Major Pharmacological Actions of Quercetin

Subjects: Infectious Diseases

Contributor: Fauzia Mahanaz Shorobi , Fatema Yasmin Nisa , Srabonti Saha , Muhammad Abid Hasan Chowdhury , Mayuna Srisuphanunt , Kazi Helal Hossain , Md. Atiar Rahman

Quercetin (3,3′,4′,5,7-pentahydroxy-2-phenylchromen-4-one), the major representative of the flavonoid subclass of flavonols, is derived from the Latin word “Quercetum,” meaning “Oak Forest”. It can be found in a variety of foods, including fruits and vegetables, and has been reported to be effective against a variety of viruses.

quercetin antiviral action flavonoid medicinal plant

1. Natural Sources of Quercetin and Its Isolation from Plants

Quercetin is one of the most consumed and important bioflavonoid components and is widely found in different varieties of fruits and vegetables. Plant species, growing conditions, harvest conditions, and storage methods can influence the polyphenolic composition of fruits and vegetables. Quercetin is found in abundance in onions, apples, and wine. According to several studies, Quercetin is also found in tea, pepper, coriander, fennel, radish, and dill [1]. More than 20 plants species produce Quercetin: *Foeniculum vulgare*, *Curcuma domestica* valeton, *Santalum album*, *Cuscuta reflexa*, *Withania somnifera*, *Emblica officinalis*, *Mangifera indica*, *Daucus carota*, *Momordica charantia*, *Ocimum sanctum*, *Psoralea corylifolia*, *Swertia chirayita*, *Solanum nigrum*, and *Glycyrrhiza glabra*, *Morua alba*, *Camellia sinensis* [2], *Allium fistulosum*, *A. cepa*, *Calamus scipionum*, *Moringa oleifera*, *Centella asiatica*, *Hypericum hircinum*, *H. perforatum*, *Apium graveolens*, *Brassica oleracea* var. *Italica, B*. oleracea var. sabellica, *Coriandrum sativum*, *Lactuca sativa*, *Nasturtium officinale*, *Asparagus officinalis*, *Capparis spinosa*, *Prunus domestica*, *P. avium*, *Malus domestica*, *Vaccinium oxycoccus*, and *Solanum lycopersicum* [3]. Quercetin is available in capsule and powder form as a dietary supplement. The plasma Quercetin concentration rises when Quercetin is consumed in the form of foods or supplements (**Table 1**). As a result, everyday consumption of Quercetin-rich foods increases Quercetin bioavailability and contributes to the prevention of lifestyle-related disorders [1].

Quercetin was isolated from a fractionated extract of *Rubus fruticosus* by using an optimized column in HPLC and increasing its concentration by using a nanofiltration membrane [4]. Extraction of Quercetin from different plant sources can be followed by effective sample preparation techniques known as the sea sand disruption method (SSDM). The SSDM is used due to its recovery efficiency [5]. During the isolation of Quercetin and its derivatives in plants’ source, SSDM is used to eliminate errors in the study [6]. Flavonoids are isolated from the crude extract of plants by using various organic solutions followed by HPLC analysis, which is further characterized by FTIR, NMR, and mass spectroscopy [7]. Quercetin-3-*O*-rhamnoside was isolated from *P. thonningii* leaves by using different organic solvents [8]. According to one study, dihydroQuercetin, one of the Quercetin derivates, was isolated from

Larix gmelinii using ultrasound-assisted and microwave-assisted alternate digestion methods because they required less extraction time, less energy, and were more cost-effective than conventional solvent extraction methods [9]. Another derivative known as Isorhamnetin was isolated from the crude extract of *Stigma maydis* through two-stage high-speed countercurrent chromatography processes, where two-phase solvent systems composed of n-hexane-ethyl acetate-methanol-water are used at volume ratios of 5:5:5:5 and 5:5:6:4 to ensure the purity [10].

Table 1. Quercetin and its derivatives from different plant sources and their biological effects in various experimental models.

Phytochemical	Plant Name	Family	Plant Parts	Virus Target	Cell	Bioassay	Viral Step or MOA	Reference
Quercetin-3-o-α-L-rhamnopyranoside (Q3R)	*Rapanea melanophloeos*	Myrsinaceae	Whole plant	IAV	MDCK cell	In vitro	Inhibit viral entry and virus replication	[11]
Quercetin 3-glucoside	*Dianthus superbus* L.	Caryophyllaceae	Whole plant	IAV	MDCK cell	In vitro and in silico	Inhibit viral replication	[12]
Quercitrin (Quercetin-3-L-rhamnoside)	*Houttuynia cordata Thunb.*	Saururaceae	Leaf (Aerial parts)	IAV (Anti-influenza A/WS/33 virus)	Mammalian kidney (BHK)	In vitro	Inhibit replication in the initial stage of virus infection by indirect interaction with virus particles	[13]
Rutin (Quercetin-3-rutinoside)	*Prunus domestica*	Rosaceae	Fruit	HCV	Human hepatocellular carcinoma cells Huh 7 and Huh 7.5	In vitro and ex vivo	Inhibit the early stage of viral entry	[14]
Quercetin	*Psidium guajava*	Myrtaceae	Bark	DENV	Epithelial VERO cells (Cercopithecus aethiops)	In vitro and in silico	Directly inhibit the viral NS3 protein and could interrupt virus entry by inhibiting fusion	[15]
Quercetin	*Embelia ribes*	Myrsinaceae	Seeds	HCV	Huh-7 cells	In vitro	Inhibit NS3 protease activity and HCV replication.	[16]
Quercetin 7-rhamnoside	*Houttuynia cordata*	Saururaceae	Aerial Parts	Porcine epidemic diarrhea virus (PEDV CV 777)	Vero (african green monkey kidney cell line; ATCC	In vitro and In vivo	Inhibit at an early stage of viral replication after infection	[17]

Phytochemical	Plant Name	Family	Plant Parts	Virus Target	Cell	Bioassay	Viral Step or MOA	Reference
					CCR-81) ST (pig testis cell line; ATCC CRL-1746)			
Quercetin and its glycoside derivatives	*Bauhinia longifolia* (Bong.)	Fabaceae	Leaves	Mayaro viruses (ATCC VR-66, lineage TR 4675)	Vero cells (African green monkey kidney, ATCC CCL-81)	In vitro	glycosilation re duces the antiviral activity of Quercetin against	[18]
DihydroQuercetin (DHQ)	*Larix sibirica* (larch wood)	Pinaceae	Wood	Coxsackie virus B4 Powers strain	Vero cells Inbred, female mice	In vivo	Decrease the replication of viral protein by reducing ROS generation	[19]
Quercetin-7-o-glucoside	*Dianthus superbus*	Caryophyllaceae	Leaves	Influenz viruses A/Vic/3/75 (H3N2, VR-822), A/PR/8/34 (H1N1, VR-1469), B/Maryland/1/59 (VR-296) and B/Lee/40 (VR-1535D)	Madin-Darby Canine Kidney (MDCK) cell	In Vitro	Inhibit influenza viral RNA polymerase PB2	[20]
Quercetin and Isoquercitrin	*Houttuynia cordata*	Saururaceae	Whole plant	Herpes simplex virus (HSV)	African green monkey kidney cells (Vero, ATCC CCL-81) and human epithelial carcinoma cells	In vitro	Quercetin and isoquercitrin inhibit NF-κB activation in HSV viral replication	[21]
Kaempferol	*Rhodioila rosea*	Crassulaceae	Roots	The influenza strains A/PR/8/34 (H1N1) (ATCC VR-1469)	Madin-Darby canine kidney (MDCK) cells were obtained	In vitro	Inhibit viral replication by blocking neuraminidases	[22]
Myricetin	*Marcetia taxifolia*	Melastomataceae	Aerial parts	HIV-1 (HTLV-IIIB/H9)	MT4 cells	In silico	May Bind to NNRTI pocket of NNRTI resistant HIV-1	[23]
Apigein	*Gentiana veitchiorum*	Gentianaceae	Flower	Foot-and-mouth disease virus	BHK-21 cells	In vitro	Block the internal ribosome entry	[24][25]

Phytochemical	Plant Name	Family	Plant Parts	Virus Target	Cell	Bioassay	Viral Step or MOA	Reference
				(FMDV)			site (IRES) mediate translational activity	
Quercetin 3-o-β-glucopyranoside	*Morus Alba*	Moraceae	Leaf	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chair termination	[26]
Quercetin 3-o-β-(6”-o-galloyl)-glucopyranoside	*Morus Alba*	Moraceae	Leaf	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chair termination	[26]
Quercetin-3-o-β-L-rhamnopyranosyl	*Acacia albdai*	Fabaceae	Leaf	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chain termination	[26]
Quercetin-3-*O*-α-L-rhamnopyranoside	*Acacia albdai*	Fabaceae	Leaf	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chain termination	[26]
6-o-methoxy Quercetin-7-o-β-D-glucopyranoside	*Centaurea glomerata*	Asteraceae	Aerial parts	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chain termination	[26]
4’,6-o-dimethoxy Quercetin-7-o-β-D-glucopyranoside	*Centaurea glomerata*	Asteraceae	Areal Parts	*Herpes simplex* Virus type 1	Vero cell line no ATCC CCL-81)	In vitro	Inhibit DNA chain termination	[26]
Quercetin-3-β-o-D-glucoside	*Allium cepa*	Amaryllidaceae	Root	Ebolaviruses (EBOV-Kikwit-GFP, EBOV Makona, SUDV-Boniface, mouse-adapted EBOV)	Vero E6 cells	In vitro	Block glycoprotein mediated step during viral entry	[27][28]
Isorhamnetin	*Ginkgo biloba*	Ginkgoaceae	Leaf	Influenza A virus Puerto Rico/8/34 (H1N1)	Madin Darby Canine Kidney (MDCK) cells	In vitro and In vivo	Inhibit neuraminidase and hemagglutination, suppress ROS generation and ERK phosphorylation	[29][30]
Luteolin	*Elsholtzia rugulosa*	Lamiaceae	Whole Plant	Influenza viruses A/PR/8/34(H1N1), A/Jinan/15/90(H3N2)	MDCK cells	In vitro	Inhibit the neuraminidase	[31]

Quercetin is taken as glycosides, with glycosyl groups released during chewing, digestion, and absorption. In humans, only a small percentage of Quercetin is absorbed in the stomach, and the primary site of absorption is the small intestine [44]. Two methods allow Quercetin glycosides to be absorbed in the intestine. One method is lactose polarizing hydrolase (LPH) in the brush border membrane, and another method is the interaction with the sodium-dependent glucose transporter (SGLT1) [2]. The gut microbiota plays a crucial role in the absorption of Quercetin by enzymatic hydrolysis. After absorption, the metabolism of Quercetin takes place in various organs, including the small intestine, colon, liver, and kidney. Biotransformation enzymes in the small intestine and liver create methylated, sulfated, and glucuronate forms of Quercetin metabolites due to phase II metabolism [1]. After that, these are released into the bloodstream via the portal vein of the liver. In the small intestine and colon, Quercetin metabolism leads to the generation of phenolic acids. The metabolites of Quercetin are found in human plasma as methylated glucuronide or unmethylated sulfate. The major metabolite of Quercetin, Quercetin-3-o-b-D-glucuronide, is delivered to target tissues via plasma to exert biological activity [1]. Quercetin had a short half-life

Phytochemical	Plant Name	Family	Plant Parts	Virus Target	Cell	Bioassay	Viral Step or MOA	Reference
				[45] and B/ Jiangsu/10/2003				
Luteolin	*Cynodon dactylon*	Poaceae	Whole Plant	Chikungunya virus	Vero cells	In vitro	Inhibit intracellular viral replication	[32]
Quercetin	*Illicium verum*	Schisandraceae		Singapore grouper iridovirus (SGIV)	Grouper spleen (GS) cells	In vitro	Interrupt SGIV binding to host cell by blocking membrane receptor on host cell which	[33]
Naringenin	*Citrus sinensis*	Rutaceae	Fruit	Zika Virus	Human A549 cells	In vitro	Inhibit NS2B-NS3 protease	[34][35]
Hesperidin	*Citrus sinensis* (sweet orange)	Rutaceae	Fruit Peel	SARS-CoV-2 virus	[46]	In silico	Binds to main protease and angiotensin converting enzyme 2	[36]
[47] Hesperidin	*Citrus sinensis*	Rutaceae	Fruit Peel	Sindbis virus	BHK-2	In vitro	Inhibitory activity on viral replication	[37][38]
Naringenin	*Citrus paradisi*	Rutaceae	Fruit Peel	Hepatitis C virus (HCV)	Huh7.5.1 human hepatoma cell	In vitro and In vivo	inhibits ApoB lipoprotein reduce secretion of HCV	[39][40]
Luteolin	*Achyrocline satureioides* [49]	Asteraceae	Whole Plant	Influenza virus A/Fort Monmouth/1/1947 (H1N1)	Madin-Darby canine kidney (MDCK) cells and Vero cells	In vitro	Block absorption to the cell surface or receptor binding site leads to the suppress of the expression of coat protein I	[41][42]
Naringenin	*Citrus paradisi*	Rutaceae	Fruit Peel	Dengue virus (DENV)	Huh7.5 cells	In vitro	Act as antiviral cytokine during DENV replication	[40][43]

however, s a high an food. through etin [1].

se days. models. cervical ve action er option tment in owth [48]. nethods. and cell nine and effective ative and enerative as anti- cognitive

deficits, and reduces neurodegeneration [1].

References

1. Ulusoy, H.G.; Sanlier, N. A minireview of quercetin: From its metabolism to possible mechanisms of its biological activities. Crit. Rev. Food Sci. Nutr. 2019, 60, 3290–3303.
2. Shakya, A.; Correspondence, A. Medicinal plants: Future source of new drugs. Int. J. Herb. Med. 2016, 4, 59–64.
3. David, A.V.A.; Arulmoli, R.; Parasuraman, S. Overviews of biological importance of quercetin: A bioactive flavonoid. Pharmacogn. Rev. 2016, 10, 84–89.
4. Zahoor, M.; Shah, A.B.; Naz, S.; Ullah, R.; Bari, A.; Mahmood, H.M. Isolation of Quercetin from Rubus fruticosus, Their Concentration through NF/RO Membranes, and Recovery through Carbon Nanocomposite. A Pilot Plant Study. BioMed. Res. Int. 2020, 2020, 8216435.

5. Wianowska, D. Application of Sea Sand Disruption Method for HPLC Determination of Quercetin in Plants. J. Liq. Chromatogr. Relat. Technol. 2015, 38, 1037–1043.
6. Wianowska, D.; Dawidowicz, A.L.; Bernacik, K.; Typek, R. Determining the true content of quercetin and its derivatives in plants employing SSDM and LC–MS analysis. Eur. Food Res. Technol. 2017, 243, 27–40.
7. Saraswathi, V.S.; Saravanan, D.; Santhakumar, K. Isolation of quercetin from the methanolic extract of Lagerstroemia speciosa by HPLC technique, its cytotoxicity against MCF-7 cells and photocatalytic activity. J. Photochem. Photobiol. B Biol. 2017, 171, 20–26.
8. Tsague, R.K.T.; Kenmogne, S.B.; Tchienou, G.E.D.; Parra, K.; Ngassoum, M.B. Sequential extraction of quercetin-3-O-rhamnoside from Piliostigma thonningii Schum. leaves using microwave technology. SN Appl. Sci. 2020, 2, 1–17.
9. Yang, X.; Zhu, X.; Ji, H.; Deng, J.; Lu, P.; Jiang, Z.; Li, X.; Wang, Y.; Wang, C.; Zhao, J.; et al. Quercetin synergistically reactivates human immunodeficiency virus type 1 latency by activating nuclear factor-κB. Mol. Med. Rep. 2017, 17, 2501–2508.
10. Cao, X.; Wei, Y.; Ito, Y. Preparative Isolation of Isorhamnetin from Stigma Maydis using High Speed Countercurrent Chromatography. J. Liq. Chromatogr. Relat. Technol. 2009, 32, 273–280.
11. Mehrbod, P.; Abdalla, M.A.; Fotouhi, F.; Heidarzadeh, M.; Aro, A.O.; Eloff, J.N.; McGaw, L.J.; Fasina, F.O. Immunomodulatory properties of quercetin-3-O-α-L-rhamnopyranoside from Rapanea melanophloeos against influenza a virus. BMC Complement. Altern. Med. 2018, 18, 184.
12. Nile, S.H.; Kim, D.H.; Nile, A.; Park, G.S.; Gansukh, E.; Kai, G. Probing the effect of quercetin 3-glucoside from Dianthus superbus L against influenza virus infection- In vitro and in silico biochemical and toxicological screening. Food Chem. Toxicol. 2019, 135, 110985.
13. Chiow, K.; Phoon, M.; Putti, T.; Tan, B.K.; Chow, V.T. Evaluation of antiviral activities of Houttuynia cordata Thunb. extract, quercetin, quercetrin and cinanserin on murine coronavirus and dengue virus infection. Asian Pac. J. Trop. Med. 2016, 9, 1–7.
14. Bose, M.; Kamra, M.; Mullick, R.; Bhattacharya, S.; Das, S.; Karande, A.A. Identification of a flavonoid isolated from plum (Prunus domestica) as a potent inhibitor of Hepatitis C virus entry. Sci. Rep. 2017, 7, 3965.
15. Trujillo-Correa, A.I.; Quintero-Gil, D.C.; Diaz-Castillo, F.; Quiñones, W.; Robledo, S.M.; Martinez-Gutierrez, M. In vitro and in silico anti-dengue activity of compounds obtained from Psidium guajava through bioprospecting. BMC Complement. Altern. Med. 2019, 19, 298.
16. Bachmetov, L.; Gal-Tanamy, M.; Shapira, A.; Vorobeychik, M.; Giterman-Galam, T.; Sathiyamoorthy, P.; Golan-Goldhirsh, A.; Benhar, I.; Zemel, R. Suppression of hepatitis C virus by

the flavonoid quercetin is mediated by inhibition of NS3 protease activity. J. Viral. Hepat. 2012, 19, e81–e88.

17. Choi, H.J.; Song, J.H.; Park, K.S.; Kwon, D.H. Inhibitory effects of quercetin 3-rhamnoside on influenza A virus replication. Eur. J. Pharm. Sci. 2009, 37, 329–333.
18. dos Santos, A.E.; Kuster, R.M.; Yamamoto, K.A.; Salles, T.S.; Campos, R.; de Meneses, M.D.; Ferreira, D. Quercetin and quercetin 3-O-glycosides from Bauhinia longifolia (Bong.) Steud. show anti-Mayaro virus activity. Parasit Vectors 2014, 7, 130.
19. Galochkina, A.V.; Anikin, V.B.; Babkin, V.A.; Ostrouhova, L.A.; Zarubaev, V.V. Virus-inhibiting activity of dihydroquercetin, a flavonoid from Larix sibirica, against coxsackievirus B4 in a model of viral pancreatitis. Arch. Virol. 2016, 161, 929–938.
20. Gansukh, E.; Kazibwe, Z.; Pandurangan, M.; Judy, G.; Kim, D.H. Probing the impact of quercetin-7-O-glucoside on influenza virus replication influence. Phytomedicine 2016, 23, 958–967.
21. Hung, P.-Y.; Ho, B.-C.; Lee, S.-Y.; Chang, S.-Y.; Kao, C.-L.; Lee, S.-S.; Lee, C.-N. Houttuynia cordata Targets the Beginning Stage of Herpes Simplex Virus Infection. PLoS ONE 2015, 10, e0115475.
22. Jeong, H.J.; Ryu, Y.B.; Park, S.-J.; Kim, J.H.; Kwon, H.-J.; Kim, J.H.; Park, K.H.; Rho, M.-C.; Lee, W.S. Neuraminidase inhibitory activities of flavonols isolated from Rhodiola rosea roots and their in vitro anti-influenza viral activities. Bioorganic Med. Chem. 2009, 17, 6816–6823.
23. Ortega, J.T.; Suárez, A.I.; Serrano, M.L.; Baptista, J.; Pujol, F.H.; Rangel, H.R. The role of the glycosyl moiety of myricetin derivatives in anti-HIV-1 activity in vitro. AIDS Res. Ther. 2017, 14, 57.
24. Dou, X.; Zhou, Z.; Ren, R.; Xu, M. Apigenin, flavonoid component isolated from Gentiana veitchiorum flower suppresses the oxidative stress through LDLR-LCAT signaling pathway. Biomed. Pharmacother. 2020, 128, 110298.
25. Qian, S.; Fan, W.; Qian, P.; Zhang, D.; Wei, Y.; Chen, H.; Li, X. Apigenin Restricts FMDV Infection and Inhibits Viral IRES Driven Translational Activity. Viruses 2015, 7, 1613–1626.
26. El-Toumy, S.A.; Salib, J.Y.; El Kashak, W.A.; Marty, C.; Bedoux, G.; Bourgougnon, N. Antiviral effect of polyphenol rich plant extracts on herpes simplex virus type 1. Food Sci. Hum. Wellness 2018, 7, 91–101.
27. Qiu, X.; Kroeker, A.; He, S.; Kozak, R.; Audet, J.; Mbikay, M.; Chrétien, M. Prophylactic Efficacy of Quercetin 3-β- O-d-Glucoside against Ebola Virus Infection. Antimicrob. Agents Chemother. 2016, 60, 5182–5188.
28. Quecan, B.X.V.; Santos, J.T.C.; Rivera, M.L.C.; Hassimotto, N.M.A.; Almeida, F.A.; Pinto, U.M. Effect of Quercetin Rich Onion Extracts on Bacterial Quorum Sensing. Front. Microbiol. 2019, 10,

867.

29. Sati, P.; Dhyani, P.; Bhatt, I.D.; Pandey, A. Ginkgo biloba flavonoid glycosides in antimicrobial perspective with reference to extraction method. J. Tradit. Complement. Med. 2019, 9, 15–23.
30. Dayem, A.A.; Choi, H.Y.; Kim, Y.B.; Cho, S.-G. Antiviral Effect of Methylated Flavonol Isorhamnetin against Influenza. PLoS ONE 2015, 10, e0121610.
31. Liu, Z.; Zhao, J.; Li, W.; Shen, L.; Huang, S.; Tang, J.; Duan, J.; Fang, F.; Huang, Y.; Chang, H.; et al. Computational screen and experimental validation of anti-influenza effects of quercetin and chlorogenic acid from traditional Chinese medicine. Sci. Rep. 2016, 6, 19095.
32. Murali, K.S.; Sivasubramanian, S.; Vincent, S.; Murugan, S.B.; Giridaran, B.; Dinesh, S.; Gunasekaran, P.; Krishnasamy, K.; Sathishkumar, R. Anti—Chikungunya activity of luteolin and apigenin rich fraction from Cynodon dactylon. Asian Pac. J. Trop. Med. 2015, 8, 352–358.
33. Liu, A.-L.; Liu, B.; Qin, H.-L.; Lee, S.; Wang, Y.-T.; Du, G.-H. Anti-Influenza Virus Activities of Flavonoids from the Medicinal Plant Elsholtzia rugulosa. Planta Med. 2008, 74, 847–851.
34. Ahmed, O.M.; Fahim, H.I.; Ahmed, H.Y.; Almuzafar, H.; Ahmed, R.R.; Amin, K.A.; El-Nahass, E.-S.; Abdelazeem, W.H. The Preventive Effects and the Mechanisms of Action of Navel Orange Peel Hydroethanolic Extract, Naringin, and Naringenin in N-Acetyl-p-aminophenol-Induced Liver Injury in Wistar Rats. Oxidative Med. Cell. Longev. 2019, 2019, 2745352.
35. Cataneo, A.H.D.; Kuczera, D.; Koishi, A.C.; Zanluca, C.; Silveira, G.F.; de Arruda, T.B.; Suzukawa, A.A.; Bortot, L.O.; Dias-Baruffi, M.; Verri, W.A.V., Jr.; et al. The citrus flavonoid naringenin impairs the in vitro infection of human cells by Zika virus. Sci. Rep. 2019, 9, 16348.
36. Bellavite, P.; Donzelli, A. Hesperidin and SARS-CoV-2: New Light on the Healthy Function of Citrus Fruits. Antioxidants 2020, 9, 742.
37. Paredes, A.; Alzuru, M.; Mendez, J.; Rodríguez-Ortega, M. Anti-Sindbis Activity of Flavanones Hesperetin and Naringenin. Biol. Pharm. Bull. 2003, 26, 108–109.
38. Al-Ashaal, H.A.; El-Sheltawy, S.T. Antioxidant capacity of hesperidin from Citrus peel using electron spin resonance and cytotoxic activity against human carcinoma cell lines. Pharm. Biol. 2011, 49, 276–282.
39. Nahmias, Y.; Goldwasser, J.; Casali, M.; van Poll, D.; Wakita, T.; Chung, R.T.; Yarmush, M.L. Apolipoprotein B-dependent hepatitis C virus secretion is inhibited by the grapefruit flavonoid naringenin. Hepatology 2008, 47, 1437–1445.
40. Si-Si, W.; Liao, L.; Ling, Z.; Yun-Xia, Y. Inhibition of TNF-α/IFN-γ induced RANTES expression in HaCaT cell by naringin. Pharm. Biol. 2011, 49, 810–814.
41. Yan, H.; Ma, L.; Wang, H.; Wu, S.; Huang, H.; Gu, Z.; Jiang, J.; Li, Y. Luteolin decreases the yield of influenza A virus in vitro by interfering with the coat protein I complex expression. J. Nat. Med.

2019, 73, 487–496.

42. De Sousa, L.R.F.; Wu, H.; Nebo, L.; Fernandes, J.B.; das Graças Fernandes da Silva, M.F.; Kiefer, W.; Kanitz, M.; Bodem, J.; Diederich, W.E.; Schirmeister, T.; et al. Flavonoids as noncompetitive inhibitors of Dengue virus NS2B-NS3 protease: Inhibition kinetics and docking studies. Bioorg. Med. Chem. 2015, 23, 466–470.
43. Frabasile, S.; Koishi, A.C.; Kuczera, D.; Silveira, G.F.; Verri, W.A., Jr.; Duarte Dos Santos, C.N.; Bordignon, J. The citrus flavanone naringenin impairs dengue virus replication in human cells. Sci. Rep. 2017, 7, 41864.
44. Almeida, A.F.; Borge, G.I.A.; Piskula, M.; Tudose, A.; Tudoreanu, L.; Valentová, K.; Williamson, G.; Santos, C.N. Bioavailability of Quercetin in Humans with a Focus on Interindividual Variation. Compr. Rev. Food Sci. Food Saf. 2018, 17, 714–731.
45. Moon, J.H.; Nakata, R.; Oshima, S.; Inakuma, T.; Terao, J. Accumulation of quercetin conjugates in blood plasma after the short-term ingestion of onion by women. Am. J. Physiol. Regul. Integr. Comp. Physiol. 2000, 279, R461–R467.
46. Batiha, G.E.-S.; Beshbishy, A.M.; Ikram, M.; Mulla, Z.S.; El-Hack, M.E.A.; Taha, A.E.; Algammal, A.M.; Elewa, Y.H.A. The Pharmacological Activity, Biochemical Properties, and Pharmacokinetics of the Major Natural Polyphenolic Flavonoid: Quercetin. Foods 2020, 9, 374.
47. Gibellini, L.; Pinti, M.; Nasi, M.; Montagna, J.P.; De Biasi, S.; Roat, E.; Bertoncelli, L.; Cooper, E.L.; Cossarizza, A. Quercetin and Cancer Chemoprevention. Evid. -Based Complement. Altern. Med. 2011, 2011, 591356.
48. Du, G.; Lin, H.; Yang, Y.; Zhang, S.; Wu, X.; Wang, M.; Ji, L.; Lu, L.; Yu, L.; Han, G. Dietary quercetin combining intratumoral doxorubicin injection synergistically induces rejection of established breast cancer in mice. Int. Immunopharmacol. 2010, 10, 819–826.
49. Sakai-Kashiwabara, M.; Asano, K. Inhibitory Action of Quercetin on Eosinophil Activation In Vitro. Evid. -Based Complement. Altern. Med. 2013, 2013, 127105.