Guarana (*Paullinia cupana*) hydro-alcoholic extract attenuates the phenotype of neurodegenerative diseases in transgenic *Caenorhabditis elegans* models for Alzheimer and Huntington diseases

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Guarana (*Paullinia cupana*) is a Brazilian plant which has emerged as a key ingredient in various sports and energy drinks because of its antioxidant property and several pharmacological activities on the central nervous system. Composition analysis shows that guaraná contains epicatechin, procyanidins, and phenolic compounds mainly caffeine. In vitro studies showed that the hydroalcoholic extract of guaraná (HEG) presents strong antioxidant activity against DPPH (1, 1'-diphenyl -2-picryl-hydrazyl) radicals. Here we employed the *C. elegans* model to investigate the potential effects of HEG in vivo. HEG treatment increased *C. elegans* tolerance to heat shock independently of any effect on *C. elegans* development and bacterial growth. Analysis with GFP reporter strains revealed that HEG treatment increased the expression of heat shock protein *hsp16.2::GFP* and superoxide dismutase *sod-3*::*GFP* but not glutathione-S transferase *gst-4::GFP*. To determine whether the increased thermotolerance and chaperonin expression induced by HEG has an effect on protein homeostasis, we measured proteasome and lysosomal activity. HEG increased proteasome degradation activity by 2-fold relative to the control. We also observed the accumulation of autophagosomes marked by GFP::LGG-1 transgenic line. Next we evaluated whether HEG treatment has an effect on protein misfolding diseases associated with pathological behaviors in the transgenic *C. elegans* models for Alzheimer and Huntington diseases. HEG decreased polyglutamine protein aggregation in *unc-54::Q40::YFP* transgenic worms. Also, HEG delayed b-amyloid (Ab) induced paralysis in the transgenic *C. elegans* model which expresses human Ab1–42 in the muscle. Inactivation of *skn-1* by RNAi blocked the protective effects of EHG, indicating that transcription factor SKN-1, the ortholog of Nrf2 in mammals is involved in the mechanism of EHG protection. Taken together, these results suggest that in *C. elegans* HEG alleviated polyglutamine protein aggregation and b-amyloid induced toxicity in part, through up-regulation of heat shock protein, increased protein degradation and SKN-1 pathway.

Palavra chave: *Caenorhabditis elegans*, guaraná, *Paullinia cupana*, mal de Alzheimer, doença de Huntington, b-amilóide

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