Quercetin (Q) is a natural heterocyclic compound with various bioactivities: antioxidant, antimicrobial, antiparasitic, antitumor, anticancerogenic, antiprotective, anti-inflammatory, etc. Good antioxidant potential makes Q good lipid peroxidation inhibitor (which is involved in development of various diseases). Lipid oxidation of biomolecules, such as LDL, may lead to the development of atherosclerotic plaques responsible for development of cardiovascular diseases. Damage of cellular membranes in the brain via lipid peroxidation leads to neurodegenerative conditions, such as Alzheimer and Parkinson disease. Bustos et al. (2016) – Q is more efficient in inhibition of ROS production and lipid peroxidation than ascorbic acid.

### Antimicrobial activity

Q inhibits growth of *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Staphylococcus aureus*, *Escherichia coli*, *Proteus* and *Aspergillus flavus*. Antibacterial mechanism of activity of Q includes destruction of bacterial cell membrane, changes in membrane permeability, impact on protein synthesis and expression, enzyme inhibition and inhibition of nucleic acids synthesis. Wang et al. (2018) – Q can damage cell membrane of *S. aureus*; treatment of *E. coli* with Q leads to bacterial cell death. Huang et al. (2005) – in mice, Q inhibits *sulphydin* (*S. suis*) and reduces cytotoxicity induced by this bacteria. Q reduces concentration of IL-1β, IL-6 and Tumour Necrosis Factor α.

### Antiviral activity (enzyme inhibition)

Antiviral activity of Q in its related to its structure. In case of HIV – inhibition of key enzymes: reverse transcriptase, integrase, protease → reduced virus replication (Biancatelli et al. [2020]). Inhibition of activity of NS3 serine protease of hepatitis C virus → virus RNA production is blocked and so is replication (Bachmetov et al. [2012]).

### Antitumor and anticancer activity

Q may have an impact on cancer cell apoptosis and induce tumor cell death. Q may increase proapoptotic protein expression and reduce antiapoptotic protein expression. Teekaraman et al. (2019) studied role of Q in apoptosis of PA-1 cell line of human metastatic ovarian cancer → Q induces apoptosis and inhibits cancer cell growth. Seo et al. (2016) – Q induces apoptosis by inhibiting STAT3 signalisation and could be used in treatment of breast cancer. Hamidullah et al. (2015) – in PC-3 and DU145 prostate cancer cell lines; Q-6-C-β-glucopiranoside blocks cell cycle in G2/G1. This is a result of reduced expression of cyclin E and D, PNA and CDK2 and increased expression of p21 and p27. Also, Q may disable cardiomyocytes apoptosis, induced by ischemia and myocardium reperfusion. Mechanism of Q cardioprotective activity is related to the inhibition of proteasom-peptidase, which controls and regulates key intracellular processes that lead to apoptosis.

### Allergies, anti-inflammatory and immunosuppressive activity

Several studies deal with these activities of Q, their general conclusions are as follows: Q is anti-hypersecretary agent (Chang et al. [2010]), Q is useful with respiratory system inflammation (Joskova et al. [2011]), Q helps with asthma (Jung et al. [2007]; Moon et al. [2008]), Q can help with exercise stress (Nieman et al. [2009]), cellular and humoral immunity (Nieman et al. [2009]).

### Cardiovascular diseases

Q reduces heart abnormalities caused by LPS and protects form myocardial infarction (Shebeko et al. [2018]). Wei et al. (2018) – Q may be used in treatment of heart diseases. Q may control dyslipidaemia and functioning of fatty liver. Gnoni et al. (2009) studied impact of Q on fat production in rat hepatocytes → Q may inhibit fatty acids synthesis in liver cells. Tian et al. (2017) – Q when applied orally protects rats from myocardial infarction. Kleemann et al. (2011) – Q may reduce CRP and fibrinogen expression in mice. Q also protected mice fed with high fat diet from endothelial dysfunction and atherosclerosis, indicating that Q has potential cardiovascular protective effect.

### Neurodegenerative diseases

Q reduces ROS production, protects from induced cellular death of primary neurons, but higher conc. of Q has the opposite effect (Zhu et al. [2007]). Possible ACH inhibitory effect (in silico study → bonding strength of Q on the enzyme is better than in case of appropriate medicines, 4-OH methylated Q has an even higher bonding affinity than Q (Islam et al. [2013]). Neuroprotective role against 6-OHDA-induced neurotoxicity by increasing conc. of enzymes involved in ROS removal, lipid peroxidation reduction, reduction of lipid hydroperoxides conc., etc. (Magalingam et al. [2014]). Q increases PNO2 expression in macrophages, brain cells, astrocytes and neurons (Sigaliz et al. [2016]).

### Diabetes mellitus

Q has hypoglycaemic, hypolipidemic and antioxidant effect. Jeong et al. (2012) – mice fed with LQ or HQE → lower glucose conc. in both cases, increased adiponectin, reduced total cholesterol, reduced conc. of thiobarbituric acid reactive compounds leading to liver enzymes increased activity (enzymes involved in ROS detoxification). Q may improve kidney shape (when kidney is changed due to hyperglycaemia) by inhibiting PKC activity, regulating expression of growth factor β 1, reducing formation of extracellular matrix and delaying of kidney hypertrophy. Q may stop kidney pathological changes, delay progress of diabetic nephropathy and improve glycolipid metabolism in rats with type 2 diabetes.

### Interaction with medication and toxicity

Q inhibits *in vivo* CYP3A4 and CYP1A2, and activates CYP2A6, xanthine oxidase and N-acetyltransferase. Interaction between Q and medicines was studied primarily due to its interaction with CYP3A4 and Pgp. In most interactions, Q reduces level or efficiency of medication via Pgp. Q has synergistic effect with chemotherapeutic substances. While Q is not carcinogenic, it is mutagen (Ames). Toxic effects of Q are probably related to production of toxic products of Q oxidation during ROS elimination. Hence, when using Q supplementation, should pay attention due to possible toxic effect of Q metabolites, especially in long term supplementation.

### Conclusion

Q is responsible for Q properties and bioactivity. Q may help prevent onset of disease or with disease progression in case of various diseases. Q has synergistic effect with various medication, and also shows toxicity due to its oxidation during ROS removal. Despite many studies, application of Q in medicine is limited due to various reasons. Hence, it would be useful to compare efficiency of various doses of Q, study bioactivity of Q aglycone vs Q glycosides and Q metabolites. Additional studies for better assessment of Q antioxidant activity and other bioactivities are also necessary.