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Exploring the Interplay of Phytochemicals, Nutrients, and Liver-Kidney Markers: Implications for Metabolic Health and Disease Prevention

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ABSTRACT

This study explores the intricate relationship between dietary phytochemicals, nutrients, and metabolic health, with a particular focus on their impact on chronic disease prevention. By reviewing current literature and research findings, this paper elucidates the mechanisms through which phytochemicals and nutrients influence metabolic markers, especially in the liver and kidneys. It discusses the potential benefits of consuming whole plant-based foods rich in these compounds and provides insights into their role in mitigating the risk of conditions such as obesity, diabetes, and cardiovascular diseases. Furthermore, it offers recommendations for future research directions and public health interventions aimed at promoting optimal metabolic health.

Keywords: Liver, Kidney Markers, Metabolic Health and Disease

INTRODUCTION

The American Cancer Society recommends a minimum of five servings of vegetables and fruits daily to reduce the risk of chronic diseases [1-4]. Earlier cancer-prevention recommendations had set a goal of seven to nine daily servings [5-8]. However, recent updates to the recommendations suggest higher consumption targets due to accumulating evidence of the benefits of these plant foods rich in compounds known to lessen cancer risk [9-12]. The ancient Ayurvedic principles of medicinal herbs to improve human health are currently being explored through scientific studies to reveal the chemistry behind the traditional human benefits [13-17]. A current-traditional phytochemical approach towards chronic disease prevention appears to be at the forefront of the Human-Plant interrelational alliance that holds significant potential advantages for human health [18-20]. This novel realization appears to be reinforced by studies being conducted the world over and has potential repercussions not only for human health benefit but also for crop selections and cultivations at the global scale. However, current opinion-based or some statistically driven conclusions alone may not conclusively elucidate the individual or cumulative roles of various classes of phytochemicals towards overall health benefits [21]. Hepatocytes and nephrons are the principal frontline components of body detoxification mechanisms [22-24]. The liver serves a major role for body detoxification processes by processing ingested xenobiotic compounds in addition to several endogenously generated compounds, such as broken down kidney hemoglobin, which ultimately get excreted via urine [25-28]. However, the liver itself is protected from its own detoxification products, such as free radicals, by the synergistic functioning of several liver enzymes and antioxidants. The kidney is directly responsible for flushing out the detoxified compounds from the body, making it a major organ of body excretory mechanisms [29-32]. The transport proteins present in these organs work round the clock, functioning in tight timelines to safeguard homeostasis [33-35].

Phytochemicals and their role in metabolic health

Polyphenols are a group of molecules found in all vegetal food products (fruits and vegetables, nuts, seeds, cereals, olive oil, chocolate, tea, and wine) that have antioxidant capacity, i.e., they can act as radical scavengers. While the potential antioxidant capacity of polyphenols is clearly an important determinant of their capacity to prevent diseases, there is now substantial evidence that polyphenols also interfere with certain signaling pathways that are responsible for health benefits that have been proven in vitro, in animals, and recently in longitudinal studies with humans [36-38]. Furthermore, if we consider the complexity of the antioxidant mechanisms in humans, which could be more than those resulting from the ability to scavenge free radicals, other benefits apart from its possible pro-oxidant activity could also explain part of their health benefits [39-43]. The prevention of insulin resistance, or diabetes, and cardiovascular diseases can be explained through interactions of these compounds with important macromolecules in the body, where laboratory studies, with in vitro cellular models exposed to different polyphenols, showed positive effects on insulin sensitivity, lipid profile, blood pressure, endothelial function, and obesity. In recent years, concern about the prevention of chronic diseases has led to increasing interest in bioactive compounds contained in foods as one of the health promotion strategies. Epidemiological and experimental findings have shown that the presence of these compounds in the diet can improve health and prevent chronic diseases, in addition to providing nutrition [44-48]. Today, health, nutrition, and biochemistry professionals agree that these molecules can prevent diseases such as obesity, insulin resistance, or diabetes, cardiovascular diseases, and certain types of cancer. Among the best known bioactive compounds, phytochemicals from plants, and especially polyphenols, are receiving special attention since there is increasing evidence that their consumption is inversely related to these health problems in people.

Definition and types of phytochemicals

Chemically, phytochemicals are divided into groups, using the similarities shared by their carbon structure and the impact they may have on human health. The list of phytochemicals includes carotenoids, flavonoids, organosulfur compounds, polyphenols, lignans, phytosterols, and glycosinolates. Many of the foods that contain the most phytochemicals are plant foods that also deliver vital nutrients such as minerals, vitamins, and fiber. For example, fruits, vegetables, grains, and legumes contain hundreds of biologically active compounds that provide crucial energy, fiber, vitamins A, C, and E, potassium, magnesium, and other phytochemical elements that are essential for overall health and wellness. Nuts and seeds as well as herbs and spices are also significant sources of many vital vitamins and minerals, along with powerful phytochemicals [30-38]. Consuming a balanced diet that is mostly composed of fresh, whole, and minimally processed foods is a good way to get necessary nutrients, vitamins, and minerals, and an assortment of healthful phytochemicals that can help to maintain optimal health and reduce the risk of developing chronic diseases such as cancer, diabetes, obesity, and cardiovascular diseases. Phytochemical is a term that refers to a wide variety of biologically active compounds found in plants [25-38]. These compounds give plants their color, flavor, and natural disease resistance, as well as provide a number of health benefits when consumed by humans. There is no single list of all the thousands of known phytochemicals categorized by the specific health benefits they may provide, although some types are recognized more than others for their individual health-promoting properties. As an example, plant sterols can lower blood cholesterol because they are structurally similar to cholesterol and can inhibit its absorption in the gastrointestinal tract. Other phytochemicals, including flavonoids, saponins, phytates, and tannins, are famous for their antioxidant and anticancer properties, as well as in slowing the aging process. Other phytochemicals are known to improve cognitive functions, protect against cardiovascular diseases, and insulin resistance [20-25].

Mechanisms of action in metabolic health

The approach consists of reviewing findings of in vitro and in vivo experiments on 'bioprocessed' materials naturally rich in these biocompounds and which were related to different 'metabolic markers' (blood and tissue concentrations of glucose, insulin, cholesterol, triglycerides) [26-36]. For a number of putative 'bioactives' identified during the various fractionation procedures, 'mechanisms' by which they do have the potential to: (1) limit adipogenesis and intracellular fat accumulation (through their capacity of modulating the activity of a number of molecular pathways), (2) increase thermogenesis, fat utilization and protection from mitochondrial dysfunction (mediated by their pro-oxidative properties), and (3) sensitize tissues to insulin actions (several phytochemicals acting as 'extreme' polar metabolites of a number of intermediates from major carbon pathways). In health, these compounds exemplify an inverse prooxidant pathophysiological property aiming at limiting the endogenous production or effects of chronic exaggerated oxidative stress [20-24]. Experimental evidence found in vitro as well as in vivo reflects that these biocompounds are able to modulate the activity of various enzymes and metabolic pathways, affecting the mobilization and oxidation/reduction of macronutrients, the availability of precursor molecules or metabolites in primary metabolic pathways, and the purity of reduced species. It seems that the antioxidative/anti-inflammatory properties particularly triggered by these biocompounds in in vivo involve cross-talking systems necessary to maintain optimal cellular functionality under physiological and stress conditions. The present chapter will draw up an overview focusing more on the interplay between some of these biocompounds and the biomarkers used as surrogate markers for the detection of major metabolic health risk factors in humans [12-16].

Examples of phytochemical-rich foods

Moving on to the whole grains, it is a huge category of food that is known or recommended to be when complex carbohydrates typically dominate, delivering a vast array of phytochemicals. Some examples of the antioxidant capacity of some of these whole grains are quinoa that represents 13.0 μmol TE/g, buckwheat 11.4, barley 8.0, eggplant 8.8, millet 7.03, bulgur 6.28, steel cut oats 4.73, brown rice 3.83, and pearled barley 3.43. Sadly, not much attention on this food group as sources of bioactive nutrients, except from anointed products such as pomegranate juice or cranberry (i.e. Vaccinium macrocarpon) supplements, and to a lesser extent, blueberry since there are additional benefits carried within those grains [20-25]. Recent comprehensive analyses including monocots (the well-defined categories of Triticum, Oryza, Hordeum, Secale, Zea, Saccharum, Sorghum, Musa...), and eudicots, such as peanut and soybean, determined that: "whole wheat (553 μmol equiv/100 g), rice bran (422), corn bran (320), sorghum bran (238), oat bran (217), barley bran (190), and rice bran (135) with respect to other plant-based foods". The bioactives in sweet, white potatoes are one of the highest in the vegetable world, unrelated to anthocyanins and they reflect catechins, chlorogenic and ferulic acids, the tocopherol (-ve vitamers E), and trace concentrations of goitrogens such as cyanoglycosides amably, when properly prepared in a meal, other domestication features. For example, key vegetables include members of the cabbage family (cruciferous), such as radishes, cauliflower, arugula, broccoli, Bok Choy or Chinese Cabbage, napa cabbage, Brussels sprouts, plus a few outliers, such as watercress and horseradish. Other crucial vegetables or culinary staples that provide such polyphenols include alliums (e.g., garlic or leeks), carrots, beets, onions, potatoes (sweet and white), tomatoes; and of course, legumes, including all lentil varieties, garbanzo beans, flat beans, peanuts, and soybeans. With color or deep desirability, the fruit family should also deserve clear mention, since phytochemicals are usually what gives fruits their extraordinary coloration [12-15].

Nutrients and their impact on liver-kidney markers

Carotenoids are dietary sources of vitamin A and have antioxidant properties. In Asian countries, there is extensive consumption of fresh vegetables such as carrots and spinach, which are sources of carotenoids and fiber. Provitamin A carotenoids providing half of the vitamin A supply in the human diet are also precursors of physiologically active retinoids. Plants are rich sources of non-provitamin A carotenoids with several biological activities and health-benefiting properties [7-9]. The more common type of β-carotene in natural sources is all-trans-β-carotene in the form of crystalline. The all-trans isomer is absorbed more than the various cis isomers of β-carotene in crystalline form. Among foods involving high amounts of β-carotene are dark green leafy vegetables, tubers such as sweet potato and carrot, orange-colored fruits such as cantaloupe, apricots, and dark fruits such as berries, prunes, and plums. All-trans-β-carotene is also found in several selected vegetables and fruits frequently consumed by people in Bali, such as long purple beans, spinach. Among the fruits consuming β-carotene are jackfruit, papaya, starfruit, and mango [10]. Among the plethora of studies on the beneficial effects of edible plant products, there is evidence corroborated through epidemiological studies that the regular consumption of vegetables and fruits is thought to protect humans against chronic diseases such as obesity, diabetes, cardiovascular diseases, various cancers, and aging. Edible plants occur in nature as fruits, leaves, grains, buds, stems, bulbs, and root tubers and contain numerous bioactive compounds, including carotenoids, vitamins, phenolic compounds, fibers, and other non-nutritional factors. Information on the utilization of these bioactive molecules in metabolic health, which involves the prevention and treatment of metabolic diseases, as well as well-being, seems to be increasing. It is encouraging to observe that studies on the potential impact of active molecules on markers associated with kidneys and liver functions are conducted [12].

Key nutrients for liver health

Choline and carnitine are abundant in animal-source foods and are interrelated metabolically. Available evidence suggests that dietary choline and carnitine could be useful in preventing fatty liver disease as a consequence of naturally occurring choline in meat from beef, pork, and poultry, and carnitine being present in red meats such as beef, pork, and lamb in high amounts. Other animal-source good choices include cod, milk, coffee, beer, and whole grains because they are rich in vitamin B6 and amino acids [10-15]. A collaborative interaction between choline and carnitine is evident in disease prevention with animal-source foods; choline in red meats helps in the maturation of carnitine, and carnitine transports energy from the cytoplasm to the mitochondria to fuel oxidative phosphorylation in the liver, heart, and kidneys. This transportation is part of a larger process that prevents depletion of the liver and kidney of these essential micronutrients, thus protecting against fatty disease. In omnivores and vegetarians or simply in individuals who consume diets that suit disease risks, together with the beneficial hemorrhagic stroke prevention effects of choline in meat, carnitine actively protects vulnerable populations during critical developmental periods and throughout life. The liver is involved in many metabolic processes that are essential for human life, such as bile production and secretion; degradation, synthesis, and conversion of nutrients; and detoxification. Many nutrients that the liver uses to maintain its function are obtained through diet-derived intermediates that the body cannot synthesize independently and are essential for body homeostasis. Key nutrients for the liver include vitamins (ascorbic acid, vitamin A, vitamin D, and B vitamins), vitamin-like compounds (choline, carnitine), and essential minerals including zinc, iron, copper, selenium, and magnesium. Human studies show that under conditions of adequate energy and protein intake, it is possible to establish optimal protein and adequate energy intake (protein 5g/kg/day for those with hepatic encephalopathy). In addition, the nutrient profile should have enriched protein/energy with adequate lipids, vitamins, and minerals. On the other hand, when liver disease is a consequence of protein-energy malnutrition (PEM), certain nutrients like vitamin D, choline, and zinc become depleted and are potential therapeutic strategies for targeting PEM in liver disease [10-14].

Key nutrients for kidney health

Vitamin and mineral levels have immense influence on metabolic health. Vitamins, along with other nutrients like lipids, protein, and polyphenols, form an important component of complex dietary matrices like fruits, vegetables, grains, and food products. In numerous observational studies, higher consumption of several vitamins and minerals has been associated with better metabolic health, with intake inversely associated with long-term disease or health risks such as cardiovascular disease, cancer, and mortality. Specifically, in humans, there is evidence that levels of certain nutrients such as folic acid, niacin, pyridoxine, folate, antioxidants vitamin E, and minerals such as zinc and magnesium are related to somatic diseases like heart disease, stroke, and some types of cancer. Moreover, cross-sectional relationship of nutrient biomarker levels with metabolic traits have also been reported. Recent evidence suggests that herbal components such as polyphenols, flavonoids, isoflavonoids, saponins, sulfides, and polymers may have additional health benefits like helping in the prevention of obesity and its complications. Milk, soy, and rice are all staple ingredients in their own right when it comes to beverages. Vitamins and minerals might be added or subtracted depending on the desired product characteristics. Vitamins and minerals are important for proper body functions, and their levels largely depend on the content of raw materials added or removed as per the regulatory guidelines. In fruits and vegetables, the levels of both the macro-nutrients and the micro-nutrients show wide variability [1-5].

Interactions between nutrients and liver-kidney markers

Altogether, liver-kidney damage may not only modulate body weight but may directly and indirectly play a significant role in the regulation of systemic Ca^{2+} through the modulation of the concentration of gut-liver-skeleton axis borne (a)P2, ionized Ca^{2+}, and parathormone levels. Studies with cows, sheep, swine, rabbits, and guinea pigs as pertinent animal models reveal negative effects of in-vivo liver-kidney damage on the concentration of (a)Pi and ionic Ca^{2+} in blood, liver, kidney, and subcutaneous tissue as well as the capacity for intestinal absorption of (a)Pi and Ca^{2+} concerning liver-kidney damage and improved parameters of nutrient homeostasis with improved dietary vitamin D status [11-16]. Recent increases in the prevalence of obesity and associated bone-related morbidities indicate a potential interrelationship between nutrient homeostasis and the constitutive structural and functional integrity of the liver-kidney axis in maintaining metabolic homeostasis. In this review, we explore the potential synergy between nutrient and non-nutritive bioactive phytochemical constituents through their role in promoting metabolic health, and the implication of their imbalance in metabolic disorders and bone-related co-morbidities. Using published reports and a search of accredited databases, the current state of knowledge on the interplay of nutrient homeostasis, liver and kidney marker enzymes, and metabolic balance was reviewed. In summary, while imbalances in enzymatic and non-enzymatic markers of liver and kidney function can be proxies for clinical conditions and biochemical abnormalities that have the potential to disrupt nutrient homeostasis and metabolic balance, the degree of their perturbations can also reflect genotypic and phenotypic and the extent of mutagen insults poised by antithetical constituents of the diet that cannot be offset by endogenous scavengers [16-18].

Implications for disease prevention

Current dietary recommendations suggest that both the macro- and micronutrient contents of food must be increased in order to improve health and control (or prevent) specific diseases. However, scientists are struggling with developing a working definition for "nutritious" and to determine the appropriate quantities and ratios needed to support and maintain good health and to prevent the onset of disease. This is complicated by the individual genetic profile of disease susceptibility that everyone possesses [8-10]. The individualized consideration of genetic and metabolic profiles to create personalized approaches to disease prevention is the premise of the field of Metabolism, Pharmaco- & Nutrigenetics (MPNG).

Considering the blended beneficial effects of dietary phytochemicals and nutrients, it is clear that the consumption of whole plant-based foods and products such as rosemary, honeybush, and rooibos (as opposed to isolated phytochemicals and nutrients in the form of supplements or extracts) is the key to protective effects against metabolic disease development. Any single phytochemical may have the potential to be used in the prevention or management of some of the disorders encountered during the course of systemic metabolic diseases. Appropriate dosages of antioxidants like vitamin E and plant-derived compounds like curcumin, omega-3 polyunsaturated fatty acids, non-nutritive sweeteners, and glucosidase inhibitors such as acarbose have shown protective effects in T2DM development and lead to improved glucose control in patients diagnosed with T2DM. There are also numerous reports highlighting the antidiabetic effects of isolated compounds with known polyphenolic structures. For example, hesperidin, quercetin, and berberine have been found to have antihyperglycemic activities and can influence the expression of transcription factors involved in insulin-signaling pathways such as PPAR-alpha, PPAR-gamma, and GLUT-2 [12-16].

Role of phytochemicals and nutrients in preventing metabolic diseases

Selenium provides resistance against cadmium-induced nephrotoxicity as well as hepatotoxicity. In the NHANES, serum selenium was negatively correlated with urinary excretion of beta-2-microglobulin, an indicator of renal proximal tubule function, when urinary cadmium levels are elevated [8]. Despite the potential benefits of consuming these foods, nutrients, and their combination, research involving the interactions of these dietary agents with liver-kidney markers is sparse. Therefore, the primary objective is to elucidate the protective effects of these dietary agents against metabolic diseases through liver-kidney markers. Such knowledge is necessary for nutritional screening and dietary interventions to safeguard public health and health economics. Public health guidelines have increased the importance of more plant-based diets, owing to an increasing aging population. However, it is important to understand that too much of some nutrients or phytochemicals may not be beneficial since phytochemicals and nutrients can interact with each other [30-34]. Nutrient-based approaches, such as consuming fruits and vegetables, have made an impact in combating metabolic diseases. Fresh mushrooms elevated HDL cholesterol and lowered serum triglycerides and insulin in genetically predisposed mice. In a prospective study of 1482 adults without metabolic syndrome, grain protein intake improved serum levels of alanine aminotransferase, a liver marker, from the baseline to 14 years later. In the Health Professionals Follow-Up, grain intake was inversely associated with liver stiffness. Carotenoids in mushrooms can suppress hepatic stearoyl CoA desaturase-1, an enzyme involved in lipid metabolism. Beta-glucans in oats and barley improve lipid metabolism, with a potential sparing effect on the liver. Minerals such as selenium, zinc, and magnesium have chelating properties. One third of global mortality is attributed to metabolic diseases, such as cardiovascular diseases, diabetes, and chronic kidney diseases. Furthermore, metabolic diseases are increasing across the globe, rendering novel methods of preventing metabolic diseases necessary. Turmeric, mushrooms, onions, and plantains have been used to prevent (or manage) metabolic diseases. Lycopene, present in tomatoes, safeguards the liver and kidneys of rats exposed to high doses of aluminum. Onions and plantains possess high antioxidant capacities. However, patients suffering from chronic liver diseases are recommended to avoid consuming nightshades, such as tomatoes. Phytochemicals such as lycopene and quercetin, combined with vitamin E, appear to protect the kidneys and liver from damage caused by drugs [35-38].

Recommendations for dietary interventions

Dietary interventions aimed at improving overall health and reducing the risk of chronic diseases such as CVD, cancers, and type 2 diabetes have focused mainly on the content of macronutrients and several essential micronutrients but have failed to focus on the interactions between these nutrients, the established health-promoting dietary guidelines for acceptable macronutrient distribution ranges and adequate intake levels and non-nutrient phytochemicals. While it is true that several guidelines and recommendations consider the interplay between nutrients, such as fat, cholesterol, and protein, and a few between nutrients and some phytochemicals, such as fibers and antioxidant vitamins, there is still, to our knowledge, no dietary recommendation or intervention that has had as its primary objective the complex interactions among the established nutrition guidelines, phytochemicals from different food groups, and several health-promotion and disease-prevention outcomes.

CONCLUSION

The investigation underscores the pivotal role of phytochemicals and nutrients from whole plant-based foods in maintaining metabolic health and preventing chronic diseases. Through their synergistic interactions and multifaceted mechanisms of action, these compounds demonstrate significant potential in modulating metabolic markers and reducing disease risk. Embracing dietary patterns rich in phytochemicals and nutrients emerges as a promising strategy for enhancing overall health and well-being. Moving forward, it is imperative to continue exploring the complex interplay between dietary components and metabolic health to inform evidence-based interventions and public health policies.

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