated fatty acids (PUFA) content of the products [28]. Researchers from Czech Republic showed, that feeding rapeseed oil for just four weeks before slaughter was sufficient for improving fatty acid profile, without negative effect on the backfat [29]. Danish studies with dietary manipulation showed, that it is possible to lower cholesterol in humans by providing meat from specially grown designer pigs. By increasing the content of rapeseed oil in pig feed, the researchers were able to change the fatty acid composition of the pig fat, in a way that it now has the potential to reduce blood cholesterol in human subject [30].

Like the plant scientists, animal scientists have also been taking advantage of the advances made in the area of biotechnology, genetic engineering, and genomics. Major source of food worldwide, is of animal origin as only 25% of the human population seems to be vegetarian. Australian researchers have developed, a high-resolution 'atlas of gene expression' in the domestic sheep [31,32]. This gene expression atlas for sheep, seems to be the largest transcriptomic dataset. Freeman and associates have described, the first genome-wide association analysis of the transcriptional landscape of 62 pig tissue/cell types [33]. In India, National Dairy Development Board has developed, a genome assembly named "NDDB-ABRO Murrah" of riverine buffaloes with a claim that, it is the first

complete parent-wise genome assembly of buffalo (https://www.nddb.coop). Similar to the green revolution, National Dairy Board of India launched "Operation Flood" called white revolution, with the leadership of Dr Veghese Kurien. This development of the genome assembly comes on the back of another successful launch of INDUSCHIP, a customized genotyping for indigenous cattle and their crosses.

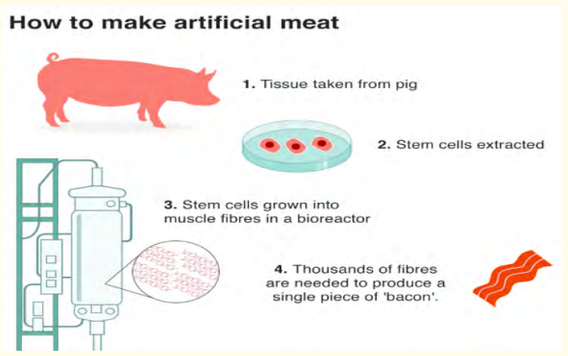

Figure 5: Cutting edge technologies for developing synthetic meat. (Public Domain).

The new start-ups are racing to develop lab-grown meat, using cutting-edge-technologies. Clean meat is the term, used for genuine animal meat grown in the laboratory using cell culture and appropriate nutrients. In August of 2013, a Dutch scientist Mark Post, presented a first lab-grown burger ever created. It costed 250,000 Euros. Mosa Meat for instance, harvests muscle tissue from a living cow using a biopsy, the muscle cells are then cultured and grown to produce mass of customized designer tissue. Scientists at Israel are working in this cutting-edge technology for developing lab-grown meat (https://www.specialtyfood.com).

Now that we have briefly discussed the advances made in developing designer plant and animal foods, let us consider another very important part of healthy foods; dietary supplements. Scientists from Tehran University, Iran, claim that higher intake of phytochemical-rich foods is inversely related to prediabetes [34]. In this study, they demonstrated that higher dietary intake of phytochemicals, correlated with lower prediabetes- odds ratio. In countries with large diabetic population, like China and India, there is a great opportunity to develop indigenous dietary supplements, enriched with phytochemicals, known to have anti-diabetic potential [35-39]. Most promising phytochemical groups are the alkaloids, glycosides, polysaccharides, and phenolics as well as flavonoids, terpenoids and steroids. If we extend this logic further, we can develop dietary supplements for intervention of most of the early metabolic risks, such as oxidative stress, chronic inflammation, excess weight, endothelial dysfunction, and subclinical atherosclerosis. For instance, Kasliwal and associates at the Medanta Hospital, New Delhi, India, have shown that just (figure 6) eating pistachio nuts for a few weeks can reduce or normalizes endothelial dysfunction, which is one of the earliest signs of vascular diseases [40]. Dr. Jay N. Cohn, a pioneering Professor of Cardiology, Director of Rasmussen Center for Prevention of Cardiovascular Disease, University of Minnesota says, "No cardiovascular diseases without endothelial dysfunction." [41].

Figure 6: Common Tropical Diabetes Herbal Plants. (Public Domain).

Oxidative stress is another early metabolic risk, and at present clinicians are not treating diabetics with any drugs for this clinical condition. The most healthful diets like Mediterranean and Okinawa diets, are rich in Nrf2 raising nutrients. The transcription factor Nrf2 (nuclear factor, erythroid -2 related factor) is a master regulator of detoxification, anti-oxidant, anti-inflammatory and also possess other cytoprotective functions. Recent studies have demonstrated, that Protandim (a mixture of five phytochemicals; Ashwagandha, Indian Bacopa, Indian Green Tea, China Milk Thistle, and China Turmeric) is associated with reduction in oxidative stress and fibrosis, preservation of the right ventricular (RV) microcirculation and RV function [42]. Since early metabolic risks such as oxidative stress, inflammation, free radical mediated pathology and ageing are associated with multiple mechanisms modulated by scores of genes and gene expressed proteins, we feel that a combination therapy using potent phytochemical extracts may be useful. Having said that, we strongly emphasize the need for a well thought-out randomized clinical trials, for validating the effectiveness of these phytochemical-based complementary therapies. In a short overview like this, we will not be able to cover all aspect of this very important topic, readers are urged to consult original articles, reviews, and comprehensive monographs on this topic. We also want to inform the readers, that at the suggestion of the editors of this journal, we had to delete more than half of our references.

Conclusion

Metabolic diseases such as hypertension, excess weight, obesity, type-2 diabetes, and vascular disease have rapidly increased in the last three decades, to epidemic proportions worldwide. Seems like the increased incidence and prevalence of these diseases, paral-

lels the introduction of the modern processed foods and sugary beverages. A collaborative study between the Imperial College of London and the World Health Organization demonstrated, that childhood and adolescent obesity has increased by ten-fold in the last four decades. An analysis of 45 countries representing 90% of the population, estimated that in 2018, there were more than 500 million type-2 diabetes worldwide. NCD Risk Factor Collaboration group, used data from 751 studies from 146 of the 200 countries for their estimate. According to them, if post -2000 trends in the increased incidence of diabetes continue, the probability of meeting the global target of halting the rise in prevalence of diabetes by 2025 to the level of 2010 level worldwide is lower than 1%. No country has reduced, reversed, or prevented the increase in the incidence or prevalence of chronic metabolic diseases. In an earlier article, we articulated a novel approach for early diagnosis of metabolic risks and developing appropriate intervention strategies. These chronic metabolic diseases are more or less life style diseases. In view of this observation, we would like to encourage holistic lifestyle, emphasize the need for robust physical activity, wellness and heart healthy diet. In this overview we have briefly discussed the concept of designer food for better cardiovascular health, with some selected examples from plant foods (cereals) and animal foods (eggs, and animal products) enriched with value added micronutrients and fats.

Food therapy of traditional Chinese medicine aims, to maintain balanced nutrition through diet. Medical diet therapy on the other hand, tries to achieve the balance of 'Yin and Yang' through the combination of nutrition and medicine. What we have discussed in this overview, is more or less a working model for how staple foods, whether from plant source (cereals, pulses and millets) or from animal sources, could be enriched with essential nutrients, balanced in terms of quality of carbohydrates, proteins and fats content. Furthermore, we also have briefly discussed, the need to develop dietary supplements for complementary therapy, so that we need not depend on the mercy of pharma industries for all our medical needs. According to WHO, over 80% of the world population rely on the traditional plant based-system of medicine. Over 50,000 plant species are in use in herbal sector. The market for herbal products runs into trillions of dollars. We would like to see that the hidden potential of this untapped market is explored. There are of course, great opportunities and challenges in developing evidence-based support for these herbal products.

Currently, there are more prediabetics, than diabetics in the world. If we add the number of prediabetics and diabetics, it will be almost close to the number of hypertensives, and obese individuals (over a billion) worldwide. These three metabolic diseases, contribute significantly to the excess morbidity and mortality, associated with cardiovascular disease. Early intervention of these "at risk" population, will go a long way, in reducing the healthcare burden of these diseases. These at-risk individuals, are not covered by any prevention programs and providing affordable health care for such a large population (several billion), is almost unaffordable in many countries. We and others working in this area feel, that the major contributing factor for metabolic risks is unhealthy lifestyle. Therefore, development of a robust education program for creating awareness, and encouragement of healthy living will go a long way, to reduce the disease burden. Such a possibility is documented by a Harvard study with the conclusion that, "Even among participants with high genetic risk, a favorable lifestyle, was associated with a nearly 50% lower relative risk of coronary artery disease, than was an unfavorable lifestyle." Considering the rapidity with which the metabolic diseases are increasing, the time for action is now. Public health policy makers should focus on prevention, and encourage healthy diet, physical activity, and a healthy lifestyle. As a part of our prevention efforts, we have articulated the benefits of physical fitness, wellness and a healthy lifestyle.

Acknowledgements

This article was prepared as a part of my presentation on 'this topic', for invited lectures at the Wellness Conference-2019 at Kanpur University, Kanpur, India, and at the Indian Science Congress-2020, Bengaluru, India. Figures 1, 2, 5, and 6 are from public (INTERNET) source. Author thanks the individuals, who posted these figures in the public domain.

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