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Low Molecular Weight Antioxidant versus Flavonoids in Combating Oxidative Stress: Which One is Superior?

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According to the free radical theory of aging, firstly proposed by Denham Harman, the most prominent cause of aging and degenerative diseases (DD) is continuously chemical reaction in cells and tissues. In this context aging and or DD is manifested as chemical composition, whilst aging process is reflected by chemical reaction affected by environment (Harman, 1981). Thus, both aging and DD have similar process, predisposed with oxidative stress and characterized by the progressive cellular alteration accumulation in line with time and account for increase in susceptibility to diseases and death. The most prevalent chemical reaction is between free radical reactive oxygen species (ROS) and reactive nitrogen species (RNS) with cellular biomolecules such as lipids, protein, carbohydrate, and DNA (Lamichhane et al., 2013). In order to prevent the deleterious effect of that chemical reaction, human's body provides an antioxidant defense system to counterbalance the free radical dangerous effect. However, owing to inappropriate life style, eating style, physical activity, and poor environment, production of ROS and RNS may be increased and induce cellular damages. Numerous publications indicated that oxidative stress and cellular damages can be reduced even prevented by exogenous antioxidant, thus intake antioxidant from external sources is necessary. There are two type of exogenous antioxidant consisting of low molecular weight antioxidant (LMWA) and flavonoids. Unfortunately, the effect of LMWA on delaying aging and ameliorating DD remain inconsistent. On the other hand, numerous data indicate that flavonoids a botanical antioxidant was capable of improving oxidative stress and emerging as an alternative promising antioxidant (Sudhakaran et al., 2019). However, the effect of LMWA and flavonoids in combating oxidative stress remain unknown which one is better.

Oxidative stress is the imbalance between free radical and antioxidants status in cellular systems, by which the alteration and damaging cells are occur. Free radical is defined as any molecular species that contain an unpaired electron in atomic orbital result in unstable molecule and therefore react easily to other molecule (Lobo et al., 2010). The reaction between free radical and other molecule is called oxidation. Free radicals in low concentration have beneficial effect on cell to cell communication, but very harmful in high concentration. Whilst antioxidant is any substances when exist in low concentration is able to inhibit the oxidation of cellular molecule and prevent tissue damages. In the human body, various systems are capable of generating free radical ROS and RNS from numerous causes. Consequently, both ROS and RNS free radical continuously exposure to cell and tissues and may induce DNA fragmentation and cell death (Syslová et al., 2014; Widayati and Nasihun, 2018). For this reason antioxidant consumption is recommended particularly to people in whom free radical daily exposure can't be evaded.

Nowadays, many people have used LMWA as antioxidant to prevent oxidative stress and damaging cell, despite the result remain unclear. Some studies reported that administration of LMWA in whole organism suffering from oxidative damages no successful effect can be achieved (Etminan et al., 2005; Nasihun and Widayati, 2016). A meta-analysis on randomized control trial was reported by Etminan M, et al. displayed that treatment with various LWMA on cardiovascular disease and degenerative diseases showed no beneficial effect (Etminan et al., 2005). One possible explanation is ROS, RNS, and other free radical are short-lived molecule that able to react really fast with biological target to be found in its surroundings. Accordingly, to scavenge free radical molecule LMWA must be in uninterrupted high concentration at free radical production site, by which fight with free radical will be occur and biological target can be protected. Unfortunately, administration of high dose LMWA is not possible, considering overloading LMWA will induce pro oxidant forming, oxidative stress, and eventually cellular damages. It was supported by the study from Podmore ID, et al. demonstrated that high dose intake (500 mg/day) of ascorbic acid in healthy individual have been proven capable of increasing oxidative stress and DNA damage in lymphocyte cells marked by increasing in 8-oxoadenin (Podmore ID et al., 1998). Moreover, considering intracellular total antioxidant capacity is tightly regulated, hence treatment with high dose LMWA, despite capable of increasing TAC in plasma, nevertheless unable to alter TAC within cell (Berry and Kohen, 1999). As

have been proven by in vitro study was reported by Koren et al. suggested that treatment with LMWA on cell culture of HaCaT, Caco-2, PC3 and Hep3B unable to increase TAC (Koren et al., 2008). Another evidence also pointed out that treatment with LMWA consisting of alfa tocopherol, ascorbic acid, and Q10 in combination was failed to decrease concentration of 8-OHdG in smokers (Priemn et al., 1997). Last but not least, supplementation with high dose LMWA is potentially reduces beneficial concentration of ROS required for cellular communication optimally (Bouayed and Bohn, 2010). The result of these studies suggested that any supplementation of high dose LMWA is invariably followed by increasing in oxidative stress, cellular damage, and at least decrease in optimal cellular function. Refer to these data, the result of supplementation of high dose LMWA have no clearly beneficial effect on degenerative diseases and oxidative stress, thus flavonoids intake become an alternative to replace LMWA for ameliorating oxidative stress.

Flavonoids are hydroxyphenolic compound synthesized in photosynthesizing cells, accordingly abundant in fruits and vegetables (Huxley and Neil, 2003; Kumar and Pandey, 2013) Recently, flavonoids are very popular because of their potential health benefit particularly arising from antioxidant, anti inflammation, and immunomodulator activity. The antioxidant activity of flavonoids was mediated by functional hydroxyl groups that able to scavenge free radical and or chelating metal ion (Singh et al., 2013). Numerous evidences showed that flavonoids possess antioxidant activity characterized by the capability to scavenge free radical superoxide anion (O2-) and peroxynitrite anion (ONOO-), bring about increasing Nitric Oxide (NO) level that beneficial for vascular dilation (Chen WS et al., 2010). Another study was reported by Huxley et al also demonstrated that flavonoids has been proven capable of inhibiting xanthine oxidase activity, hence inhibit superoxide anions production in eukaryotic cells (Mahmoud et al., 2019). Another study was conducted on diabetic rats reported by Punithavathi VR, et al. also indicated that flavonoids was able to improve antioxidant enzymes activity including superoxide dismutase, catalase, and glutathione peroxidase (Punithavathi et al., 2008). A meta-analysis of prospective cohort studies was reported by Huxley et al. indicated that high intake of fruits and vegetables containing flavonoids associated with reducing risk factor of coronary heart disease mortality in population (Huxley and Neil, 2003). Based on these data conclusion can be drawn tentatively that high intake of dietary flavonoids is better than LMWA, however long term clinical study is needed.

REFERENCES

Berry, E., Kohen, R., 1999. Is the biological antioxidant system integrated and regulated? Med. Hypotheses 53, 397–401.

Bouayed, J., Bohn, T., 2010. Exogenous antioxidants — Double-edged swords in cellular redox state Health beneficial effects at physiologic doses versus deleterious effects at high doses. Oxid. Med. Cell. Longev. 3, 228–237. https://doi.org/10.4161/oxim.3.4.12858

Chen WS, Lee YJ, Yu YC, Hsaio CH, Yen JH, Yu SH, Tsai YJ, Chiu SJ, 2010. Enhancement of p53-mutant human colorectal cancer cells radiosensitivity by flavonoid fisetin. Int. J. Radiat. Oncol. Biol. Phys. 77, 1527–1535. https://doi.org/10.1016/j.ijrobp.2010.02.043

Etminan, M., Gill, S.S., Samii, A., 2005. Intake of vitamin E , vitamin C, and carotenoids and the risk of Parkinson's disease: a meta-analysis. Lancet Neurol 4, 362–5.

Harman, D., 1981. The aging process. Proc. Natl. Acad. Sci. U. S. A. 78, 7124–8. https://doi.org/10.1073/pnas.78.11.7124

Huxley, R., Neil, H., 2003. The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies. Eur. J. Clin. Nutr. 57, 904–908. https://doi.org/10.1038/sj.ejcn.1601624

Koren, E., Zverev, I., Ginsburg, I., Kohen, R., 2008. Supplementation with antioxidants fails to increase the total antioxidant capacity of several cell lines in culture. Biomed. Pharmacother. 62, 179–88. https://doi.org/10.1016/j.biopha.2007.12.012

Kumar, S., Pandey, A.K., 2013. Chemistry and Biological Activities of Flavonoids: An Overview. Sci. J. 2013.

Lamichhane, A., Chaudhary, V., Nk, S., Singh, M., Pandey, R., Sk, A., 2013. Low Molecular Weight Antioxidants (lmwa) and their Orchestration. Nepal J. Med. Sci. 2, 171–80.

Lobo, V., Patil, A., Phatak, A., Chandra, N., 2010. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn. Rev. 4, 118–126. https://doi.org/10.4103/0973-7847.70902

Mahmoud, A.M., Bautista, R.J.H., Sandhu, M.A., Hussein, O.E., 2019. Review Article Beneficial Effects of Citrus Flavonoids on

Cardiovascular and Metabolic Health. Oxid. Med. Cell. Longev. 2019, 1–19. https://doi.org/10.1155/2019/5484138

Nasihun, T., Widayati, E., 2016. Administration of Purwoceng (Pimpinella alpins Molk) improves oxidative stress following UVC irradiation in Spargue-Dawley male rats. J. Nat. Remedies 16, 82–91. https://doi.org/10.18311/jnr/2016/7684

Podmore ID, Griffiths HR, Herbert KE, Mistry N, Mistry P, Lunec J, 1998. Vitamin C exhibits pro-oxidant properties. Nature 392, 559. https://doi.org/10.1038/33308

Priemn, H., Loft, S., Nyyssonen, K., Salonen, J.T., Potilsen, H.E., 1997. No effect of supplementation with vitamin E , ascorbic acid , or coenzyme Qi 0 on oxidative DNA damage estimated by. Am J Clin Nutr. 65, 503–7.

Punithavathi, V.R., Anuthama, R., Prince, P.S.M., 2008. Combined treatment with naringin and vitamin C ameliorates streptozotocin-induced diabetes in male Wistar rats. J. Appl. Toxicol. 28, 806–813. https://doi.org/10.1002/jat

Singh, A.R., Bajaj, V.K., Shekhawat, P.S., Singh, K., 2013. Screening Of Potential Male Contraceptive Drugs From Natural Resources: An Overview Int. J. Pharm. Sci. Res. 4, 1654–1668.

Sudhakaran, M., Sardesai, S., Dose, A.I., 2019. Flavonoids: New Frontier for Immuno-Regulation and Breast Cancer Control. Antioxidants 8, 103. https://doi.org/10.3390/antiox8040103

Syslová, K., Böhmová, A., Mikoška, M., Kuzma, M., Pelclová, D., I, P.K., 2014. Multimarker Screening of Oxidative Stress in Aging. Oxid. Med. Cell. Longev. 2014, 1–14. https://doi.org/10.1155/2014/562860

Widayati, E., Nasihun, T., 2018. Treatment of Pimpinella Alpina Molk Improve Oxidative stress and Inhibit Liver Cellular Apoptosis in Rats Following UVB Irradiation: Is there Any Correlation? Bangladesh J. Med. Sci. 17, 18–128.