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Review

A comprehensive review on role of phytochemicals in human health

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Abstract

Phytochemicals are plant extracts that are widely used due to their ability to provide health benefits and their therapeutic activity against several disorders. They are also called phytonutrients as they are not really the part of our diet but have several positive effects on our health. They are found to decrease the risk factor of cardiovascular disorders and coronary heart disorders. It has also been found that phytochemicals diminish the risk ratio of several types of cancers including breast, colon and skin cancers. This article revolves around taking carotenoids, chlorophyll and fibers as examples of phytonutrients to evaluate their beneficial role in several diseases. These phytochemicals have been found to be associated with antioxidant activity, retinol activity, cell signaling, improvement of glycemic control, protection against high blood pressure, facilitation in defecation and anti-cancerous activity.

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Introduction: Since the beginning of human society, plants and their extracts have always been used as medicine by man. Even today, all dieticians advise people to increase their consumption of natural products derived from plants. These are based on the studied facts that plant-based products like fruits, vegetables, grains etc. provide immunity against many illnesses such as cancer, heart diseases, diabetes mellitus(insulin-dependent) and neurodegeneration.

Phytochemicals, also known as phytonutrients, are considered to be responsible for the above stated effects of the plants in which they are found. They can be literally defined as "plant chemicals". They are the chemicals that are plant-based and are not the essential part of our food but have many positive effects on our health. Innumerable types of phytochemicals have been discovered, yet scientists believe that many more are still hidden in the complexities of nature. Although phytochemicals have been divided into three broad groups, namely phenolic acids, flavonoids and lignans, and these groups are considered homogeneous, yet every compound in these groups is metabolized differently and may have different effects. Phytochemicals are of different types including carotenoids, curcumin, chlorophyll and chlorophyllin, flavonoids, indole-3-carbinol, isothiocyanates, garlic derived compounds, lignans, fiber, phytosterols, soy isoflavones, resveratrol etc.

Role of Phytochemicals in Human Health: The research on the role of phytochemicals in good health is limited. It is not, yet, known the exact cause of the positive effects of phytochemical containing products in food. In other words, it is not yet known if these phytochemicals work independently, if they work together with one another or if they work with other compounds found in the matrix of food in which they are present. But it is a certified fact that phytochemicals rich diet can prevent from many diseases. Some important diseases and the roles of phytochemicals in their prevention are as under:

Cardiovascular Diseases: Enough evidence is present to show that phytochemical rich diet can prevent from heart diseases. Studies suggest that every portion of daily consumption of vegetables and fruits decreases the risk of coronary heart disease. Furthermore, many researches have been conducted on soy, tea leaves and cocoa for their effects on cardiovascular system and each of them is found to decrease the risk for cardiovascular disorders. These foods help against high blood pressure, inflammation and are involved in decreasing LDL oxidation, dilating blood vessels etc. In addition, other phytochemicals also help in lowering the risk of heart diseases [1,2].

Tumor: It is observed that phytochemicals decrease the risk of various types of cancers such as lung, colon, skin or breast cancer. It is shown that whole grains reduce the risk of colorectal cancer. Similarly, many phytochemicals are linked with the reduction in the risk of cancer. These include cruciferous vegetables, isothiocyanates, isoflavones and many more.

Insulin Dependent Diabetes: Phytochemicals are observed to reduce the risk of diabetes type-2 by lowering inflammation, increasing the sensitivity of insulin and most importantly, decreasing the chances of weight gain. These inhibit carbohydrate digestion, stimulate insulin production and secretion from pancreas, activate insulin receptors etc. Almost all types of phytochemicals are found to have the diabetes reducing effect on patients.

Neurodegeneration: Certain neurodegenerative disorders can be prevented using phytochemicals in food. These include Alzheimer's disease, Parkinson's disease etc. It is found out that phytochemicals, such as capsaicin, curcumin, flavonoids and resveratrol, have neuroprotective effect. These phytochemicals increase inter-neuron connections and increase the blood supply to the brain. This protects the neurons and increases the functioning of neurons [3,4].

Important Phytochemicals and their Uses: As stated above, phytochemicals are of various types. Many are present in plain-sight in front of us in our daily lives. For example, carotenoids, a group of important phytochemicals, are present in many fruits and vegetables like carrots, broccoli, mangoes, oranges etc. Following is the detailed explanation of some of the phytochemicals found in our daily routine foods and their roles in human health.

Carotenoids: Carotenoids are natural phytochemicals present in plants, algae, and chlorophyll containing bacteria. These are colored pigments and contain more than 750 compounds. Carotenoids give orange, red and yellow colors to many plants, vegetables and fruits. Structurally, they consist of a long unsaturated polymer chain and two end groups at the ends. Carotenoids consist of two sub-groups; xanthophylls and carotenes. Carotenes are long chain organic compounds. Examples of carotenes are α -carotene, Q -carotene, -carotene, lycopene. 50 kinds of carotenes have been discovered in natural compounds. Meanwhile, xanthophylls contain oxygen atoms in their chains in the form of hydroxy, aldehyde, ketonic, carboxyl, epoxide and furan oxide groups. Some are present in the form of fatty acid esters, glycosides, sulphates and protein complex[5]. The most commonly found carotenoids in our diet are α -carotene, Q -carotene, Q - cryptoxanthin, lutein, zeaxanthin and lycopene. Carotenoids are divided into two types:

(i) Provitamin A: These carotenoids are split into retinols in the body.

(ii) Non-provitamin A: These carotenoids are not fragmented into retinols in the body [7].

Metabolism: In the enterocytes, retinol forming carotenoids are cleaved by either of two enzymes, Q - carotene oxygenase-1 (BCO1) or Q-carotene oxygenase-2 (BCO2). BCO1 breaks the vitamin A producing carotenoids and retinal is formed as a result. This can be, then, converted into retinols or retinoic acids which are different forms of vitamin A. BCO2 breaks carotenes into β-apocarotenal. It is then acted upon by BCO1 to form retinal. BCO2 has greater affinity for non-provitamin A carotenoids but not for pro-vitamin A ones. The inverse holds true for BCO1 [6]. When BCO2 acts upon the non-provitamin A carotenoids, it breaks lutein and zeaxanthin into apocarotenals and lycopene into apolycopenals.

Roles in Human Health: Carotenoids have many important functions in the maintenance of the human health. These roles are primarily determined by their structural and chemical properties.

Provitamin A role: Vitamin A is an important component of our nutrition. It plays fundamental roles in our immune system, normal growth and development and eyesight. The retinol forming carotenoids are involved in this function. These carotenoids have to be converted into retinols which depend upon many factors[7] .

Retinol activity equivalent (RAE) is currently used as a standard for measuring vitamin A activity. It has been observed that the dietary preformed vitamin A is the most efficient as it has 1:1 RAE ratio, which means that 1μg of dietary preformed vitamin A produces 1μg of retinol. The RAE ratio order then decreases from supplemental β -carotene to dietary β -carotene to dietary α-carotene to dietary β-cryptoxanthin[8].

(i) Antioxidant Role: The action of phytochemicals as antioxidants is quite complex in humans. It is proposed that the oxidation of fats in liver could be inhibited by phytochemicals under certain conditions, which would deactivate the singlet oxygen species produced in this process [9]. Certain recent studies showed that carotenoids are involved in the upregulation of anti-oxidant activity. For example, lycopene is involved in diluting the TNF α induced oxidative stress in the RPE (Retinal Pigment Epithelial) cells by increasing the level of phase II detoxification enzymes (including GCL, GSTs, NQO-1, HO-1) via stimulation of Nrf2 pathway. In addition, it was observed that lycopene triggers Nrf2 mediated antioxidant mechanism in many types of cells [10-14].

(ii) Blue Light Filtering: Carotenoids have a structural significance in filtering blue light. The conjugating double bonds enable the carotenoids to absorb visible light. This property comes in effect in the eye, where the non-provitamin A carotenoids i.e. meso-zeaxanthin, lutein and zeaxanthin are involved in the absorption of blue light. These carotenoids are present in the macular region of the eye. It is shown that zeaxanthin and lutein can protect against age mediated ocular disorders by protecting against oxidative damage of the eye. Lutein and zeaxanthin can enhance the contrast sensitivity of the eye and can protect against eye fatigue in young people. Lutein has also been proposed to stimulate the neuronal signaling efficiency of the eye, thereby enhancing eye functioning [11,15,16].

(iii) Cell signaling: Carotenoids are found to enhance cell-to-cell signaling. They play a key role in the intercellular communication [17].

(iv) Role in Immune System: For standard immune functioning, vitamin A is important. Intake of β -carotene causes improvement of certain biomarkers of the immune system [18].

(v) Cancer: Certain researches have been done in regard of the effects of carotenoids in reducing the risks of cancer but more work has to be done. It is carried out by extensive studies and researches that the risks of lung, prostate, mouth, pharyngeal, laryngeal, breast and colorectal cancers can be significantly dropped by the intake of certain carotenoids. For example, β-carotene has been found to be involved in the reduction of the risks of lung cancer [19]. Similarly, lycopene is shown to be promising in prostate cancer. Studies showed that people with high intake of tomatoes or dietary lycopene had 11-19% low risk of developing prostate cancer. Likewise, β-carotene was found to be effective against breast cancer and colorectal cancer [20].

(vi) Cardiovascular Diseases: As carotenoids are non-polar, they travel in lipoproteins in the body, along with other fats. Studies show that high blood carotenoid concentrations are related to the reduction in the measure of the width of the arteries and have a positive effect on the function of endothelial cells. Similarly, a recent study showed that carotenoids reduce the blood concentration of cardiovascular risk factors (total homocysteine and CRP) [21-23]. A recent study reports that high lutein blood concentration is related to low risk of coronary diseases and strokes [22,24].

Chlorophylls and metallo-chlorophylls: In plants and photosynthetic protists (algae), a green color pigment is present known as chlorophyll. It is an important component of the process of photosynthesis, as it traps light energy in the process. Chlorophyll consists of four heterocyclic pyrrole subunits which collectively makes a porphyrin ring with a magnesium ion in its center. The two naturally occurring types of chlorophyll are chlorophyll A and chlorophyll B. Both have a long hydrophobic hydrocarbon chain, called phytol tail. The only difference is the substitution of an aldehyde group in chlorophyll b with a methyl group in chlorophyll a, in the porphyrin ring. These comprise almost 99% of the chlorophyll species in plants. Some photosynthetic species have small amounts of chlorophyll c. Unlike chlorophylls A and B, it does not have a phytol tail. Metallo-chlorophylls differ from naturally occurring chlorophyll due to the presence of iron, copper or zinc instead of magnesium in the porphyrin ring [25]. These are chemically synthesized in industries. The most common type of metallo-chlorophyll is sodium copper chlorophyllin (SCC). It is derived from chlorophyll and consists of a partially natural mixture of sodium copper salts. The phytol tail is lost in its synthesis due to which it is water soluble. The most common commercial SCC compound are trisodium copper chlorin e6 and disodium copper chlorin.

Roles in Human Health: Chlorophylls and metallo-chlorophylls are involved in many ways in enhancing the human health. These are following:

(i) Formation of Coordination compounds: The absorption of many carcinogens in GIT such as polyaromatic hydrocarbons, AFB1(aflatoxin-B1) and heterocyclic amines in food is observed to be decreased by the intake of chlorophyll and its derivatives (SCC) due to the tendency of chlorophyllin to form complexes with these carcinogens.

(ii) Antioxidant Effects: Although the antioxidant effect of chlorophyll and metallo-chlorophyll is not clear in in-vivo conditions in humans, the oxidative damages of radiations and carcinogens is found to be decreased by the intake of SCC compounds in animals [26-32].

(iii) Detoxification of Carcinogens: Cancer development requires activation of procarcinogens into active carcinogens. Cytochrome P450 enzymes are required for this process. Certain studies suggest that SCC can inhibit the cytochrome P450 enzymes as it inhibits all the activities of it. In addition, chlorophyll has been found to form complexes with carcinogens. The most notable of these carcinogens are IQ, Trp- P-2, aflatoxinB1and benzo[a]pyrene. Similarly, SCC are found out to be involved in promoting the activity of phase II quinone reductase, which is involved in the excretion of toxic chemicals and carcinogens from the body. An experiment showed that CYP1A1 and CYP1B1 was strongly induced by the introduction of BP (benzo[a]pyrene; a strong pro-carcinogen), while the introduction of chlorophyllin before inducting BP gave a sharp drop in the concentrations of CYP1A1 and CYP1B1. This was followed by another experiment in which the induction of BPdG adducts was examined with the introduction of only BP and then BP with chlorophyllin. The introduction of chlorophyllin reduced the induction of BPdG adducts. This showed that chlorophyllin has the potential of being a pretty good chemoprotective agent [27,33–35].

(iv) Therapeutic Activity: The effect of SCC on the human colon cancer cells was reported in a study. It was reported that chlorophyllin (CHL), introduced to tumorous cells in their synthesis stages of cell cycles, is involved in the downregulation of p21, p53, and some G1/S checkpoint controls. It was shown that CHL treatment resulted in the reduction of the ribonucleotide reductase enzyme in cancer cells, which is essential for DNA repair and synthesis. This effect is still to be examined in in vivo conditions but it has potential of being effective as a cancer therapeutic agent. Additionally, chlorophyll activities have been found to produce therapeutic effect via various pathways [36].

(v) Metal Absorption: The metal absorption role of chlorophyll is attributed to its porphyrin ring. The iron porphyrin compounds are readily assimilated than non-heme bound iron. Due to this, according to an in vitro study, iron chlorophyllin has been observed to be an equal potent source of delivering iron to intestinal Caco-2 cells as heme is. The commonly used supplemental form of iron used for this purpose is FeSO4. Sodium iron chlorophyllin has been observed to be better than it in transporting bioavailable iron to the intestinal cells [37]. Validation of this role is still to be done in humans but scientists are hopeful that this mechanism will be much efficient in in vivo conditions.

(vi) Aflatoxin Liver Cancer: Aflatoxin-B1 is a carcinogen which affects the liver and causes hepatocellular carcinoma. It is converted into aflatoxin-8,9-epoxide in the liver which causes the DNA damage and mutations. It has been observed that CHL is capable of reducing the urine level of a hepatocellular carcinoma biomarker, AFB1-N7-Guanine. A trial showed that people taking SCC had 55% lower urine AFB1-N7-guanine levels than those not taking SCC [38].

Fiber

According to the National Academy of Medicine, fibers are classified into two categories; dietary fiber and functional fiber. These two categories collectively form total fiber. According to the National Academy of Medicine, "Dietary fiber is the non-digestible carbohydrates that are intrinsic and intact in plants." The other category, functional fiber, is defined as "isolated, nondigestible carbohydrates that have beneficial physiological effects in humans." The functional fiber can be isolated from plants or can be synthesized artificially. Chemically, they contain the β -glycosidic linkages which cannot be hydrolyzed by human hydrolytic enzymes. Some examples of dietary fibers include hemicelluloses, cellulose, gum, pectins, inulin, lignin, oligofructose, resistant starch, and Q-glucans. Examples of functional fibers are isolated or extracted forms of dietary fibers, chitin, polydextrose and polyols, fructo-oligosaccharides, galacto-oligosaccharides, psyllium, resistant dextrin. In addition of the above stated categories, another classification system is used for fibers. This classification depends upon their physiochemical properties. Under this system, fibers are classified as soluble, fermentable and gel forming fibers, soluble, fermentable and non- viscous fibers, soluble, non- fermentable and viscous fibers, and insoluble, non-fermentable fibers.

i. Soluble, fermentable and gel forming fibers: These fibers are dissolved in water and form gels in it. These are metabolized by bacteria of the gut into SCFAs (short chain fatty acids) and gases. These fatty acids, mostly butyrate, are the source of energy for many of the intestinal cells. These fibers are also called pre-biotic fibers. They aid in the maintenance of blood glucose concentration and lessen the blood cholesterol level. Examples include pectins, and glucomannan.

ii. Soluble, viscous, nonfermented fibers: These are water soluble and gel forming fibers. They are used for controlling glycemic control and in lowering the blood cholesterol concentration. As these fibers are nonfermentable, they form viscous gels in the large intestine and help in stool-normalizing role of the intestine. Examples include psyllium.

iii. Soluble, non-viscous, fermentable fibers: These can be easily dissolved in water. They are fermentable and so, have no laxative effect. They have no prominent health benefits. An in vitro study shows that inulin can elevate the levels of gut bacteria while suppressing the reproduction of disease-causing bacteria. Examples include wheat dextrin, inulin, polydextrose etc.

iv. Insoluble, nonfermented fibers: These are insoluble in water and nonfermentable fibers. A laxative effect is produced by large particles of these fibers as they trigger the walls of large intestine to release water and mucus which makes the stool soft by increasing the water contents of the stool. The small fiber particles produce constipating effect by increasing the dry stool mass.

Examples include wheat bran, cellulose and lignin.

Roles in Human Health: Fibers play several roles in human health. These are as follows:

(i) Lowering Serum Cholesterol: Most viscous fibers are found out to have blood lipid abnormality improving capabilities. These include renal illnesses, dyslipidemia, hypothyroidism, and obesity. Viscous fibers are found to be associated with decrease in the total and LDL cholesterol level [39]. Another study shows that increased intake of psyllium and statin is related with significant increase in LDL cholesterol level reduction than with the intake of statin only [40]. It has also been found that the ability of soluble fibers to diminish cholesterol levels is associated to its viscosity and that the reduction in the viscosity of these fibers lead to reduction in their cholesterol lowering ability. The mechanism of this process has been studied. It has been found out that the viscous fibers in the food trap the bile salts and prevent them to be absorbed in the ileum. This facilitates their elimination with the stool [39].

(ii) Improving Glycemic Control: It has been found in several studies that fibers are associated with the increased glycemic control. This capability of fibers is also linked with their viscosity. Studies have shown that non-viscous fibers have no effect on blood glucose concentration. On the other hand, viscous fibers are found to have glycemic control effect through many studies. A study in 2015 showed that psyllium is related to decrease in postprandial glucose concentration in insulin dependent diabetics and also in euglycemic people. Postcibal blood insulin levels are found to be dropped in the presence of these fibers in people except insulin dependent diabetics [41].

The mechanism of action of fibers in this role involves the ability of fiber to increase the chyme viscosity. This decreases the breakdown of high molecular weighted compounds and promotes glucose absorption in the entire small intestine rather than in its first part only. The absorption in the latter parts of the small intestine has been found to lower enteric emptying and bowel transit which reduces hunger and food intake [39]. GLP-1(glycogen-like peptide 1) is produced as a result of the effect of fibers on the absorption of sugars, which further stimulates the production of insulin in pancreas and adjusts the food uptake at the CNS level [42].

(iii) Effect against HBP (High Blood Pressure): Studies show that soluble, viscous fibers are involved in the reduction of systolic and diastolic pressure. It has been observed that soluble viscous fiber (namely β-glucan, guar gum, konjac glucomannan, pectin and psyllium) intake in normotensive or hypertensive individuals resulted in 0.39mmHg drop in diastolic and 1.59mmHg drop in systolic pressure. Extensive studies suggest that among all these fibers, psyllium is responsible for the reduction in systolic pressure [43]. The mechanism of action for this effect is unclear but it may be related to the serum cholesterol level lowering and glycemic controlling roles of soluble, viscous fibers.

(iv) Facilitating Defecation: Fibers facilitate in stool elimination. This is best examined through the increased fecal output and increased water content in stool. This function is best achieved through the two mechanisms:(A) Large particles of insoluble fibers are involved in increasing the water content of stool. This is because these fibers irritate the mucosa lining of large intestine and triggers the release of water and mucus, resulting in the laxative effect. These fibers include cellulose and wheat bran. (B) The dehydration effect in colon is opposed by the viscous, soluble fibers [39]. Due to these factors, the fibers that are nonfermentable have the potential laxative effect.

(v) Cardiovascular Diseases: Fibers are found to have positive impacts on the cardiovascular diseases. It has been recognized that the risk level of coronary heart diseases (CHD) and cardiovascular diseases (CVD) is diminished by the intake of diet rich in fibers. The most recent study showed 7% lower chance of CHD and 17% lower chance of CVD [44]. Several subgroup analyses shows that soluble fiber containing foods such as cereal or fruits are closely related to decrease in the risks of CHD. The biochemistry of the cardiovascular diseases risk is mostly linked with the cholesterol lowering effects of the soluble and viscous fibers. In addition, some other mechanisms may be related to this effect. A study shows the negative effect of total fiber intake on CVD and CDH respectively[45].

(vi) Type 2 Diabetes Mellitus: Fibers play an important role against type 2 mellitus due to their glycemic control ability. It has been observed in several studies that total fiber intake is associated with a significant drop in the risk ratio of insulin dependent diabetes mellites. More studies have shown that the soluble, viscous fibers are responsible for this effect.

The reason of the glucose concentration controlling of viscous fibers has been associated with its viscosity. In addition, some other compounds, such as magnesium, in the cereal are involved in improving the glycemic control in glucose intolerant people [46].

(vii) Cancer: It has been found that fibers have certain effects on cancer. Several cohort studies have been done in this regard and a recent study suggests that the more fiber intake is associated with decrease in the colorectal, breast and liver cancers. However, these fibers have not been observed to have any influence on other kinds of cancer such as prostate, endometrial, biliary tract, kidney or bladder. Other studies in this regard suggest that cereal fibers are linked with the decrease in the risk of colorectal, stomach and liver cancers while vegetable fibers are associated with the decrease in the risk of breast cancer [47,48].

Colorectal Cancer: Many mechanisms of action for the effect of fibers on colorectal cancer have been proposed. According to one mechanism, the insoluble fibers in the diet sweep away the carcinogens quickly through the intestine before they can affect the colon cells. Meanwhile, the soluble fibers in the food are metabolized by the microbiota of the gut into short chain fatty acids (SCFAs), mainly butyrate. Butyrate acts as one of the energy sources of the colon cells. The normal colon cells metabolize butyrate in their mitochondria. The colon consists of several ditches called colonic crypts. The cells in the base of these crypts perform the above function as they face low-moderate concentrations of butyrate. The cells on the surface face high concentrations of butyrate, which are too much for the colonocytes to metabolize. Thus, butyrate molecules enter their nuclei and acts as histone deacetylase (HDAC) inhibitor. This inhibits cell proliferation and induces apoptosis and the cells are exfoliated into the lumen. This mechanism occurs in the cancerous cells too and is more effective due to the Warburg effect of the cancer cells in which the cells prefer glucose over butyrate as the energy source. Due to this, even moderate concentrations of butyrate have the same effect as that of high concentrations i.e., inhibition of proliferation and induction of apoptosis [49]. Secondly, certain in vitro studies show the positive effect of inulin on the growth of "good" bacteria and negative effect on the growth of disease causing bacteria. The imbalance of gut bacteria, known as dysbiosis, is linked with many diseases which also include colorectal cancer [50]. Thirdly, the gut microbiota converts soluble fibers into acetate, propionate and butyrate. These SCFAs are involved in anti-inflammatory and anti-carcinogenic actions. Briefly, the SCFAs produced from dietary fibers by the gut bacteria induce the production of IL- 10 and retinoic acids in the dendritic cells, which stimulate the conversion of naïve T cells into Treg cells and inhibit the production of Th17 cells. SCFAs activate GPR43 which cause the proliferation of Treg cells. These cells are known to have colonic anti-inflammatory and anti-carcinogenic effects. On the other hand, Th17 cells are known to cause inflammation and promote carcinogenesis in colon. In addition, the GPR109A receptor is involved in the transcription of IL-18 which is matured from its pro-peptide by the activation of NLRP3 inflammasome by the $K+$ efflux, indued by the signaling of GPR43. The activation of GPR43 by the SCFAs also inhibits chemotaxis in neutrophils through the downregulation of CXCR2 receptor in them. Additionally, the activation of GPR109A causes the inhibition of the NF-κB activation in the epithelial cells of colon [51,52].

Breast Cancer: Recent studies show 7-9% decrease in the breast cancer risk with increased dietary fiber intake [53]. It has been shown that prolonged estrogen exposure is one of the causes of breast cancer. Low lipid and high fiber diet results in drop of blood estrogen levels by pacing up the estrogen metabolism rate and its excretion from the body.

Conclusion:

In a nutshell, phytochemicals are one of the most important constituents of our nutrition. From the above stated details, it is clear that they are involved in numerous mechanisms and have numerous roles in the good health of the human body. Generally speaking, people taking phytochemical rich diets are less likely to be affected by diseases or other conditions than those which consume low or no phytochemicals in their diet. The most noticeable among these conditions or diseases are cardiovascular diseases and cancer. Some of the prominent and common roles of phytochemicals in this regard are as anti-oxidant, as anti-carcinogenic and the reduction of risks of cardiovascular diseases.

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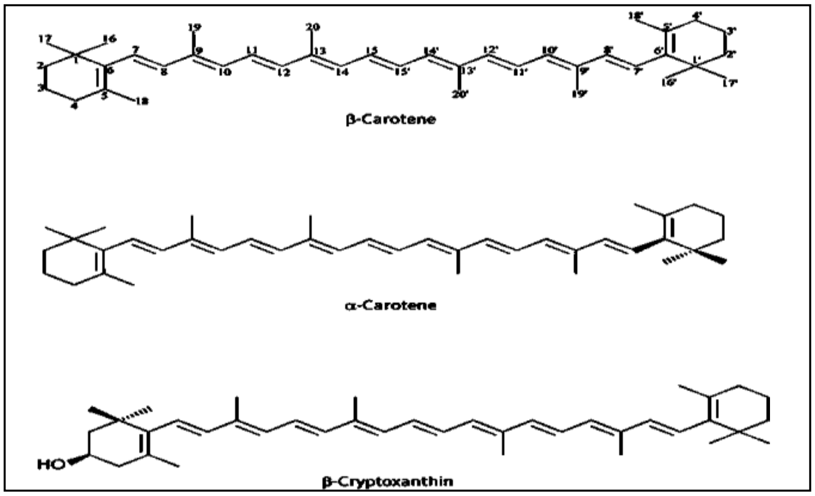


Figure 1: Pro-vitamin A carotenoids (trans chemical structures) [8]

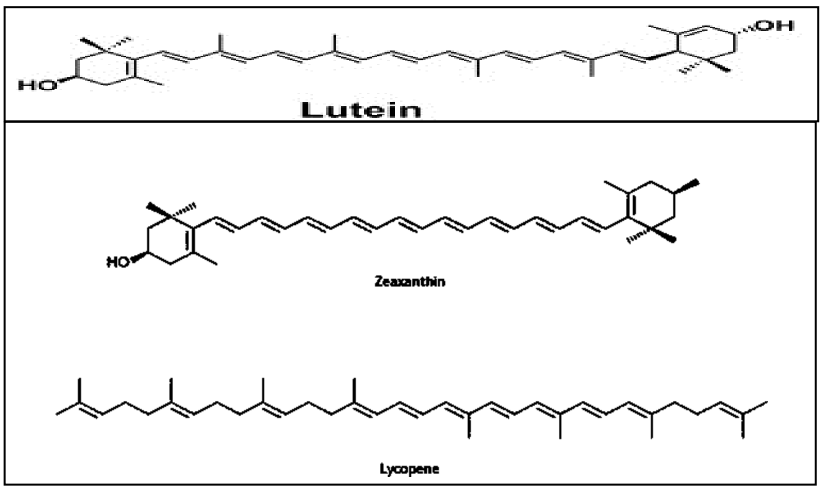
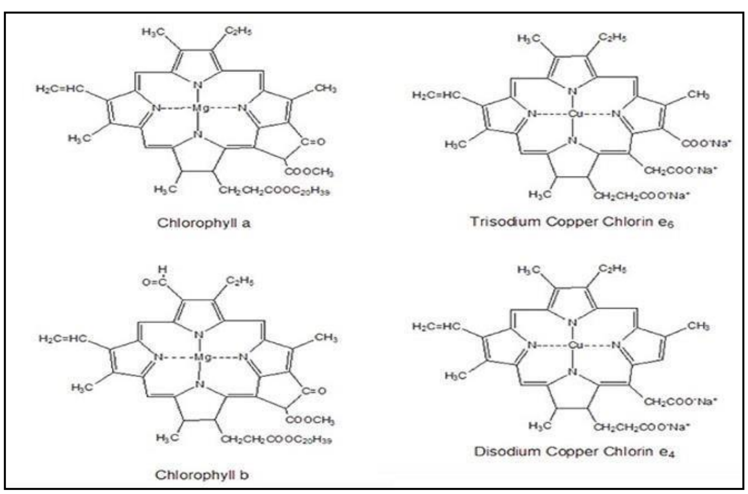


Figure 2: Non-provitamin A Carotenoids (trans chemical structures)[8]



***F*igure 3**: Structures of Chlorophyll a, Chlorophyll b and two commonly found SCC compounds

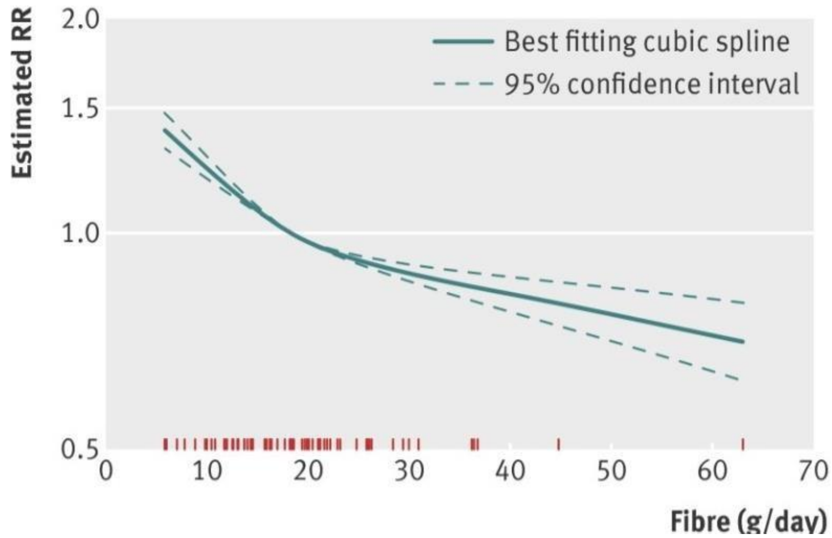


Figure 4: Inverse effect of increase fiber intake on CDH risk ratio. RR=risk ratio

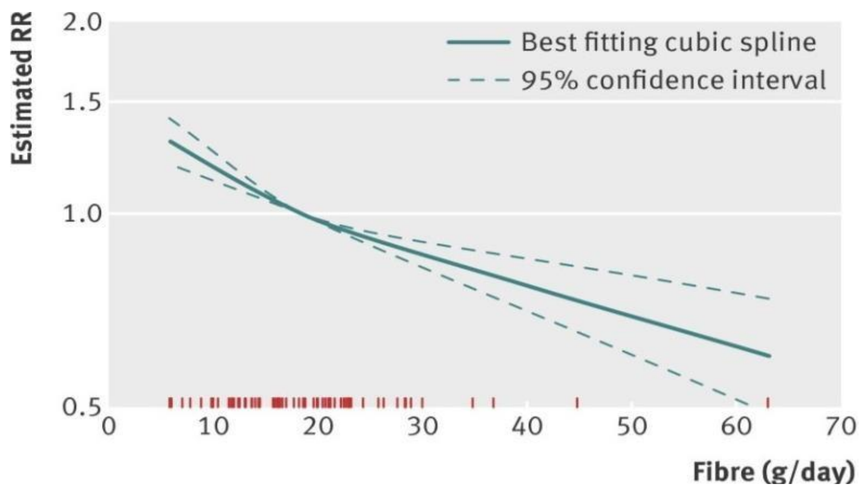


Figure 5: Inverse effect of increased fiber intake on CVD risk ratio. RR=riskratio

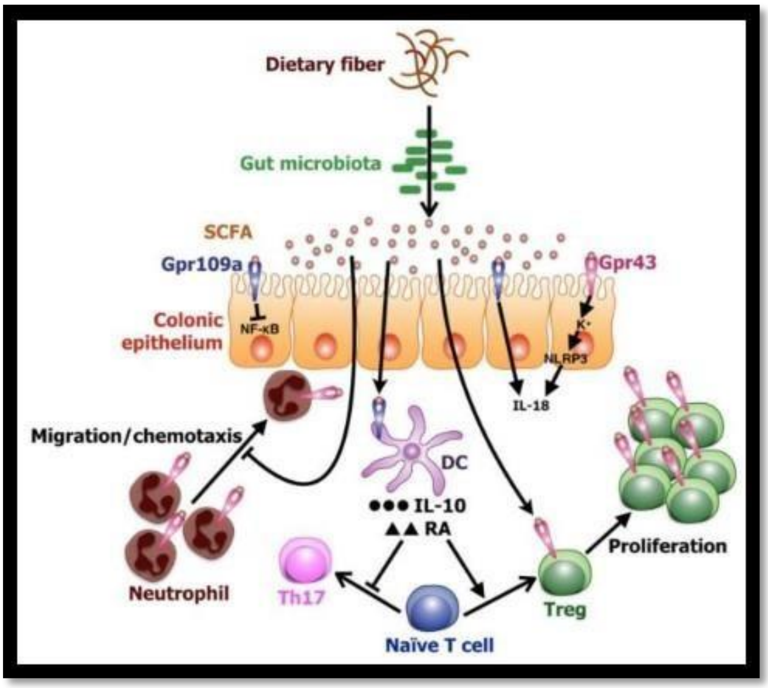


Figure 6: A simplified model showing regulation of gut homeostasis bySCFA receptors

Table 1: RAE ratios for Performed and Pro-formed vitamin A phytochemicals

Consumption	Weightage of Retinol formed	RAE Proportion
1µg of performed vitamin A	1µg	1:1
2µg of supplemental Q-carotene	1µg	2:1
12µg of dietary Q-carotene	1µg	12:1
24µg of *a*-carotene	1µg	24:1
24µg of Q-cryptoxanthin	1µg	24:1