

# Enhancing the Bioavailability of Quercetin by Concomitant Administration with Enzyme Inhibitor

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## Abstract

**Background:** Quercetin is a food supplement with multiple biological activities including antihypertensive, vasodilator effects, antiobesity, antihypercholesterolemic, antiatherosclerotic and other activities, it is available in wide range of dietary supplement and daily food intake, after oral ingestion, quercetin is metabolized by intestinal enzymes and absorbed by the duodenum, then be transported to the liver where is transformed into its glucuronidated, methylated and sulfo-substituted metabolites.

**Aim of Study:** Boosting the bioavailability of Quercetin by enzyme inhibitor effect of ketoconazole

**Method:** 10 apparently healthy adult, male (5) and female (5) were grouped A and B, with a 1-week wash-period, Group A received Quercetin 1000 mg, group B received Quercetin 1000 mg and Ketoconazole 400 mg, and 15 blood samples are collected on the following timing 0, 0.5 - 12.5 by 1 hour interval and other by hour 24 for HPLC Assay.

**Results:** Concurrent ketoconazole administration with Quercetin significantly improves the mean plasma concentration under the curve from zero time to infinity ( $AUC_{0-\infty}$ ) by 176% ( $403.41 \pm 62.28$  vs.  $228.51 \pm 28.67$   $\mu\text{g}\cdot\text{h}/\text{mL}$ ;  $P < 0.0001$ ) and prolonged time to complete elimination ( $44.66 \pm 9.17$  vs.  $12.93 \pm 1.4$  hr.;  $P < 0.0000$ ) compared with Quercetin alone.

**Conclusion:** Bioavailability of Quercetin will be increased by its administration together with ketoconazole, due to enzyme inhibiting effect of ketoconazole which delay elimination and increase the AUC of Quercetin.

**Keywords:** Quercetin, Ketoconazole, bioavailability, enzyme inhibitor.

## INTRODUCTION

Quercetin (Que) is a pentahydroxyflavone (C<sub>15</sub>H<sub>10</sub>O<sub>7</sub>). (1, 2) It is polyphenolic flavonoid compound (3, 4) used as a food supplement and has numerous biological activities; (5) it is taken as a single ingredient or in combination with other vitamin supplements. (6, 7) Que is a needle crystal of brilliant citron yellow it is insoluble in frigid water, poorly soluble in wormed water, while it is quite soluble in the lipids and alcohol. (5) The term "quercetin" has been used since 1857; (1) (8) it is originated from quercetum or quercus which means oak wood forest. (9) It is an aglycone, (lacking an attached sugar molecule). (10) Because the presence of hydrophilic sugar moiety which improves the solubility of a glycosyl group, the Que glycoside is soluble in water. (11) Que and its derivatives are of the most powerful antioxidants found in plants and contains several OH groups in its structure, which may further contribute to photodegradation. (8, 12) It is one of more than 4000 plant phenolics that are naturally available, (13) in many vegetables, fruits and drinks ingested from the daily diet, (14) including onions, broccoli, apples, berries, (15) and citrus fruits, (9) it is ubiquitously present in wine and tea. (16, 17)

Que is well known for its vasodilator, antihypertensive effects, antiatherosclerotic, antiobesity, antihypercholesterolemic, and antidiabetic activities. (18-20) Que's mechanisms of action are pleiotropic, involves the decrease of glucose absorption from the intestine, insulin secretory and insulin-sensitizing effects, and the enhancement of glucose uptake in the muscles. (21) Epidemiological studies indicate an inverse association between dietary intake of Que and cancer; (22) Que is empirically used for the treatment of asthma, hay fever, eczema, hives, and gout as examples of allergic disorders (14) Moreover, flavonoids