**Rutin**

**DESCRIPTION**
The flavonoid rutin is a flavonol glycoside comprised of the flavonol quercetin (see Quercetin) and the disaccharide rutinose. Rutin is found in many plants, especially the buckwheat plant *Fagopyrum esculentum* Moench, the flour of which is used to make pancakes. Other rich dietary sources of rutin include black tea and apple peels.

Rutin is a solid substance, pale yellow in appearance and only slightly soluble in water. It is, however, much more soluble in water than its aglycone quercetin. Rutin’s molecular formula is C_{27}H_{30}O_{16}, its molecular weight is 610.53 daltons, and its structural formula is:

![Rutin molecular structure]

The disaccharide moiety of rutin, rutinose, is comprised of the sugars rhamnose (6-deoxy-L-mannose) and glucose. Many names are used for rutin in the literature. They include rutoside, quercetin-3-rutinoside and sophorin. Also, 3, 3', 4', 5, 7-pentahydroxyflavone-3-rutinoside, 3-rhamnosyl-glucosyl quercetin and 3-[[6-O-(6-deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl oxy] 2-(3, 4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one.

**ACTIONS AND PHARMACOLOGY**

**ACTIONS**
Rutin may have antioxidant, anti-inflammatory, anticarcinogenic, antithrombotic, cytoprotective and vasoprotective activities.

**MECHANISM OF ACTION**
Many, if not most, of rutin’s possible activities can be accounted for, in part, by rutin’s antioxidant activity. Rutin is a phenolic antioxidant and has been demonstrated to scavenge superoxide radicals. Rutin can chelate metal ions, such as ferrous cations. Ferrous cations are involved in the so-called Fenton reaction, which generates reactive oxygen species. Rutin may also modulate the respiratory burst of neutrophils. The *in vivo* antioxidant activity of rutin is most likely due to its aglycone quercetin, to which it is metabolized following ingestion. Although most studies show rutin to inhibit lipid peroxidation, a few studies do not. Rutin may also help maintain levels of the biological antioxidant reduced glutathione. Importantly, under certain conditions, rutin or its metabolite quercetin may become a pro-oxidant. For example, nitrosation of rutin/quercetin may produce a pro-oxidant molecule that may have mutagenic potential.

**PHARMACOKINETICS**
The pharmacokinetics of rutin in humans is still under investigation. It appears that only about 17% of an ingested dose is absorbed. Absorption appears to occur mainly from the colon following the removal of the carbohydrate moiety by bacterial enzymes to form quercetin. Quercetin may undergo glucuronidation in the colonocytes. It is unclear to what extent there is absorption of quercetin glycosides. Quercetin and glucuronide conjugates of quercetin are transported to the liver via the portal circulation, where they undergo significant first pass metabolism. Metabolites may include isorhamnetin, kaempferol and tamarixetin. Quercetin itself may undergo glucuronidation and sulfation. Quercetin and its metabolites are distributed from the liver to various tissues in the body. Quercetin is strongly bound to albumin in the plasma.

**INDICATIONS AND USAGE**
Rutin may be useful in the management of venous edema. It may help strengthen capillaries, protect against some toxins and have anti-inflammatory effects, as well as some anticancer effects. It may also help prevent the oxidation of vitamin C and have some positive lipid effects.

**RESEARCH SUMMARY**
Some of the earliest research related to rutin found that, in daily doses of 200 to 600 mg, it is useful in treating some with conditions characterized by capillary fragility and attendant easy bruising. There was the suggestion in some of this early work that it might help decrease the incidence of cerebral hemorrhage, though no research was conducted to
specifically confirm this. An early placebo-controlled study reported a significant reduction in mid-cycle menstrual bleeding in rutin-supplementated women.

Several placebo-controlled trials have demonstrated that rutin has significant efficacy in diminishing the venous edema that is an early sign of chronic venous disease of the leg.

Rutin’s anti-inflammatory potential has been demonstrated in a number of animal studies. In experimentally induced colitis, both pre- and post-induction treatment with rutin conferred significant preventive and healing effects. Rutin was shown to increase colonic glutathione levels, thus reducing oxidative tissue damage in this inflammatory condition. It has also shown cytoprotective effects against ethanol injury in an animal model of ethanol-induced gastric lesions.

Rutin’s radical-scavenging and, possibly, its iron-chelating abilities were said, in other animal studies, to significantly protect against asbestos-induced oxidative cellular injury.

Very preliminary animal research has found some evidence that rutin can inhibit some cancerous and pre-cancerous conditions, including chemically induced colonic neoplasia. Results, however, have been mixed. Far more research is required.

Although in most studies rutin has been found to inhibit lipid peroxidation, in one study rutin was not found to block cellular lipid peroxidation. However, according to the researchers, rutin may still potentially play a positive role in helping to prevent atherogenesis by inhibiting the depletion of cellular glutathione and ATP, thus perhaps reducing the cytotoxicity of oxidized LDL-cholesterol.

Finally, there is some evidence suggesting that rutin, taken with vitamin C, may help inhibit the oxidation of vitamin C and thus make it safer and more useful in some conditions. More research is needed to elucidate the relationship between the flavonoids and vitamin C.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS
Rutin is contraindicated in those who are hypersensitive to any component of a rutin-containing product.

PRECAUTIONS
Pregnant women and nursing mothers should avoid using rutin supplements.

There is some suggestion that rutin may undergo nitrosation with, for example, nitrates and nitrites found in some processed meat products to form potentially mutagenic substances. Those who supplement with rutin should avoid using it concomitantly with such products.

ADVERSE REACTIONS
Rutin is generally well tolerated. Adverse reactions include gastrointestinal ones, such as nausea. There are rare reports of headache and mild tingling of the extremities.

INTERACTIONS

DRUGS
Quinolone antibiotics: Quercetin binds in vitro to the DNA gyrase site in bacteria. Therefore, theoretically, it can serve as a competitive inhibitor to the quinolone antibiotics, which also bind to this site.

NUTRITIONAL SUPPLEMENTS
Vitamin C: The interaction between flavonoids, such as rutin and quercetin, and vitamin C is unclear. It has been believed for some time that flavonoids work synergistically with vitamin C, enhancing the absorption of the vitamin and preventing it from oxidation. However, recent research indicates that flavonoids may actually inhibit the uptake of vitamin C into cells. More research is necessary in order to clarify this issue.

FOODS
Rutin may undergo nitrosation with nitrates and nitrites found in some processed meat products to form potentially mutagenic substances.

DOSAGE AND ADMINISTRATION
Typical doses used are 500 mg once or twice daily. Those with venous insufficiency/varicose veins often use 500 mg taken twice daily.

LITERATURE


Kostyuk VA, Potapovich AI, Sperensky SD, Maslova GT. Protective effect of natural flavonoids on rat peritoneal...


Park JB, Levine M. Intracellular accumulation of ascorbic acid is inhibited by flavonoids via blocking of dehydroascorbic acid and ascorbic acid uptakes in HL-60, U937 and Jurkat cells. *J Nutr.* 2000; 130:1297-1302.


**S-Adenosyl-L-Methionine (SAMe)**

**DESCRIPTION**

S-adenosyl-L-methionine (SAMe) is a natural substance present in the cells of the body. It is a direct metabolite of the essential amino acid L-methionine. It is variously known as ademetionine, S-adenosylmethionine, SAM, SAMe and SAM-e. It is represented structurally as:

![Structural formula of SAMe](image)

SAMe is used as a drug in Europe for the treatment of depression, liver disorders, osteoarthritis and fibromyalgia. Recently, SAMe has been introduced into the United States as a dietary supplement for the support of bone and joint health, as well as mood and emotional well being.

**ACTIONS AND PHARMACOLOGY**

**ACTIONS**

SAMe plays a crucial biochemical role in the body by donating a one-carbon methyl group in a process called transmethylation. SAMe, formed from the reaction of L-methionine and adenosine triphosphate catalyzed by the enzyme S-adenosylmethionine synthetase, is the methyl group donor in the biosynthesis of both DNA and RNA nucleic acids, phospholipids, proteins, epinephrine, melatonin, creatine and other molecules.

Supplemental SAMe may have antidepressant and hepatoprotective activities.

**MECHANISM OF ACTION**

The mechanism of action of supplemental SAMe is unclear. Much is known, however, of the mechanism of action of endogenous SAMe.

Methylation of DNA is critical in the biological phenomenon known as gene silencing. Gene silencing helps suppress genes that may give rise to cancer or those that may carry information for endogenous retroviruses. Methylation of RNA, particularly transfer RNA, is similarly important in safeguarding the form and function of these molecules in protein synthesis.

SAMe is the methyl donor to phosphatidylethanolamine in the formation of phosphatidylcholine (PC). PC is a major component of cell membranes and is vital for maintenance of cellular membrane fluidity, important in sustaining the bioenergetics and information-processing functions of cells.

SAMe is also involved in the methylation of histones, major elements in chromosomal structure. This methylation is believed to play a key role in the regulation of DNA transcription, the process by which RNA is formed. The carbon and nitrogen atoms of L-carnitine are derived from methylated lysine residues, which are formed by methylating certain proteins with SAMe’s methyl group.

SAMe’s importance in the body is further emphasized by the fact that it is also the methyl donor for the synthesis of epinephrine (adrenaline), creatine, melatonin, glutathione, the polyamines spermine and spermidine, and the amino acids L-cysteine and taurine, all of which play vital roles in human health.