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EDITORIAL

# Rutin: A Potential Therapeutic Agent for Alzheimer Disease

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Rutin is a flavonoid glycoside found in Citrus plants. It has been reported for its neuroprotective effects, probably due to its antioxidant and anti-inflammatory properties. Rutin protects the membranes by enhancing their rigidity through interaction with phospholipids preventing their oxidative damage [1].

Xu et al. reported that rutin decreases β-amyloid plaque aggregation, nitric oxide production, the pro-inflammatory cytokines, cytotoxicity and oxidative stress *in-vitro*. They additionally investigated its *in-vivo* neuroprotective effects on alzheimer-diseased transgenic mice, where they reported an attenuation of the memory deficits, increase of antioxidant parameters as reduced glutathione and super oxide dismutase, decrease in lipid peroxidation levels, as indicated by malondialdehyde, as well as decreased brain interleukin-1β and interleukin-6 levels [2].

Habtemariam reported that rutin can modify both the cognitive and behavioral symptoms that are associated with neurodegenerative diseases by its ability to cross the blood brain barrier and by acting as both an antioxidant in neuronal cells and an anti-inflammatory drug. In addition, it showed effects on amyloid beta (Aβ) aggregates and processing in Alzheimer disease [3].

Enogieru et al. reported the use of plant-derived bioactive components as rutin in many neurodegenerative diseases. They attributed its mechanism of action to amelioration of the antioxidant enzymes, decreasing the pro-inflammatory cytokines, anti-apoptotic effects, restoring the activity of complex enzymes in the mitochondria and activating the MAPK cascade, thus aids in neuronal survival [4].

Jiménez-Aliaga et al. reported the effects of rutin *in-vitro* in decreasing Aβ25–35 fibril formation and accumulation thus decreasing neurotoxicity [5], while Wang et al. reported the inhibition of Aβ aggregation and cytotoxicity by rutin, in addition to the prevention of mitochondrial damage, reducing the production of pro-inflammatory cytokines by reducing TNF-α and interleukin-(IL-) 1 *in-vitro*, and increasing the levels of catalase and superoxide dismutase enzymes as well as reduced glutathione levels [6].

Interestingly, the administration of (Congo red/rutin) magnetic nanoparticles intravenously in transgenic mice resulted in the amelioration of neurologic changes and the decrease of memory deficits in their brains [7]. Additionally, Xu et al. showed that rutin reduced oligomeric Aβ, IL-1 and IL-6 levels in the brains of transgenic mice [8].

Ramalingayya et al. reported that rutin improved recognition in a dose-dependent manner against scopolamine-induced memory deficit alzheimer model without any disturbance to the locomotor activity [9].

Javed et al. stated that rutin improved cognition and attenuated streptozotocin-induced inflammation in another Alzheimer model by decreasing the expression of IL-8, COX-2 enzyme, NF-κB as well as inducible iNOS and ameliorating the hippocampal histological abnormalities [10]. While in a zebrafish model of Alzheimer, Richetti et al. showed that rutin inhibited scopolamine-induced amnesia without affecting the zebrafish locomotor activity [11].

The restriction of rutin use as a therapeutic agent may be attributed to its rapid metabolism and excretion as well as poor absorbtion [4]. Mostafa et al. reported that flavonoids rapid metabolism can be overcome by their methoxylation which also improve their intestinal absorption, bioavailability and stability [12]. Also recently, loading rutin that was extracted from *Calendula officinalis* L. flowers onto a novel nanoparticled-lipid polymer hybrid has shown efficacy for targeting rutin delivery to the brain. These nanoparticle were found to be both biocompatible, as tested by a hemolysis test, and bioavailable. Thus, these results open the era for the formulation of novel neuro-pharmaceuticals for brain targeting using natural products [13].

## REFERENCES

1. Mostafa NM. Comparative analysis of rutin content in some Egyptian plants: A validated RP-HPLC-DAD approach. European J Med Plants. 2017;19:1-8.
2. Xu PX, Wang SW, Yu XL, Su YJ, Wang T, Zhou WW, et al. Rutin improves spatial memory in Alzheimer's disease transgenic mice by reducing Aβ oligomer level and attenuating oxidative stress and neuroinflammation. Behav Brain Res. 2014; 264:173-180.
3. Habtemariam S. Rutin as a natural therapy for Alzheimer's disease: Insights into its mechanisms of action. Curr Med Chem. 2016;23:860-873.
4. Enogieru AB, Haylett W, Hiss DC, Bardien S, Ekpo OE. Rutin as a potent antioxidant: implications for neurodegenerative disorders. Oxid Med Cell Longev. 2018.

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5. Jiménez-Aliaga K, Bermejo-Bescós P, Benedí J, Martín-Aragón S. Quercetin and rutin exhibit antiamyloidogenic and fibril-disaggregating effects in vitro and potent antioxidant activity in APPswe cells. Life Sci. 2011;89:939-945.

6. Wang SW, Wang YJ, Su YJ, Zhou WW, Yang SG, Zhang R, et al. Rutin inhibits β-amyloid aggregation and cytotoxicity, attenuates oxidative stress, and decreases the production of nitric oxide and proinflammatory cytokines. Neurotoxicology. 2012;33:482-490.

7. Hu B, Dai F, Fan Z, Ma G, Tang Q, Zhang X. Nanotheranostics: Congo red/rutin-MNPs with enhanced magnetic resonance imaging and $H_2O_2$-responsive therapy of Alzheimer's disease in APPswe/PS1dE9 transgenic mice. Adv Mater. 2015;27:5499-5505.

8. Xu PX, Wang SW, Yu XL, Su YJ, Wang T, Zhou WW, et al. Rutin improves spatial memory in Alzheimer's disease transgenic mice by reducing Aβ oligomer level and attenuating oxidative stress and neuroinflammation. Behav Brain Res. 2014;264:173-180.

9. Ramalingayya GV, Nampoothiri M, Nayak PG, Kishore A, Shenoy RR, Mallikarjuna Rao C, et al. Naringin and rutin alleviates episodic memory deficits in two differentially challenged object recognition tasks. Pharmacogn Mag. 2016;12:S63-70.

10. Javed H, Khan MM, Ahmad A, Vaibhav K, Ahmad ME, Khan A, et al. Rutin prevents cognitive impairments by ameliorating oxidative stress and neuroinflammation in rat model of sporadic dementia of Alzheimer type. Neurosci. 2012;210:340-352.

11. Richetti SK, Blank M, Capiotti KM, Piato AL, Bogo MR, Vianna MR, et al. Quercetin and rutin prevent scopolamine-induced memory impairment in zebrafish. Behav Brain Res. 2011;217:10-15.

12. Mostafa NM, Abd El-Ghffar EA, Hegazy HG, Eldahshan OA. New methoxyflavone from *Casimiroa sapota* and the biological activities of its leaves extract against lead acetate induced hepatotoxicity in rats. Chem Biodivers. 2018;15:e1700528.

13. Ishak RAH, Mostafa NM, Kamel AO. Stealth lipid polymer hybrid nanoparticles loaded with rutin for effective brain delivery - comparative study with the gold standard (Tween 80): optimization, characterization and biodistribution. Drug Deliv. 2017;24:1874-1890.