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Mini Review

A Note on the Importance of Phytonutrients in Rehabilitation of Cancer Survivors with Cognitive Impairment

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Abstract

Toxicological studies have revealed that certain chemical pesticides and chlorine could cause abnormal changes in the CNS of animal models. These chemicals being the uncouplers of oxidative phosphorylation may destabilize the mitochondrial functions. In recent years the cancer survivors were reported to exhibit cognitive impairment and dementia. Phytochemical compounds have been documented to reinstate athe brain functions to normalcy, in animal models. Hence phytochemicals may be of use in reinstating the brain functions in cancer survivors suffering dementia/cognitive memory loss.

Keywords: Toxicology; Chlorine; Phytochemical; Brain; Mitochondrial; Cognitive Impairment

Introduction

Among all cancer treatment type's chemotherapy represents the most successful mode of therapy, since it has improved the survival period of the patient for a long term. Survival in cancer patients was found to be higher i.e. 23% in women with breast cancer followed 19% prostate cancer individuals and 10% of the survival in individuals with colorectal cancers. However the above prolonged survival period is determined by several factors besides the detection of cancer stage I and II levels. Viz.,

- Immune tolerance of the individual
- The impact of diets and supplement in the post-treatment period.
- Regular exercise with sun exposures to derive D_3 vitamin.
- Stress free psycho somatic conditions.
- Sleep behavior of the patient.
- Pollution free environment
- Self hygiene of the patient etc.

Chemotherapy induced peripheral neuropathy(CIPN) is an important side effect due to various drugs such as taxanes, platinum agents, epothilones and vinca alkaloids etc. and their cumulative toxicity. The severity of CIPN has been attributed to single drugs used for long times, multiple drugs and their combined toxicity dosage between successive dosage regimens etc. Although the treatment to these individuals with drugs has been conducted, there are no reports of established cure for the CIPN.

A larger percentage of cancer survivors reported memory loss and concentration deficiency. 20 to 30 percent of breast cancer and colorectal cancer survivors showed cognitive impairment. The various domains in cognitive impairment include failure in working memory, deficits in executive function, information

processing speed, and memory retrieval etc., Vardy., *et al*. [1]. In cancer survivors unlike the cortical deficits characteristics of age related Alzheimer's dementia, the CIPN, related dementia involves sub cortical regions and their impairment which are reversible and treatable. Thus cognitive retrieval is a very important aspect for the survivors from cancer and is one of the strategies in rehabilitation programmes. Our studies and observation of toxicity stress on animal models have elucidated the effects of chemical micro contaminants like pesticides, chlorines on the physiological functioning of the central nervous system.

Though chlorine represents an important element of public health importance by its disinfecting property, in the *in vivo* and dichloromines which converted into chlorinated compounds and chlorine complexed compounds like monochloramines environment it is powerful mutagenic and carcinogenic compounds that affect the brain histology and CNS function. Moreover these free and combined chlorine can act as potent oxidizing agents. Chlorine toxicity in fishes caused the following changes Viz., sparse disposition of neuronal cells with increase in the inter cellular spaces in the F.B region, clustering of more glial cells in the mid brain and hind brain region (glyosis), scar formations, loss of neural cells in F.B region than M.B and H.B regions etc. Ramalingam [2]. Harvey., *et al*. [3] brave also reported the selective neuro toxic action of P-chloro-amphetamine in the brain of rats with changes like neural cells shrinkage, perineuronal space, and cellular debris etc. Toth., *et al*. [4] have reported reduction of forebrain weight with no gross lesions by chlorine dioxide in developing rat brain. These studies have opined that the changes in brain are likely events to happen since blood brain barrier regions, and some zones in situ may allow the free passage of toxicants and/or biocides like chlorine compounds and pesticides. Balasundaram., *et al*. [5] in their study on phosalone poisoning on the cation linked ATPases of CNS of *Rana tigrina* revealed failure of neuronal activity by the LD_{50} concentration (3.953 g/Kg body weight) of the organo phosphate pesticide, phosalone, They have revealed the inhibitory action of phosalone on the Na^+ K^+ - ATPase; mg^{2+} ATPase and Ca^{2+} ATPase; invariably in all the sixregions of CNS Viz Rhombancephalon, Lumbar spinal cord, cervical spinal cord, thoracic spinal cord, midbrain and Telencephalon.

Effect of uncouplers on brain

It is known that uncouplers are compounds which can inhibit phosphorylation in cellular mitochondria but stimulate respiration and ATP hydrolysis. Uncouplers in appropriate concentrations can prevent the phosphorylation of ATP without interfering the electron transport. Pesticide like Dinitro phenol derivatives, penta-chlorophenol and hexachlorophene and organophosphates can act as uncoupling agents interfering oxidative phosphorylation but enhancing the O_2 uptake in cells Corbett [6].

Michaelis ML., *et al*. [7] have also envisaged that inhibition of Ca^{2+} ATPase cause accumulation and enhancement of intracellular calcium due to efflux of Ca^{2+} from mitochondria as well as influx of Ca^{2+} from the external environment of the neural cells and may cause continuous release of neurotransmitter molecules and subsequent convulsions. Balasundaram and selvarajan [8] have reported inhibition of Acetyl cholinesterase/enzyme and attributed disturbance in adrenergic and cholinergic functionalities leading to fatigue and morbidity in frogs.

The above information's of toxicological studies and stress biology provide us more insights regarding cognitive impairment in cancer survivors. That is, a plethora cellular/neural mechanism may operate to disturb the functionalities of the different brain regions in cancer survivors, to bring homeostatic disturbances, in order to manifest their cognitive abnormalities.

Recent studies on the actions of phytonutrients molecules or phytochemicals revealed their ameliorative properties in the neuronal tissues (antineuopathic). Towards this line the phytoremedial properties of the antioxidant compounds on neural functions are paramount to elucidate their potential in cognitive rehabilitation in cancer survivors.

Several phytochemical compounds exhibit neuroprotective effects. Quercetin: (Qc): is a polyphenolic compound found in vegetables, fruits, seeds etc. In-situ model studies have revealed that quercetin can pass through the blood brain barrier. Marcus., *et al*. [9] studies have also revealed that quercetin significantly protected the neuronal cells from the oxidative stress induced neurodegeneration in Alzheimer's disease, and decreased lipid peroxidation by the improved activity of catalase and superoxide dismutase, and glutathione depletion.

The herbal medicine Ginkgo biloba containing the Querectin in high amount exhibit neuro- protective effect against the oxidative damage inflicted by 6-OHDA. It also attenuated the neuronal death

in the hippocampus and improved the learning and memory in rats. Napatr Sriraksa., *et al*. [10] in their study on rat model with Quercetin suggest the use of Quercetin as an adjuvant therapeutic agent for the treatment of cognitive impairment.

Conclusion

Quercetin belongs to flavonoid group of phytochemicals which is ubiquitously found in such fruits as citrus, apple, berries and in onions, parsly green tea and red wine. It's highly anti-inflammatory and antioxidant functions are attributed for the restoration of brain health and better cognitive output and restitution of memory Elumalai and Lakshmi [11]. In the light of these reports it may be concluded that phytochemical adjuvants may be the best choice for treatment of cognitive impairment of cancer patients who survived the chemotherapy.

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