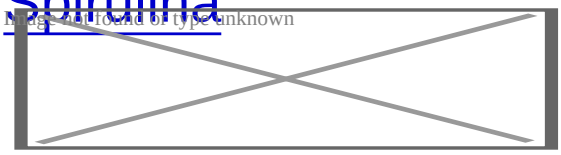
Detoxification

Description

Silymarin
Quercetin
Astaxanthin
Melatonin
Spirulina



Silymarin

Kiruthiga, P. V., Shafreen, R. B., Pandian, S. K., & Devi, K. P.. (2007). Silymarin Protection against Major Reactive Oxygen Species Released by Environmental Toxins: Exogenous H 2 O 2 Exposure in Erythrocytes. Basic & Clinical Pharmacology & Toxicology, 100(6), 414–419.

Plain numerical DOI: 10.1111/j.1742-7843.2007.00069.x
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“Silymarin is a polyphenolic plant flavonoid (a mixture of flavonoid isomers such as silibinin, isosilibinin, silidianin and silichristin) derived from silymarin marianum that has anti-inflammatory, hepatoprotective and anticarcinogenic effects. our earlier studies have shown that silymarin plays a protective role against the oxidative damage induced by environmental contaminants like benzo(a)pyrene in erythrocyte haemolysates. during the detoxification of these environmental contaminants, the major reactive oxygen species generated is hydrogen peroxide (h2o2). because h2o2can easily penetrate into the cell and cause damage to biomolecules, the protective role of silymarin was further assessed against this cytotoxic agent in vitro in erythrocyte haemolysates. the protective effect was monitored by assessing the levels of the antioxidant enzymes superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, glutathione-s-transferase, glutathione peroxidase and malondialdehyde (lpo) in three groups: vehicle control, h2o2-exposed groups and drug co-incubation group (h2o2 + silymarin). the protective effect of silymarin on the non-enzymic antioxidant glutathione and haemolysis, methaemoglobin content and protein carbonyl content were also assessed. it was observed that the activities of antioxidant enzymes and glutathione were reduced and the

malondialdehyde levels were elevated after h2o2exposure. there were also alterations in haemolysis, methaemoglobin content and protein carbonyl content, whereas after the administration of silymarin, the antioxidant enzyme activities reversed to near normal with reduced malondialdehyde content and normalized haemolysis, methaemoglobin content and protein carbonyl content. the results suggest that silymarin possesses substantial protective effect and free radical scavenging mechanism against exogenous h2o2-induced oxidative stress damages, hence, can be used as a protective drug against toxicity induced by environmental contaminants. © 2007 the authors."
Kiruthiga, P., Karthikeyan, K., Archunan, G., Pandian, S. K., & Devi, K. P.. (2015). Silymarin prevents benzo(a)pyrene-induced toxicity in Wistar rats by modulating xenobiotic-metabolizing enzymes. Toxicology and Industrial Health

Plain numerical DOI: 10.1177/0748233713475524
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"Benzo(a)pyrene (b(a)p), which is commonly used as an indicator species for polycyclic aromatic hydrocarbon (pah) contamination, has a large number of hazardous consequences on human health. in the presence of the enzyme cytochrome-p-450 1a1 (cyp1a1), it undergoes metabolic activation to form reactive intermediates that are capable of inducing mutagenic, cytotoxic, teratogenic and carcinogenic effects in various species and tissues. research within the last few years has shown that flavonoids exhibit chemopreventive effect against these toxins. in the present study, the protective effect of silymarin (a flavonoid) against b(a)p-induced toxicity was monitored in wistar rats by evaluating the levels of hepatic phase i (cyp1a1), phase ii enzymes (glutathione-s-transferase, epoxide hydroxylases, uridinediphosphate glucuronosyltransferases, nad(p)h: quinone oxidoreductase 1, sulfotransferases), cellular antioxidant enzyme heme oxygenase and total glutathione. the results reveal that silymarin possesses substantial protective effect against b(a)p-induced damages by inhibiting phase i detoxification enzyme cyp1a1 and modulating phase ii conjugating enzymes, which were confirmed by histopathological analysis. overall, the inhibition of cyp1a1 and the modulation of phase ii enzymes may provide, in part, the molecular basis for the effect of silymarin against b(a)p. © 2013, sage publications. all rights reserved."
Elyasi, S.. (2021). Silybum marianum, antioxidant activity, and cancer patients. In Cancer

Plain numerical DOI: 10.1016/b978-0-12-819547-5.00043-2
DOI URL
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"Silymarin, a flavonoid extracted from silybum marianum, displays antioxidant, and antiinflammatory activities. silybin is the major constituent and is often proposed as the substance responsible for silymarin biological activity. these properties seem to have resulted from their ability to scavenge free radicals, reactive oxygen species (ros), and to chelate metal ions. traditionally, it has been used to treat hepatic and biliary disorders. however, milk thistle is increasingly being evaluated for its use in adult and pediatric populations for oncology indications. usual indications during cancer treatment include cleansing and detoxification after chemotherapy, preventing chemotherapy and radiotherapy induced

adverse reactions like hepatotoxicity cardiotoxicity, nephrotoxicity, etc., and potentiating chemotherapy and radiation therapy as an adjunctive treatment. primary studies are considering its use as a chemopreventive agent and possibly to assist in cancer treatment. so milk thistle's current clinical use is growing by an increasing number of clinical trials and animal studies. this article provides an overview of the current clinical applications of s. marianum in the oncology setting, considering its antioxidant and antiinflammatory properties."
Kwon, D., Jun, D., & Kim, Y.. (2014). A novel mechanism involved in the enhancement of glutathione synthesis in liver by silymarin and its pharmacological significance. Planta Medica

Plain numerical DOI: 10.1055/s-0034-1394493
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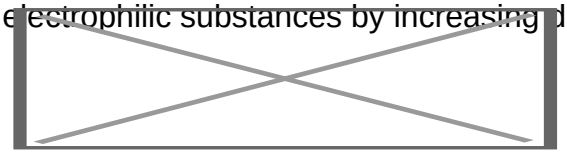
"Silymarin has been used for the treatment of liver injury. we investigated the alterations in sulfur amino acid metabolism induced by silymarin and its pharmacological significance. male mice were treated with silymarin (100 or 200 mg/kg, po) every 12h for a total of 3 doses. silymarin elevated hepatic methionine level by 24% at the lower dose and by 34% at the higher dose when measured at 6h after the last dosing, but decreased methionine adenosyltransferase expression in a dose-dependent manner. s-adenosylmethionine or homocysteine concentration was not changed, whereas cystathionine, cysteine and glutathione (gsh) were increased significantly. cystathionine ?-synthase was induced, but cysteine dioxygenase was down-regulated in liver. total oxygen radical scavenging capacity of liver was increased and hepatic lipid peroxidation was diminished significantly. in mice pretreated with silymarin the hepatotoxicity induced by acetaminophen (apap; 500 mg/kg, ip) was reduced as measured by elevation of serum enzyme activities and histopathological examination. plasma apap level was not changed, while apap-gsh, apap-cysteine and apap-mercapturate were elevated significantly. however, expression of cyp2e1, cyp1a or cyp3a was not increased by silymarin. these results indicate that the increment of apap-gsh conjugates should be attributed to the increase in conjugation of n-acetyl-p-benzoquinoneimine with gsh. in conclusion, the results show that silymarin enhances hepatic gsh generation by elevating cysteine availability via an increment in cysteine synthesis and an inhibition of its catabolism to taurine, which subsequently contributes to the antioxidant defense of liver. it is also suggested that silymarin may protect the liver from reactive electrophilic substances by increasing detoxification via conjugation with gsh."



Quercetin

Zhao, Y., Tang, Y., & Sang, S.. (2021). Dietary Quercetin Reduces Plasma and Tissue Methylglyoxal and Advanced Glycation End Products in Healthy Mice Treated with Methylglyoxal. Journal of Nutrition

Plain numerical DOI: 10.1093/jn/nxab176

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“Background: methylglyoxal (mgo), a precursor of advanced glycation end products (ages), has been linked to ages-associated diseases. objectives: this study investigated the efficacy and mechanisms of dietary quercetin in decreasing plasma and tissue concentrations of mgo and ages in mgo-administered mice. methods: male, 6-wk-old cd-1 mice were administered ain-93g diet and water (con) or 0.12% mgo in water (mgo) or mgo plus 0.2% (0.2q) dietary quercetin for 1 wk (n = 5) (experiment 1), and water (con), 0.12% mgo (mgo), or mgo plus 0.1% (0.1q), 0.2% (0.2q), or 0.4% (0.4q) dietary quercetin for 6 wk (n = 10) (experiment 2). the plasma, kidney, and liver concentrations of mgo, quercetin, and isorhamnetin and their trapping adducts with mgo were determined by lc-ms, and age concentrations were measured by the fluorescent method. furthermore, the expressions of glyoxalase i/ii (glo i/ii) and aldose reductase (ar), mgo detoxification enzymes, were determined by western blot. one-factor anova and post hoc dunnett’s or tukey’s test were used to analyze the data. results: after 1 wk of treatment, the mgo concentrations in plasma (20.2%) and kidney (29.9%) in 0.2q mice were significantly lower than those in mgo mice. after 6 wk of treatment, the concentrations of mgo in the plasma (14.7-18.6%), kidney (20-20.8%), liver (15.4-18.6%), and tissue ages (28-36.8%) in 0.1q, 0.2q, and 0.4q mice were significantly lower than those in mgo mice. the plasma concentrations of quercetin, isorhamnetin, and their mgo adducts were dose-dependently increased after quercetin administration. in addition, after 6 wk of quercetin administration, the expressions of glo i/ii and ar in the liver and kidney were significantly upregulated to promote mgo detoxification compared with mgo-treated mice. conclusions: quercetin reduced plasma and tissue mgo concentrations and inhibited age formation by trapping mgo and regulating the mgo detoxification systems in mgo-administered healthy mice.”
Kim, M., Jee, S. C., Kim, K. S., Kim, H. S., Yu, K. N., & Sung, J. S.. (2021). Quercetin and isorhamnetin attenuate benzo[a]pyrene-induced toxicity by modulating detoxification enzymes through the ahr and nrf2 signaling pathways. Antioxidants

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“Benzo[a]pyrene, classified as a group 1 carcinogen, is metabolized to b[a]p-7,8-dihydrodiol-9,10-epoxide (bpde), causing dna mutations and eventually cancer. quercetin is a dietary flavonoid abundant in fruits and vegetables. after quercetin intake, quercetin’s metabolites isorhamnetin and miquelianin are more highly concentrated than quercetin in the human plasma. in this study, we investigated the molecular mechanisms associated with the cytoprotective effect of quercetin and its metabolites against benzo[a]pyrene from a detoxification perspective. quercetin and its metabolite isorhamnetin reduced benzo[a]pyrene-induced cytotoxicity, whereas the metabolite miquelianin did not mitigate benzo[a]pyrene-induced cytotoxicity. moreover, quercetin and isorhamnetin reduced intracellular levels of bpde-dna adducts. the formation and elimination of bpde is mediated by the xenobiotic detoxification process. quercetin and isorhamnetin increased the gene and protein expression levels of phase i, ii, and iii enzymes involved in xenobiotic detoxification. further-more,

quercetin and isorhamnetin induced the translocation of aryl hydrocarbon receptor (ahr) and nuclear factor erythroid 2-related factor 2 (nrf2), which regulate the expression level of phase enzymes. our results suggest that quercetin and isorhamnetin promote the metabolism, detoxifi-cation, and elimination of b[a]p, thereby increasing anti-genotoxic effects and protecting against b[a]p-induced cytotoxicity."
Bagheri, A., Ebrahimpour, S., Nourbakhsh, N., Talebi, S., & Esmaeili, A.. (2021). Protective effect of quercetin on alteration of antioxidant genes expression and histological changes in the dental pulp of the streptozotocin-diabetic rats. Archives of Oral Biology

Plain numerical DOI: 10.1016/j.archoralbio.2021.105088
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"Objective: we aimed to assess the effect of quercetin as one of the most common polyphenols with anti-inflammatory and antioxidant properties on expression levels of catalase (cat), superoxide dismutase 1 (sod1), and glutathione peroxidase 1 (gpx1), involved in the detoxification of reactive oxygen species (ros), and histology of dental pulp in streptozotocin-diabetic rats. design: type 1 diabetes mellitus (t1dm) was induced by intraperitoneal injection of streptozotocin in adult male wistar rats. animals (n = 24) were equally distributed into control, diabetes, and diabetes treated with quercetin groups. rats were gavaged daily with quercetin (25 mg/kg) for forty days. to measure the mrna levels of antioxidant genes, quantitate real-time pcr was applied. the oxidative stress parameters such as total antioxidant capacity (tac) and histopathological assessments were performed. results: a significant increase in the relative quantification mrna levels of sod1, cat, gpx1 was detected in diabetic rat dental pulp. besides, persistent hyperglycemia led to the enhancement of tac level and degeneration of connective tissue of the dental pulp. interestingly, quercetin normalized the expression mrna levels of cat, sod1, gpx1 to near the normal level. moreover, quercetin treatment normalized tac levels. conclusions: because of the crucial role of antioxidants in diabetic complications, the findings of the current study presented a molecular basis for the protective effect of quercetin on dental pulp in diabetic conditions."
Ibrahim, K. A., Eleyan, M., Khwanes, S. A., Mohamed, R. A., & Abd El-Rahman, H. A.. (2021). Quercetin ameliorates the hepatic apoptosis of foetal rats induced by in utero exposure to fenitrothion via the transcriptional regulation of paraoxonase-1 and apoptosis-related genes. Biomarkers

Plain numerical DOI: 10.1080/1354750X.2021.1875505
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"Background & purpose: exposure to organophosphorus during different phases of pregnancy induces many adverse impacts on the developing foetuses due to their immature detoxification system. we have estimated the potential amelioration role of quercetin against hepatic injury-induced apoptosis in rat foetuses following gestational exposure to fenitrothion and probable involvement of paraoxonase-1. methods: forty pregnant rats were allocated into four groups; the first one kept as control, the second intubated with quercetin (100 mg/kg), the third orally administrated fenitrothion (4.62 mg/kg) and the

last group received quercetin two hours before fenitrothion intoxication. results: fenitrothion significantly elevated the foetal hepatic levels of thiobarbituric acid reactive substances, protein carbonyl, and nitric oxide, but it reduced the enzymatic activities of glutathione-s-transferase, superoxide dismutase, catalase, and acetylcholinesterase. furthermore, fenitrothion provoked many histopathological changes in the foetal liver and markedly up-regulated the mrna gene expression of p53, caspase-9 along with elevation in the immunoreactivity of bax and caspase-3, but it down-regulated the expression level of paraoxonase-1. remarkably, quercetin co-treatment successfully ameliorated the hepatic oxidative injury and apoptosis prompted by fenitrothion. conclusions: dietary supplements with quercetin can be used to reduce the risk from organophosphorus exposure probably through paraoxonase-1 up-regulation and enhancement of the cellular antioxidant system."
Cui, B., Huang, X., Li, S., Hao, K., Chang, B. H., Tu, X., … Zhang, Z.. (2019). Quercetin Affects the Growth and Development of the Grasshopper Oedaleus asiaticus (Orthoptera: Acrididae). Journal of Economic Entomology

Plain numerical DOI: 10.1093/jee/toz050
DOI URL
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"Flavonoids are secondary metabolites that help plants resist insect attack, but pest insects have evolved enzymes that reduce the toxicity of these secondary metabolites. we studied the response of the grasshopper oedaleus asiaticus bey-bienko fed different concentrations of quercetin, a representative flavonoid. oedaleus asiaticus growth (survival rate and growth rate) was significantly reduced at high quercetin concentrations. reactive oxygen species (ros) increased significantly in response to the diet stress associated with high quercetin concentrations. gene expression and protein phosphorylation level of the igf?foxo cascade related to the stress response in the o. asiaticus insulin-like signaling pathway (ilp) were also reduced. multiple protective enzyme activities were regulated by foxo. mixed-function oxidase (mfo), superoxide dismutase (sod), peroxidase (pod), and catalase (cat), were all significantly increased with exposure to high quercetin concentrations. quercetin negatively regulated the ilp pathway, and was detrimental to o. asiaticus growth and survival, as more energy was required for detoxification. this study showed how flavonoids impact on o. asiaticus biochemical pathways, physiology, and development. flavonoids offer a new option for the development of biological pesticides for application to grasshopper biological control."
Gao, Y., Fang, L., Wang, X., Lan, R., Wang, M., Du, G., … Zhao, H.. (2019). Antioxidant activity evaluation of dietary flavonoid hyperoside using Saccharomyces cerevisiae as a model. Molecules

Plain numerical DOI: 10.3390/molecules24040788
DOI URL
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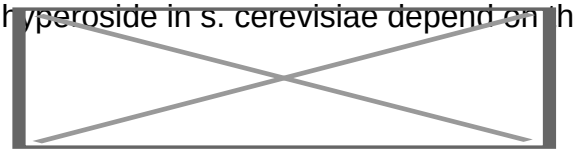
"Oxidative stress leads to various diseases, including diabetes, cardiovascular diseases, neurodegenerative diseases, and even cancer. the dietary flavonol glycoside, hyperoside (quercetin-3-o-galactoside), exerts health benefits by preventing oxidative damage. to further understand its antioxidative defence mechanisms, we systemically investigated the regulation of hyperoside on

oxidative damage induced by hydrogen peroxide, carbon tetrachloride, and cadmium in saccharomyces cerevisiae. hyperoside significantly increased cell viability, decreased lipid peroxidation, and lowered intracellular reactive oxygen species (ros) levels in the wild-type strain (wt) and mutants gtt1? and gtt2?. however, the strain with ctt1? showed variable cell viability and intracellular ros-scavenging ability in response to the hyperoside treatment upon the stimulation of h2o2 and ccl4. in addition, hyperoside did not confer viability tolerance or intercellular ros in cdso4-induced stress to strains of sod1? and gsh1?. the results suggest that the antioxidative reactions of hyperoside in s. cerevisiae depend on the intercellular ros detoxification system."



Astaxanthin

Hoshi, H., Monoe, F., Ohsawa, I., Ohta, S., & Miyamoto, T.. (2020). Astaxanthin improves osteopenia caused by aldehyde-stress resulting from Aldh2 mutation due to impaired osteoblastogenesis. Biochemical and Biophysical Research Communications

Plain numerical DOI: 10.1016/j.bbrc.2020.04.013
DOI URL
directSciHub download

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"Aldehyde dehydrogenase 2 (aldh2) plays major roles in aldehyde detoxification and in the catalysis of amino acids. aldh2?2, a dominant-negative transgenic expressing aldehyde dehydrogenase 2 (aldh2) protein, is produced by a single nucleotide polymorphism (rs671) and is involved in the development of osteoporosis and hip fracture with aging. in a previous study, transgenic mice expressing aldh2?2(aldh2?2 tg) osteoblastic cells or acetaldehyde -treated mc3t3-e1 showed impaired osteoblastogenesis and caused osteoporosis [1]. in this study, we demonstrated the effects of astaxanthin for differentiation to osteoblasts of mc3t3-e1 by the addition of acetaldehyde and aldh2?2 tg mesenchymal stem cells in bone marrow. astaxanthin restores the inhibited osteoblastogenesis by acetaldehyde in mc 3t3-e1 and in bone marrow mesenchymal stem cells of aldh2?2 tg mice. additionally, astaxanthin administration improved femur bone density in aldh2?2 tg mice. furthermore, astaxanthin improved cell survival and mitochondrial function in acetaldehyde-treated mc 3t3-e1 cells. our results suggested that astaxanthin had restorative effects on osteoblast formation and provide new insight into the regulation of osteoporosis and suggest a novel strategy to promote bone formation in osteopenic diseases caused by impaired acetaldehyde metabolism."
Kavitha, K., Thiyagarajan, P., Rathna, J., Mishra, R., & Nagini, S.. (2013). Chemopreventive effects of diverse dietary phytochemicals against DMBA-induced hamster buccal pouch carcinogenesis via the induction of Nrf2-mediated cytoprotective antioxidant, detoxification, and DNA repair enzymes. Biochimie

Plain numerical DOI: 10.1016/j.biochi.2013.05.004

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“Identifying agents that activate nuclear factor erythroid-2 related factor-2 (nrf2), a key regulator of various cytoprotective antioxidant, and detoxifying enzymes has evolved as a promising strategy for cancer chemoprevention. in the present study, we investigated the effect of dietary supplementation of structurally diverse phytochemicals- astaxanthin, blueberry, chlorophyllin, ellagic acid, and theaphenon-e on nrf2 signaling, and xenobiotic-metabolizing and antioxidant enzymes in the 7,12-dimethylbenz[a] anthracene (dmba)-induced hamster buccal pouch (hbp) carcinogenesis model. we observed that these phytochemicals induce nuclear accumulation of nrf2 while downregulating its negative regulator, keap-1. this was associated with reduced expression of cyp1a1 and cyp1b1, the cytochrome p450 isoforms involved in the activation of dmba, and the oxidative stress marker 8-hydroxy-2?-deoxyguanosine coupled with upregulation of the phase ii detoxification enzymes glutathione s-transferases and nad(p)h:quinone oxidoreductase 1 and the antioxidant enzymes superoxide dismutase, catalase, and glutathione peroxidase. in addition, these dietary phytochemicals also enhanced the dna repair enzymes 8-oxoguanine glycosylase 1 (ogg1), xeroderma pigmentosum d (xpd), xeroderma pigmentosum g (xpg), and x-ray repair cross complementing group 1 (xrcc1). our data provide substantial evidence that the dietary phytochemicals inhibit the development of hbp carcinomas through the activation of nrf2/keap-1 signaling and by upregulating cytoprotective enzymes. the extent of the chemopreventive effects of the phytochemicals was in the order: chlorophyllin > blueberry > ellagic acid > astaxanthin > theaphenon-e. thus these dietary phytochemicals that function as potent activators of nrf2 and its orchestrated response are novel candidates for cancer chemoprevention. © 2013 elsevier masson sas. all rights reserved.”
Gradelet, S., Astorg, P., Bon, A. M. Le, Bergès, R., & Suschetet, M.. (1997). Modulation of aflatoxin B1 carcinogenicity, genotoxicity and metabolism in rat liver by dietary carotenoids: Evidence for a protective effect of CYP1A inducers. In Cancer Letters

Plain numerical DOI: 10.1016/S0304-3835(97)04668-5
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“The effects of several carotenoids of vitamin a and of s-methylcholanthrene have been tested on the initiation of hepatocarcinogenesis by aflatoxin b1, using the sequential protocol of solt and farber. afb1-induced dna single-strand breaks and afb1-metabolism were also assessed. the p4501a inducer carotenoids (canthaxanthin, astaxanthin, ?-apo-8’-carotenal) and 3-methylcholanthrene reduce the carcinogenicity of afb1, divert afb1-metabolism into the less genotoxic aflatoxin m1 and reduce afb1-induced dna single-strand breaks: we conclude that these carotenoids exert their protective effect through the deviation of afb1 metabolism towards detoxification pathways. ?-carotene decreased afb1 carcinogenicity but did not alter its metabolism, probably acting by other mechanisms.”
P., P., M.C., M., A., C., & M., M.. (2011). Potential interactions of carotenoids with other bioactive food components in the prevention of chronic diseases. Current Bioactive Compounds

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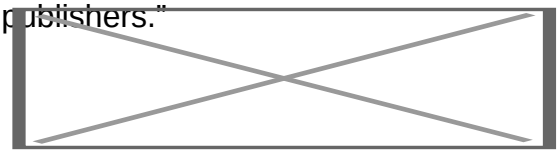
“Epidemiological studies have consistently shown that regular consumption of fruits and vegetables, as well as whole grains and fish oils, is strongly associated with reduced risk of developing chronic diseases, such as cancer and cardiovascular diseases. over the years, numerous bioactive compounds have been identified that contribute to these beneficial health effects. in particular, carotenoids have been shown to exhibit potential antioxidant, anti-atherogenic and anti-carcinogenic properties in several experimental studies. more recently, evidence is emerging that specific combinations of carotenoids with other bioactive food components may be far more effective in protecting against cancer and cardiovascular diseases than isolated compounds. the present review summarizes the in vitro and in vivo evidence for additive and synergistic interactions of carotenoids with various dietary bioactive food components, including vitamin e, vitamin c, phenolics, n-3 polyunsaturated fatty acids (pufas) and lipoic acid, in preventing oxidative stress, cancer and cardiovascular diseases. our understanding of the molecular mechanisms underlying such synergistic effects, as well as the number of the studies, is still limited, but it appears that different combinations of complementary modes of actions may be an appropriate strategy for significantly reducing the risk of chronic diseases and to meet nutrient requirements for optimum health.© 2011 bentham science publishers.”



Melatonin

He, J., Zhuang, X., Zhou, J., Sun, L., Wan, H., Li, H., & Lyu, D.. (2020). Exogenous melatonin alleviates cadmium uptake and toxicity in apple rootstocks. Tree Physiology

Plain numerical DOI: 10.1093/TREEPHYS/TPAA024
DOI URL
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“To examine the potential roles of melatonin in cadmium (cd) uptake, accumulation and detoxification in malus plants, we exposed two different apple rootstocks varying greatly in cd uptake and accumulation to either 0 or 30 ?m cd together with 0 or 100 ?m melatonin. cadmium stress stimulated endogenous melatonin production to a greater extent in the cd-tolerant malus baccata borkh. than in the cd-susceptible malus micromalus ‘qingzhoulinqin’. melatonin application attenuated cd-induced reductions in growth, photosynthesis and enzyme activity, as well as reactive oxygen species (ros) and malondialdehyde accumulation. melatonin treatment more effectively restored photosynthesis, photosynthetic pigments and biomass in cd-challenged m. micromalus ‘qingzhoulinqin’ than in cd-stressed m. baccata. exogenous melatonin lowered root cd2+ uptake, reduced leaf cd accumulation, decreased cd translocation factors and increased root, stem and leaf melatonin contents in both cd-exposed rootstocks. melatonin application increased both antioxidant concentrations and enzyme

activities to scavenge cd-induced ros. exogenous melatonin treatment altered the mrna levels of several genes regulating cd uptake, transport and detoxification including ha7, nramp1, nramp3, hma4, pcr2, nas1, mt2, abcc1 and mhx. taken together, these results suggest that exogenous melatonin reduced aerial parts cd accumulation and mitigated cd toxicity in malus plants, probably due to the melatonin-mediated cd allocation in tissues, and induction of antioxidant defense system and transcriptionally regulated key genes involved in detoxification."
Tordjman, S., Chokron, S., Delorme, R., Charrier, A., Bellissant, E., Jaafari, N., & Fougerou, C.. (2017). Melatonin: Pharmacology, Functions and Therapeutic Benefits. Current Neuropharmacology

Plain numerical DOI: 10.2174/1570159×14666161228122115
DOI URL
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"© 2017 bentham science publishers. background: melatonin synchronizes central but also peripheral oscillators (fetal adrenal gland, pancreas, liver, kidney, heart, lung, fat, gut, etc.), allowing temporal organization of biological functions through circadian rhythms (24-hour cycles) in relation to periodic environmental changes and therefore adaptation of the individual to his/her internal and external environment. measures of melatonin are considered the best peripheral indices of human circadian timing based on an internal 24-hour clock. methods: first, the pharmacology of melatonin (biosynthesis and circadian rhythms, pharmacokinetics and mechanisms of action) is described, allowing a better understanding of the short and long term effects of melatonin following its immediate or prolonged release. then, research related to the physiological effects of melatonin is reviewed. results: the physiological effects of melatonin are various and include detoxification of free radicals and antioxidant actions, bone formation and protection, reproduction, and cardiovascular, immune or body mass regulation. also, protective and therapeutic effects of melatonin are reported, especially with regard to brain or gastrointestinal protection, psychiatric disorders, cardiovascular diseases and oncostatic effects. conclusion: this review highlights the high number and diversity of major melatonin effects and opens important perspectives for measuring melatonin as a biomarker (biomarker of early identification of certain disorders and also biomarker of their follow-up) and using melatonin with clinical preventive and therapeutic applications in newborns, children and adults based on its physiological regulatory effects."
Samanta, S.. (2020). Physiological and pharmacological perspectives of melatonin. Archives of Physiology and Biochemistry

Plain numerical DOI: 10.1080/13813455.2020.1770799
DOI URL
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"The pineal gland is a interface between light-dark cycle and shows neuro-endocrine functions. melatonin is the primary hormone of pineal gland, secreted at night. the night-time melatonin peak regulates the physiological functions at dark. melatonin has several unique features as it synchronises internal rhythm with daily and seasonal variations, regulates circadian rhythm and sleep-wake cycle. physiologically melatonin involves in detoxification of free radicals, immune functions, neuro-protection,

oncostatic effects, cardiovascular functions, reproduction, and foetal development. the precise functions of melatonin are exhibited by specific receptors. in relation to pathophysiology, impaired melatonin secretion promotes sleep disorder, cancer progression, type-2 diabetes, and neurodegenerative diseases. several reports have highlighted the therapeutic benefits of melatonin specially related to cancer protection, sleep disorder, psychiatric disorders, and jet lag problems. this review will touch the most of the area of melatonin-oriented health impacts and its therapeutic aspects."
Luchetti, F., Canonico, B., Betti, M., Arcangeletti, M., Pilolli, F., Piroddi, M., … Galli, F.. (2010). Melatonin signaling and cell protection function. FASEB Journal

Plain numerical DOI: 10.1096/fj.10-154450
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"Besides its well-known regulatory role on circadian rhythm, the pineal gland hormone melatonin has other biological functions and a distinct metabolism in various cell types and peripheral tissues. in different tissues and organs, melatonin has been described to act as a paracrine and also as an intracrine and autocrine agent with overall homeostatic functions and pleiotropic effects that include cell protection and prosurvival factor. these latter effects, documented in a number of in vitro and in vivo studies, are sustained through both receptor-dependent and -independent mechanisms that control detoxification and stress response genes, thus conferring protection against a number of xenobiotics and endobiotics produced by acute and chronic noxious stimuli. redox-sensitive components are included in the cell protection signaling of melatonin and in the resulting transcriptional response that involves the control of nf-?b, ap-1, and nrf2. by these pathways, melatonin stimulates the expression of antioxidant and detoxification genes, acting in turn as a glutathione system enhancer. a further and converging mechanism of cell protection by this indoleamine described in different models seems to lie in the control of damage and signaling function of mitochondria that involves decreased production of reactive oxygen species and activation of the antiapoptotic and redox-sensitive element bcl2. recent evidence suggests that upstream components in this mitochondrial route include the calmodulin pathway with its central role in melatonin signaling and the survival-promoting component of mapks, erk1/2. in this review article, we will discuss these and other molecular aspects of melatonin signaling relevant to cell protection and survival mechanisms. © faseb."
Li, M. Q., Hasan, M. K., Li, C. X., Ahammed, G. J., Xia, X. J., Shi, K., … Zhou, J.. (2016). Melatonin mediates selenium-induced tolerance to cadmium stress in tomato plants. Journal of Pineal Research

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"Both selenium (se) and melatonin reduce cadmium (cd) uptake and mitigate cd toxicity in plants. however, the relationship between se and melatonin in cd detoxification remains unclear. in this study, we investigated the influence of three forms of se (selenocysteine, sodium selenite, and sodium selenate) on the biosynthesis of melatonin and the tolerance against cd in tomato plants. pretreatment with different forms of se significantly induced the biosynthesis of melatonin and its precursors

(tryptophan, tryptamine, and serotonin); selenocysteine had the most marked effect on melatonin biosynthesis. furthermore, se and melatonin supplements significantly increased plant cd tolerance as evidenced by decreased growth inhibition, photoinhibition, and electrolyte leakage (el). se-induced cd tolerance was compromised in melatonin-deficient plants following tryptophan decarboxylase (tdc) gene silencing. se treatment increased the levels of glutathione (gsh) and phytochelatins (pcs), as well as the expression of gsh and pc biosynthetic genes in nonsilenced plants, but the effects of se were compromised in tdc-silenced plants under cd stress. in addition, se and melatonin supplements reduced cd content in leaves of nonsilenced plants, but se-induced reduction in cd content was compromised in leaves of tdc-silenced plants. taken together, our results indicate that melatonin is involved in se-induced cd tolerance via the regulation of cd detoxification."
Reiter, R. J., Mayo, J. C., Tan, D. X., Sainz, R. M., Alatorre-Jimenez, M., & Qin, L.. (2016). Melatonin as an antioxidant: under promises but over delivers. Journal of Pineal Research

Plain numerical DOI: 10.1111/jpi.12360
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"Melatonin is uncommonly effective in reducing oxidative stress under a remarkably large number of circumstances. it achieves this action via a variety of means: direct detoxification of reactive oxygen and reactive nitrogen species and indirectly by stimulating antioxidant enzymes while suppressing the activity of pro-oxidant enzymes. in addition to these well-described actions, melatonin also reportedly chelates transition metals, which are involved in the fenton/haber–weiss reactions; in doing so, melatonin reduces the formation of the devastatingly toxic hydroxyl radical resulting in the reduction of oxidative stress. melatonin's ubiquitous but unequal intracellular distribution, including its high concentrations in mitochondria, likely aid in its capacity to resist oxidative stress and cellular apoptosis. there is credible evidence to suggest that melatonin should be classified as a mitochondria-targeted antioxidant. melatonin's capacity to prevent oxidative damage and the associated physiological debilitation is well documented in numerous experimental ischemia/reperfusion (hypoxia/reoxygenation) studies especially in the brain (stroke) and in the heart (heart attack). melatonin, via its antiradical mechanisms, also reduces the toxicity of noxious prescription drugs and of methamphetamine, a drug of abuse. experimental findings also indicate that melatonin renders treatment-resistant cancers sensitive to various therapeutic agents and may be useful, due to its multiple antioxidant actions, in especially delaying and perhaps treating a variety of age-related diseases and dehumanizing conditions. melatonin has been effectively used to combat oxidative stress, inflammation and cellular apoptosis and to restore tissue function in a number of human trials; its efficacy supports its more extensive use in a wider variety of human studies. the uncommonly high-safety profile of melatonin also bolsters this conclusion. it is the current feeling of the authors that, in view of the widely diverse beneficial functions that have been reported for melatonin, these may be merely epiphenomena of the more fundamental, yet-to-be identified basic action(s) of this ancient molecule."
Reiter, R. J., Tan, D. X., & Galano, A.. (2014). Melatonin: Exceeding expectations. Physiology

Plain numerical DOI: 10.1152/physiol.00011.2014
DOI URL

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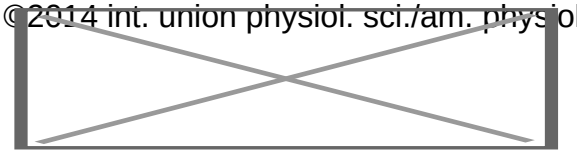
“Melatonin is a small, highly conserved indole with numerous receptor-mediated and receptor-independent actions. receptor-dependent functions include circadian rhythm regulation, sleep, and cancer inhibition. the receptor-independent actions relate to melatonin’s ability to function in the detoxification of free radicals, thereby protecting critical molecules from the destructive effects of oxidative stress under conditions of ischemia/reperfusion injury (stroke, heart attack), ionizing radiation, and drug toxicity, among others. melatonin has numerous applications in physiology and medicine. ©2014 int. union physiol. sci./am. physiol. soc.”



Spirulina

Dasgupta, T., Banerjee, S., Yadav, P. K., & Rao, A. R.. (2001). Chemomodulation of carcinogen metabolising enzymes, antioxidant profiles and skin and forestomach papillomagenesis by Spirulina platensis. Molecular and Cellular Biochemistry

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“Numerous reports have revealed an inverse association between consumption of some selective natural products and risk of developing cancer. in the present study the effect of 250 and 500 mg/kg body wt. of spirulina was examined on drug metabolising phase i and phase ii enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase and lipid peroxidation in the liver of 7-week-old swiss albino mice. the implications of these biochemical alterations have been further evaluated adopting the protocol of benzo(a)pyrene induced forestomach and 7,12 dimethylbenz(a)anthracene (dmba) initiated and croton oil promoted skin papillomagenesis. our primary findings reveal the ‘Monofunctional’ nature of spirulina as deduced from its potential to induce only the phase ii enzyme activities associated mainly with carcinogen detoxification. the glutathione s-transferase and dt-diaphorase specific activities were induced in hepatic and all the extrahepatic organs examined (lung, kidney and forestomach) by spirulina pretreatment (significance level being from $p < 0.05$ to $p < 0.005$) except for the low dose treatment in forestomach. with reference to antioxidant enzymes viz., superoxide dismutase, catalase, glutathione reductase, glutathione peroxidase and reduced glutathione were increased significantly by both the chosen doses of spirulina from $p < 0.01$ to $p < 0.005$. chemopreventive response was quantitated by the average number of papillomas per effective mouse (tumor burden) as well as percentage of tumor bearing animals. there was a significant inhibition of tumor burden as well as tumor incidence in both the tumor model systems studied. in the skin tumor studies tumor burden was reduced from 4.86 to 1.20 and 1.15 by the low and high dose

treatment respectively. in stomach tumor studies tumor burden was 2.05 and 1.73 by the low and high doses of spirulina treatment against 3.73 that of control."
Premkumar, K., Pachiappan, A., Abraham, S. K., Santhiya, S. T., Gopinath, P. M., & Ramesh, A.. (2001). Effect of Spirulina fusiformis on cyclophosphamide and mitomycin-C induced genotoxicity and oxidative stress in mice. Fitoterapia

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"Spirulina fusiformis was tested for its possible in vivo protective effects against cyclophosphamide (cp) and mitomycin-c (mmc) induced genotoxicity and oxidative stress in mice. pre-treatment with s. fusiformis (250, 500 and 1000 mg kg-1, p.o., daily for 5 days) significantly reduced the chromosomal damage and lipid peroxidation with concomitant changes in antioxidants and detoxification systems. all the three tested doses were effective in exerting a protective effect against cp and mmc. © 2001 elsevier science b.v. all rights reserved."
Yener, N. A., Sinanoglu, O., Ilter, E., Celik, A., Sezgin, G., Midi, A., … Aksungar, F.. (2013). Effects of spirulina on cyclophosphamide-induced ovarian toxicity in rats: Biochemical and histomorphometric evaluation of the ovary. Biochemistry Research International

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"Cyclophosphamide (cyc) is known to cause ovotoxicity and infertility in women. our aim is to investigate the possible ovotoxic effects of cyc and possible antioxidant and protective effects of blue-green algae, spirulina (sp), in rat ovaries. eighteen rats were given: group i (n = 6, control); group ii (n = 6, cp), a single dose cyc; group iii (n = 6, sp+cyc), 7 days sp+single dose cyc. tissue malondialdehyde (mda) levels, superoxide dismutase (sod), and catalase (cat) activities are assessed biochemically. normal and atretic primordial and primary follicle counts for all sections obtained for each ovary are calculated. mean number of follicle counts for each group are compared. in sp+cyc group, tissue mda levels were significantly lower than those in the cp and higher than those in the c group (cp > sp + cyc > c). tissue sod activity was significantly higher in sp+cyc group than that in the cp group and lower than that in the c group (c > sp + cyc > c). no statistically significant difference was found between the ovarian cat activities in any group. histomorphometrically, there was also no significant difference between the mean numbers of normal and atretic small follicle counts. our results suggest that single dose cyc has adverse effects on oxidant status of the ovaries and sp has protective effects in cyc-induced ovotoxicity. © 2013 nese arzu yener et al."
Yigit, F., Gurel-Gurevin, E., Isbilen-Basok, B., Esener, O. B. B., Bilal, T., Keser, O., … Ikitimur-Armutak, E. I.. (2016). Protective effect of Spirulina platensis against cell damage and apoptosis in hepatic tissue caused by high fat diet. Biotechnic and Histochemistry

Plain numerical DOI: 10.3109/10520295.2015.1114142
DOI URL
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“Spirulina platensis is a microalga that may be a source of antioxidants that can reduce body fat deposition. consumption of a high fat diet produces elevated blood lipid levels, inflammation and apoptosis. we investigated the possible effects of s. platensis on the blood lipid profile, and liver inflammation and apoptosis in rats fed a high fat diet. sixty-four young male rats were divided into eight equal groups. the control group was fed a basic diet. the experimental groups were fed a diet for 60 days that was prepared by mixing variable amounts of 43% vegetable oil and 10% cholesterol with or without 3% s. platensis mixed with the basal diet. blood and liver tissue samples were collected from each animal. serum samples were used to analyze lipid parameters, total antioxidant status and total oxidant status. inos and enos were determined by immunohistochemistry. tunel staining was used to detect apoptosis to investigate a possible connection between inflammation and apoptosis in the liver tissue. the relations between fat deposition and liver degeneration were assessed by sirius red staining and alpha-smooth muscle actin immunostaining. s. platensis reduced serum hdl-c, ldl-c and triglyceride, increased hdl-c levels in rats fed a high fat diet to near control levels, and reduced inos levels and increased enos levels in the liver tissue compared to vegetable oil and cholesterol treated groups. the apoptotic index was reduced in the groups that were fed a high fat or a basic diet when supplemented with s. platensis.”
McCarty, M. F., & Lerner, A.. (2020). Nutraceuticals targeting generation and oxidant activity of peroxynitrite may aid prevention and control of parkinson’s disease. International Journal of Molecular Sciences

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“Parkinson’s disease (pd) is a chronic low-grade inflammatory process in which activated microglia generate cytotoxic factors—most prominently peroxynitrite—which induce the death and dysfunction of neighboring dopaminergic neurons. dying neurons then release damage-associated molecular pattern proteins such as high mobility group box 1 which act on microglia via a range of receptors to amplify microglial activation. since peroxynitrite is a key mediator in this process, it is proposed that nutraceutical measures which either suppress microglial production of peroxynitrite, or which promote the scavenging of peroxynitrite-derived oxidants, should have value for the prevention and control of pd. peroxynitrite production can be quelled by suppressing activation of microglial nadph oxidase—the source of its precursor superoxide—or by down-regulating the signaling pathways that promote microglial expression of inducible nitric oxide synthase (inos). phycocyanobilin of spirulina, ferulic acid, long-chain omega-3 fatty acids, good vitamin d status, promotion of hydrogen sulfide production with taurine and n-acetylcysteine, caffeine, epigallocatechin-gallate, butyrogenic dietary fiber, and probiotics may have potential for blunting microglial inos induction. scavenging of peroxynitrite-derived radicals may be amplified with supplemental zinc or inosine. astaxanthin has potential for protecting the

mitochondrial respiratory chain from peroxynitrite and environmental mitochondrial toxins. healthful programs of nutraceutical supplementation may prove to be useful and feasible in the primary prevention or slow progression of pre-existing pd. since damage to the mitochondria in dopaminergic neurons by environmental toxins is suspected to play a role in triggering the self-sustaining inflammation that drives pd pathogenesis, there is also reason to suspect that plant-based diets of modest protein content, and possibly a corn-rich diet high in spermidine, might provide protection from pd by boosting protective mitophagy and thereby aiding efficient mitochondrial function. low-protein diets can also promote a more even response to levodopa therapy."
Ebrahim, R. M.. (2020). Prophylactic effect of Spirulina platensis on radiation-induced thyroid disorders and alteration of reproductive hormones in female albino rats. International Journal of Radiation Research

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"Background: ionizing-radiation induces oxidative stress and thyroid toxicity. thyroid function disorders have a great impact on fertility in both sexes. materials and methods: forty female rats were divided into four groups. control, spirulina-treated (300 mg/kg); given orally for 15 days, ?-irradiated; given (5 gy whole body ?-rays) and spirulina+irradiated; given spirulina for 15 days before irradiation. animals were sacrificed the 3rd day post-irradiation. the level of the oxidant/antioxidant markers: malondialdehyde (mda), superoxide dismutase (sod), catalase (cat) and glutathione peroxidase (gsh-px) was evaluated. in addition, caspase-3 activity was measured as apoptotic marker and comet assay to detect dna-damage. serum thyroid stimulating hormone (tsh), triiodothyronine (t3) and thyroxine (t4) were determined to evaluate the thyroid function alterations. also, analysis of reproductive hormones; follicle stimulating hormone (fsh), luteinizing hormone (lh), estradiol (e2) and progesterone (p4) was detected. results: whole body ?-irradiation-induced oxidative stress, denoted by significant decreases of antioxidant markers and an increase in mda content. the activity of caspase-3 was significantly increased and comet assay revealed dna damage. also, serum level of tsh was significantly increased, while t3, and t4, significantly decreased in irradiated rats. moreover, the reproductive hormones showed significant decreases. spirulina treatment has significantly attenuated oxidative stress in thyroid tissues, decreased caspase-3 activity and ameliorated dna damage, concomitant with significant amelioration in the levels of thyroid and reproductive hormones. conclusion: spirulina may alleviate ?-rays-induced thyroid damage and play a significant role in the regulation of thyroid and reproductive hormones in female rats."

Tags

1. chemtrails
2. geoengineering

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