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REVIEW ARTICLE

Vitamin C is not just an antioxidant

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Introduction

Vitamin C is engaged with the support of body capacities. Nonetheless, many concentrates show conflicting outcomes about its belongings. From the time it was first detached in 1928, various investigations have been done on its biochemical and pharmacokinetic properties, its capacities and even the job of this molecule in neurophysiology. It is critical to distinguish the job vitamin C has in the upkeep of oxide/decrease (redox) balance; just as the conceivable impact, it might have on the treatment of constant degenerative maladies, immune system illnesses and malignancy [9]. Vitamin C is considered as one of the best examples of antioxidants that play role in maintaining the body from free radicals. Therefore, this paper explains the reality of vitamin C as an antioxidant and its role and mechanism specifically in the brain.

Vitamin C and its forms

Ascorbic acid is an impartially charged particle, which can be protonated and moved toward becoming ascorbate. Contingent upon the pH of the medium in which it is found, ascorbic acid may lose the hydrogen particles joined to one of its two ionizable groups situated at carbons 2′ and 3′, creating ascorbate mono anion or di anions (figure 1) [1]. Ascorbic acid is a white crystalline strong solvent in water; one of its essential jobs lies in its biochemical capacity in redox forms. When we discuss vitamin C, we allude to the groups of ascorbic acid analogs that can be both systemic and natural molecules [2].

Mechanism of absorption

Ascorbate is the fundamental type of vitamin C in the human body [3]. This particle goes about as a co-substrate for a few catalysts that are vital for the working of organisms. Its action as an antioxidant incorporates the capacity to be reversibly oxidized to ascorbyl radical and after that to dehydroascorbate [4]. The two structures are ingested in the eating routine, since ascorbate can be oxidized in the gastrointestinal tract (GIT) by the nearness of different substances that go about as oxidizing agents such as Iron (F3+) and some flavonoids. Ascorbate may likewise be oxidized because of sustenance handling, either by cooking methods or lack of awareness of storage techniques while packaging products [5].

The organs with the most elevated convergence of ascorbate are the adrenal organs (550mg/kg), the brain (140mg/kg), the liver (125mg/kg), and as far as size, the skeletal muscle with a centralization of 35mg/kg [6]. The capacity

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performed by ascorbate in every cell of these organs will decide the kind of transporter that is most appropriate for their nearby prerequisites. With respect to central nervous system (CNS), the ascorbate situated in the cerebrospinal fluid diffuses unreservedly into the extracellular space of neurons and glia, where it is caught by both cell types by means of SVCT2 (aside from astrocytes) [7].

SVCT2 is the principle transporter in the adrenal organs; it keeps up high concentration of ascorbate in the chromaffin cells of the adrenal medulla, which are fundamental for the blend of catecholamines [8].

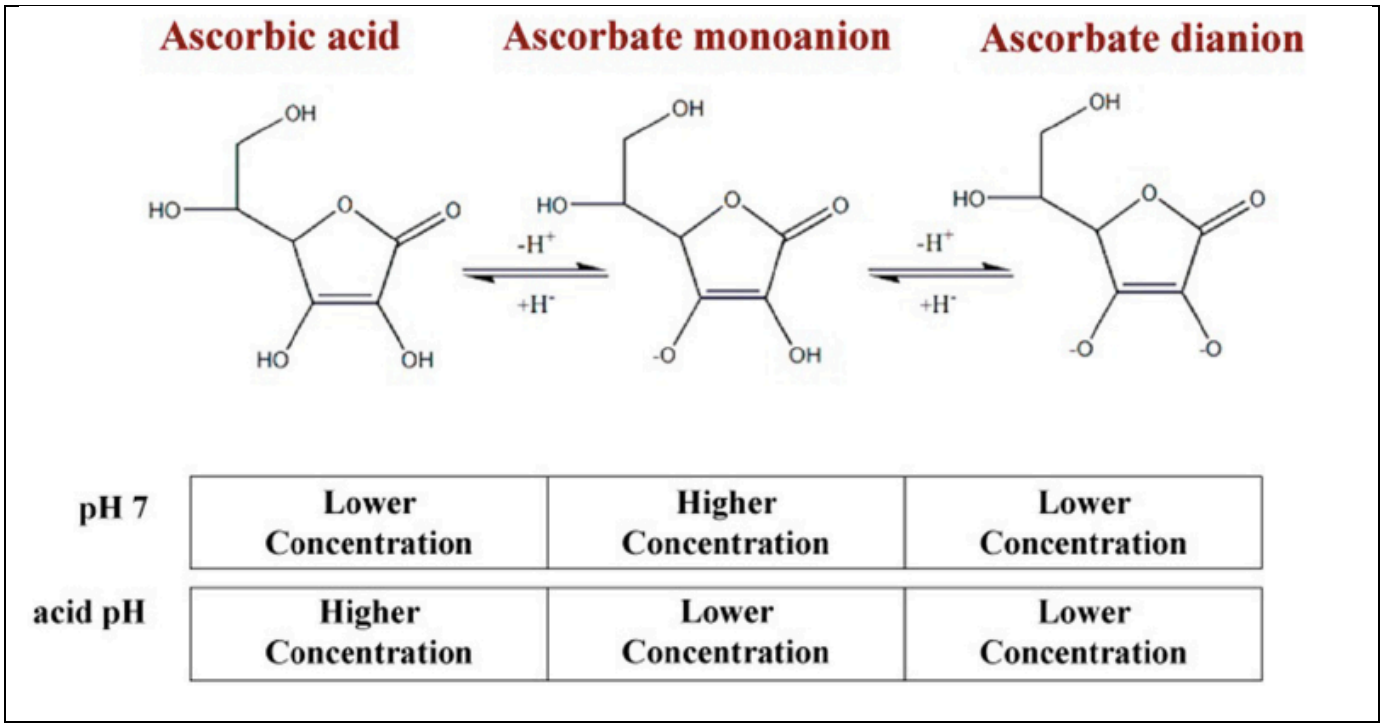

Figure 1. Forms of Vitamin C according to pH.

Its role in CNS

There are different functions of ascorbate in nervous system such as the association of ascorbate with the blood- brain barrier just as its therapeutic purposes; besides, its consequences for the procedure of neuronal differentiation, development and survival; thirdly, its impact on modulating neuro transmission and its cooperation in catecholamine production. Finally, it has a cell antioxidant impact and it additionally assumes a role in the learning and memory process just as in the structure and backing of the sensory system [9].

Its role in memory and learning

Parle and Dhingra infused portions of 60 and 120mg/kg of ascorbic acid intraperitoneally to mice with medication-instigated amnesia through "administration of diazepam and scopolamine and to mice that acquired amnesia naturally with age [10]. Utilizing “the elevated plus maze and the

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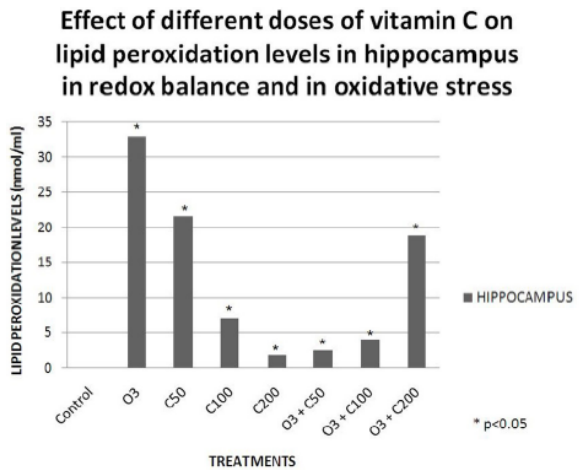
passive avoidance test" [10]. The authors inferred that ascorbic acid improved learning and memory in old mice and saved the mice in the group that got the medications [10]. Likewise, different examinations have demonstrated that the mix of vitamin C and vitamin E can have valuable impacts counteracting memory modifications [11].

n any case, it has not been conceivable to show the reproducibility of these outcomes nor their viability in human investigations concentrated on the anticipation and treatment of dementia and Alzheimer's disease [12]. Some Studies have exhibited that vitamin C impacts on learning and memory are subject to the redox balance state. When a low portion of vitamin C (50mg/kg) was given to healthy rats, the retention latency decreased in the passive avoidance test. At that point, a group of rats were given a portion of ozone (0.7 ppm) without Vitamin C, the retention latency decreased too. The study also practically stated that "when we gave the same dose of vitamin C to rats exposed to ozone, the retention latency was similar to that of the control, demonstrating a protective effect of the vitamin" [12]. Along these lines, it could be contrasted these outcomes and the lipid peroxidation levels in the hippocampus and it is been observed the relation between the oxidative damage and the decline in the passive avoidance test. This demonstrated a pro-oxidant impact of low portion vitamin C in a redox equilibrium and an antioxidant agent impact at any oxidative stress state [12]. The below figures (Figure 2 & Figure 3) show the effect of vitamin C on memory as well as on lipid peroxidation.

Its antioxidant's role in CNS

Two amazing facts of the brain that make it a readily oxidizable tissue are the 20% consumption of the total body oxygen by the brain as well as it is composed of a high metabolic rate [13].

These conditions legitimize the significance of antioxidants agents in the brain, which are expected to keep up the redox



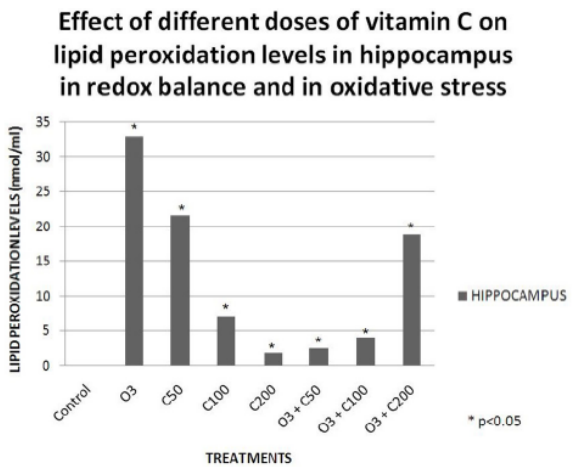


Figure 2. Effects of different doses of vitamin C on memory in redox balance and in oxidative stress. **Figure 3.** Effects of different doses of vitamin C on lipid peroxidation levels in hippocampus in redox balance and in oxidative stress.

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balance. The dispersion of these antioxidants is not uniform since neurons can achieve intracellular ascorbate concentration of 10mM and glutathione of 2.5 Mm as restricted to what occurs in glia where the concentration of ascorbate is 2.5 mM and the one of glutathione is 3.8 mM [14].The unbalanced dispersion of ascorbate is because of the way that SVCT2 is specially expressed in neurons; while in astrocytes ascorbate focuses through the intracellular decrease of DHA, which enters the cell by means of GLUT1. The physiological note worthiness of this unequal appropriation is the supply of ascorbate to the neuron. An expansion in the expression of mRNA identified with the translation of SVCT2 in the two neurons and astrocytes has been demonstrated in rats with prompted cerebral ischemia, likely as a cell defensive component against oxidative stress actuated by ischemia [15].

Some scientists have contemplated the cooperation of ascorbate with different antioxidants, for example, a-tocopherol [16] and glutathione [17] just as the possible therapeuticapplications of this interaction, e.g., in the anticipation of Alzheimer's disease [18].

Its role in redox balance

The body always maintains a balanced hemostasis oxidants and antioxidants and that is simply means, if there is a slight increase in the production of Reactive Oxygen Species (ROS), the immediate response of the body by increasing the activity of endogenous antioxidant system through redox signaling mechanism [19]. Along with endogenous antioxidants, there are exogenous antioxidants that are obtained by the diet and they play a very good role in maintaining the redox balance. As a result, vitamin C can also be obtained from diet to comprise antioxidant enzymes (e.g., catalase, superoxide dismutase, and glutathione peroxidase) and antioxidant molecules (e.g., glutathione and thioredoxin) [20]. Sometimes the body gets attacked by oxidative stress when there is unbalanced between the release of free radicals and activity of antioxidants. As other antioxidants, ascorbate has an effect against oxidative stress due to its power of donating electrons from both the second and third carbon [21].

Studies have shown the effectiveness of ascorbate is more than thiols, a-tocopherol, and urate to inhibit lipid peroxidation in plasma. Equally, when there is a high concentration of ascorbate in blood, it will have a longer time to enhance lipid peroxidation with no-pro-oxidant effects and “even in ascorbate serum concentrations of 5mM achievable only parenterally” [22].

Vitamin C and Alzheimer’s disease

It is expected naturally that the levels of ascorbic acid decline as people age , however many data have shown that ascorbic acid plays a big role in the health of neurons while it is been observed naturally that Alzheimer’s population’s ascorbic acid level in the blood is lower than other older population [23], [24], [25]. When oxidative stress occurs in patients with Alzheimer’s disease, the best first live of defiance is a conjunction of ascorbic acid with glutathione. Consequently, it has been approved that this conjunction of two molecules can be the driving force behind the inhibition of pathological factors associated with AD [26]. As soon as these factors appear, they play a contribution role in oxidative environment, as well as declining antioxidant reserves [27].

A recent research was done in animal models in which it showed that ascorbic acid can play a role in reducing the progression of disease out of its general antioxidant capacity, thus includes mitochondrial function, enzymatic co-factor and DNA methylation[28], [29]. At the same time, deficiency of ascorbic acid should be avoided in the early stages of disease pathology because it might help in increasing the protection of neuronal health as well as protecting against

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accelerating of oxidative damage. As it has been mentioned previously that AD patient tend to have lower ascorbic acid which that would affect them in reducing the progression of the disease if early detections were not proposed, therefore, in this case many clinical studies have suggested that supplementation of ascorbic acid along with non-enzymatic antioxidants for patients with AD [30], [31]

CONCLUSION

Vitamin C is considered as one of the important antioxidants in the body and that is either found in the body or acquired from the diet. It has different role as an antioxidant in body and more specifically in the brain. It plays very good roles during redox reactions that occur within the brain and it has been mentioned above as well as the neuron developmental. Along with that, studies have shown that vitamin C can be of the best solution for reducing the progression of neurodegenerative diseases such as Alzheimer's disease. Therefore, it can be concluded that vitamin C with its other forms are essential antioxidants for the brain.

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