BETTER DIETS, BETTER HEALTH

Antioxidants and Polyphenols

Briefing Paper 4

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ANTIOXIDANT AND POLYPHENOLS

SUMMARY

Protective foods and diets are intended to protect people and our planet. Food systems are the source of many problems and of their solutions. We have to shift our consumption to more protective foods that are intended to reduce human disease and enhance planetary sustainability. Our intention in this briefing paper is threefold: to explain the roles of antioxidants; to introduce the sources of antioxidants especially as 'protective diets', and; to explain how such diets can protect us from the burden of non-communicable diseases.

Oxygen is essential for us to live. All cells in our body can create energy and process metabolism only if they have enough oxygen. Through the biochemical processes, however, some oxygen becomes a different form, i.e., a free radical. These free radicals, natural by-products of the normal functions of the body, are harmful to our health. Free radicals usually lack an electron of the outer shell, and this makes them unstable enough to quickly search for other stable molecules and steal their electrons for the stability of free radicals. This deprivation of electrons, oxidation, leads to cellular damage. However, our body has a natural defence mechanism against it, i.e., the antioxidant defence. Antioxidants fight against oxidation by deactivating free radicals through donating their electrons (reduction). This natural duel between free radicals and antioxidants happens every day in our body.

However, free radicals can overwhelm antioxidants once their numbers become excessive. It leads to oxidative stress if the antioxidant defence does not keep up with the growing numbers of free radicals. Depending on where the oxidative stress occurs, it causes a wide range of diseases, including arteriosclerosis, cardiovascular diseases, cerebrovascular accidents, cancers, and ageing. Fortunately, we can deliver reinforcements for the antioxidant defence through our diet. Antioxidants are rich in ACE (Vitamin A, C, and E), minerals, and polyphenols which have been increasingly in the spotlight for their various effects beyond antioxidation. Effective intake of antioxidants varies depending on food; how it is cooked and which part of the food has antioxidants. Synthetic sources are also available but recent studies recommend natural sources. Proactive and balanced consumption of antioxidant-rich foods should be promoted to protect our health.

POLICY PRIORITIES

- Search for effective and nontoxic natural compounds with antioxidative activity, and reduce dependency on synthetic antioxidants which may be dangerous to human health
- Promote diets with rich antioxidant ingredients
- Include antioxidant-rich foods in national Food Based Dietary Guidelines (FBDG)
- Promote such foods in public health and agriculture policies
- Research to identify optimal intake of antioxidants and any risks caused due to excessive intake
- Promote research to identify non-antioxidative effects of polyphenols that are beneficial to our health

This Briefing Paper is the Fourth of a series of papers entitled 'Better Diets, Better Health

BACKGROUND

What we take in has profound effects on our health and communities. Much of what we eat is not good for us or for the planet. We consume many foods that appear to contribute to poor health and increase mortality. Moreover, producing these foods contributes substantially to overuse of pesticides and fertilisers, depletion of water reserves, soil erosion and emissions of greenhouse gases. Unhealthy diet is also one of the greatest risk factors for non-communicable diseases, equivalent to 71% of deaths globally.[1]

Eating is an intimate act: we think about what we are eating several times a day, even superficially. *'You are What you Eat'* is a phrase from the influential 18th century French gastronome, Jean-Anthelme Brillat-Savarin, author of the classic *The Physiology of Taste*.[2] Today it is even more pertinent given that our dietary intake could be unhealthy.

What is the Purpose of this Briefing Paper?

Antioxidants are good for us. In this briefing paper we focus on the roles that antioxidants play in keeping us healthy and demonstrate why antioxidant-rich foods should be considered as protective foods. We begin by describing the generation and behaviour of free radicals and the phenomenon of oxidative stress that results in an extraordinarily wide range of diseases. The duel pits free radicals against antioxidants. Free radicals are implicated in cardiovascular and inflammatory disease, cataract, and cancer. Antioxidants prevent tissue damage by preventing the formation of radicals, scavenging them, or by promoting their decomposition. Polyphenols are not only one of the most important and common antioxidants but also can have non-antioxidant properties.

The Rockefeller Foundation initiative funds our work the objective of which is to counter the aforementioned unhealthy and environmentally damaging trends of diets, in part by shifting food consumption towards diets that protect against disease.[3] Figure 1 outlines the Rockefeller Foundation's *Theory of Change* that

[1] https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

[2] "Tell me what you eat: I will tell you who you are". Quote attributed to Jean Anthelme Brillat-Savarin (1755-1826), French lawyer and politician, well-known for his work as an epicure and gastronome. Wikipedia, The Free Encyclopedia. Available from: https://en.wikipedia.org/wiki/Jean_Anthelme_Brillat-Savarin (Accessed:06.04.20)

[3] Flor, R. 2019. The Rockefeller Foundation. Focusing on "Protective Foods" to Reduce the Global Burden of Disease. Available from: https://www.rockefellerfoundation.org/blog/focusing-protective-foods-reduce-global-burden-disease/ (Accessed 22.04.20)

emphasises the potential role of protective foods in improving human and planetary health.

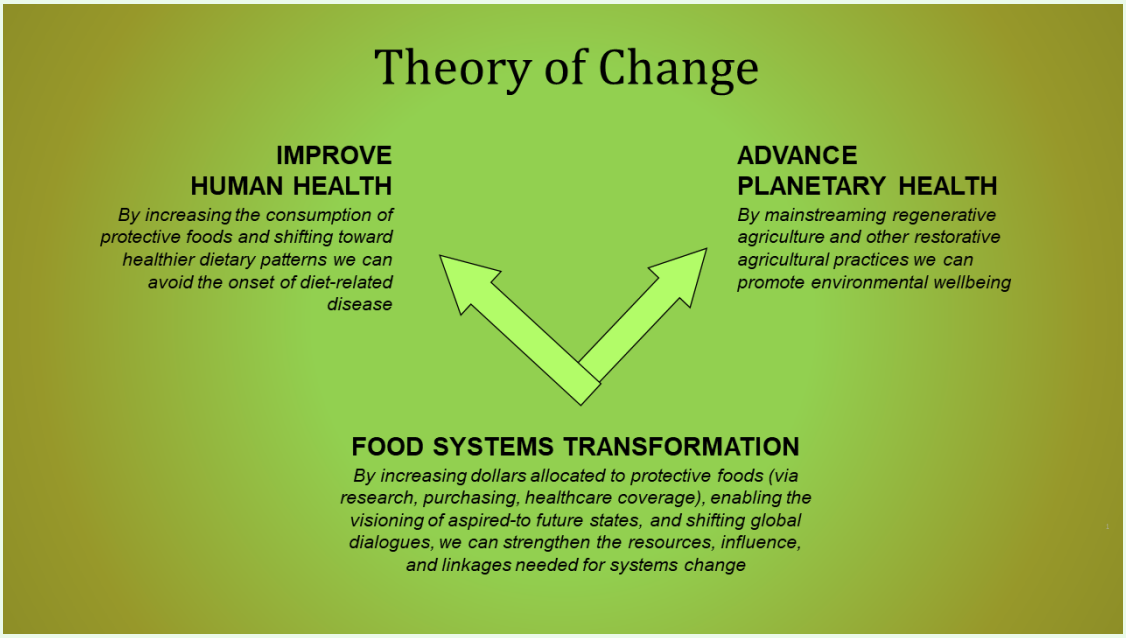

Figure 1: Theory of Change from The Rockefeller Foundation

THE NATURE OF THE DUEL

Human body is carefully designed and built on very delicate yet wonderful balance. There is no doubt that one of the most vital chemicals for the balance and life itself is oxygen (O2) that when taken into our body, it helps to create energy and transform what we ate into nutrients for all cells and organs. It is over the oxygen and cells where "the duel" occurs between two groups: free radicals and antioxidants. Antioxidants are the goodies whereas free radicals are the baddies. Free radicals can act independently but their destructive power can be substantial anywhere in the body. The influence of the destruction is called oxidative stress. Antioxidants can inhibit both the free radicals and the oxidative stress.

In this briefing paper, we would like to tell you what amazing things antioxidants can do for us. But first, we would like to introduce you to the main characters and a situation of the duel: oxygen, free radicals, oxidative stresses, and antioxidants.

Oxygen

In many aspects, oxygen is one of the most important chemicals in our lives. As we studied in our chemistry classes in school, an oxygen molecule (O2) consists of two oxygen atoms (O). An oxygen atom is composed of one atomic nucleus surrounded by two shells/orbitals; inner and outer shells (Figure 2).[4] Inner shell contains two electrons and the outer one has 6 electrons. Electrons are usually stabilised when one electron pairs up with another one, but two out of six electrons of the outer shell do not have an electron to be paired. In order to stabilise, an oxygen atom (O) then searches for another oxygen atom (O) which is also looking for a pair for its own stabilisation. When the two unstable oxygen atoms find each other, they connect to each other by pairing up their two singled out electrons. This

[4] https://www.chegg.com/learn/chemistry/introduction-to-chemistry/covalent-bonding

is how two oxygen atoms (O) become one stable oxygen molecule (O2), the oxygen that we breathe in.

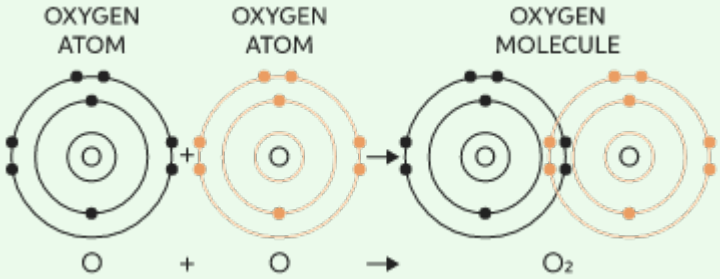

Figure 2: 2 Oxygen Atoms and 1 Oxygen Molecule

Oxygen unites with the iron of haemoglobin. Blood transports that union to all the cells every one of which has hundreds if not thousands of mitochondria. These metabolize oxygen with nutrients such as sugar, fat, and protein to generate adenosine triphosphate (ATP).[5] ATP is an energy for our growth and existence.

Free Radicals

All matter consists of molecules. Molecules are composed of atoms that contain an atomic nucleus and electrons. As already mentioned, molecules are stable if their electrons are paired. But there are also atoms and molecules which contain unpaired electrons. Free radicals refer to these unstable atoms and molecules.

All cells in the human body decompose nutrients to create energy with the oxygen. It is in these ordinary metabolic processes and immune system responses where 2-3% of oxygen becomes unstable through losing electron(s). In other words, this unstable oxygen is a free radical, one of the most significant free radicals in our bodies.[6] Typically, a free radical lacks an electron (Figure 3).[7]

[5] S.E. Cox, Energy Metabolism, Editor(s): Benjamin Caballero, Encyclopedia of Human Nutrition (Third Edition), Academic Press, 2013,

Pages 177-185, https://doi.org/10.1016/B978-0-12-375083-9.00091-X

[6] https://www.verywellhealth.com/information-about-free-radicals-2249103

[7] Anne Marie Helmenstine, Healthvalue Wikimedia Commons

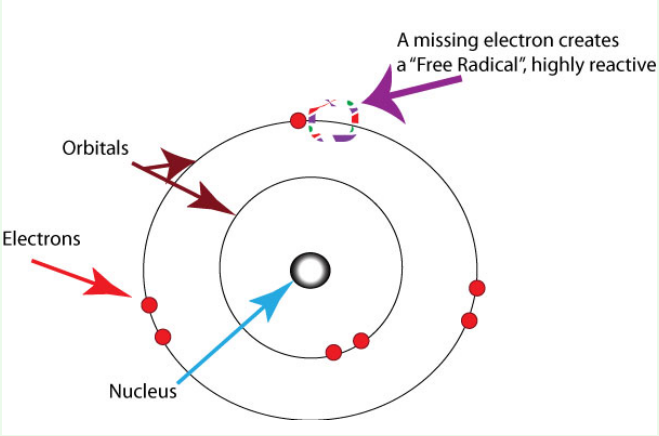

Figure 3: A Free Radical, with a Missing Electron

Free radicals are capable of independent existence but are unstable and highly reactive as their name suggests. In order to stabilise, they steal electrons from other atoms and molecules. This reaction is called oxidation that causes damage to proteins, DNA, carbohydrates, and to lipids.[8] Apart from normal metabolic processes in the human body, free radicals can be also derived from external sources such as X-rays, ozone, cigarette smoking, air pollutants, and industrial chemicals. Excessive production of free radicals results in serious damage and diseases (Figure 4).[9][10]

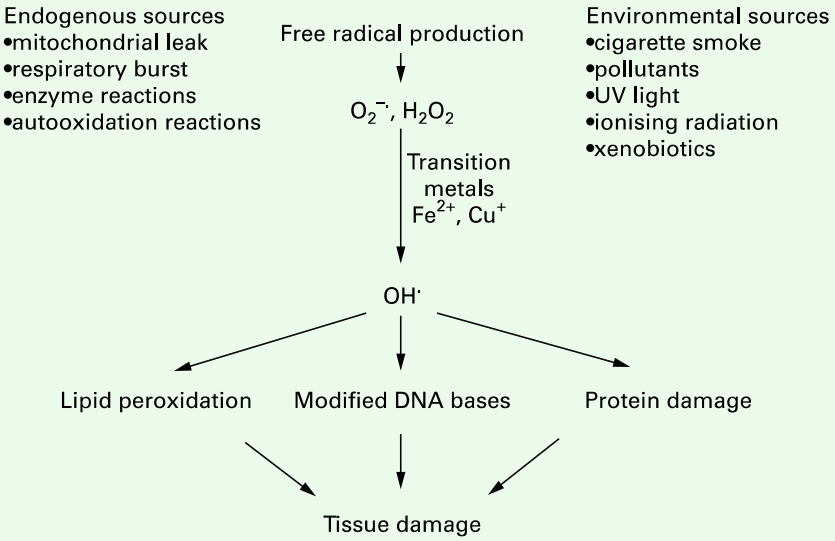

Figure 4: Sources of Free Radicals and Their Damaging Consequences

[8] Lobo, V., Patil, A., Phatac, A. and Chandra, N. 2010 Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacogn Rev.* 4: 118-126

[9] Liou, S. 2011 About free radical damage. Huntington's Outreach Project for Education at Stanford. 29 June 2011

[10] Young, I.S and Woodside, J.V. 2001 Antioxidants in health and disease. J. Clin.Pathol. 54: 176-186

Although endogenous sources can be sources of free radicals as listed in Figure 4, probably the most impactful free radicals enter our body from external sources; from the food we eat, the medicines we take, the air we breathe, and the water we drink.[11] Consumption of fried foods and alcohol, smoking tobacco, inhaling pesticides and air pollutants could be the main external sources of free radicals. Oxidation of cells by free radicals also leads to pathological conditions associated with aging.[12]

Although free radicals are generally regarded as baddies, they are very beneficial in some circumstances. For example, free radicals are generated by the mitochondria, organelles in all or cells producing huge amounts of energy. These free radicals are beneficial in healing wounds. In fact, reactive oxygen species (ROS) that include both free and non-free radicals[13] can heal wounds faster. This is of potential benefit to the elderly and people with diabetes who have chronic issues with wound healing.[14]

Oxidative stress

Oxidative stress arises as a result of an imbalance between production of active oxygen such as free radicals and their antioxidant defences, resulting in damage to the body's cells. Excessive as well as too little exercise, imbalanced diet, smoking, exposure to ultraviolet, radioactivity, air pollution, and chronic inflammation can accelerate oxidative stress.[15]

Through oxidation of lipids and proteins, oxidative stress leads to a range of diseases, including[16]

- inflammatory diseases: arthritis, respiratory diseases;
- ischemic diseases: heart diseases, stroke;

[11] Liou, S. 2011 About free radical damage. Huntington's Outreach Project for Education at Stanford. 29 June 2011

[12] Liquori, I. *et al.* 2018 Oxidative stress, aging, and diseases. *Clin Interv Aging* 13: 757-772

[13] https://www.vmi.pitt.edu/EPR-ROS/index.html

[14] McDonald, K. 2014. Moderate Levels of 'Free Radicals' Found Beneficial to Healing Wounds. UC San Diego News Center; Niethammer, P. 2014 Stress Heals. Developmental Cell *31*, October 13, 2014

[15] Aseervatham, G.S.B., Sivasudha, T., Jeyadevi, R. *et al. 2013* Environmental factors and unhealthy lifestyle influence oxidative stress in humans—an overview. *Environ Sci Pollut Res* 20, 4356–4369 https://doi.org/10.1007/s11356-013-1748-0; Kandola, K., Bowman, A. and Birch-Machin, M.A. 2015, Oxidative stress – a key emerging impact factor in health, ageing, lifestyle and aesthetics. *Int J Cosmet Sci*, 37: 1-8. https://doi.org/10.1111/ics.12287

[16] Lobo, V. *et al* 2010 Free radicals, antioxidants and functional foods: impact on human health. Pharmacogn Rev. 2010 4: 118–126.

- acquired immunodeficiency, gastric ulcers, and hypertension;
- neurological disorders: Alzheimer's disease, Parkinson's disease;
- alcoholism and smoking-related diseases;
- Short-term oxidative stress may occur in tissues injured by trauma, infection, hit injury, hyperoxia, toxins and excessive exercise.

ANTIOXIDANTS

In practice, 'oxidation' is defined as a chemical reaction involving the loss of electrons and an increase in the oxidative state. This chain reaction of oxidation can be stopped by antioxidants, defined as any molecule that inhibits the oxidation of another molecule. An antioxidant is a molecule stable enough to donate an electron to a free radical and neutralize it (this stabilisation through receiving an electron is called reduction) (Figure 5).[17] Such antioxidants can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged.[18]

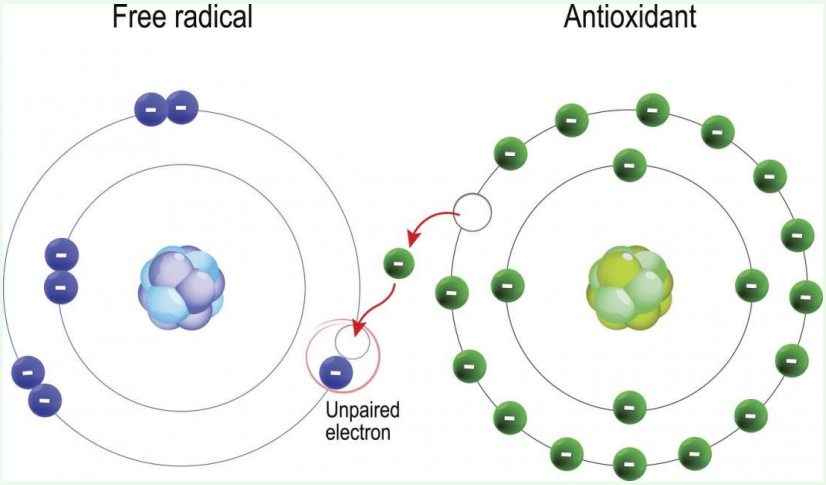

Figure 5: An Antioxidant Donating an Electron to a Free Radical

[17] https://www.medicalnewstoday.com/articles/318652#How-do-free-radicals-damage-the-body

[18] Lobo, et al.

Effects

Antioxidants were originally important in industrial processes. It was the identification of vitamins A, C, and E as antioxidants that revolutionized the field, underlining the importance of antioxidants in biochemistry of living organisms. Today, they are involved in various biological processes such as tissue protection, immunity, health, maintaining homeostasis, aging, growth and development. The beneficial effects for our health include:

1) **Protection against Heart Disease:** Diets high in fruits, vegetables and other foods contain antioxidants that help fight cardiovascular disease.
2) **Protection against Cancer:** Lycopene, rich in tomato, and lutein can prevent cancers of the mouth, pharynx, esophagus, stomach, colon and rectum.
3) **Boosting of Immunity:** Vitamin C is able to reduce the severity of the common cold.
4) **Fight against Aging:** Antioxidants may protect against some of the degenerative effects on the body of age-related diseases that can lead to early death.

Antioxidants can contribute in the reduction of four groups of non-communicable diseases that account for over 80% of all premature death (age range 30 to 69 years). They include cardiovascular diseases, cancers, respiratory diseases, and diabetes.[19]

Sources

Antioxidants can be natural or artificial. Some are produced during normal metabolism. They are enzymes, such as digestive and metabolic enzymes, protecting cells by an interacting network of antioxidant enzymes. Other lighter antioxidants are non-enzymatic antioxidants including ascorbic acid or vitamin C, glutathione, melatonin, vitamin E and uric acid.

Natural Sources

Important antioxidants from dietary sources are vitamin E, vitamin C, and β-carotene. Because the body cannot manufacture them, they have to be acquired externally through dietary intake. Green and yellow vegetables such as paprika,

[19] https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

broccoli, kale, fruits such as kiwi, strawberry, and potato are rich in vitamin C.[20] Tomato, spinach, paprika, broccoli, and citrus fruits are good β-carotene providers.[21] Vitamin E is rich in nuts and seeds such as sesame, almond, peanut, as well as pumpkin and avocado.[22]

Minerals form another group of antioxidant-providers are also available through diets. Seafoods such as salmon, trout, and shellfish such as crab and shrimp are rich in astaxanthin.[23] Polyphenols are the most abundant antioxidants in our diets.[24] In this briefing paper, we discuss polyphenols in next section since their benefits go beyond antioxidation.

Synthetic Sources

Synthetic and natural food antioxidants are used routinely in foods, especially those containing oils and fats to protect food against oxidation. Some synthetic compounds, substances created from chemical processes, have been widely used as antioxidants in the food industry, cosmetics, and therapeutic industry. For example, some representative synthetic antioxidants in the food industry are BHA (E-320), BHT (E-321), TBHQ (E-319), and Propyle Galate (E-310).[25] The primary purpose of these food additives is to delay the deterioration of food due to oxidation. But consumers are showing a preference for natural antioxidants, and the health regulation bodies in many countries also prohibit or limit the use of synthetic ones.

There has been a global trend toward the use of natural substance present in medicinal plants and dietary plants as therapeutic antioxidants, regarding natural antioxidants as a promising alternative for synthetic antioxidant; they are cheaper, highly compatible with dietary intake, and have no harmful effects in the body. It has been reported that there is an inverse relationship between the dietary intake of antioxidant-rich food and the incidence of human diseases.

[20] https://www.hsph.harvard.edu/nutritionsource/antioxidants/

[21] https://www.hsph.harvard.edu/nutritionsource/antioxidants/

[22] https://www.hsph.harvard.edu/nutritionsource/antioxidants/

[23] https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/astaxanthin

[24] Harvard T.H. Chan School of Public. Antioxidants. The Nutrition Source. URL https://www.hsph.harvard.edu/nutritionsource/antioxidants/ (accessed 27.04.2020).

[25] https://www.btsa.com/en/examples-of-natural-and-synthetic-antioxidants/

Recent studies highlight that synthetic antioxidants may be dangerous to human health and have led to a search for effective, nontoxic natural compounds with antioxidative activity. In addition to endogenous antioxidant defence systems, consumption of dietary and plant-derived antioxidants appears to be a suitable alternative. Dietary and other components of plants form a major source of antioxidants.

POLYPHENOLS

Polyphenols are not new compounds, but it is only in the past ten years that their contribution to healthy foods and diets has been recognized. There are several thousand different kinds of polyphenols.[26] They protect the body's tissues against oxidative stress as antioxidants, but as we shall see they play other roles, such as reducing blood pressure and cholesterol and preventing neurogenerative diseases.

The total dietary intake of polyphenols may be as high as 1 g/d, 10 times higher than the intake of vitamin C and 100 times higher than the intakes of vitamin E and carotenoids.[27] Their main dietary sources are fruits and plant-derived beverages.[28] Anthocyanin (prune, blueberry), quercetin (onion, asparagus, lettuce), isoflavone (soybean), resveratrol (red wine), chlorogenic acid (coffee), catechin (green tea), and theaflavin (black tea) are well-known polyphenols found in our diet.[29]

Antioxidant Effects

The following three examples are of reasonably well-established sources of polyphenols as antioxidants:

Grapes

[26] Williamson, G. 2017. The role of polyphenols in modern nutrition. *Nutr Bull* 42, 226–235. https://doi.org/10.1111/nbu.12278

[27] Scalbert, A., Johnson,I.T. and Saltmarsh, M. 2005 Polyohenols; antioxidants and beyond. *The American Journal of Clinical Nutrition*, 8: 215S–217S,

[28] Scalbert, *et al.*

[29] https://academic.oup.com/ajcn/article/79/5/727/4690182

- Consuming foods rich in polyphenols from grapes—including red wine—is known to help reduce the risk of heart disease.[30] One of the grape polyphenols is resveratrol in the skin of red grapes.
- They decrease the oxidation of "bad" cholesterol (low-density lipoprotein cholesterol) that plays a role in the hardening of arteries (the development of atherosclerosis).
- It is yet to be discovered how the benefits occur, but grape polyphenols also reduce blood clotting, abnormal heart rhythms, and blood vessel narrowing.

Green Tea[31]

- Tea has one of the highest contents of polyphenols among common food and beverages, representing 30% of fresh leaf dry weight. In addition to tea, polyphenols are very abundant in cocoa and berries.[32] Of the green, black or Oolong teas, green tea produces the most significant health effect.
- Most important flavonoids in tea are various catechins, especially epigallocatechin gallate (EGCG), that are potent antioxidants. Tea catechins also appear to have anti-obesity and antidiabetic effects.
- Green tea consumption has also been linked to the prevention of many types of cancer and may reduce the risk of chronic diseases.

Olives[33]

- A Mediterranean diet has high consumption of olives. Olive oil is particularly high in antioxidants.
- Hydroxytyrosol is a rich source of polyphenols and is the most powerful antioxidant discovered to date, accounting for most of the beneficial properties of olive products. It absorbs free radicals 15 times higher than green tea and has antioxidant, anti-atherogenic, anti-thrombotic, anti-inflammatory and cardioprotective properties.
- Olive polyphenols may stimulate olive's own antioxidant defense system.

[30] Elsevier. Press Release. Mounting Evidence Shows Health Benefits of Grape Polyphenols (28.10.2008) URL https://www.elsevier.com/about/press-releases/research-and-journals/mounting-evidence-shows-health-benefits-of-grape-polyphenols (accessed 27.04.2020); Leifert, W.R., Abeywardena, M.Y. (2008). Cardioprotective actions of grape polyphenols. Nutr Res 28, 729–737. https://doi.org/10.1016/j.nutres.2008.08.007

[31] Chacko, S.M., Thambi, P.T., Kuttan, R., Nishigaki, I. (2010). Beneficial effects of green tea: A literature review. Chin Med 5, 13. https://doi.org/10.1186/1749-8546-5-13

[32] Catechin - an overview. ScienceDirect Topics. URL: https://www.sciencedirect.com/topics/neuroscience/catechin (accessed 27.04.2020).

[33] Raederstorff, D. (2009) Antioxidant activity of olive polyphenols in humans: A review. Int.J. Vitam. Nutr. Res. 79: 15-165; Richards, K.L. 2019; The most powerful natural anti-oxidant discovered to date-Hydroxytyrosol. Prohealth.com. Mounting evidence shows health benefits of grape polyphenols; Leiferts, W.R. and Abeywardena, M, Y. 2008. Cardioprotective actions of grape polyphenols. Nutrition Research 28:729-737

Beyond Antioxidant Effects

It has become increasingly apparent that the effects of dietary polyphenols go beyond their antioxidant effect:[34]

- Antioxidants may prevent growth of tumours as pro-oxidants.[35]
- The interaction of soy isoflavones with estrogen receptors and their effects on endocrine function.[36]
- Epidemiological, experimental, and clinical studies suggested several beneficial effects from consuming green tea: antioxidant and anti-inflammatory activities, cancer and cardiovascular disease prevention and anti-obesity.[37]
- Long-term consumption of diets rich in polyphenols protects against certain cancers, cardiovascular diseases, type 2 diabetes, osteoporosis, pancreatitis, gastrointestinal problems, lung damage, and neurodegenerative diseases[38]

CONCLUSION

One of the most critical and often overlooked component of our diets is antioxidant rich foods. Improvement of our general health condition through intake of antioxidant rich foods would also alleviate the public health burden. In order to describe the benefits of antioxidants, this paper firstly presented the process as well as the damage of intracorporal oxidation by free radicals. Secondly, how the antioxidant defence mechanism fights against the oxidation was explained. Thirdly, the paper not only introduced different kinds of antioxidants and their sources but

[34] Scalbert, A., Johson, I.T. and Saltmarsh, M. 2005 Polyphenols: antioxidants and beyond. *Am J Clin Nutr 81(suppl):215S–7S.*

[35] Scalbert, Johnson and Saltmarsh, 2005

[36] Scalbert, Johnson and Saltmarsh, 2005

[37] Meydani, M. and Hasan, S.T. 2010 **Dietary Polyphenols and Obesity**

Nutrients 2: 737-751; doi:10.3390/nu2070737

[38] Cory, H. et al. 2018. The Role of Polyphenols in Human Health and Food Systems: A Mini-Review. Front Nutr. 5:87

also the benefits of polyphenols, the most abundant antioxidants in our diets, that have other beneficial properties in addition to antioxidation.

Policy recommendations for inclusion of antioxidant and polyphenol into our diet are laid out at the beginning of the paper. The policy suggestions can be useful both for programs and research for this very relevant and important issue.