= Antioxidant =

An antioxidant is a molecule that inhibits the oxidation of other molecules . Oxidation is a chemical reaction that can produce free radicals , leading to chain reactions that may damage cells . Antioxidants such as thiols or ascorbic acid (vitamin C) terminate these chain reactions . The term " antioxidant " is mainly used for two different groups of substances : industrial chemicals which are added to products to prevent oxidation , and natural chemicals found in foods and body tissue which are said to have beneficial health effects .

To balance the oxidative state , plants and animals maintain complex systems of overlapping antioxidants , such as glutathione and enzymes (e.g. , catalase and superoxide dismutase) produced internally or the dietary antioxidants , vitamin A , vitamin C and vitamin E.

Diets containing antioxidant dietary supplements do not improve health nor are they effective in preventing diseases . Randomized clinical trials including supplements of beta @-@ carotene , vitamin A and vitamin E singly or in different combinations found no effect on mortality rate and cancer risk , or may even increase cancer risk . Supplementation with selenium or vitamin E does not reduce the risk of cardiovascular disease . Oxidative stress can be considered as either a cause or consequence of some diseases , an area of research stimulating drug development for antioxidant compounds for use as potential therapies .

Industrial antioxidants have diverse uses , such as food and cosmetics preservatives and inhibitors of rubber or gasoline deterioration .

= = Health effects = =

= = = Relation to diet = = =

Although certain levels of antioxidant vitamins in the diet are required for good health , there is considerable doubt as to whether antioxidant @-@ rich foods or supplements have anti @-@ disease activity ; and if they are actually beneficial , it is unknown which antioxidant (s) are needed from the diet and in what amounts beyond typical dietary intake . Some authors dispute the hypothesis that antioxidant vitamins could prevent chronic diseases , while others maintain such a possibility is unproved and misguided from the beginning .

Polyphenols , which have antioxidant properties in vitro , are not proven as dietary antioxidants in vivo , yet may have non @-@ antioxidant roles in minute concentrations that affect cell @-@ to @-@ cell signaling , receptor sensitivity , inflammatory enzyme activity or gene regulation .

Although dietary antioxidants have been investigated for potential effects on neurodegenerative diseases such as Alzheimer 's disease , Parkinson 's disease , and amyotrophic lateral sclerosis , these studies have been inconclusive .

= = = Drug candidates = = =

Tirilazad is an antioxidant steroid derivative that inhibits the lipid peroxidation that is believed to play a key in neuronal death in stroke and head injury . It demonstrated activity in animal models of stroke , but human trials demonstrated no effect on mortality or other outcomes in subarachnoid haemorrhage and worsened results in ischemic stroke .

Similarly , the designed antioxidant NXY @-@ 059 exhibited efficacy in animal models , but failed to improve stroke outcomes in a clinical trial . As of November 2014 , other antioxidants are being studied as potential neuroprotectants .

Common pharmaceuticals (and supplements) with antioxidant properties may interfere with the efficacy of certain anticancer medication and radiation .

= = = Physical exercise = = =

During exercise , oxygen consumption can increase by a factor of more than 10 . However , no benefits for physical performance to athletes are seen with vitamin E supplementation and 6 weeks of vitamin E supplementation had no effect on muscle damage in ultramarathon runners . Some research suggests that supplementation with amounts as high as 1000 mg of vitamin C inhibits recovery . Other studies indicated that antioxidant supplementation may attenuate the cardiovascular benefits of exercise .

= = = Adverse effects = = =

Relatively strong reducing acids can have antinutrient effects by binding to dietary minerals such as iron and zinc in the gastrointestinal tract and preventing them from being absorbed . Notable examples are oxalic acid , tannins and phytic acid , which are high in plant @-@ based diets . Calcium and iron deficiencies are not uncommon in diets in developing countries where less meat is eaten and there is high consumption of phytic acid from beans and unleavened whole grain bread .

Nonpolar antioxidants such as eugenol ? a major component of oil of cloves ? have toxicity limits that can be exceeded with the misuse of undiluted essential oils . Toxicity associated with high doses of water @-@ soluble antioxidants such as ascorbic acid are less of a concern , as these compounds can be excreted rapidly in urine . More seriously , very high doses of some antioxidants may have harmful long @-@ term effects . The beta @-@ carotene and Retinol Efficacy Trial (CARET) study of lung cancer patients found that smokers given supplements containing beta @-@ carotene and vitamin A had increased rates of lung cancer . Subsequent studies confirmed these adverse effects .

These harmful effects may also be seen in non @-@ smokers , as a recent meta @-@ analysis including data from approximately 230 @,@ 000 patients showed that ? @-@ carotene , vitamin A or vitamin E supplementation is associated with increased mortality but saw no significant effect from vitamin C. No health risk was seen when all the randomized controlled studies were examined together , but an increase in mortality was detected when only high @-@ quality and low @-@ bias risk trials were examined separately . As the majority of these low @-@ bias trials dealt with either elderly people , or people with disease , these results may not apply to the general population . This meta @-@ analysis was later repeated and extended by the same authors , with the new analysis published by the Cochrane Collaboration ; confirming the previous results . These two publications are consistent with some previous meta @-@ analyzes that also suggested that Vitamin E supplementation increased mortality , and that antioxidant supplements increased the risk of colon cancer . Beta @-@ carotene may also increase lung cancer . Overall , the large number of clinical trials carried out on antioxidant supplements suggest that either these products have no effect on health , or that they cause a small increase in mortality in elderly or vulnerable populations .

While antioxidant supplementation is widely used in attempts to prevent the development of cancer , antioxidants may interfere with cancer treatments , since the environment of cancer cells causes high levels of oxidative stress , making these cells more susceptible to the further oxidative stress induced by treatments . As a result , by reducing the redox stress in cancer cells , antioxidant supplements (and pharmaceuticals) could decrease the effectiveness of radiotherapy and chemotherapy . On the other hand , other reviews have suggested that antioxidants could reduce side effects or increase survival times .

= = Oxidative challenge in biology = =

A paradox in metabolism is that , while the vast majority of complex life on Earth requires oxygen for its existence , oxygen is a highly reactive molecule that damages living organisms by producing reactive oxygen species . Consequently , organisms contain a complex network of antioxidant metabolites and enzymes that work together to prevent oxidative damage to cellular components such as DNA , proteins and lipids . In general , antioxidant systems either prevent these reactive species from being formed , or remove them before they can damage vital components of the cell . However , reactive oxygen species also have useful cellular functions , such as redox signaling .

Thus , the function of antioxidant systems is not to remove oxidants entirely , but instead to keep them at an optimum level .

The reactive oxygen species produced in cells include hydrogen peroxide (H_2O_2) , hypochlorous acid (HClO) , and free radicals such as the hydroxyl radical (· OH) and the superoxide anion (O_2 ?) . The hydroxyl radical is particularly unstable and will react rapidly and non @-@ specifically with most biological molecules . This species is produced from hydrogen peroxide in metal @-@ catalyzed redox reactions such as the Fenton reaction . These oxidants can damage cells by starting chemical chain reactions such as lipid peroxidation , or by oxidizing DNA or proteins . Damage to DNA can cause mutations and possibly cancer , if not reversed by DNA repair mechanisms , while damage to proteins causes enzyme inhibition , denaturation and protein degradation .

The use of oxygen as part of the process for generating metabolic energy produces reactive oxygen species . In this process , the superoxide anion is produced as a by @-@ product of several steps in the electron transport chain . Particularly important is the reduction of coenzyme Q in complex III , since a highly reactive free radical is formed as an intermediate (Q · ?) . This unstable intermediate can lead to electron " leakage " , when electrons jump directly to oxygen and form the superoxide anion , instead of moving through the normal series of well @-@ controlled reactions of the electron transport chain . Peroxide is also produced from the oxidation of reduced flavoproteins , such as complex I. However , although these enzymes can produce oxidants , the relative importance of the electron transfer chain to other processes that generate peroxide is unclear . In plants , algae , and cyanobacteria , reactive oxygen species are also produced during photosynthesis , particularly under conditions of high light intensity . This effect is partly offset by the involvement of carotenoids in photoinhibition , and in algae and cyanobacteria , by large amount of iodide and selenium , which involves these antioxidants reacting with over @-@ reduced forms of the photosynthetic reaction centres to prevent the production of reactive oxygen species .

= = Metabolites = =

Antioxidants are classified into two broad divisions , depending on whether they are soluble in water (hydrophilic) or in lipids (lipophilic) . In general , water @-@ soluble antioxidants react with oxidants in the cell cytosol and the blood plasma , while lipid @-@ soluble antioxidants protect cell membranes from lipid peroxidation . These compounds may be synthesized in the body or obtained from the diet . The different antioxidants are present at a wide range of concentrations in body fluids and tissues , with some such as glutathione or ubiquinone mostly present within cells , while others such as uric acid are more evenly distributed (see table below) . Some antioxidants are only found in a few organisms and these compounds can be important in pathogens and can be virulence factors .

The relative importance and interactions between these different antioxidants is a very complex question , with the various metabolites and enzyme systems having synergistic and interdependent effects on one another . The action of one antioxidant may therefore depend on the proper function of other members of the antioxidant system . The amount of protection provided by any one antioxidant will also depend on its concentration , its reactivity towards the particular reactive oxygen species being considered , and the status of the antioxidants with which it interacts .

Some compounds contribute to antioxidant defense by chelating transition metals and preventing them from catalyzing the production of free radicals in the cell . Particularly important is the ability to sequester iron , which is the function of iron @-@ binding proteins such as transferrin and ferritin . Selenium and zinc are commonly referred to as antioxidant nutrients , but these chemical elements have no antioxidant action themselves and are instead required for the activity of some antioxidant enzymes , as is discussed below .

= = = Uric acid = = =

Uric acid is by far the highest concentration antioxidant in human blood . Uric acid (UA) is an antioxidant oxypurine produced from xanthine by the enzyme xanthine oxidase , and is an intermediate product of purine metabolism . In almost all land animals , urate oxidase further catalyzes the oxidation of uric acid to allantoin , but in humans and most higher primates , the urate oxidase gene is nonfunctional , so that UA is not further broken down . The evolutionary reasons for this loss of urate conversion to allantoin remain the topic of active speculation . The antioxidant effects of uric acid have led researchers to suggest this mutation was beneficial to early primates and humans . Studies of high altitude acclimatization support the hypothesis that urate acts as an antioxidant by mitigating the oxidative stress caused by high @-@ altitude hypoxia . In animal studies that investigate diseases facilitated by oxidative stress , introduction of UA both prevents the disease or reduces it , leading researchers to propose this is due to UA 's antioxidant properties . Studies of UA 's antioxidant mechanism support this proposal .

With respect to multiple sclerosis , Gwen Scott explains the significance of uric acid as an antioxidant by proposing that " Serum UA levels are inversely associated with the incidence of MS in humans because MS patients have low serum UA levels and individuals with hyperuricemia (gout) rarely develop the disease . Moreover , the administration of UA is therapeutic in experimental allergic encephalomyelitis (EAE) , an animal model of MS. " In sum , while the mechanism of UA as an antioxidant is well @-@ supported , the claim that its levels affect MS risk is still controversial , and requires more research .

Likewise , UA has the highest concentration of any blood antioxidant and provides over half of the total antioxidant capacity of human serum . Uric acid 's antioxidant activities are also complex , given that it does not react with some oxidants , such as superoxide , but does act against peroxynitrite , peroxides , and hypochlorous acid . Concerns over elevated UA 's contribution to gout must be considered as one of many risk factors . By itself , UA @-@ related risk of gout at high levels (415 ? 530 ?mol / L) is only 0 @.@ 5 % per year with an increase to 4 @.@ 5 % per year at UA supersaturation levels (535 + ?mol / L) . Many of these aforementioned studies determined UA 's antioxidant actions within normal physiological levels , and some found antioxidant activity at levels as high as 285 ?mol / L.

= = = Vitamin C = = =

Ascorbic acid or " vitamin C " is a monosaccharide oxidation @-@ reduction (redox) catalyst found in both animals and plants . As one of the enzymes needed to make ascorbic acid has been lost by mutation during primate evolution , humans must obtain it from the diet ; it is therefore a vitamin . Most other animals are able to produce this compound in their bodies and do not require it in their diets . Ascorbic acid is required for the conversion of the procollagen to collagen by oxidizing proline residues to hydroxyproline . In other cells , it is maintained in its reduced form by reaction with glutathione , which can be catalysed by protein disulfide isomerase and glutaredoxins . Ascorbic acid is a redox catalyst which can reduce , and thereby neutralize , reactive oxygen species such as hydrogen peroxide . In addition to its direct antioxidant effects , ascorbic acid is also a substrate for the redox enzyme ascorbate peroxidase , a function that is particularly important in stress resistance in plants . Ascorbic acid is present at high levels in all parts of plants and can reach concentrations of 20 millimolar in chloroplasts .

= = = Glutathione = = =

Glutathione is a cysteine @-@ containing peptide found in most forms of aerobic life . It is not required in the diet and is instead synthesized in cells from its constituent amino acids . Glutathione has antioxidant properties since the thiol group in its cysteine moiety is a reducing agent and can be reversibly oxidized and reduced . In cells , glutathione is maintained in the reduced form by the enzyme glutathione reductase and in turn reduces other metabolites and enzyme systems , such as ascorbate in the glutathione @-@ ascorbate cycle , glutathione peroxidases and glutaredoxins , as well as reacting directly with oxidants . Due to its high concentration and its central role in maintaining the cell 's redox state , glutathione is one of the most important cellular antioxidants . In some organisms glutathione is replaced by other thiols , such as by mycothiol in the Actinomycetes , bacillithiol in some Gram @-@ positive bacteria , or by trypanothione in the Kinetoplastids .

= = = Melatonin = = =

Melatonin is a powerful antioxidant . Melatonin easily crosses cell membranes and the blood ? brain barrier . Unlike other antioxidants , melatonin does not undergo redox cycling , which is the ability of a molecule to undergo repeated reduction and oxidation . Redox cycling may allow other antioxidants (such as vitamin C) to act as pro @-@ oxidants and promote free radical formation . Melatonin , once oxidized , cannot be reduced to its former state because it forms several stable end @-@ products upon reacting with free radicals . Therefore , it has been referred to as a terminal (or suicidal) antioxidant .

= = = Vitamin E = = =

Vitamin E is the collective name for a set of eight related tocopherols and tocotrienols , which are fat @-@ soluble vitamins with antioxidant properties . Of these , ? @-@ tocopherol has been most studied as it has the highest bioavailability , with the body preferentially absorbing and metabolising this form .

It has been claimed that the ? @-@ tocopherol form is the most important lipid @-@ soluble antioxidant , and that it protects membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction . This removes the free radical intermediates and prevents the propagation reaction from continuing . This reaction produces oxidised ? @-@ tocopheroxyl radicals that can be recycled back to the active reduced form through reduction by other antioxidants , such as ascorbate , retinol or ubiquinol . This is in line with findings showing that ? @-@ tocopherol , but not water @-@ soluble antioxidants , efficiently protects glutathione peroxidase 4 (GPX4) -deficient cells from cell death . GPx4 is the only known enzyme that efficiently reduces lipid @-@ hydroperoxides within biological membranes .

However , the roles and importance of the various forms of vitamin E are presently unclear , and it has even been suggested that the most important function of ? @-@ tocopherol is as a signaling molecule , with this molecule having no significant role in antioxidant metabolism . The functions of the other forms of vitamin E are even less well @-@ understood , although ? @-@ tocopherol is a nucleophile that may react with electrophilic mutagens , and tocotrienols may be important in protecting neurons from damage .

= = Pro @-@ oxidant activities = =

Antioxidants that are reducing agents can also act as pro @-@ oxidants . For example , vitamin C has antioxidant activity when it reduces oxidizing substances such as hydrogen peroxide , however , it will also reduce metal ions that generate free radicals through the Fenton reaction .

2 Fe3 + + Ascorbate ? 2 Fe2 + + Dehydroascorbate

2 Fe2 + + 2 H2O2 ? 2 Fe3 + + 2 OH · + 2 OH ?

The relative importance of the antioxidant and pro @-@ oxidant activities of antioxidants is an area of current research , but vitamin C , which exerts its effects as a vitamin by oxidizing polypeptides , appears to have a mostly antioxidant action in the human body . However , less data is available for other dietary antioxidants , such as vitamin E , or the polyphenols . Likewise , the pathogenesis of diseases involving hyperuricemia likely involve uric acid 's direct and indirect pro @-@ oxidant properties .

That is , paradoxically , agents which are normally considered antioxidants can act as conditional pro @-@ oxidants and actually increase oxidative stress . Besides ascorbate , medically important conditional pro @-@ oxidants include uric acid and sulfhydryl amino acids such as homocysteine . Typically , this involves some transition @-@ series metal such as copper or iron as catalyst . The potential role of the pro @-@ oxidant role of uric acid in (e.g.) atherosclerosis and ischemic stroke is considered above . Another example is the postulated role of homocysteine in atherosclerosis .

= = = Negative health effects = = =

Some antioxidant supplements may promote disease and increase mortality in humans under certain conditions . Hypothetically , free radicals induce an endogenous response that protects against exogenous radicals (and possibly other toxic compounds) . Free radicals may increase life span . This increase may be prevented by antioxidants , providing direct evidence that toxic radicals may mitohormetically exert life extending and health promoting effects .

= = Enzyme systems = =

As with the chemical antioxidants , cells are protected against oxidative stress by an interacting network of antioxidant enzymes . Here , the superoxide released by processes such as oxidative phosphorylation is first converted to hydrogen peroxide and then further reduced to give water . This detoxification pathway is the result of multiple enzymes , with superoxide dismutases catalysing the first step and then catalases and various peroxidases removing hydrogen peroxide . As with antioxidant metabolites , the contributions of these enzymes to antioxidant defenses can be hard to separate from one another , but the generation of transgenic mice lacking just one antioxidant enzyme can be informative .

= = = Superoxide dismutase , catalase and peroxiredoxins = = =

Superoxide dismutases (SODs) are a class of closely related enzymes that catalyze the breakdown of the superoxide anion into oxygen and hydrogen peroxide . SOD enzymes are present in almost all aerobic cells and in extracellular fluids . Superoxide dismutase enzymes contain metal ion cofactors that , depending on the isozyme , can be copper , zinc , manganese or iron . In humans , the copper / zinc SOD is present in the cytosol , while manganese SOD is present in the mitochondrion . There also exists a third form of SOD in extracellular fluids , which contains copper and zinc in its active sites . The mitochondrial isozyme seems to be the most biologically important of these three , since mice lacking this enzyme die soon after birth . In contrast , the mice lacking copper / zinc SOD (Sod1) are viable but have numerous pathologies and a reduced lifespan (see article on superoxide) , while mice without the extracellular SOD have minimal defects (sensitive to hyperoxia) . In plants , SOD isozymes are present in the cytosol and mitochondria , with an iron SOD found in chloroplasts that is absent from vertebrates and yeast .

Catalases are enzymes that catalyse the conversion of hydrogen peroxide to water and oxygen , using either an iron or manganese cofactor . This protein is localized to peroxisomes in most eukaryotic cells . Catalase is an unusual enzyme since , although hydrogen peroxide is its only substrate , it follows a ping @-@ pong mechanism . Here , its cofactor is oxidised by one molecule of hydrogen peroxide and then regenerated by transferring the bound oxygen to a second molecule of substrate . Despite its apparent importance in hydrogen peroxide removal , humans with genetic deficiency of catalase ? " acatalasemia " ? or mice genetically engineered to lack catalase completely , suffer few ill effects .

Peroxiredoxins are peroxidases that catalyze the reduction of hydrogen peroxide , organic hydroperoxides , as well as peroxynitrite . They are divided into three classes : typical 2 @-@ cysteine peroxiredoxins ; atypical 2 @-@ cysteine peroxiredoxins ; and 1 @-@ cysteine peroxiredoxins . These enzymes share the same basic catalytic mechanism , in which a redox @-@ active cysteine (the peroxidatic cysteine) in the active site is oxidized to a sulfenic acid by the peroxide substrate . Over @-@ oxidation of this cysteine residue in peroxiredoxins inactivates these enzymes , but this can be reversed by the action of sulfiredoxin . Peroxiredoxins seem to be important in antioxidant metabolism , as mice lacking peroxiredoxin 1 or 2 have shortened lifespan and suffer from hemolytic anaemia , while plants use peroxiredoxins to remove hydrogen peroxide generated in chloroplasts .

Thioredoxin and glutathione systems

The thioredoxin system contains the 12 @-@ kDa protein thioredoxin and its companion thioredoxin reductase . Proteins related to thioredoxin are present in all sequenced organisms . Plants , such as Arabidopsis thaliana , have a particularly great diversity of isoforms . The active site of thioredoxin consists of two neighboring cysteines , as part of a highly conserved CXXC motif , that can cycle between an active dithiol form (reduced) and an oxidized disulfide form . In its active state , thioredoxin acts as an efficient reducing agent , scavenging reactive oxygen species and maintaining other proteins in their reduced state . After being oxidized , the active thioredoxin is regenerated by the action of thioredoxin reductase , using NADPH as an electron donor .

The glutathione system includes glutathione , glutathione reductase , glutathione peroxidases and glutathione S @-@ transferases . This system is found in animals , plants and microorganisms . Glutathione peroxidase is an enzyme containing four selenium @-@ cofactors that catalyzes the breakdown of hydrogen peroxide and organic hydroperoxides . There are at least four different glutathione peroxidase isozymes in animals . Glutathione peroxidase 1 is the most abundant and is a very efficient scavenger of hydrogen peroxide , while glutathione peroxidase 4 is most active with lipid hydroperoxides . Surprisingly , glutathione peroxidase 1 is dispensable , as mice lacking this enzyme have normal lifespans , but they are hypersensitive to induced oxidative stress . In addition , the glutathione S @-@ transferases show high activity with lipid peroxides . These enzymes are at particularly high levels in the liver and also serve in detoxification metabolism .

Oxidative stress in disease

Oxidative stress is thought to contribute to the development of a wide range of diseases including Alzheimer 's disease , Parkinson 's disease , the pathologies caused by diabetes , rheumatoid arthritis , and neurodegeneration in motor neuron diseases . In many of these cases , it is unclear if oxidants trigger the disease , or if they are produced as a secondary consequence of the disease and from general tissue damage ; One case in which this link is particularly well @-@ understood is the role of oxidative stress in cardiovascular disease . Here , low density lipoprotein (LDL) oxidation appears to trigger the process of atherogenesis , which results in atherosclerosis , and finally cardiovascular disease .

Oxidative damage in DNA can cause cancer . Several antioxidant enzymes such as superoxide dismutase , catalase , glutathione peroxidase , glutathione reductase , glutathione S @-@ transferase etc. protect DNA from oxidative stress . It has been proposed that polymorphisms in these enzymes are associated with DNA damage and subsequently the individual 's risk of cancer susceptibility .

A low calorie diet extends median and maximum lifespan in many animals . This effect may involve a reduction in oxidative stress . While there is some evidence to support the role of oxidative stress in aging in model organisms such as Drosophila melanogaster and Caenorhabditis elegans , the evidence in mammals is less clear . Indeed , a 2009 review of experiments in mice concluded that almost all manipulations of antioxidant systems had no effect on aging .

Diets high in fruit and vegetables , and so possibly being rich in antioxidant vitamins , have no established effect on status of health or aging , yet may have more subtle physiological effects , such as modifying cell @-@ to @-@ cell communication .

Uses in technology

Food preservatives

Antioxidants are used as food additives to help guard against food deterioration . Exposure to oxygen and sunlight are the two main factors in the oxidation of food , so food is preserved by keeping in the dark and sealing it in containers or even coating it in wax , as with cucumbers . However , as oxygen is also important for plant respiration , storing plant materials in anaerobic conditions produces unpleasant flavors and unappealing colors . Consequently , packaging of fresh fruits and vegetables contains an ~ 8 % oxygen atmosphere . Antioxidants are an especially important class of preservatives as , unlike bacterial or fungal spoilage , oxidation reactions still occur relatively rapidly in frozen or refrigerated food . These preservatives include natural antioxidants such as ascorbic acid (AA , E300) and tocopherols (E306) , as well as synthetic antioxidants such as propyl gallate (PG , E310) , tertiary butylhydroquinone (TBHQ) , butylated hydroxyanisole (BHA , E320) and butylated hydroxytoluene (BHT , E321) .

The most common molecules attacked by oxidation are unsaturated fats ; oxidation causes them to turn rancid . Since oxidized lipids are often discolored and usually have unpleasant tastes such as metallic or sulfurous flavors , it is important to avoid oxidation in fat @-@ rich foods . Thus , these foods are rarely preserved by drying ; instead , they are preserved by smoking , salting or fermenting . Even less fatty foods such as fruits are sprayed with sulfurous antioxidants prior to air drying . Oxidation is often catalyzed by metals , which is why fats such as butter should never be wrapped in aluminium foil or kept in metal containers . Some fatty foods such as olive oil are partially protected from oxidation by their natural content of antioxidants , but remain sensitive to photooxidation . Antioxidant preservatives are also added to fat based cosmetics such as lipstick and moisturizers to prevent rancidity .

= = = Industrial uses = = =

Antioxidants are frequently added to industrial products . A common use is as stabilizers in fuels and lubricants to prevent oxidation , and in gasolines to prevent the polymerization that leads to the formation of engine @-@ fouling residues . In 2007 , the worldwide market for industrial antioxidants had a total volume of around 0 @.@ 88 million tons . This created a revenue of circa 3 @.@ 7 billion US @-@ dollars (2 @.@ 4 billion Euros) .

They are widely used to prevent the oxidative degradation of polymers such as rubbers , plastics and adhesives that causes a loss of strength and flexibility in these materials . Polymers containing double bonds in their main chains , such as natural rubber and polybutadiene , are especially susceptible to oxidation and ozonolysis . They can be protected by antiozonants . Solid polymer products start to crack on exposed surfaces as the material degrades and the chains break . The mode of cracking varies between oxygen and ozone attack , the former causing a " crazy paving " effect , while ozone attack produces deeper cracks aligned at right angles to the tensile strain in the product . Oxidation and UV degradation are also frequently linked , mainly because UV radiation creates free radicals by bond breakage . The free radicals then react with oxygen to produce peroxy radicals which cause yet further damage , often in a chain reaction . Other polymers susceptible to oxidation include polypropylene and polyethylene . The former is more sensitive owing to the presence of secondary carbon atoms present in every repeat unit . Attack occurs at this point because the free radical formed is more stable than one formed on a primary carbon atom . Oxidation of polyethylene tends to occur at weak links in the chain , such as branch points in low @-@ density polyethylene .

= = Measurement and levels in food = =

Antioxidant vitamins are found in vegetables , fruits , eggs , legumes and nuts . Vitamins A , C , and E can be destroyed by long @-@ term storage or prolonged cooking . The effects of cooking and food processing are complex , as these processes can also increase the bioavailability of antioxidants , such as some carotenoids in vegetables . Processed food contains fewer antioxidant vitamins than fresh and uncooked foods , as preparation exposes food to heat and oxygen .

Other antioxidants are not vitamins and are instead made in the body . For example , ubiquinol (coenzyme Q) is poorly absorbed from the gut and is made in humans through the mevalonate pathway . Another example is glutathione , which is made from amino acids . As any glutathione in

the gut is broken down to free cysteine , glycine and glutamic acid before being absorbed , even large oral doses have little effect on the concentration of glutathione in the body . Although large amounts of sulfur @-@ containing amino acids such as acetylcysteine can increase glutathione , no evidence exists that eating high levels of these glutathione precursors is beneficial for healthy adults . Supplying more of these precursors may be useful as part of the treatment of some diseases , such as acute respiratory distress syndrome , protein @-@ energy malnutrition , or preventing the liver damage produced by paracetamol overdose .
Other compounds in the diet can alter the levels of antioxidants by acting as pro @-@ oxidants whereby consuming the compound may cause oxidative stress , possibly resulting in higher levels of antioxidant enzymes .

= = = Invalidation of ORAC = = =

Measurement of antioxidant content in food is not a straightforward process , as this is a diverse group of compounds with different reactivities to various reactive oxygen species . In food science , the oxygen radical absorbance capacity (ORAC) used to be the industry standard for antioxidant strength of whole foods , juices and food additives . However , the United States Department of Agriculture (USDA) withdrew these ratings in 2012 as biologically invalid , stating that no physiological proof in vivo existed to support the free @-@ radical theory , especially for polyphenols . Consequently , the ORAC method , derived only from in vitro experiments , is no longer considered relevant to human diets or biology .
Alternative in vitro measurements include the Folin @-@ Ciocalteu reagent , and the Trolox equivalent antioxidant capacity assay .

= = History = =

As part of their adaptation from marine life , terrestrial plants began producing non @-@ marine antioxidants such as ascorbic acid (vitamin C) , polyphenols and tocopherols . The evolution of angiosperm plants between 50 and 200 million years ago resulted in the development of many antioxidant pigments ? particularly during the Jurassic period ? as chemical defences against reactive oxygen species that are byproducts of photosynthesis . Originally , the term antioxidant specifically referred to a chemical that prevented the consumption of oxygen . In the late 19th and early 20th centuries , extensive study concentrated on the use of antioxidants in important industrial processes , such as the prevention of metal corrosion , the vulcanization of rubber , and the polymerization of fuels in the fouling of internal combustion engines .
Early research on the role of antioxidants in biology focused on their use in preventing the oxidation of unsaturated fats , which is the cause of rancidity . Antioxidant activity could be measured simply by placing the fat in a closed container with oxygen and measuring the rate of oxygen consumption . However , it was the identification of vitamins A , C , and E as antioxidants that revolutionized the field and led to the realization of the importance of antioxidants in the biochemistry of living organisms . The possible mechanisms of action of antioxidants were first explored when it was recognized that a substance with anti @-@ oxidative activity is likely to be one that is itself readily oxidized . Research into how vitamin E prevents the process of lipid peroxidation led to the identification of antioxidants as reducing agents that prevent oxidative reactions , often by scavenging reactive oxygen species before they can damage cells .