

Mini Review

Considering antioxidant supplements as a means to prevent diseases

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Oxidative stress has been implicated in Alzheimer's and many other diseases and more recently, it has been linked to various COVID-19-related symptoms. Many diseases do not develop immediately as a result of the accumulated causes or injury, but rather, as a result of prolonged exposure to elevated oxidative stress, which disrupts the body's natural homeostatic functions.

Elevated oxidative stress causes lipids, proteins, and sugars in the body to oxidise, genetic damage, mitochondrial dysfunction, and poor antioxidant defense. As well, oxidative stress induces inflammation by elevating active inflammatory factors. It is widely believed that when this vicious cycle is prolonged, it promotes disease conditions, therefore, breaking this cycle of oxidative stress is paramount for preventing the onset of disease.

Multiple research projects have been targeting single antioxidants such as vitamin C and vitamin E, due to their antioxidant properties that can mitigate oxidative stress. However, these efforts have not yielded much results so far. In contrast to single antioxidants, supplements containing a well-balanced combination of several antioxidants may be more effective for addressing the myriad of symptoms associated with established diseases and more current concerns such as Alzheimer's and COVID-19 infection.

This review discusses oxidative stress and its relationship to Alzheimer's and COVID-19 infection. In addition, we propose the use of Twendee X, a super antioxidant complex, which aids in preventing cognitive decline in Alzheimer's patients and assists in preventing and treating COVID-19 infection and its related symptoms. Pub Med (<https://pubmed.ncbi.nlm.nih.gov>) was employed as bibliographic research.

Oxidative stress and Alzheimer's disease

High oxidative stress is a state that occurs when the reactive oxygen species (ROS) being produced in the body exceed the supply of antioxidants available in the body to counteract them.

More Information

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ROS are the primary cause of oxidative stress and are mainly produced as bi-products of mitochondrial energy production, and when leukocyte aggregation and phagocytosis activate the immune system in response to viruses and bacteria that invade the body.

ROS are also generated in the body due to stimuli from the natural environment, such as air pollution, ultraviolet radiation, ageing, and lifestyle factors such as smoking, alcohol consumption, and diet. Once generated, ROS triggers inflammation that damages genes, proteins, lipids, enzymes, and cells and also increases inflammatory factors. In particular, mitochondria and leukocytes, which are the sites of adenosine triphosphate (ATP) production, are also sites of active oxygen production, hence these immune cells are particularly affected. When these immune cells are exposed to high levels of chronic oxidative stress, it results in reduced ATP production and compromised immune function.

The nervous system is vulnerable to oxidative stress due to its high levels of polyunsaturated fatty acids and iron, as well as its heavy reliance on oxygen. Experiments that examined the brains of Alzheimer's patients postmortem, have reported oxidative damage to lipids and proteins, reduced ATP production, and neuronal depletion. Furthermore, researchers



have also associated mild cognitive impairment with increased oxidative damage prior to the onset of dementia symptoms [1,2].

Oxidative stress and COVID-19 infection

In other research, COVID-19 infection triggered an increase in oxidative stress in the body; this oxidative stress was implicated in exacerbated and persistent cytokine storms and impaired coagulation [3]. Even after the virus is reduced to undetectable levels, the persistence of high oxidative stress in recovered patients can develop into other conditions such as COVID sequelae. It has also been reported that the lipid nanoparticles (LNPs), which are the protective agent in the mRNA-based COVID-19 vaccine, have strong inflammatory properties, which may be responsible for the adverse reactions people experience soon after being vaccinated [4]. The examples of Alzheimer's and COVID-19 demonstrate that oxidative stress and inflammation are closely intertwined and can be implicated in various diseases.

Twendee X super antioxidant complex

Twendee X (henceforth referred to as TwX) is a patented supplement containing a proprietary blend of eight varieties of antioxidants: vitamin C, glutamine, cysteine, coenzyme Q10, fumaric acid, succinic acid, niacin and vitamin B2 [5,6]. Strong antioxidant effects of TwX on different human tissues were already confirmed and may have prevention and therapeutic effects on various diseases. Similar to regular pharmacological medicines, TwX has passed all safety tests namely: chromosomal aberration, toxicity, and mutation tests.

To assess even more of TwX's antioxidant potential, we measured the reduction of ROS induced by hydrogen peroxide, an oxidising agent, in the cells and mitochondria of HepG2 cells. Hydrogen peroxide increases both intracellular and intramitochondrial ROS by more than 60%, however treating the cells with 60 µg/ml of TwX reduced the aforementioned ROS to 45% and 63%, in cells and the mitochondria respectively. In addition, we observed that superoxide dismutase (SOD), which acts as an antioxidant, also increased by 60% in cells and 147% in the mitochondria. These results strongly suggest that TwX not only suppresses oxidative stress but concurrently protects the mitochondria from oxidative stress as well.

Effects of TwX on Alzheimer's disease

The effects of the antioxidant TwX on Alzheimer's disease are being tested in both animal experiments and clinical trials.

In an Alzheimer's model mouse (APP23 mice), treatment with TwX (20 mg/kg/day) for 7.5 months reduced not only phospho-tau (AT8) immunoreactivity, but also the expression of oxidative stress markers [7]. It should be noted that TwX has also been shown to reduce tumor necrosis factor- α (TNF- α) and inflammation markers in mice with cerebral infarction [8].

In 2019, a prospective, randomized, double-blind, placebo-controlled intervention clinical trial was conducted with mild cognitive impairment (MCI), the pre-stage of dementia. Two assessment methods, the MMSE and Hasegawa dementia score, showed that TwX made a significant difference in significantly improving MCI [9]. Considering that the experiment used the most stringent of all clinical trials, it is fair to say that these results demonstrate that TwX can effectively reduce the risk of dementia.

Effectiveness of TwX on COVID-19

The effectiveness of TwX against COVID-19 has been investigated in a web-based survey of actual patients with COVID-19 sequelae and COVID-19 vaccine adverse reactions.

More than 100 patients suffering from multiple symptoms of COVID-19 infection sequelae and COVID-19 vaccine sequelae each took TwX for one month, and a comparative analysis was conducted of patients' symptoms before and after taking the supplement. Sequelae symptoms were similar in both groups with the main symptoms being: fatigue, breathlessness, chest pain, abnormal taste and smell, headache, brain fog, joint pain, and dizziness. Patients reported a significant improvement in all symptoms after one month of taking TwX [10,11].

Conclusion

Alzheimer's and COVID-19 infection-related conditions are just two of more than 120 oxidative stress-related diseases. As the body has numerous functions that rely on antioxidants, it is believed that antioxidant supplements may help normalize the body's natural homeostasis when multiple antioxidants are taken in the required dose. There are many antioxidant supplements worldwide that claim to offer therapeutic benefits, however, so far, very few have shown efficacy against oxidative stress-related diseases. Two possible explanations for this are that most of these supplements contain a single antioxidant, and/or are formulated in concentrations that are inadequate to have a positive effect. In contrast to these supplements, TwX contains adequate amounts of all the main antioxidants the body needs.

Many of the symptoms associated with COVID-19 infection directly affect patients' daily lives and there are no effective treatments. Therefore, the fact that COVID patients were aware of their improvement is considered a very significant endorsement of the efficacy of TwX as a supplement. It is also important that supplements are guaranteed to be not only safe in general but also safe for long-term consumption, as is required in the case of Alzheimer's patients. TwX has met all these safety standards, and this, in addition to its high concentration of multiple antioxidants, strongly suggests that TwX is worth considering as a therapeutic option for preventing and treating oxidative stress-related diseases including Alzheimer's and COVID.



References

1. Tadokoro K, Ohta Y, Inufusa H, Loon AFN, Abe K. Prevention of Cognitive Decline in Alzheimer's Disease by Novel Antioxidative Supplements. *Int J Mol Sci*. 2020 Mar 13;21(6):1974. doi: 10.3390/ijms21061974. PMID: 32183152; PMCID: PMC7139972.
2. Praticò D, Clark CM, Liun F, Rokach J, Lee VY, Trojanowski JQ. Increase of brain oxidative stress in mild cognitive impairment: a possible predictor of Alzheimer disease. *Arch Neurol*. 2002 Jun;59(6):972-6. doi: 10.1001/archneur.59.6.972. Erratum in: *Arch Neurol* 2002 Sep;59(9):1475. PMID: 12056933.
3. Cecchini R, Cecchini AL. SARS-CoV-2 infection pathogenesis is related to oxidative stress as a response to aggression. *Med Hypotheses*. 2020 Oct;143:110102. doi: 10.1016/j.mehy.2020.110102. Epub 2020 Jul 13. PMID: 32721799; PMCID: PMC7357498.
4. Ndeupen S, Qin Z, Jacobsen S, Bouteau A, Estambouli H, Igyártó BZ. The mRNA-LNP platform's lipid nanoparticle component used in preclinical vaccine studies is highly inflammatory. *iScience*. 2021 Dec 17;24(12):103479. doi: 10.1016/j.isci.2021.103479. Epub 2021 Nov 20. PMID: 34841223; PMCID: PMC8604799.
5. Haruhiko I. Composition for protection against cytotoxic effects. Tima Foundation. Patent No. 5777821. 2015-9-9.
6. Inufusa H. Characterization of cell protection effects of Twendee X by oxidative stress. *J World Mitochondria Soc*. 2016; 2: 42.
7. Liu X, Yamashita T, Shang J, Shi X, Morihara R, Huang Y, Sato K, Takemoto M, Hishikawa N, Ohta Y, Abe K. Clinical and Pathological Benefit of Twendee X in Alzheimer's Disease Transgenic Mice with Chronic Cerebral Hypoperfusion. *J Stroke Cerebrovasc Dis*. 2019 Jul;28(7):1993-2002. doi: 10.1016/j.jstrokecerebrovasdis.2019.03.029. Epub 2019 Apr 24. PMID: 31029568.
8. Kusaki M, Ohta Y, Inufusa H, Yamashita T, Morihara R, Nakano Y, Liu X, Shang J, Tian F, Fukui Y, Sato K, Takemoto M, Hishikawa N, Abe K. Neuroprotective Effects of a Novel Antioxidant Mixture Twendee X in Mouse Stroke Model. *J Stroke Cerebrovasc Dis*. 2017 Jun;26(6):1191-1196. doi: 10.1016/j.jstrokecerebrovasdis.2017.01.003. Epub 2017 Feb 9. PMID: 28190603.
9. Tadokoro K, Morihara R, Ohta Y, Hishikawa N, Kawano S, Sasaki R, Matsumoto N, Nomura E, Nakano Y, Takahashi Y, Takemoto M, Yamashita T, Ueno S, Wakutani Y, Takao Y, Morimoto N, Kutoku Y, Sunada Y, Taomoto K, Manabe Y, Deguchi K, Higashi Y, Inufusa H, You F, Yoshikawa T, von Greiffenclau MM, Abe K. Clinical Benefits of Antioxidative Supplement Twendee X for Mild Cognitive Impairment: A Multicenter, Randomized, Double-Blind, and Placebo-Controlled Prospective Interventional Study. *J Alzheimers Dis*. 2019;71(3):1063-1069. doi: 10.3233/JAD-190644. PMID: 31476161.
10. You F, Tanaka S, Inufusa H. Effects of Antioxidant composition Twendee X on side effects of SARS-CoV-2 mRNA vaccine. *Brain Supplement*. 2022; 4: 1-6.
11. You F, Tanaka S, Inufusa H. Antioxidant composition Twendee X may improve long COVID symptoms. *Brain Supplement*. 2022; 4: 7-12.