Opinion



# Effects of quercetin from microorganism to metabolic diseases

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## Opinion

Since ancient times, natural products have been a feasible and effective strategy for prevention and treatment of various diseases. During the last decades, utilization of naturally occurring compounds of plant origin has been noticed. Flavonoids, secondary metabolites in plants, are a group of compounds with two or more aromatic rings, each bearing at least one aromatic hydroxyl and connected with a carbon bridge. They were present in the diet representing promising agents for a variety of diseases including cardiovascular disease, diabetes mellitus, hypertension and cancer. Among them, quercetin (QCT), a plant derived flavonoid, highly enriched in plant food including vegetables and fruits (e.g. tomatoes, grapes, onions and apples) as well as in tea.[1,2] There are several health and physiological benefits of QCT administration including cardioprotective, anti-diabetic, anti-carcinogenic, antioxidant, anti-inflammatory, anti-apoptotic and anti-microbial effects.[1,3,4]

For the microorganism, quercetin has shown anti-bacterial, anti-biofilm and microbiota-regulating properties. Quercetin could inhibit the growth of planktonic *Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis, Actinomyces viscosus, Fusobacteriumnucleatum,* and *Actinomyces naeslundii* and *Helicobacter pylori*.[5–7] When quercetin was used in combination with antibiotics including amoxicillin, ampicillin, cephradine, ceftriaxone, imipenem or methicillin, they were found to increase each other's activity against *Staphylococcus aureus*.[8] Aside from planktonic bacteria, quercetin has also been reported to inhibit biofilm development for multiple bacteria such as *Enterococcus faecalis*, *Staphylococcus aureus*, *Streptococcus mutans*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Bacterial biofilm is multicellular aggregates enclosed in a self-created biopolymer matrix and could enable these microorganisms to evade host.Qayyum et al demonstrated that quercetin (256mg/L) could inhibit 95% biofilm formation of *E. faecalis* MTCC 2729 through crystal violet assay. The anti-biofilm effect of quercetin was confirmed by scanning electron microscopy (SEM) and CLSM.[9] As far as Gram-negative bacterium *Pseudomonas aeruginosa*, Ouyang et al. reported quercetin is an effective inhibitor of quorum sensing, biofilm formation and virulence factors at a low concentration (16mg/L).

Base on the effects on these microorganisms, their biofilm and related factors, quercetin may influence the gut microbiota which is an ecosystem consisted of an estimated 10-100 trillion microorganisms, including bacteria, fungi, archaea and viruses and exerts diverse physiological functions, such as modulation of immune system, regulation of the gut barrier integrity and biosynthesis of vitamins.[10] Zhao et al demonstrated that combination of quercetin and resveratrol could reduce obesity in high-fat diet-fed rats by modulation of gut microbiota composition, decreasing the abundance of *Firmicutes, Desulfovibrionaceae*, *Acidaminococcaceae, Coriobacteriaceae, Bilophila, Lachnospiraceae* and its genus *Lachnoclostridium*, which were reported to be potentially related to diet-induced obesity, increasing the abundance of *Bacteroidales, Christensenellaceae, Akkermansia, Ruminococcaceae*.*Akkermansia*has been considered as a next-generation of beneficial probiotic and to be associated with metabolic disorders.[11,12]

Metabolic disorders include multiple clinical manifestations, like central obesity and impaired fasting blood glucose, ultimately increasing the risk for type 2 diabetes or cardiovascular disease.[12] In rat models, accumulating evidence showed the effects of quercetin on diabetes and diabetic related diseases, including lowering of glucose in blood plasma, preservation of β-cell activity in the pancreas, and attenuating diabetic nephropathy.[13–15] In mouse models, quercetin could interfere in both key proatherogenic activities of macrophages, namely foam cell formation and pro-oxidant/proinflammatory responses, to further exert the atheroprotective properties.[16] Moreover, the anti-obesity effects of quercetin in adipocyte cultures and animal models have been well reviewed recently.[17] Therefore, these studies suggest quercetin is a promising treatment option for metabolic disorders, although the mechanism remains unclear.

Notably, recent evidence indicated the association between metabolic disorders and dysregulation of gut microbiota composition, also known as dysbiosis. Dysbiosis may lead to gut barrier dysfunction and intestinal homeostasis disruption through translocation of microbial products and pro-inflammatory factors.[18] Interestingly, quercetin has a relatively low bioavailability, and large proportion remains in the gut and may interplay with microbiota. Moreover, given its effects on microorganism, especially increasing beneficial bacterium Akkermansia, we speculate quercetin may exert anti-inflammatory effects and alleviate metabolic disorders through modulating gut microbiota. However, more evidences are still needed in the future, as the effects of quercetin are complicated and the relative underlying mechanisms are not completely clear yet.

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## Conflicts of interest

The author declares that there are no conflicts of interest.

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