





Cocoa Polyphenols as Functional Food to counteract the Spinocerebellar Ataxia Type 3 disease

<u>Sciandrone B.1</u>, Palmioli A.1, Airoldi C.1, Regonesi M.E.¹ *E-mail: Barbara.sciandrone@unimib.it*

¹ Bioscience and Biotechnology dept., Università Milano-Bicocca, Milano, Italy

Keywords: Cocoa, polyphenols, ATX3, SCA3, nutraceuticals, functional food.

Abstract:

Spinocerebellar Ataxia Type 3 (SCA3) is an incurable neurodegenerative disease in which all the therapeutic approaches used are only palliative. The SCA3 is caused by an abnormal expansion of the polyQ track present in the C-terminal of the ATX3 protein. It is the second polyQ disease for incident worldwide and its principal hallmark is a progressive ataxia. The onset of the SCA3 occurs when the ATX3 polyQ track exceeds the threshold of 55 glutamines, causing ATX3 aggregation and leading to the formation of intra-neuronal aggregates and amyloid fibrils.

One of the possible therapeutic strategies is based on the discovery of compounds capable to counteract the ATX3 aggregation. Cocoa seeds from *Theobroma cacao* are a rich source of polyphenols and, thanks to its delicious flavours and world diffusion, it can be used as powerful functional foods. It has already demonstrated its biological activity in delaying aging and inhibit A β aggregation (causing Alzheimer disease) both *in vitro* and *in vivo*, and now we tested its capability to counteract the SCA3 disease.

Firstly, we assayed *in vitro* the anti-aggregation proprieties of the polyphenols enriched fraction of cocoa seeds on ATX3 aggregation by Thioflavin T (ThT) assay and solubility test. ThT profiles of ATX3 treated with cocoa polyphenols clearly displayed a dose-dependent decrease in fluorescent values, compared with the untreated ATX3. On the other hand, the solubility test showed a significant decrease of monomeric ATX3 protein on SDS-PAGE gels, in concomitance with the formation of SDS-resistant aggregates at high cocoa polyphenols concentrations. Moreover, we used our *Caenorhabditis elegans* SCA3 model expressing in neuronal cells the ATX3 protein carrying 130 glutamines. We fed daily nematodes with 0,5 mg/ml of cocoa polyphenols fraction from the first day of adulthood and we observed an increase in the mean lifespan from 3 to 7 days, and also an increase of 20% in body bands numbers in respect to the untreated nematodes and to the control strain expressing a non-pathological ATX3 variant.

Take together, our results demonstrate the capability of cocoa polyphenols to interfere with ATX3 aggregation and to ameliorate the helthspan of our *C. elegans* SCA3 model. This strongly supports their employment as a potential functional food capable of prevent and counteract the SCA3 development.