Quantification of acetogenins in Annona muricata linked to atypical parkinsonism in Guadeloupe.


Source

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Abstract

Atypical parkinsonism in Guadeloupe has been associated with the consumption of fruit and infusions or decoctions prepared from leaves of Annona muricata L. (Annonaceae), which contains annonaceous acetogenins, lipophilic inhibitors of complex I of the mitochondrial respiratory chain. We have determined the concentrations of annonacin, the major acetogenin in A. muricata, in extracts of fruit and leaves by matrix-assisted laser desorption-ionization mass spectrometry. An average fruit is estimated to contain about 15 mg of annonacin, a can of commercial nectar 36 mg, and a cup of infusion or decoction 140 microg. As an indication of its potential toxicity, an adult who consumes one fruit or can of nectar a day is estimated to ingest over 1 year the amount of annonacin that induced brain lesions in rats receiving purified annonacin by intravenous infusion.

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Annonacin, a lipophilic inhibitor of mitochondrial complex I, induces nigral and striatal neurodegeneration in rats:
possible relevance for atypical parkinsonism in Guadeloupe.


Source

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Abstract

In Guadeloupe, epidemiological data have linked atypical parkinsonism with fruit and herbal teas from plants of the Annonaceae family, particularly Annona muricata. These plants contain a class of powerful, lipophilic complex I inhibitors, the annonaceous acetogenins. To determine the neurotoxic potential of these substances, we administered annonacin, the major acetogenin of A. muricata, to rats intravenously with Azlet osmotic minipumps (3.8 and 7.6 mg per kg per day for 28 days). Annonacin inhibited complex I in brain homogenates in a concentration-dependent manner, and, when administered systemically, entered the brain parenchyma, where it was detected by matrix-associated laser desorption ionization-time of flight mass spectrometry, and decreased brain ATP levels by 44%. In the absence of evident systemic toxicity, we observed neuropathological abnormalities in the basal ganglia and brainstem nuclei. Stereological cell counts showed significant loss of dopaminergic neurones in the substantia nigra (-31.7%), and cholinergic (-37.9%) and dopamine and cyclic AMP-regulated phosphoprotein (DARPP-32)-immunoreactive GABAergic neurones (-39.3%) in the striatum, accompanied by a significant increase in the number of astrocytes (35.4%) and microglial cells (73.4%). The distribution of the lesions was similar to that in patients with atypical parkinsonism. These data are compatible with the theory that annonaceous acetogenins, such as annonacin, might be implicated in the aetiology of Guadeloupean parkinsonism and support the hypothesis that some forms of parkinsonism might be induced by environmental toxins.

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