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## Possible protective strategies of “queen of tropical fruits”: *Garcinia mangostana* in age related neurodegenerative disorder like Huntington’s disease

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Huntington’s disease (HD) is an autosomal dominantly inherited progressive neurodegenerative disorder, characterized by progressively worsening chorea, psychiatric disturbances, cognitive impairment and weight loss. The degenerative process primarily involves medium spiny striatal neurons (MSN) and to a lesser extent cortical neurons. Importantly,  $\gamma$ -amino butyric acid (GABA)ergic projection neurons of the striatum, which make up roughly 90% of the striatal neurons are the most vulnerable in HD and their early dysfunction is responsible for the development of chorea. Fruits of *G. mangostana* are the most treasured part of this plant and are famous for the remarkably pleasant flavour. Over the past decades, it is shown that mangosteen contains high amounts of xanthenes, a class of polyphenolic compounds which are shown to have significant biological activities in in-vitro systems. Dried and powdered fruit hull is used as antimicrobial agents and for the anti-parasitic treatments in dysentery as well as externally for healing wounds, suppurations and chronic ulcers. 1,2-Dihydro-1,8,10-trihydroxy-2-(2-hydroxypropan-2-yl)-9-(3-methylbut-2-enyl)furo[3,2-a] xanthen-11-one, 6-deoxy-7-demethylmangostanin, 1,3,7-trihydroxy-2,8-di-(3-methylbut-2-enyl)-xanthone and mangostanin induced quinone reductase in the Hepa 1c1c7 cell line in an in vitro screening assay (IC<sub>50</sub>, 0.68-2.2  $\mu$ g/mL) whereas  $\gamma$ -mangostin exhibited hydroxyl radical-scavenging activity (IC<sub>50</sub>, 0.20  $\mu$ g/mL). Antioxidant activities are also shown for 8-hydroxycudraxanthone, gartanin,  $\alpha$ -mangostin,  $\gamma$ -mangostin and smeachxanthone A using authentic and morpholinosydnonimine-derived peroxyxynitrite methods. An extract of *G. mangostana* is reported to have very good antioxidant action in the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) assay. The extract inhibited 50% of free radicals at a concentration of 6.13  $\mu$ g/mL. In addition, this extract showed high inhibition on TNF- $\alpha$  production generated from peripheral blood mononuclear cells (PBMC) stimulated with *Propionibacterium acnes*. Therefore this plant is claimed to have a remarkable antiinflammatory effect and to reduce cell damage. A vast number of studies have demonstrated the anti-inflammatory properties of mangosteen. In a clinical study, mangosteen juice exhibited potential anti-inflammatory potential. Primary human adipocytes treated with xanthenes, the major bioactive compounds found in mangosteen, demonstrated reduced LPS-induced expression of pro-inflammatory genes (i.e. TNF- $\alpha$ , IL-6, IFN- $\gamma$  and IL-10) In RAW264.7 macrophage cells, mangosteen extract,  $\alpha$ -mangostin and  $\gamma$ -mangostin demonstrated a clear ability to inhibit NO and PGE<sub>2</sub> release, along with the gene encoding iNOS and COX-2. Anti-inflammatory mechanism of  $\gamma$ -Mangostin via inhibition of spontaneously PGE<sub>2</sub> release in a concentration-dependent manner as well as inhibit of lipopolysaccharide (LPS)-induced expression of COX-2 protein and its mRNA.  $\gamma$ -Mangostin also inhibits cyclooxygenase and prostaglandin E<sub>2</sub> synthesis. Where, both  $\alpha$ -Mangostin &  $\gamma$ -Mangostin showed anti-inflammatory activity by inhibition of inducible NO synthase. Currently available drugs provide symptomatic relief but do not stop progression of disease. Thus, the development of new therapeutic strategies remains an unmet medical need. Failure of current drug therapy may be due to their action at only one of many neurotransmitters involved or their inability to upregulate signaling messengers reported to have important role in neuronal functioning, neurotransmitter biosynthesis and release neuronal growth and differentiation, synaptic plasticity and cognitive functioning. Therefore, as already mentioned above, one of the alternatives to restore the anti-oxidant defence mechanism as well to inhibit inflammatory cytokines which are mainly involved in the pregression of Huntington’s diseases. Based on important and versatile role of Mangosteen in prevention of oxidation and inflammation, it may be possible protective strategies of Mangosteen: *Garcinia Mangostana* in Huntington’s disease and to find out if both complications are equally implicated in the disease pathogenesis or progression.

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