

Review Article : Open Access

Special Issue2 (COVID-19)

Significance and importance of fruits in strengthening immune system during COVID-19

Johra Khan^{♦*}

Department of Medical Laboratory Sciences, College of Applied Medical Sciences, Majmaah University, Al Majmaah, 11952, Saudi Arabia
*Health and Basic Sciences Research Center, Majmaah University, Al Majmaah, 11952, Saudi Arabia

Article Info

Article history

Received 1 November 2021
Revised 25 December 2021
Accepted 26 December 2021
Published Online 30 December 2021

Keywords

Citrus fruits
Apple
Berries
Phytochemicals
ACE2
Kiwi

Abstract

The outbreak of COVID-19 in 2019 followed by its new variants till now in 2021, made it more necessary to find more identify effective antiviral agents to be included in daily life to combat SARS-CoV-2 and support vaccines and their effect. Fruits are always considered good for health and many studies are trying to find the solution and different compounds with antiviral properties in fruits. Recently, many *in vivo* and docking studies found many phytochemical compounds effective against COVID-19. In this review, we tried to collect data from different studies. We found that fruits are most valuable gift with great healing property.

1. Introduction

The new decade of the 21st century started with the emergence of a novel coronavirus SARS-CoV-2 or COVID-19 in December 2019, which is another community health problem and has been the focus of global attention due to a pneumonia epidemic of unknown cause (Kumar *et al.*, 2021). It has emerged in the huanan seafood market, where livestock animals are also traded, in Wuhan State of Hubei Province in China (Lai *et al.*, 2020). The first case of the COVID-19 epidemic was discovered with unexplained pneumonia on December 12, 2019, and 27 viral pneumonia cases with 7 being severe were officially announced on December 31, 2019 and possible influenza and other CoVs were ruled out by laboratory testing. Chinese authorities announced on January 7, 2020 that a new type of coronavirus (novel coronavirus, nCoV) was isolated (Imperial College of London. Report 2: estimating the potential total number of novel coronavirus cases in Wuhan City, China, Jan 2020 (Imai *et al.*, 2020). This virus was named as COVID-19 by WHO on January 2019. New variant cases are still being identified, primarily in other Asian and African countries and in many countries such as the trans-oceanic USA and UK (Pulliam *et al.*, 2021).

During COVID-19, World Health Organization (WHO) announced special dietary suggestion and guidelines for maintaining strong immunity to combat chronic diseases like viral infection including COVID-19. As per WHO, a person should take 5 fruits and vegetables

per day but during COVID-19, the serving recommendation was increased to 9 (5 fruits and 4 vegetable) per day (Moreb *et al.*, 2021). Many researches confirmed the entry of SARS-CoV-2 in human is aided by angiotensin-converting enzyme (ACE2) which is a transmembrane enzyme and its level was associated with dietary patterns of the population are found related to ACE levels in their body and in some researches rate of mortality is also connected to the deity intake (Chew *et al.*, 2011; Jaiswal, 2020).

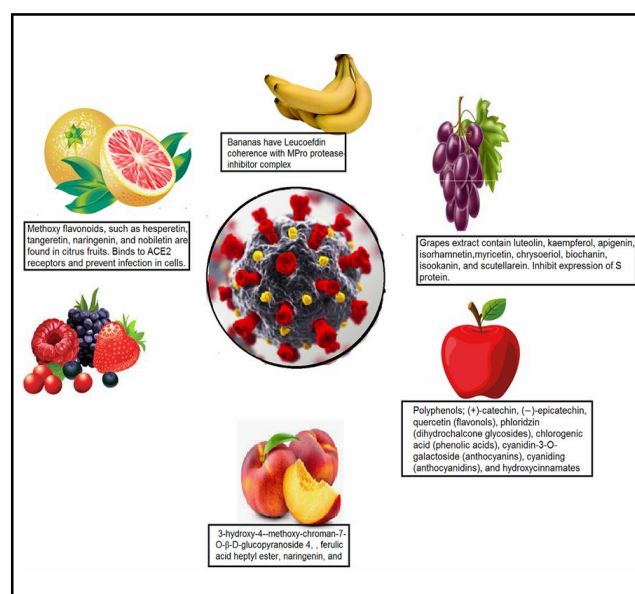


Figure 1: Different fruits and the phytochemical components against SARS-CoV-2.

Corresponding author: Dr. Johra Khan

Assistant Professor, Department of Medical Laboratory Sciences, College of Applied Medical Sciences, Majmaah University, Al Majmaah, 11952, Saudi Arabia

E-mail: j.khan@mu.edu.sa

Tel.: +966-538077360

Copyright © 2021 Ukaaz Publications. All rights reserved.

Email: ukaaz@yahoo.com; Website: www.ukaazpublications.com

From the studies till now, it is identified that protein deficiency can cause the low antibody production and more chances of getting infection (Martindale *et al.*, 2020). The level of nutrition in a body is fundamental necessity for controlling inflammation and oxidative stress, which are directly and indirectly connected to immune system (Cena and Chieppa, 2020). Many nutrients like omega-3 fatty acids, vitamins, and minerals with many phytochemicals (polyphenols, carotenoids) contain anti-inflammatory properties (Garofolo *et al.*, 2021; Rothenberg, 2021). The dietary fibre found in fruits and vegetables helps in gut microbiota stimulation and produce probiotic effect by supporting the growth of bacteria like *Bifidobacterium* sp., also help in reducing pathogenic bacteria such as *Clostridium* sp. (O'Shea *et al.*, 2012; Egbuna *et al.*, 2021). These are important to be considered especially in case of SARS-CoV-2 infection due to gastrointestinal problems during COVID-19 and even after recovery (Khan *et al.*, 2021; Rudrapal *et al.*, 2021). In this article, we are providing the information regarding intake of fruits in COVID-19 and their role as immunity booster to combat and recover from this pandemic (Komarayanti *et al.*, 2020; Khanna *et al.*, 2021; Yedjou *et al.*, 2021).

2. Fruits with healing properties

2.1 Citrus fruits

Fruits are good source of vitamins, alkaloids, and flavonoids with many other phytochemicals which are beneficial for human health. They are also useful for treating many diseases (Rudrapal *et al.*, 2021; Shaikh *et al.*, 2021). The six common flavonoids found in citrus fruits including *Citrus reticulata* (mandarin), *Citrus maxima* (pummelo), and *Citrus sinensis* (sweet orange) are naringin, naringenin, hesperetin, hesperidin, neohesperidin, and nobiletin (Asjad *et al.*, 2013; Cheng *et al.*, 2020). In COVID-19 chronic patient, cytokine storm is observed increase in concentrations of interleukins (IL-1 β , IL-10), TNF- α , and IFN γ in plasma (Peterson and Dwyer, 1998; Tripoli *et al.*, 2007). Corticosteroids are recommended to reduce inflammation in lungs, indicating use of anti-inflammatory substances, can help in reducing the severity of COVID-19 clinical symptoms. Anti-inflammatory activity of Citrus naringin was tested in lipopolysaccharide (LPS) treated rats as LPS was found to induce COX-2, IL-1 β , and IL-6 (Meneguzzo *et al.*, 2020). Naringin in 10, 20, 40 μ g/ml concentration significantly reduce the effect of COX-2, iNOS, IL-1 β , and IL-6 and help in lowering the cytokine storm (Tutunchi *et al.*, 2020). As per WHO and different studies on WH-Human_1 sequence of SARS-CoV S-protein shares identical structure of 3-D structure in RBD domain and significant binding affinity toward human ACE2 which is expressed in lungs, kidney, brain, and digestive tract and critical for SARS-CoV-2 entry in host cell (Liu *et al.*, 2016). Zheng and Liu (2020) did docking study to find the interaction of flavonoids with ACE2 (Zheng and Liu *et al.*, 2020). The results showed high binding activity between naringin and ACE2 with docking energy of -6.85 kcal/mol and potential binding site at TYR-515, GLU-402, GLU-398, and ASN394, similarly, naringenin shows bind with ACE2 with docking energy of -6.05 kcal/mol and with possible binding site at LEU-143, PRO-146, and LYS-131 (Muchtaridi *et al.*, 2020). Hesperidin and hesperetin also showed potential binding affinity to ACE2 with docking energy of -4.21 kcal/mol and -6.09 kcal/mol with binding sites at ASN-277, ARG-273, HIS-505 with hesperetin, and TRP-69, LEU-351, ASP-350 with hesperidin (Biagioli *et al.*, 2021). This study also focused

on comparison between the docking studies between chloroquine, baicalin with hesperetin, naringenin, and naringin reporting good potentials of these three flavonoids similar to chloroquine to inhibit the ACE2 (Guler *et al.*, 2021).

2.2 Kiwi as immunity booster

Kiwi fruit is also known with names like “China Miracle fruit”, “Horticulture wonder of New Zealand”, and so on. Kiwi contains good amount of vitamin C, carotenoids, polyphenols, and dietary fibres (Arshad *et al.*, 2020). Researches on kiwi found it to a potential immunity booster. *In vitro* and *in vivo* studies on animal models shows significant influence of different biomarkers related to oxidative stress and immune system and also recorded to reduce the frequency and severity of upper respiratory tract infection in comparison to vitamin C supplements alone (Aslam *et al.*, 2017). Kiwi fruit contains the ability of DNA protection from free radicals (Kim *et al.*, 2020; Öztürk and Yücedag, 2021). The flavonoids and phytonutrients present in kiwi was found to reduce shortness of breath by 32%, night cough by 27%, running nose by 28%, and chronic cough by 25% (Reddy, 2020). Doctors observed that COVID-19 patients who eat three kiwis a day, had low risk of age related muscular degeneration (ARMD) (Arumugam *et al.*, 2021).

2.3 Apples

Apples are always considered best for as per the famous saying, “an apple a day, keeps a doctor away”. Apples contain high amount of vitamin B, C, and antioxidants, which not only helps in promoting immunity, but also improves digestive system (Kamal *et al.*, 2019). Riboflavin (vitamin B2), a photosensitizer that was used together with UV light to reduce the viral load of batches of blood transfusion and in controlling the titer of MERS-CoV (Middle East respiratory syndrome) related coronavirus which cannot be detected (Cardoso *et al.*, 2012). *In vivo* study in mice reported that riboflavin decreases inflammation in lungs with significant reduction in neutrophil infiltration (Lu *et al.*, 2004). Some studies also suggest that vitamin B6 supplementation increases total lymphocyte, T-helper and T-suppressor cells. It is also found to significantly reduce inflammation (Nieva *et al.*, 2006). Apples are also reported to show anti-inflammatory activity in human lung cells and tracheal epithelial cells by increasing the pro-inflammatory cytokines and chemokine signalling effect (Chaudhuri *et al.*, 2015). Apple and its juice were found to decrease cell proliferation and allergic reactions of IgE and mast cell. Apple peels also found to activate macrophages to facilitate tissue repair and direct inhibition of pro-inflammatory pathway by increasing expression of Arg1 gene in lungs (Chaudhuri *et al.*, 2015). Combinations of boysenberry with apple reduce lung inflammation by increasing granulocyte apoptosis mediated interleukin 17A and F (Pajares *et al.*, 2011).

2.4 Some other fruits

Other than citrus fruits and apple, some other fruits are also recorded to have nitrate contents present in their flesh, seeds, and skin. Fruits like grapes and berries contain nitrate, resveratrol, anthocyanin, and quercetin which shows protective activity in lung damages and injuries inhibiting TNF- α , IL-8, modulation Th1 and 2 cells, holding neutrophil and eosinophil recruitment. All of these are responsible of causing cytokine storm in lungs of a COVID-19 patient (Criado and García, 2004). The extract of grape seeds also

reported to relive viral complications by stopping viral replication, it reduce pro-inflammatory IL-6, IL-8, IL-1 β , reduce the expression of mucins (Swathi Krishna *et al.*, 2021). The strawberry and blackberry are also big source of dietary nitrates. Study on rat's shows that strawberry extract reduce level of IgG and IgM in hepatic cells. The extracts of blueberry and strawberry helps in cell survival, and DNA repair (Zhang and Liu, 2020). They are also found to work as immune modulator (Wang *et al.*, 2014).

These fruits also contain flavonoids which help in regulating immune response by regulating receptors and BRD4 (bromodomain containing protein 4) (Nagarajan *et al.*, 2014). Some researchers reported them also to activate nuclear factor erythroid derived 2 related factor 2 (Nrf2), which help in regulating cytokine storm

during SARS-CoV-2 infection (Liskova *et al.*, 2021). Pedunculagin, tercatain, and castalin are some hydrolysable tannin showing strong connection sites like Cys145 and His41 on 3 CL pro protein of SARS-CoV-2 (Mendonca and Soliman, 2020). Studies by Mazza and Miniati (2018) reported the presence of anthocyanin in strawberry and high amount of it in bush blueberries (Chrz *et al.*, 1993; Mazza and Miniati, 2018). The molecular docking studies of anthocyanin's ligands from berries shows three compounds, pelargonidin-3-glucose, pelargonidin 3 rhamnoside, and procyanidin B2 were targeted on amino acid responsible for interaction between S protein and ACE2 (Karppinen *et al.*, 2018). This will cause disturbance in attachment of SARS-CoV-2 virus with ACE2 in host cell receptor preventing viral infection (Karppinen *et al.*, 2018).

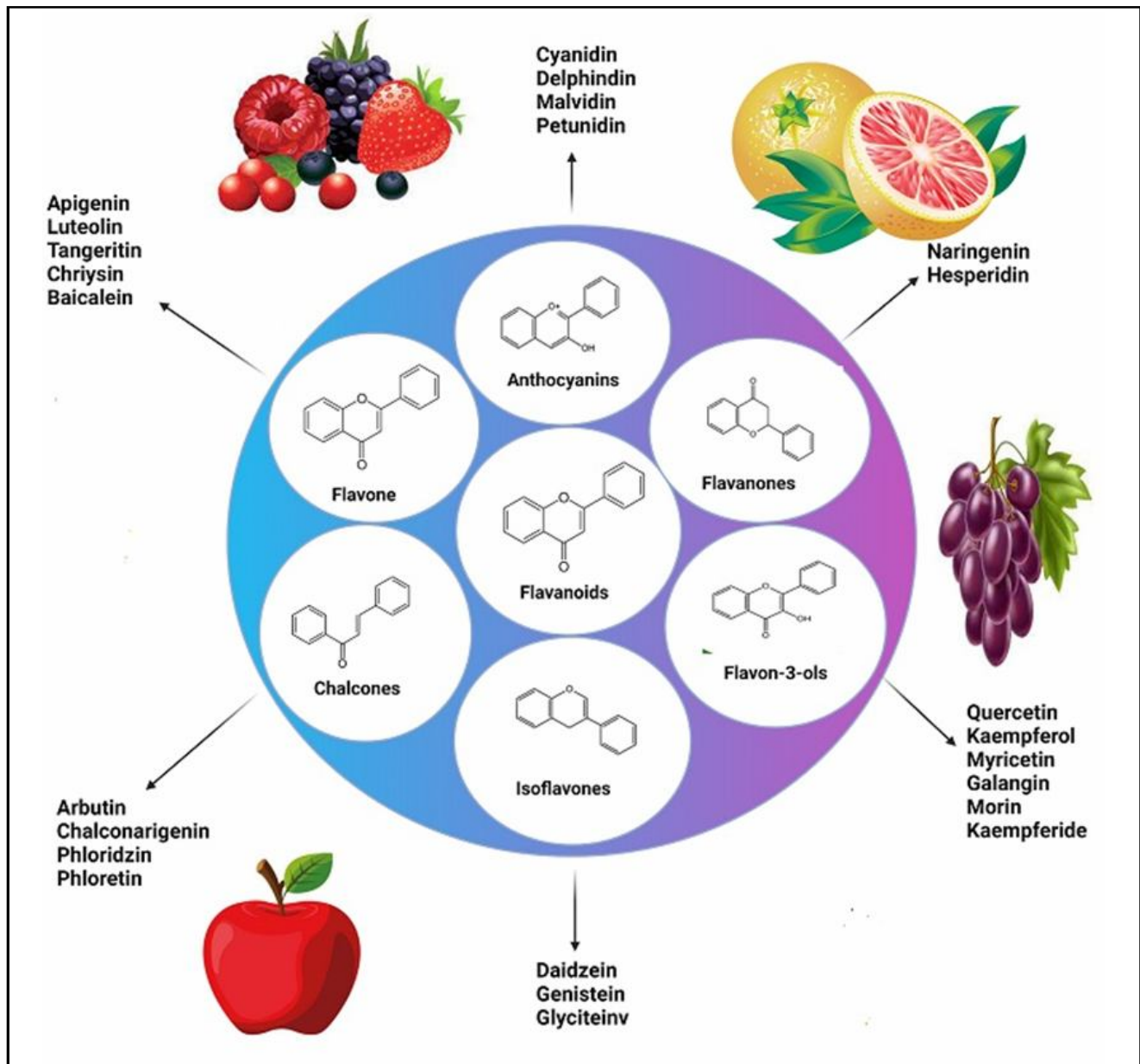


Figure 2: Different phytochemicals found in fruits to fight against COVID-19.

3. Conclusion

Fresh fruits are very important for health especially during this COVID-19, when need of strong immunity is very high. Fruits which contain significant amount of nitrate can hold the progression of viral disease immediately by either activating or inhibiting different pathways related to SARS-CoV-2 progression. Fruits are home based cheap and readily available remedies that can be implemented to limit the spread of COVID-19 pandemic.

Conflict of interest

The author declares no conflicts of interest relevant to this article.

References

- Arshad, M.S.; Khan, U.; Sadiq, A.; Khalid, W.; Hussain, M.; Yasmeen, A.; Asghar, Z. and Rehana, H. (2020). Coronavirus disease (COVID 19) and immunity booster green foods: A mini review. *Food Sci. and Nu.*, **8**(8):3971-3976.
- Arumugam, T.; Sona, C. L. and Maheswari, M. U. (2021). Fruits and vegetables as superfoods: Scope and demand. *J. Pharm. Innov.*, **10**:119-129.
- Asjad, H.M. M.; Akhtar, M. S.; Bashir, S.; Din, B.; Gulzar, F., Khalid and Asad, M. (2013). Phenol, flavonoid contents and antioxidant activity of six common citrus plants in Pakistan. *J. Pharma. and Cos. Sci.*, **1**(1): 1-5.
- Aslam, M. F.; Majeed, S.; Aslam, S. and Irfan, J. A. (2017). Vitamins: Key role players in boosting up immune response. A mini review. *Vit. Miner*, **6**(1):2376-1318.
- Biagioli, M.; Marchianò, S.; Roselli, R.; Giorgio, C.; Bellini, R.; Bordoni, M.; Gidari, A.; Sabbatini, S.; Francisci, D. and Fiorillo, B. (2021). Discovery of a AHR pelargonidin agonist that counter-regulates ACE2 expression and attenuates ACE2-SARS-CoV-2 interaction. *Biochem. Pharm.*, **188**:114564.
- Cardoso, D. R.; Libardi, S. H. and Skibsted, L. H. (2012). Riboflavin as a photosensitizer. Effects on human health and food quality. *Food and Fun.*, **3**(5):487-502.
- Cena, H. and M. Chieppa (2020). Coronavirus disease (COVID-19-SARS-CoV-2) and nutrition: Is infection in Italy suggesting a connection. *Fron. In., immun.* **11**:944.
- Chaudhuri, S.; Sardar, S.; Bagchi, D.; Singha, S. S.; Lemmens, P. and Pal, S. K. (2015). Sensitization of an endogenous photosensitizer: Electronic spectroscopy of riboflavin in the proximity of semiconductor, insulator, and metal nanoparticles. *J. of Phy. Chem.*, **119**(18): 4162-4169.
- Cheng, L.; Zheng, W.; Li, M.; Huang, J.; Bao, S.; Xu, Q. and Ma, Z. (2020). Citrus fruits are rich in flavonoids for immunoregulation and potential targeting ACE2, Preprints, pp:20-313.
- Chew, L.; Prasad, K. N.; Amin, I.; Azrina, A. and Lau, C. (2011). Nutritional composition and antioxidant properties of *Canarium odontophyllum* Miq. (dabai) fruits. *J. of Food Comp. and Ana.*, **24**(4-5):670-677.
- Chrzą, D.; Maness, N. and Wahem, I. (1993). Yield and quality evaluation of seven strawberry cultivars in eastern Oklahoma. *Hort. Sci.*, **28**(4): 276F-276.
- Criado, S. and García, N.A. (2004). Vitamin B2-sensitized photooxidation of the ophthalmic drugs Timolol and Pindolol: Kinetics and mechanism. *Red. Report*, **9**(5):291-297.
- Egbuna, C.; Awuchi, C. G.; Kushwaha, G.; Rudrapal, M.; Patrick-Iwuanyanwu, K. C.; Singh, O.; Odoh, U. E.; Khan, J.; Jeevanandam, J. and Kumarasamy, S. (2021). Bioactive compounds effective against type 2 diabetes mellitus: a systematic review. *Cur. Topics in Med. Chem.*, **21**(12): 1067-1095.
- Garófalo, A.; Qiao, L. and Maia-Lemos, P. d. S. (2021). Approach to nutrition in cancer patients in the context of the Coronavirus disease 2019 (COVID-19) pandemic: Perspectives. *Nut. and Cancer*, **73**(8):1293-1301.
- Guler, H. I.; Fulya, A.; Zehra, C.; Yakup, K.; Belduz, A. O.; Canakci, S. and Kolayli, S. (2021). Targeting CoV-2 Spike RBD and ACE-2 Interaction with flavonoids of anatolian propolis by *insilico* and *in vitro* studies in terms of possible COVID-19 therapeutics. *Turk. J. Biol.*, **45**(4):530-548.
- Imai, N.; Dorigatti, I.; Cori, A.; Donnelly, C.; Riley, S. and Ferguson, N. (2020). Report 2: Estimating the potential total number of novel Coronavirus cases in Wuhan City, China.
- Jaiswal, A.K. (2020). Nutritional composition and antioxidant properties of fruits and vegetables, academic press.
- Kamal, I.; Zaffar, S.; Malik, J. A. and Ahmad, M. (2019). Effect of apple peel extract on the production of IgG immunoglobulins in immunosuppressed mice. *J. Postgrad. Med. Inst.*, **33**(3):66.219.22.243.
- Karppinen, K.; Tegelberg, P.; Häggman, H. and Jaakola, H. (2018). Abscisic acid regulates anthocyanin biosynthesis and gene expression associated with cell wall modification in ripening bilberry (*Vaccinium myrtillus* L.) fruits. *Fron. in Plant Sci.*, **9**:1259.
- Khan, J.; Deb, P. K.; Priya, S.; Medina, K. D.; Devi, R.; Walode, S. G. and Rudrapal, M. (2021). Dietary flavonoids: Cardioprotective potential with antioxidant effects and their pharmacokinetic, toxicological and therapeutic concerns. *Mol.*, **30**; **26**(13):4021, doi:10.3390/molecules26134021. PMID: 34209338; PMCID: PMC8272101.
- Khanna, K.; Kohli, S. K.; Kaur, R.; Bhardwaj, A.; Bhardwaj, V.; Ohri, P.; Sharma, A.; Ahmad, A.; Bhardwaj, R. and Ahmad, P. (2021). Herbal immune-boosters: Substantial warriors of pandemic Covid-19 battle. *Phytomed.*, **85**:153361.
- Kim, Y. M.; Park, Y. S.; Park, Y. K.; Ham, K. S.; Kang, S. G.; Barasch, D.; Nemirowski, A. and Gorinstein, S. (2020). Phytochemical analysis of two main varieties of persimmon and kiwifruit and their antioxidative and quenching capacities. *Euro. Food Res. and Tech.*, **246**(6):1259-1268.
- Komarayanti, S.; Suharso, W. and Herrianto, E. (2020). Local fruits and vegetables of Jember district that can increase immunity during the Covid-19 pandemic. *Bir. Ex. Journal*, **2**(4):492-508.
- Kumar, D.; Jahan, S.; Khan, A.; Siddiqui, A. J.; Redhu, N. S.; Khan, J.; Banwas, S.; Alshehri, B. and Alaidarous, A. (2021). Neurological manifestation of SARS-CoV-2 induced inflammation and possible therapeutic strategies against COVID-19. *Mol. Neur.*, pp:1-18.
- Lai, X.; Wang, M.; Qin, C.; Tan, L.; Ran, L.; Chen, D.; Zhang, H.; Shang, K.; Xia, C. and Wang, S. (2020). Coronavirus disease 2019 (COVID-2019) infection among healthcare workers and implications for prevention measures in a tertiary Hospital in Wuhan, China. *JAMA Netw. Open.* **3**(5):e209666.
- Liskova, A.; Samec, M.; Koklesova, L.; Samuel, S. M.; Zhai, K.; Al-Ishaq, R. K.; Abotaleb, M.; Nosal, V.; Kajo, K. and Ashrafzadeh, M. (2021). Flavonoids against the SARS-CoV-2 induced inflammatory storm. *Biomed. and Pharm.*, pp:111-430.
- Liu, X.; Wang, N.; Fan, S.; Zheng, X.; Yang, Y.; Zhu, Y.; Lu, Y.; Chen, Q.; Zhou, H. and Zheng, J. (2016). The citrus flavonoid naringenin confers protection in a murine endotoxaemia model through AMPK-

- ATF3-dependent negative regulation of the TLR4 signalling pathway. *Sci. Rep.*, 6(1):1-14.
- Lu, C.; Bucher, G. and Sander, W. (2004). Photoinduced interactions between oxidized and reduced lipoic acid and riboflavin (vitamin B2). *Chem. Phys. Chem.*, 5(1):47-56.
- Martindale, R.; Patel, J. J.; Taylor, B.; Arabi, Y. M.; Warren, M. and McClave, S. A. (2020). Nutrition therapy in critically ill patients with coronavirus disease 2019. *J. Parent. and E.N.*, 44(7):1174-1184.
- Mazza, G. and E. Miniati (2018). Anthocyanins in fruits, vegetables, and grains, CRC press.
- Mendonca, P. and Soliman, K. F. (2020). Flavonoids activation of the transcription factor Nrf2 as a hypothesis approach for the prevention and modulation of SARS-CoV-2 infection severity. *Antioxid.*, 9(8):659.
- Meneguzzo, F.; Ciriminna, R.; Zabini, N. and Pagliaro, M. (2020). Review of evidence available on hesperidin-rich products as potential tools against COVID-19 and hydrodynamic cavitation-based extraction as a method of increasing their production, *Proc.*, 8(5):549.
- Moreb, N. A.; Albandary, A.; Jaiswal, S. and Jaiswal, A. K. (2021). Fruits and vegetables in the management of underlying conditions for COVID-19 high-risk groups. *J. F.*, 10(2):389.
- Muchtaridi, M.; Fauzi, M.; Khairul Ikram, N. K.; Mohd Gazzali, A. and Wahab, H.A. (2020). Natural flavonoids as potential angiotensin-converting enzyme 2 inhibitors for anti-SARS-CoV-2. *Mol.*, 25(17):3980.
- Nagarajan, S.; Hossan, T.; Alawi, M.; Najafova, Z. ; Indenbirken, D.; Bedi, U.; Taipaleenmäki, H.; Ben-Batalla, I.; Scheller, M. and Loges, S. (2014). Bromodomain protein BRD4 is required for estrogen receptor-dependent enhancer activation and gene transcription. *Cell Rep.*, 8(2):460-469.
- Nieva, J.; Kerwin, L.; Wentworth, A. D.; Lerner, R. A. and Wentworth P. (2006). Immunoglobulins can utilize riboflavin (Vitamin B2) to activate the antibody-catalyzed water oxidation pathway. *Imm. Letters*, 103(1):33-38.
- O'Shea, N.; Arendt, E. K. and Gallagher, E. (2012). Dietary fibre and phytochemical characteristics of fruit and vegetable by-products and their recent applications as novel ingredients in food products. *Innov. F. Sci. and Emer. Tech.*, 16:1-10.
- Öztürk, B. and Yücedağ, F. (2021). Effects of methyl jasmonate on quality properties and phytochemical compounds of kiwifruit (*Actinidia deliciosa* cv. Hayward') during cold storage and shelf life. *Turk. J. of Agri. and Forest*, 45(2):154-164.
- Pajares, A.; Bregliani, M.; Natera, J.; Criado, S.; Miskoski, S.; Escalada, J. P. and García, N. A. (2011). Mechanism of the photosensitizing action of a mixture humic acid-riboflavin in the degradation of water-contaminants. *J. Photochem. and Photobio. A: Chem.*, 219(1): 84-89.
- Peterson, J. and Dwyer, J. (1998). Flavonoids: Dietary occurrence and biochemical activity. *Nut. Res.*, 18(12):1995-2018.
- Pulliam, J. R.; Van Schalkwyk, C.; Govender, N.; Von Gottberg, A.; Cohen, C.; Groome, M. J.; Dushoff, J.; Mlisana, K. and Moultrie, H. (2021). Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. *Med. Rxiv.*, pp:320.
- Reddy, A.C. (2020). Immunity: A strong defense against coronavirus.
- Rothenberg, E. (2021). Coronavirus disease 19 from the perspective of ageing with focus on nutritional status and nutrition management. A narrative review. *Nut.*, 13(4):1294.
- Rudrapal, M.; Gogoi, N.; Chetia, D.; Khan, J.; Banwas, S.; Alshehri, B.; Alaidarous, M. A.; Laddha, U. D.; Khairnar, S. J. and Walode, S. G. (2021). Repurposing of Phytomedicine-Derived Bioactive Compounds with promising Anti-SARS-CoV-2 potential: Molecular docking, MD simulation and drug-likeness/ADMET studies. *S. J. Bio. Sci.*, doi: 10.1016/j.sjbs.2021.12.018. Epub ahead of print. PMID: 34924801; PMCID: PMC8667520.
- Rudrapal, M.; Khan, J.; Dukhyil, A. A. B.; Alarousy, R. M. I. I.; Attah, E. I.; Sharma, T.; Khairnar, S. J. and Bendale, A. R. (2021). Chalcone scaffolds, bioprecursors of flavonoids: Chemistry, bioactivities, and pharmacokinetics. *Mol.*, 26(23):71-77.
- Shaikh, Z.; Sundarrajan, P.; Bhagtaney, L.; Zehra, S.; Zahra, K. F.; Badra, B.; Yigit, B. M.; Patel, N.; Alim, H. and Khan, J. (2021). Applicability of vitamins in the management of COVID-19: An overview. *Ann. Phytomed.*, S65-S76.
- Swathi Krishna, S.; Thennavan, A. and Kanthlal, S. (2021). Dietary foods containing nitric oxide donors can be early curators of SARS CoV 2 infection: A possible role in the immune system. *J. of F Biochem.*, e13884.
- Tripoli, E.; La Guardia, M.; Giammanco, S.; Di Majo, D. and Giammanco, M. (2007). Citrus flavonoids: Molecular structure, biological activity and nutritional properties: A review. *F. Chem.*, 104(2):466-479.
- Tutunchi, H.; Naeini, F.; Ostadrahimi, A. and Hosseinzadeh Attar, M. J. (2020). Naringenin, a flavanone with antiviral and anti-inflammatory effects: A promising treatment strategy against COVID 19. *Phyto. Res.*, 34(12):3137-3147.
- Wang, L.; Gao, S.; Jiang, W.; Luo, C.; Xu, M.; Bohlin, L.; Rosendahl, M. and Huang, W. (2014). Antioxidative dietary compounds modulate gene expression associated with apoptosis, DNA repair, inhibition of cell proliferation and migration. *IJMS*. 15(9):16226-16245.
- Yedjou, C. G.; Alo, R. A.; Liu, J.; Enow, J.; Ngnepiepa, P.; Long, R.; Latinwo, L. and Tchounwou, P. B. (2021). Chemo-preventive effect of vegetables and fruits consumption on the COVID-19 pandemic. *J. of Nut. Food Sci.*, 4(2).
- Zhang, L. and Liu, Y. (2020). Potential interventions for novel coronavirus in China: A systematic review. *J. of Med. Virolo.*, 92(5):479-490.

Citation

Johra Khan (2021). Significance and importance of fruits in strengthening immune system during COVID-19. *Ann. Phytomed.*, Volume10, Special Issue2 (COVID-19): S111-S115. <http://dx.doi.org/10.54085/ap.covid19.2021.10.2.12>