Title - *Drosophila* model to understand cellular and molecular basis of suppression of neurodegeneration by Ayurvedic *Amalaki Rasayana* and *Rasa-Sindoor*

Abstract - With a view to understand the basic biology underlying traditional Ayurvedic system of health care, we used the *Drosophila* model and examined biological effects of two Ayurvedic *Rasayana* formulations, viz., *Amalaki Rasayana* (AR) and *Rasa-Sindoor* (RS), at organismal, cell and molecular levels. AR is a herbal preparation from Indian Gooseberry (*Emblica officinalis*) fruits while RS is a herbo-mineral *Bhasma* containing mercury and sulphur. Biological parameters like development, life-span, fecundity, stress-tolerance etc. were affected, in a formulation-specific manner, when organisms were reared from the beginning of the 1st instar larval stage on food supplemented with 0.5% AR or RS. These effects generally agreed with their suggested Ayurvedic applications. Dietary supplement of either of these formulations during larval period substantially suppressed, without any side-effects, neurodegeneration in fly models of polyQ and Alzheimer’s disorders. AR or RS provided through food reduced the polyQ or Aβ inclusion bodies and levels of stress inducible Hsp70 and Hsp60, but elevated levels of hnRNPs and CBP, and also improved the ubiquitin proteasomal system for better protein clearance in affected cells. Additionally, either of these dietary supplements substantially inhibited induced apoptosis, which adds to the survival of diseased neuronal cells that would have otherwise died through apoptosis. AR, but not RS, substantially improved the oxidative stress tolerance of larvae and flies. Thus our studies suggest, for the first time, the potential of these Ayurvedic formulations in providing a holistic relief from the increasingly common neurodegenerative disorders.
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