

Diet, Drug and Inhibitor Therapy Prevent Toxic Protein Aggregation in Various Species

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Protein aggregation has become of major concern to diabetes and neurodegenerative diseases [1]. The reversal of various diseases such as obesity, diabetes and neurodegenerative diseases is connected to accelerated protein aggregation that can lead to endoplasmic reticulum (ER) stress and mitochondrial apoptosis [2,3]. Diet, drug and inhibitor therapy have become of importance to prevent protein aggregation and important to the cellular quality-control system to prevent protein aggregation and ER stress related cell death. Polyunsaturated fatty acids such as docosahexaenoic acid (DHA) and various inhibitors [4-8] may reduce protein aggregation and prevent programmed cell death.

The generation of toxic amyloid beta has been connected to hypercholesterolemia with various cholesterol lowering drugs such as statins [9] important to the treatment of toxic amyloid beta in man and various species. Caffeine has been shown to lower amyloid beta levels and its excessive use is critical for species survival [10]. Indian spices such as curcumin are important to the prevention of toxic amyloid beta aggregation but in the current non-alcoholic fatty liver disease (NAFLD) epidemic curcumin doses should be carefully controlled with relevance to neuron toxicity [11]. The aggregation of amyloid beta indicates central importance to toxic protein aggregation in various species with specific doses of zinc and magnesium consumption essential to prevent toxic amyloid beta aggregation [12-17]. Other components such as 4-phenylbutyric acid has been used to prevent protein aggregation and ER stress [18] but excessive butyric acid consumption may lead to cell apoptosis [19].

In recent years the heat shock proteins (HSP) have become critical to amyloid beta aggregation and tau clearance [20] with HSP now critical to various diets, drug and inhibitor therapy with relevance to protein aggregation and mitochondrial apoptosis. HSP in various species is now critical for survival with heat shock genes [21,22] and (Figure 1) their regulation by diet and core body temperature is essential for adaptation to various environments. The heat shock gene Sirtuin 1 (Sirt 1) is now critical for survival with various Sirt 1 dietary activators [22] also relevant to prevent amyloid beta protein aggregation.

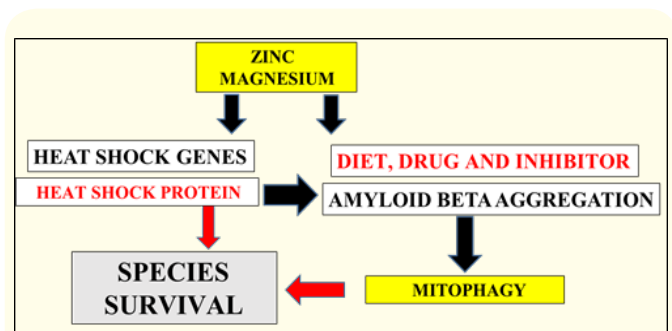


Figure 1: Zinc consumption determines heat shock gene activation and HSP-amyloid beta aggregation with relevance to mitophagy. Excessive zinc consumption may promote protein aggregation and inactivate beneficial effects of dietary magnesium, fatty acids, drug and inhibitor effects on prevention of protein aggregation.

Zinc levels with relevance to Sirt 1 expression and HSP metabolism is essential in various species [22,23] but excessive zinc levels may induce toxic immunogenic HSP-amyloid beta aggregation and mitochondrial apoptosis [12,22]. In the developing world elevated xenobiotic levels may override zinc/magnesium effects and lead to Sirt 1 inactivation with accelerated protein aggregation [13-17]. Inactivation of Sirt 1 leads to defective hepatic drug xenobiotic metabolism (statin) with delayed statin cytotoxicity associated with defective hepatic caffeine and curcumin metabolism and accelerated protein aggregation in various species [9-11].

Conclusion

Survival of the species and regulation of HSP levels are critical to prevent toxic protein aggregation and mitophagy. Dietary activators, drugs and inhibitors may reverse protein aggregation, but excessive caffeine and curcumin levels may inactivate and promote toxic amyloid beta aggregation. In various species zinc levels and core body temperature are critical to survival with HSP and amyloid regulation important to toxic protein aggregation with relevance to programmed cell death.

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Bibliography

- Eisele YS., *et al.* "Targeting Protein Aggregation for the Treatment of Degenerative Diseases". *Nature Reviews Drug Discovery* 14.11 (2015): 759-780.
- Ogen-Shtern N., *et al.* "Protein aggregation and ER stress". *Brain Research* 1648 (2016): 658-666.
- Hashimoto M., *et al.* "Role of protein aggregation in mitochondrial dysfunction and neurodegeneration in Alzheimer's and Parkinson's diseases". *Neuromolecular Medicine* 4.1-2 (2003): 21-36.
- Begum G., *et al.* "Docosahexaenoic acid reduces ER stress and abnormal protein accumulation and improves neuronal function following traumatic brain injury". *Journal of Neurosciences* 34.10 (2014): 3743-3755.
- Seung Kyun Shin., *et al.* "Docosahexaenoic acid-mediated protein aggregates may reduce proteasome activity and delay myotube degradation during muscle atrophy *in vitro*". *Experimental and Molecular Medicine* 49.1 (2017): e287.
- Pietrobono D., *et al.* "Inhibitors of protein aggregates as novel drugs in neurodegenerative diseases". *Global Drugs and Therapeutics* 2.3 (2017): 1-5.
- Saunders JC., *et al.* "An *in vivo* platform for identifying inhibitors of protein aggregation". *Nature Chemical Biology* 12.2 (2016): 94-101.
- Kim YJ and Takahashi R. "Role of polyunsaturated fatty acids for misfolding protein aggregations: implication for neurodegenerative diseases". *Annals of the New York Academy of Sciences* 1086 (2006): 11-20.
- Li HH., *et al.* "Neuroprotective effects of statins against amyloid β -induced neurotoxicity". *Neural Regeneration Research* 13.2 (2018): 198-206.
- Martins IJ. "Caffeine with Links to NAFLD and Accelerated Brain Aging. Chapter: Non-Alcoholic Fatty Liver Disease - Molecular Bases, Prevention and Treatment". *InTech-Open Science Open Minds* (2017): 155-179.
- Martins IJ. "Indian Spices and Biotherapeutics in Health and Chronic Disease". *Health* 10.4 (2018): 374-380.
- Sanna A., *et al.* "Zinc Status and Autoimmunity: A Systematic Review and Meta-Analysis". *Nutrients* 10.1 (2018): E68.
- Lee M-C., *et al.* "Zinc ion rapidly induces toxic, off-pathway amyloid- β oligomers distinct from amyloid- β derived diffusible ligands in Alzheimer's disease". *Scientific Reports* 8 (2018): 4772.
- Rezaei-Ghaleh N., *et al.* "Effect of zinc binding on β -amyloid structure and dynamics: implications for A β aggregation". *Biophysical Journal* 101.5 (2011): 1202-1211.
- Huang X., *et al.* "Alzheimer's disease, beta-amyloid protein and zinc". *Journal of Nutrition* 130.5 (2000): 1488S-1492S.
- Yu J., *et al.* "Magnesium modulates amyloid-beta protein precursor trafficking and processing". *Journal of Alzheimer's Disease* 20.4 (2010): 1091-1096.
- Martins IJ. "Magnesium Therapy Prevents Senescence with the Reversal of Diabetes and Alzheimer's Disease". *Health* 8.7 (2016): 694-710.
- Kolb PS., *et al.* "The therapeutic effects of 4-phenylbutyric acid in maintaining proteostasis". *International Journal of Biochemistry and Cell Biology* 61 (2015): 45-52.
- Wiley JC., *et al.* "Phenylbutyric acid reduces amyloid plaques and rescues cognitive behavior in AD transgenic mice". *Aging Cell* 10.3 (2011): 418-428.
- Wilhelmus MMM., *et al.* "Heat Shock Proteins and Amateur Chaperones in Amyloid-Beta Accumulation and Clearance in Alzheimer's Disease". *Molecular Neurobiology* 35.3 (2007): 203-216.

21. Garbuz DG and Evgen'ev MB. ["The evolution of heat shock genes and expression patterns of heat shock proteins in the species from temperature contrasting habitats"]. *Genetika* 53.1 (2017): 12-30.
22. Martins IJ. "Heat Shock Gene Inactivation and Protein Aggregation with Links to Chronic Diseases". *Diseases* 6.39 (2018): 1-5.
23. Martins IJ. "Overnutrition Determines LPS Regulation of Mycotoxin Induced Neurotoxicity in Neurodegenerative Diseases". *International Journal of Molecular Sciences* 16.12 (2015): 29554-29573.

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