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Review Article

Flavonoids as Antioxidants

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Abstract:

The oxidant reactions of free radicals and molecules with unpaired electrons are thought to contribute to many health problems [1]. Antioxidants restrict the deleterious effects of oxidative stress. These effects can be direct (i.e., eliminating certain free radicals) or indirect (i.e., preventing radical formation). The body produces certain endogenous antioxidants (i.e., enzymes), which can be consumed in the diet. Some dietary antioxidants such as vitamin E are essential nutrients (the body cannot function normally without them). The diet also contains other components that are capable of antioxidant action. These belong to a class of food components known as phytochemicals. These compounds, such as flavonoids, are not required parts of the diet but may confer health benefits such as antioxidant action [2]. It might be said that one can live without phytochemicals, but one might live better with them.

If phytochemicals exert antioxidant actions in humans, the body's antioxidant capacity should diminish with a low-phytochemical diet. To a limited degree, this idea has been tested in a study conducted in our laboratory.[3] ~Patients undergoing renal dialysis consumed one of three generified liquid formulas as the sole nutrition source for 3 weeks. Each formula contained essential nutrients in amounts generally considered adequate but did not contain major sources of phytochemicals. Nearly all subjects (12 = 20 for each of the three formulas) showed depressed plasma total antioxidant status (TAS) values. The decrease in TAS values could not be attributed to three major factors: vitamin E, vitamin C, or uric acid. p-Carotene was not a factor.

Keywords: flavonoids; polyphenols; quercetin; anti-oxidative neuro protective

Introduction

Flavonoids are a major class of phytochemicals in plants.[4] ~ Many flavonoid compounds, which are a family of polyphenols, may exert antioxidant effects in humans and are found in a variety of foods of plant origin. There is also the potential to use such compounds as pharmacological agents, an idea that has already been tested to a limited degree, both for naturally occurring Nanovoids and synthetic compounds. [5-6]" Health-related research on flavonoids is not new, but widespread research on the biological actions of flavonoids has accelerated only recently. A personal note c can be mentioned. alongside those lines. In 1983, I coauthored a paper on the interactions between a copper enzyme and a flavonoid in the catechin.[7] ^ At that point, numerous researchers discouraged me from pursuing addition paintings on flavonoids because "there is a little hobby in these compounds." certainly, this past mindset can be shown by a Medline search of catechin for 1983. The best 8 other papers are determined. In the evaluation, a comparable Medline looked for catechin in 1998 famous 83 papers. At gift, however, the realistic implications for flavonoids in human fitness are sketchy. However, the evidence that certain flavonoids exert health-promoting antioxidant effects in human beings is growing at a rapid pace. This study provides a brief review of the feasible mechanisms that might be related to flavonoid antioxidant moves, summarizes some of the evidence that antioxidant moves arise in humans (including evidence that entails lipoprotein oxidation), discusses evidence for the operation of specific antioxidant mechanisms, and notes the priority of the possible pro-oxidant effects of flavonoids. Many consultant references are cited, but apologies are issued to several authors who are not cited right here; however, they have contributed papers on flavonoids as antioxidants.

Chronic Catechin Feeding Effects on Plasma TAS in Rats

Treatment	TAS (mmoles/l)
Control	1.5 ± 0.3
Catechin	3.5 ± 0.3

Note: Rats were fed a semipurified AIN diet and given tap water either with or without dissolved catechin (2.1 g/l) for 45 days.

Possible Antioxidant Mechanisms of Flavonoids

Often, the antioxidant effects of flavonoids are conceived only in terms of a single biochemical action, that is, direct reactions with radicals. These direct reactions produce so-called scavenging of free radicals, [8-11] where the unpaired electron of a radical becomes paired without ultimately generating another radical.' However, the potential antioxidant actions of flavonoids must be considered multiple for two reasons. First, as listed in Table 8.1, there are at least six different possible antioxidant mechanisms for flavonoids. Second, the free radical-scavenging effects of flavonoids are not a single biochemical action.

Although Table 8.1 lists direct radical scavenging as a single mechanism, this action could involve more than one type of reaction within the oxidant process. Cook and Sammat [2] provided an example of this oxidant process given by Cook and Sammat {2}. They state that there are three different stages of radical-mediated oxidation of membrane lipids:

Initiation (free radicals remove hydrogen from a polyunsaturated fatty acid to form a lipid radical);

2. Propagation (the lipid radical plus molecular oxygen forms a lipid peroxy radical, which then breaks down to more radicals).

3. Termination (new radicals react with antioxidants to eliminate radicals). Cook and Samman4 state that flavonoids could act at any of these stages. Flavonoids can block initiation by scavenging primary radicals such as superoxide Flavonoids also react with peroxy radicals to slow their propagation. In addition, the flavonoid radical intermediates formed after a reaction with peroxy radicals can react with other radicals formed during propagation.

This accelerates the termination process.Five of the possible antioxidant mechanisms in Table 8.1 can involve, at least in part, the prevention of free radical formation (Table 8.1, Mechanisms B to F). These mechanisms may be termed indirect antioxidant actions. These mechanisms include down-regulation of the production of superoxide radical and hydrogen peroxide, a precursor of free radical.' This effect, at least in some situations, could be accomplished through regulation of protein kinase C, which is thought to trigger the secretion of superoxide and hydrogen peroxide.'[12-13],'"his protein kinase C mediation could be particularly true for the soy constituent genistein, which belongs to the flavonoid class known as isoflavone. Genistein is a classic inhibitor of protein kinase C in vitro. I2 Still, it is unlikely that this is the only way in which flavonoids can inhibit the production of superoxide and hydrogen peroxide. Another consideration regarding hydrogen peroxide is that flavonoids may also directly react with this compound in a manner that eliminates the potential for radical formation (Table 8.1, Mechanism C).'[14-15]'

Possible Antioxidant Mechanisms of Flavonoids

A.	Direct radical scavenging
B.	Downregulation of radical production
C.	Elimination of radical precursors (i.e., hydrogen pero
D.	Metal chelation
E.	Inhibition of xanthine oxidase
F.	Elevation of endogenous antioxidants

Another way flavonoids may prevent radical formation is by chelation of transition metals (Table 8.1, Mechanism D). Some transition metals, such as iron, can catalytically form reactive free radicals.' Many flavonoids' structures have the chemical properties to chelate these metals in a state where radical generation is inhibited.'"[16-I7] In addition to this action, metals, and flavonoids may also, in some circumstances, form complexes that eliminate radicals. [I8]

Flavonoids can also act as antioxidants by inhibiting pro-oxidant enzymes (Table 8.1, Mechanism E). The most prominent example is the inhibition of xanthine oxidase [19-21], which can, in certain states, produce superoxide radicaLZ2. The pathological significance of superoxide production by xanthine oxidase has been debated but could be important in some health problems such as cardiac reperfusion injury.[22]

There is another possible indirect antioxidant action of the flavonoids. Some of these compounds may elevate the body's concentrations of endogenous antioxidants, which eliminate free radicals or their precursors. An example would be superoxide dismutase l,[23], which eliminates superoxide radicals inside the cell [24]

EVIDENCE THAT FLAVONOIDS ACT AS ANTIOXIDANTS

What is the evidence that the antioxidant effects of flavonoids occur to a great extent in humans? Much evidence is based on what flavonoids can do in vitro. Studies conducted in test tubes or culture plates cannot perfectly predict what will happen in vivo. Nonetheless, in vitro, observations can provide insights into the possible actions in vivo. From this perspective, each of the potential antioxidant mechanisms of flavonoids mentioned in Table 8.1 has been noted in vitro (see

Section V). In addition, studies in experimental animals have been conducted to justify the claim that flavonoids can act as antioxidants. These studies fall into one of the four categories listed in Table 8.2.

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Flavonoids have been administered with the aid of diet or bolus administration, as either remoted compounds or as part of a more popular nutritional intervention (i.e., inexperienced tea intake). The references stated for A through E are representative; however, they are not considered exhaustive. One trouble in a lot of those experimental animal research is distinguishing whether or not an antioxidant impact is a number one or secondary impact of the flavonoids. as instance, for category C, if a carcinogen is administered to a rat, flavonoids may additionally inhibit tumor development through an antioxidant effect or a few other mechanisms. An instance of the latter will be the inhibition of cytochrome P- 450-mediated carcinogen activation. This would limit the potential of that carcinogen to supply

tumors, however, could not be attributed to the antioxidant effect of flavonoids. Even if oxidation products are measured, including lipid peroxides, this does not continually distinguish the antioxidant effect from the easy prevention of carcinogen activation. If the carcinogen is not activated properly, there will be little oxidant stress due to the carcinogen [25-29]. Regardless of this conceptual hassle, the wide range of experimental designs used in this study indicates that the antioxidant moves of flavonoids explain at least some of the consequences. This competition is supported further with the aid of the flavonoid-precipitated increases in measures of serum antioxidant capacities determined ex vivo. "[30-31]' those measurements are defined as ex vivo because flavonoid consumption is in vivo, however, the capacity of plasma or serum to scavenge radicals is decided in vitro. even though the precise

interpretation of these styles of measurements carries a few uncertainties; the consequences at the least imply that ingested flavonoids can impact radical-scavenging potential in an intact animal. The outcomes can be alternatively dramatic if the experimental situations are manipulated in positive approaches. this can be

illustrated by the facts in Table 8.3. Our laboratory fed a low-phytochemical American Institute of Vitamins (ATN) diet to rats for 45 days. Half of the rats consumed drinking water spiked with catechin (table 8.3). [32-34] The distinction in serum TAS between catechin remedy and no treatment has become extraordinarily massive. In most research on TAS or related measurements, a 20% distinction between the two corporations is considered desirable. In contrast, the difference is almost 2.5-fold.

TABLE 8.3
Chronic Catechin Feeding Effects on Plasma TAS in Rats

Treatment	TAS (mmoles/l)
Control	1.5 ± 0.3
Catechin	3.5 ± 0.3

Note: Rats were fed a semipurified AIN diet and given tap water either with or without dissolved catechin (2.1 g/l) for 45 days.

Admittedly, this rat takes a look at changes to be designed to give a large reaction. An excessive dose of catechin was used, and a fundamental weight loss plan was used to reduce the presence of phytochemicals within the eating regimen. This observation shows that flavonoids can exert a major effect on TAS values.

Human studies on flavonoids as antioxidants are still limited in scope, although many more studies are likely to come forth. Table 8.4 categorizes the current observations. Most studies conducted so far have examined flavonoid-rich foods rather than isolated flavonoids. Epidemiological studies (Observation A, Table 8.4), although very important from a practical standpoint, have the same inherent problems as studies of disease-like symptoms in animal models.

Below in Table [35-44]

TABLE 8.4
Observations from Human Studies of Flavonoids as Antioxidants

A.	In epidemiological studies, inverse correlations between flavonoid consumption and incidence of diseases thought to involve oxidant stress[4,35–37]
B.	Depression of the concentrations of oxidant products such as lipid peroxides[38]
C.	Elevation of concentrations of endogenous antioxidants, or prevention of their depletion during oxidant stress[38]
D.	Elevated measures of plasma or serum antioxidant capacities determined *ex vivo*[39–41]
E.	Inhibition of exercise-induced muscle tissue breakdown and inflammation[40]
F.	Depression of lipoprotein oxidation rates assessed *ex vivo*[42–44]

Note: References are examples, not an exhaustive list. Most of these studies involve consumption of flavonoid-rich foods, not isolated flavonoids.

Both types of studies do not always distinguish between flavonoid antioxidant effects and other flavonoid effects. Moreover, human epidemiological studies do not necessarily distinguish between a cause-and-effect relationship for flavonoids and a coincidental effect. For example, an apparent protective effect for flavonoid-rich foods could be attributable to the vitamin C content of the foods. any other possibility is that the consumption of flavonoid-wealthy ingredients occurs to the finest diploma in Individuals who emphasize a typically healthy lifestyle. As a result, the general lifestyle, in place of flavonoid consumption in keeping with se, may additionally explain the consequences. For human research, observations of flavonoid effects on oxidation products (i.e., lipid peroxides) or endogenous antioxidant concentrations (Observations B and C, Table 8.4) are still very limited in phrases of examine numbers and scope of design. for instance, on September 1,

1999, a Medline search of lipid peroxide (or peroxides), plus flavonoids or flavonoids, did now not yield an unmarried paper showing flavonoid consumption miserable lipid peroxide values in human beings in vivo. some such papers have discovered the usage of different seek strategies, but the quantity turned into small and the scope limited. For instance, one observes observed despair in plasma values for malondialdehyde (a lipid peroxide product) for the duration of an l-week duration of high consumption of sure juice^.'^ However, the contribution of flavonoids to this result remains unclear. The effects can be due to other factors together with diet C or the indirect consequences of juice intake displacing different beverages in the topics' diets. Additional work is required in this area.

As with experimental animal studies, flavonoid consumption by humans has been related to an increase in plasma or serum indices of antioxidant capacities determined ex vivo (Observation D, table eight.4). This shows that in humans consuming diverse diets, flavonoid intake can affect the general radical-scavenging capacities of the plasma or serum. However, as with experimental animal research, the potential impact of these results on fitness cannot yet be assessed quantitatively.

One technique for comparing viable antioxidant movements, such as those of flavonoids, is now not accomplished, as with ease in human beings, as it is for experimental animals. This method examines the consequences of antioxidant consumption on acute oxidant stress in otherwise wholesome topics. In experimental animals, this will be carried out using numerous methods, together with the injection of hepatotoxins, including carbon tetrachloride, management of endotoxins, induction of an inflammatory condition, or publicity of hyperoxia. Ethical concerns limit such research. One alternative can be a bout of workout. even though exercising is typically considered health-selling, it does precipitate oxidant pressure.[45] This stress is a concept to make contributes to the muscular tissues breakdown and infection that happens during exercising." therefore, a bout of exercising may be one manner of studying acute oxidant stress in otherwise healthy human beings. now not handiest does such research provide fundamental

insights into whether a meal factor exerts antioxidant effects, but these studies may also have some sensible value for health promotion. The oxidant strain of exercising is a concept to make contributes to fatigue, muscle soreness, and the chance of injury [46-49] In addition, very strenuous exercise may increase cancer risk in the case of ultra-endurance athletes, or in people who train hard, but sporadically (the "weekend ~warrior") [50]. ~Our laboratory40 has carried out a pilot study in young men that simulated the "weekend warrior" behavior (Observation E, Table 8.4). The subjects who were not highly trained aerobically consumed soy protein beverages or whey protein placebo twice a day for 3 weeks. The soy protein beverage was rich in a category of flavonoids known as isoflavones, whereas they did not contain such compounds. Before and after the 3-week consumption period, the subjects performed an exhaustive bout of aerobic exercise. The soy group, but not the whey group, showed less muscle tissue breakdown and inflammation after the second exercise bout. Our laboratory plans to conduct in-depth studies on soy and exercise. However, it should be noted that any effects of soy protein products may not be due to just the isoflavone contents

flavonoids and llpoproteln oxidation.

lipoprotein oxidation is considered highly relevant to a major human health problem, atherosclerosis. In human studies, oxidation is studied ex vivo (oxidation is initiated after the removal of lipoproteins from the subjects). However, variations in the donors' lipoprotein, such as variations in preformed lipid hydro peroxide non enzymatic contents, are assumed to influence the oxidation data.[51]" Generally, these studies have examined the oxidation of low-density lipoprotein (LDL), but some studies have examined the combination of LDL and very low-density lipoproteins (VLDL). Lipoprotein oxidation is particularly useful for studying flavonoids. For one thing, both lipoprotein oxidation and flavoid intake are thought to be relevant to cardiovascular disease.is," Another issue is that many flavonoids are potent inhibitors of lipoprotein oxidation when added to lipoproteins in vitro. In vitro, studies have initiated oxidation in various ways (metal ions, organic chemical reactions, and cell-initiated events).

The results of studies on flavonoid intake and lipoprotein oxidation vary greatly. Some have found an effect42-44and some have not. [53-57], By Some of this variability in results is likely attributable to differences in the study design. The differences are listed in Table 8.5. The first variable on the list, different types of flavonoids, could be very important but does not seem to be the whole answer. For instance, one study of tea flavonoids has found effects on LDL oxidation,[58]"

TABLE 8.5
Design Variable for Studies of Flavonoid Intake Effects on Lipoprotein Oxidation

A.	Type of flavonoids
B.	Whole foods vs. flavonoid concentrates
C.	Lipoprotein isolation method
D.	Length of flavonoid ingestion period
E.	Type of subjects
F.	Placebo control vs. no placebo control
G.	Background diet of the test subjects

while others have not. Variable B, Table 8.5, whole food vs. flavonoid concentrate, produced two hypotheses. First, the combination of whole-food ingredients may be more effective than just a single flavonoid or even just the flavonoid fraction of food (i.e., vitamin C plus flavonoids may be more effective than either alone). Two, the absorption and metabolism of the flavonoids may depend on other food

components. For example, the alcohol in red wine may make flavonoids more biologically active than they would be without the alcohol.[59] detected in a number of ways.4~'6.'8.sJ.6(1-"7 Generation methods have included enzyme systems,

supports organic chemical reactions, and metal-catalyzed events. Detection methods include direct electron spin resonance (ESR) measurements of free radical disappearance, injury to cultured cells and cc11 organelles, diminished generation of

oxidant products, and inhibition of oxidation of goal molecules, which includes lipids, lipoproteins, liposomes, or DNA. The sheer extent of information on this place provides a sturdy case wherein flavonoids are capable of direct radical scavenging. however, facts amassed in vitro have not settled three important questions:

1. Do flavonoid concentrations reach and keep values wherein scavenging could have a first-rate impact on antioxidant defenses in vivo?

2. If the solution to the first question is yes, then in what body sites does this arise?

3. Does the metabolic change of flavonoids diminish their scavenging ability?

For the first two questions, the above-cited will increase in plasma antioxidant capacities following

Flavonoid ingestion helps the idea that radical scavenging using flavonoids is viable in vivo. but, the extent to which this motion occurs and the volume to which these actions impact health remain to be decided. One wants of this study is to look for oxidation merchandise of flavonoids in vivo. If flavonoids scavenge radicals, certain flavonoid merchandise is fashioned. initially,

that merchandise will be identified after the reactions had been performed in vitro. As a result, it could be determined whether the identical merchandise may be located in vivo. If they're determined, this would be accurate proof that flavonoids scavenge radicals in vivo. For the ultimate question, the activity of metabolites, a preliminary indication of a "sure" answer, seems to be authentic for at least a few quercetin metabolites. however, many paintings remain to be performed on the flavonoid scavenging effects. every other feasible antioxidant motion of flavonoids is their ability to suppress the mobile production of radicals and their precursors, which includes hydrogen peroxide. This has been established in vitro through the use of remoted phagocytes or organelles. however, this movement is tough to evaluate in vivo. One applicable indirect dimension is the size of plasma myeloperoxidase throughout oxidative pressure. because the secretion of myeloperoxidase through sure phagocytes can occur on the same hydro peroxide non enzymatic for non-enzymatic as secretion of superoxide and hydrogen peroxide" will increase in myeloperoxidase can sometimes be construed to indicate expanded superoxide and peroxide manufacturing in vivo. In a preceding take a look at soy and workout,{40} soy isoflavone consumption decreased workout-triggered increases in myeloperoxidase. future work is needed to completely discover the relationship between flavonoids and the secretion of radicals and their precursors. Many flavonoids have chemical systems that allow the chelation of transition metals along with iron and cc) peel-, J,f~-fx.Q, which can inhibit the metallic-catalyzed formation of unfastened radicals.

This inhibition has been established in vitro, in most cases not directly using inspecting oxidant harm to a target molecule.6-1x, similarly, some flavonoids had been proven to defend cultured cells towards iron-brought about damage. ~~,~~). Some studies have proven that flavonoids can block iron-prompted accidents in rodents. ~~.~? In one of these studies, sure flavonoids dwindled the concentration of radicals detectable by ESR spin trapping. j2 however, none of those effects verified that flavonoids save your iron from forming loose radicals. instead, those effects should genuinely be due to flavonoids disposing of radicals after their formation. but, one statement shows that iron chelation is as a minimum partly concerned with safety in opposition to iron overload damage. In cultured rat hepatocytes, three flavonoids confirmed cytoprotection outcomes in proportion to their iron-chelating potential.70 Flavonoid interactions with metals could have an extra antioxidant impact apart from inhibiting metal-catalyzed radical formation. Flavonoid-metal complexes can be used as catalysts to eliminate radicals. An example of this has been demonstrated with a rutin-copper complex. f8? The complex was much more potent than rutin alone in eliminating superoxide radicals and preventing lipid peroxidation in rat liver microsomes. However, other flavonoids have not yet been tested. Rats were fed a mixed-feed diet but not a semi-purified diet. When this effect was observed, it was tissue-specific. In the pancreas, a smaller response was observed compared with the colon, and no response was observed in the liver or lung (unpublished data). In another study, little to no effect on liver SOD activity was reported after feeding any of the three flavonoids to rats. This lack of an effect occurred despite the depression of liver lipid peroxidation. Similarly, bolus quercetin treatment restricts ethanol-induced gastric mucosal injury without changing mucosal SOD activity. ~[60]"

Silymarin has been reported to increase lymphocyte SOD 1 activity. A series of studies have been conducted with silymarin on Cu-Zn SOD in erythrocytes and lymphocytes from patients with alcoholic cirrhosis in Hungary.~Silymarin consumption initially increases SOD activity and protein levels in lymphocytes and erythrocytes. The same general effect was achieved by incubating silymarin with the same cell types in vitro. However, data on silymarin actions in vivo in other types of people (i.e., healthy subjects) are lacking. The effects in patients with cirrhosis may represent a general protection of cell protein integrity rather than a specific induction of SOD 1. Some flavonoids may be able to prevent the inactivation of SOD I at a given body site during oxidative stress but do not affect activities under

normal circumstances. An example of this is seen for catechin and rat lung SOD.{29} This study reports that bolus catechin administration prevents a fall in lung SOD activities in rats treated with the oxidant stimulant diethylmaleate, but does not affect pre-stress SOD values.

Flavonoids can also affect the concentration of antioxidant glutathione. Rodent studies have shown considerable specificity for flavonoid types and tissues. Several different flavonoids have been reported to either increase gastrointestinal glutathione concentrations or to prevent their depletion by inflammatory stress 81-83Some other rodent tissues also respond to flavonoid ingestion with either increased glutathione contents or protection against stress-induced depletion.2", X4, X5 However, one study" indicates that the flavonoid silymarin does not increase glutathione contents of the kidney, lung, or spleen despite increasing levels in the intestine, liver, and stomach. In contrast, our laboratory has found that chronic ingestion of synthetic catechin has no effect on liver glutathione content, but nearly doubles these values in the lungs (unpublished results). This lung effect appears to be protective. As shown in Figure 8.2, catechin ingestion was partially protected against lung lipid peroxidation caused by diethylmaleate, a chemical that depletes lung glutathione. In contrast, in mice, administration of the two flavonoids does not block skin glutathione depletion caused by sulfur mustard dermal intoxication but still blocks lipid peroxidation.

There have been sporadic examinations of the effects of flavonoids on the antioxidant enzymes glutathione peroxidase and glutathione reductase. Both activities were increased in the mouse skin by feeding isoflavone genistein. Reductase enzyme activity is also increased in the intestine. Another study reported increases in both enzyme activities in the livers of rats fed an isoflavone-containing

soy protein isolate. In another work, the consumption of a green tea extract by mice produces moderately high activities for liver glutathione reductase and very high activities for glutathione peroxidase activity in all three tissues.~ In humans, plasma glutathione peroxidase activities increased after 10-day consumption of quercetin-rich juices.3x However, it should be recognized that for this study, as well as those with green tea or soy protein isolates, the effects may not be dependent only on flavonoids, but may also involve other food components. In contrast, consumption of pure quercetin by rats increases the gastric mucosal activity of glutathione peroxidase. #' In addition, in mice, acute treatment with a two-flavonoid combination prevents cardiac glutathione peroxidase activity depletion by the chemotherapy drug adriamycin." This study and the others noted in this paragraph indicate that flavonoids can influence glutathione peroxidase and reductase activity. Nonetheless, there is still a large information gap regarding the effects of flavonoid treatments on body sites, and to what extent. This is particularly true from the perspective of human studies.

There have been a few studies on flavonoids and catalase, another antioxidant enzyme. Some of these report that flavonoid feeding does not affect rat liver catalase activities." In contrast, one report stated that topical application of silymarin inhibits a depression in skin catalase activity in a mouse photo-carcinogenesis model.93 In addition, two mouse feeding studies mentioned above, one with genistein and one with green tea, found increased catalase activity in multiple tissues. The whole area of flavonoids affecting endogenous antioxidants is interesting, but still requires more research to elucidate the full biological importance of a flavonoid-endogenous antioxidant relationship

Prooxidant Effects of Flavonoids

Although this chapter focuses on the possible antioxidant effects of flavonoids, there are certainly a respectable number of papers concerning the pro-oxidant effects of these compounds. Some of the chemicals that can make flavonoids free of radical scavengers, under certain circumstances, can also generate oxidant reactions. These reactions can damage the same biological molecules that flavonoids are supposed to protect against oxidation. One large issue in this whole area is whether these pro-oxidant actions can occur in vivo and, if so, under what circumstances. So far, the evidence for the pro-oxidant actions of flavonoids has come primarily from in vitro studies. However, if flavonoids continue to gain attention for their possible health-promoting effects, the issue of pro-oxidant actions must also be addressed

Summaries

Many studies have provided evidence that the antioxidant actions of flavonoids can impact human health. However, this statement still has to be considered speculative, pending more studies, particularly in humans. There appear to be several different mechanisms by which flavonoids can exert direct or indirect antioxidant actions. The exact mechanisms operate under circumstances that require further illumination. As the antioxidant effects of flavonoids gain more attention, there

may also need to consider the possible pro-oxidant effects.

Research Method: The researchers performed a systematic review of the prevailing literature on the topic of flavonoids as antioxidants. They searched various scientific databases and protected research that investigated the antioxidant properties of flavonoids in vitro (cellular subculture research) and in vivo (animal or human studies). The covered studies used various experimental techniques to measure antioxidant hobbies, such as measuring reactive oxygen species (ROS) levels, lipid peroxidation, and antioxidant enzyme interest.

Result:

The systematic evaluation revealed that flavonoids show off enormous antioxidant activity in vitro and in vivo. numerous studies verified that flavonoids can scavenge unfastened radicals and reduce oxidative stress, which is a major contributor to numerous persistent illnesses, inclusive of cardiovascular diseases, neurodegenerative issues, and positive forms of most cancers.

In vitro, research consistently showed that flavonoids can at once neutralize loose radicals and inhibit oxidative harm to cells and tissues. moreover, they can modulate the pastime of antioxidant enzymes, including superoxide dismutase (SOD), catalase, and glutathione peroxidase, which similarly complements the mobile antioxidant defense machine.

In animal and human research, flavonoid-rich diets or supplementation with specific flavonoids ended in extended antioxidant capacity and reduced oxidative strain markers. these consequences were found in numerous tissues and organs, helping the belief that flavonoids can exert antioxidant consequences all through the body.

Discussion:

The findings of this systematic assessment provide strong evidence supporting the antioxidant houses of flavonoids. The ability of flavonoids to scavenge loose radicals and modulate antioxidant enzyme pastime indicates their potential in stopping oxidative damage and related diseases.

it is important to note that the antioxidant activity of flavonoids is inspired using several factors, which include their chemical shape, concentration, and bioavailability. one of the kind subclasses of flavonoids, including flavonols, flavones, and anthocyanins, may also vary in their antioxidant potency. moreover, the presence of other dietary components and character variations in metabolism can affect the absorption and bioavailability of flavonoids, in the long run influencing their antioxidant consequences.

while the consequences from in vitro and animal studies are promising, more nicely-designed human clinical trials are had to further elucidate the ability health advantages of flavonoids as antioxidants. future studies need to also discover the mechanisms underlying the antioxidant interest of flavonoids and their specific effects on unique mobile approaches related to oxidative strain.

Conclusion

Flavonoids serve a multiplicity of functions in eukaryotic cells, not only because of their region in specific cells and Subcellular booths but also because of their chemical structures. Pressure-responsive flavonoids show an extraordinary ability to reduce diverse types of reactive oxygen species, a common condition with which vegetation is faced when experiencing distinct abiotic and biotic stresses. Antioxidant flavonoids may contribute greatly to ROS-detoxing via chemical ROS quenching in plant cells, whereas, in human cells, their features as reducing retailers seem of pretty minor importance. but flavonoids may serve similar capabilities in plant life and human beings (in high nanomolar to low micro molar variety) utilizing tightly regulating the sports of various protein kinases, which, in flip, are answerable for mediating ROS-precipitated signaling cascades critical to mobile growth and differentiation. these practical roles are effectively served by ROS-quenching flavonoids. The relationships between flavonoid-protein kinases, which have been extensively investigated in humans, have not yet acquired interest in plant life. Here, we are aware that MAPKs are activated with the aid of oxidative pressure alerts and mediate the responses of flowers to hugely special stressors. Flavonoids can significantly affect MPAK signaling cascades in flowers now not best by directly binding to the active sites of proteins; however, they modulate their activation through ROS-scavenging activities.

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Conflict of Interest

The authors declare no conflict of interest

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