

GRUPPO 5 : QUERCETIN

CHEMICAL IDENTITY

- **INCI NAME:** QUERCETIN
- **CAS NO.:** 117-39-5
- **EINECS/ELINCS:** 204-187-1
- **MOLECULAR WEIGHT:** 302.23
- **CHEMICAL NAMES:**

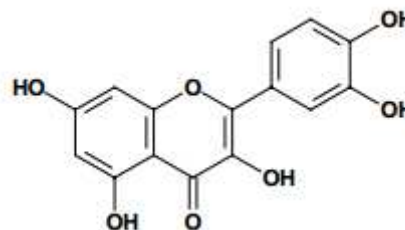
Chem. Abstr. Name: 2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran- 4-one

IUPAC Systematic Name: 3,3',4',5,7-Pentahydroxyflavone

Synonyms: CI 75670; CI Natural Yellow 10; 3,3',4',5,7- pentahydroxyflavone;

3,4',5,5',7-pentahydroxyflavone; 3,5,7,3',4'- pentahydroxyflavone; quercetine

- **STRUCTURAL AND MOLECULAR FORMULAE**



- **PARTITION COEFFICIENT: LOG POW** 1.82

GRUPPO 5 : QUERCETIN

CHARACTERISATION AND PURITY OF THE CHEMICAL VEDI TABELLA

Table 5 Physical, Chemical, and Microbiological Specifications for Quercegen's High-Purity Quercetin		
Parameter	Limit	Method of Analysis^a
Description	Yellow or greenish-yellow, crystalline powder, odorless or with a slight characteristic odor	Visual and olfactory inspection
Solubility, in 2% ethanol (NTU)	Not more than 15	Merck S/A
Solubility, 1% DMF	Clear solution	Visual inspection
Solubility, Water	Insoluble	Visual inspection
Identity	Comparable to quercetin standard	HPLC analysis
Assay (Quercetin) (dry weight basis)	Not less than 99.5% ^b	HPLC analysis
Density (g/mL)	Not less than 0.25	Merck S/A SOP 41/g/1213
Moisture (%)	Not more than 4.0	Karl-Fisher
Sulfated ash (%)	Not more than 0.15	Merck S/A
Chloride (Cl ⁻) (ppm)	Not more than 1,000	Merck S/A
Sulfate (SO ₄ ²⁻) (ppm)	Not more than 1,000	Merck S/A
Heavy Metals		
Arsenic (As) (ppm)	Not more than 1	AAS
Cadmium (Cd) (ppm)	Not more than 1	AAS
Cobalt (Co) (ppm)	Not more than 1	AAS
Lead (Pb) (ppm)	Not more than 1	AAS
Mercury (Hg) (ppm)	Not more than 1	AAS
Nickel (Ni) (ppm)	Not more than 1	AAS
Microbiological Specifications		
Aerobic bacteria (CFU/g)	Not more than 5,000	Merck General Method MG 029 ^c
Yeasts and molds (CFU/g)	Not more than 500	Merck General Method MG 029
<i>Salmonella</i> species (per 10 g)	Absent	Merck General Method MG 029
<i>Escherichia coli</i> (per 10 g)	Absent	Merck General Method MG 029
<i>Staphylococcus aureus</i> (per 10 g)	Absent	Merck General Method MG 029
<i>Pseudomonas aeruginosa</i> (per 10 g)	Absent	Merck General Method MG 029

AAS = Atomic Absorption Spectroscopy; CFU = Colony-forming units; DMF = N,N-Dimethylformamide; HPLC = high-performance liquid chromatography; NTU = Nephelometric Turbidity Unit

^a See Exhibit B-2 for details of the methods of analysis.

^b To obtain quercetin of not less than 99.5% purity, a 3-step purification process is applied.

^c Merck General Method 029 complies with U.S. Pharmacopeia Monograph for Microbiology Tests (USP, 2008 or a more recent edition) (see Exhibit B-2).

GRUPPO 5 : QUERCETIN

- **PHYSICAL-CHEMICAL SPECIFICATIONS**
- **ASPECT:** YELLOW, CRYSTALLINE SOLID
- **SOLUBILITY:** INSOLUBLE IN WATER . SLIGHTLY SOLUBLE IN ALCOHOL. SOLUBLE IN GLACIAL ACETIC ACID AND AQUEOUS ALKALINE SOLUTIONS
- **BOILING-POINT:** Sublimes (Lide, 1997)
- **MELTING-POINT:** 316.5°C (Lide, 1997)
- **STABILITY:** PH CONDITIONS RANGING FROM PH 3 TO 7.5
- **FUNCTIONS AND USES:**

Quercetin is a Flavonoid, widely distributed in nature and in foods. It has been used in medicine to decrease capillary fragility. Used in dyes and as a veterinary drug (National Toxicology Program, 1991).

Used in cosmetics as antioxidant (use level: 0.1% – 0.2%).

[Rieger MM; Kirk-Othmer Encyclopedia of Chemical Technology. (2001). NY, NY: John Wiley & Sons; Cosmetics. Online Posting Date: Dec 4, 2000.]

GRUPPO 5 : QUERCETIN

TOXICOLOGICAL EVALUTATION

Acute Toxicity

LD50 Acute Oral (Mouse) 160 mg/kg bw

LD50 Subcutaneous (Mouse) 100 mg/kg bw

(Sullivan et al., 1951).

Rabbits were unaffected by intravenous administration of 100 mg/kg bw or by diets containing 1% quercetin for 410 days (Ambrose et al., 1952).

Dermal Toxicity: No data submitted

Inhalation Toxicity: No data submitted

Irritation and corrosivity

No data submitted

Skin sensitization

No data submitted

Dermal Absorbition

No data submitted.

Repeated dose toxicity/ carcinogenicity

Species: Male and female F344DuCj rats

Route/Dose: Diet 0, 1.25, 5.0%

Period : 104 weeks

NOAEL (for males) 2.203 mg/kg body weight/day

NOAEL (for females) 2.372 mg/kg body weight/day

Findings: Negative

Ref. : Ito et al, 1989

GRUPPO 5 : QUERCETIN

Genotoxicity / Mutagenicity

in vitro: Positive

- (Mammalian polychromatic erythrocytes - Micronucleus test, chromosome aberrations) [MUTAT RES 89:69-74,1981]
- Salmonella typhimurium (one or more of the five standard strains: TA98, TA100, TA1535, TA1537, and TA1538) -Histidine reverse gene mutation, Ames assay [MUTAT RES 58:225-229,1978 ; EMICBACK/25140; SCIENCE 197:577-578,1977]

In Vivo: Negative

- Nonhuman - Sister-chromatid exchange (SCE) in vivo [MUTAT RES 124:255-270,1983]

the *in vitro* mutagenic properties of quercetin have not been observed *in vivo* following oral administration in at least 10 negative studies. This discrepancy between positive *in vitro* findings versus negative *in vivo* results may be attributed to limited *in vivo* absorption of quercetin .

GRUPPO 5 : QUERCETIN

- **ADME**

Oral absorption was estimated to range from 36 to 53% (based on total radioactivity) (Walle *et al.*, 2001).

Distributed relatively uniformly across all major tissues (Abrahamse *et al.*, 2005).

Studies conducted in rats and humans to quantify the absorption of quercetin and its metabolites from the gastrointestinal tract demonstrated highly variable results (20 to 60% in rats and 24 to 53% in humans).

Low Bioavailability due to rapid to extensive metabolism.

- **HUMAN STUDIES**

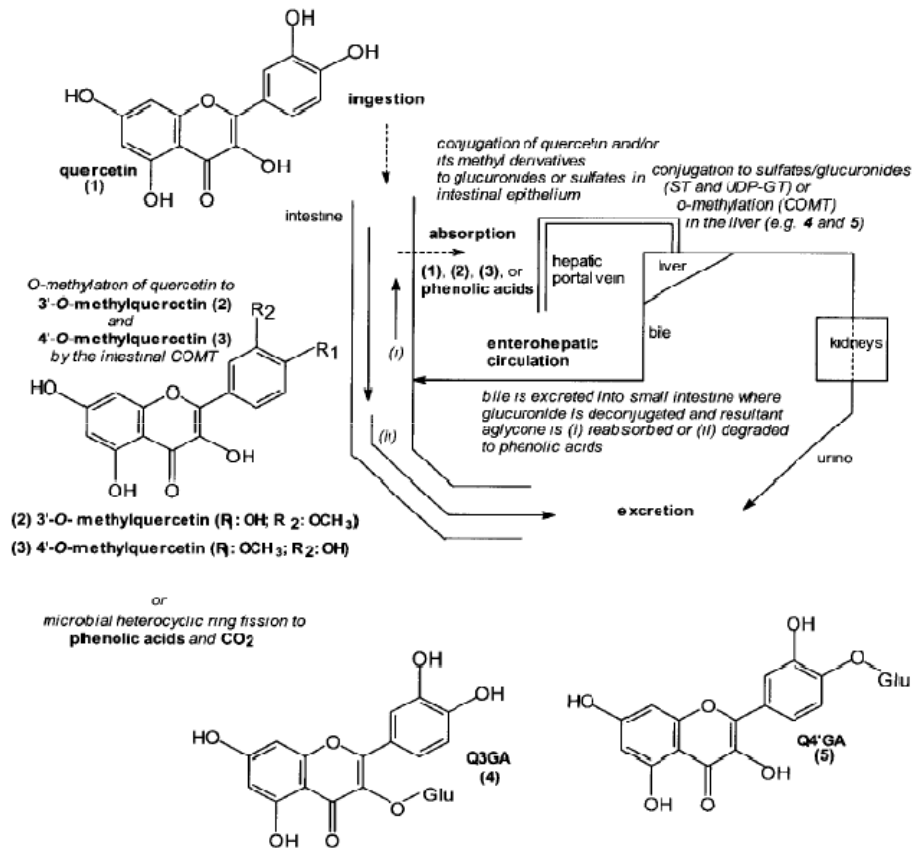
It was concluded that supplementation with 500 or 1,000 mg quercetin/day for 12 weeks was safe in this study as there were no adverse symptoms or change in blood diagnostic chemistries and GSH.

QUERCETIN has been recognised Grass by FDA (2009)

Approximated daily intake 1250 mg/day

GRUPPO 5 : QUERCETIN

Figure 3 Schematic Representation of the Absorption, Metabolism, and Excretion of Quercetin in Mammals



Adapted from Day and Williamson (1999)

GRUPPO 5 : QUERCETIN

- MOS IN UN IPOTETICO

Product: tooth paste for adult

C Quercitin in the product= 0.1%

$$SED = 2.16(\text{mg/kg bw day}) * 0.1 * 0.53$$

$$SED = 2.16 * 0,1 * 0,53 = 0,11448$$

$$MoS = 2200 / 0,11448 = 19217,33$$