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Abstract

Curcumin in Neuroprotection: From Kernicterus to Parkinson's Disease

Sri Jayanti[1*,2,3], Rita Moretti[4], Claudio Tiribelli[1] and Silvia Gazzin[1]

*[*1]Fondazione Italiana Fegato-Onlus, Basovizza, Italy*

[2] Faculty of Medicine, Hasanuddin University, Makassar, Indonesia.

[3]Molecular Biomedicine Ph.D. Program, University of Trieste, Trieste, Italy.

[4]Neurology Clinic, Department of Medical, Surgical, and Health Sciences, University of Trieste, Trieste, Italy

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ABSTRACT

Curcumin, a polyphenol derived from turmeric, has been widely known not only due to its nutraceutical benefits but also its therapeutic potential as anti-inflammatory, anti-oxidant, anti-diabetic, and anti-aging. We have previously explored curcumin in neonatal hyperbilirubinemia and have shown that it counteracts bilirubin toxicity in the animal model of Gunn rat. Curcumin protects from cerebellar hypoplasia, from the abnormalities in the Purkinje and granular cells, and abolishes the behavioral abnormalities. Genetic and proteomic analyses unraveled that Curcumin treatment has multi-targets in bilirubin-induced pathological mechanisms by reverting inflammation (interleukin-1β], tumor necrosis factor-alpha [Tnf-α]), redox stress (heme oxygenase-1 [Hmox-1]), glutamate neurotoxicity and affecting brain development (marked by intercellular adhesion molecule 1 [Icam-1], myelin-associated glycoprotein [Mag], and myelin basic protein [Mbp]). Altogether, these data indicate that Curcumin owns pleiotropic protective effects to prevent neurological damage during severe neonatal hyperbilirubinemia. The pathological mechanism described above have been also reported in Parkinson's disease (PD), a growing neurological disorder that still relies on symptomatic treatment. In an ex vivo PD model of organo typic brain cultures of substantia nigra (OBC-SN) reproducing the disease from the pre-symptomatic to the final events, we have identified in oxidative stress and inflammation the main early (3h) mechanisms responsible for dopaminergic neurons sufferance and the subsequent loss (up to 40% at 24h). Hypothesizing that the pleiotropic beneficial effects of curcumin described in the jaundice model can also be observable in the PD model, we performed a pilot study to test this challenging theory. Our preliminary experimental data showed that curcumin restores the loss in the number of dopaminergic neurons. This observation encourages us to perform additional investigation to better define the molecular effect with which Curcumin exerts the beneficial effects in PD. The study may pave the way for an earlier and more effective causal treatment of PD.

Keywords: Curumin, Neonatal hyperbilirubinemia, Cerebellar hypoplasia, Organotypic brain cultures, Dopaminergic neuron loss, Parkinson's disease

Abbreviations

I1-1β: Interleukin-1β; Tnf-α: Tumor necrosis factor-alpha; Hmox-1: Heme oxygenase-1; Icam-1: Intercellular adhesion molecule-1; Mag: Myelin-associated glycoprotein; Mbp: Myelin basic protein; PD: Parkinson's disease; OBC-SN: Organotypic Brain Cultures of Substantia Nigra

Corresponding author: Sri Jayanti, Fondazione Italiana Fegato-Onlus, Bldg. Q, AREA Science Park, ss14, Km 163.5, Basovizza, 34149 Trieste, Italy, E-mail: sri.jayanti@fegato.it

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