Publications Template

#	Research Title	Field	Abstract	Year of Publication Publishing	Publishing Link "URL"
1	Neuroprotective role of galantamine with/without physical exercise in experimental autoimmune encephalomyelitis in rats. Life Sciences Journal. 277 (2021), 119459.	Drug repurposing In multiple sclerosis (autoimmune disease)	Aims The fact that physical activity besides central cholinergic enhancement contributes in improving neuronal function and spastic plasticity, recommends the use of the anticholinesterase and cholinergic drug galantamine with/without exercise in the management of the experimental autoimmune encephalomyelitis (EAE) model of multiple sclerosis (MS). Materials and methods Sedentary and 14 days exercised male Sprague Dawley rats were subjected to EAE. Hereafter, exercised rats continued on rotarod for 30 min for 17 consecutive days. At the onset of symptoms (day 13), EAE sedentary/exercised groups were subdivided into untreated and post-treated with galantamine. The disease progression was assessed by EAE score, motor performance, and biochemically using cerebrospinal fluid (CSF). Cerebellum and brain stem samples were used for histopathology and immunohistochemistry analysis. Key findings Galantamine decreased EAE score of sedentary/exercised rats and enhanced their motor performance. Galantamine with/without exercise inhibited CSF levels of tumor necrosis factor (TNF)-α, interleukin (IL)-6), and Bcl-2-associated X protein (Bax), besides caspase-3 and forkhead box P3 (Foxp3) expression in the brain stem. Contrariwise, it has elevated CSF levels of brain derived neurotrophic factor (BDNF) and B-cell lymphoma (Bcl-2) and enhanced remyelination of cerebral neurons. Noteworthy, exercise boosted the drug effect on Bcl-2 and Bax. Significance	2021	https://www.sciencedirect.com/science/article/pii/S0024320521004446

			The neuroprotective effect of galantamine against EAE was associated with anti-inflammatory and anti-apoptotic potentials, along with increasing BDNF and remyelination. It also normalized regulatory T-cells levels in the brain stem. The impact of the add-on of exercise was markedly manifested in reducing neuronal apoptosis.		
2	Does physical exercise improve or deteriorate treatment of multiple sclerosis with mitoxantrone? Experimental autoimmune encephalomyelitis study in rats. BMC Neuroscience 23,11 (2022).	Drug repurposing In multiple sclerosis (autoimmune disease)	Background Mitoxantrone has proved efficacy in treatment of multiple sclerosis (MS). The fact that physical exercise could slow down the progression of disease and improve performance is still a debatable issue, hence; we aimed at studying whether combining mitoxantrone with exercise is of value in the management of MS. Methods Thirty-six male rats were divided into sedentary and exercised groups. During a 14-day habituation period rats were subjected to exercise training on a rotarod (30 min/day) before Experimental Autoimmune Encephalomyelitis (EAE) induction and thereafter for 17 consecutive days. On day 13 after induction, EAE groups (exercised &sedentary) were divided into untreated and mitoxantrone treated ones. Disease development was evaluated by motor performance and EAE score. Cerebrospinal fluid (CSF) was used for biochemical analysis. Brain stem and cerebellum were examined histopathological and immunohistochemically. Results Exercise training alone did not add a significant value to the studied parameters, except for reducing Foxp3 immunoreactivity in EAE group and caspase-3 in the mitoxantrone treated group. Unexpectedly, exercise worsened the mitoxantrone effect on EAE score, Bcl2 and Bax. Mitoxantrone alone decreased EAE/demyelination/inflammation scores, Foxp3 immunoreactivity, and interleukin-6, while increased the re-myelination marker BDNF without any change in tumor necrosis factor-α. It clearly interrupted the apoptotic pathway in brain stem, but worsened EAE mediated changes of the anti-apoptotic Bcl2 and pro-apoptotic marker Bax in the CSF. Conclusions The neuroprotective effect of mitoxantrone was related with remyelination, immunosuppressive and anti-inflammatory potentials. Exercise training did not show added value to mitoxantrone, in contrast, it disrupts the apoptotic pathway.	2022	https://link.springer.com/article/10.1186/s12868-022-00692-1

3	Morin suppresses mTORc1/IRE-1α/JNK and IP3R-VDAC-1 pathways: Crucial mechanisms in apoptosis and mitophagy inhibition in experimental Huntington's disease, supported by in silico molecular docking simulations. Life Sciences Journal. 338 (2024), 122362.	Drug repurposing In Huntington's disease (neurodegenerative disease)	Aims Endoplasmic reticulum stress (ERS) with aberrant mitochondrial-ER contact (MERC), mitophagy, and apoptosis are interconnected determinants in neurodegenerative diseases. Previously, we proved the potential of Morin hydrate (MH), a potent antioxidant flavonoid, to mitigate Huntington's disease (HD)-3-nitropropionic acid (3-NP) model by modulating glutamate/calpain/Kidins220/BDNF trajectory. Extending our work, we aimed to evaluate its impact on combating the ERS/MERC, mitophagy, and apoptosis. Methods Rats were subjected to 3-NP for 14 days and post-treated with MH and/or the ERS inducer WAG-4S for 7 days. Disease progression was assessed by gross inspection and striatal biochemical, histopathological, immunohistochemical, and transmission electron microscopical (TEM) examinations. A molecular docking study was attained to explore MH binding to mTOR, JNK, the kinase domain of IRE1-α, and IP3R. Key findings MH decreased weight loss and motor dysfunction using open field and rotarod tests. It halted HD degenerative striatal neurons and nucleus/mitochondria ultra-microscopic alterations reflecting neuroprotection. Mechanistically, MH deactivated striatal mTOR/IRE1-α/XBP1s&JNK/IP3R, PINK1/Ubiquitin/Mfn2, and cytochrome c/caspase-3 signaling pathways, besides enhancing p-PGC-1α and p-VDAC1. WAG-4S was able to ameliorate all effects initiated by MH to different extents. Molecular docking simulations revealed promising binding patterns of MH and hence its potential inhibition of the studied proteins, especially mTOR, IP3R, and JNK. Significance MH alleviated HD-associated ERS, MERC, mitophagy, and apoptosis. This is mainly achieved by combating the mTOR/IRE1-α signaling, IP3R/VDAC hub, PINK1/Ubiquitin/Mfn2, and cytochrome c/caspase 3 axis to be worsened by WAG-4S. Molecular docking simulations showed the promising binding of MH to mTOR and JNK as novel identified targets.	2024	https://www.sciencedirect.com/science/article/pii/S0024320523009979