The isothiocyanate isolated from *Moringa oleifera* shows potent anti-inflammatory activity in the treatment of murine sub-acute Parkinson's disease

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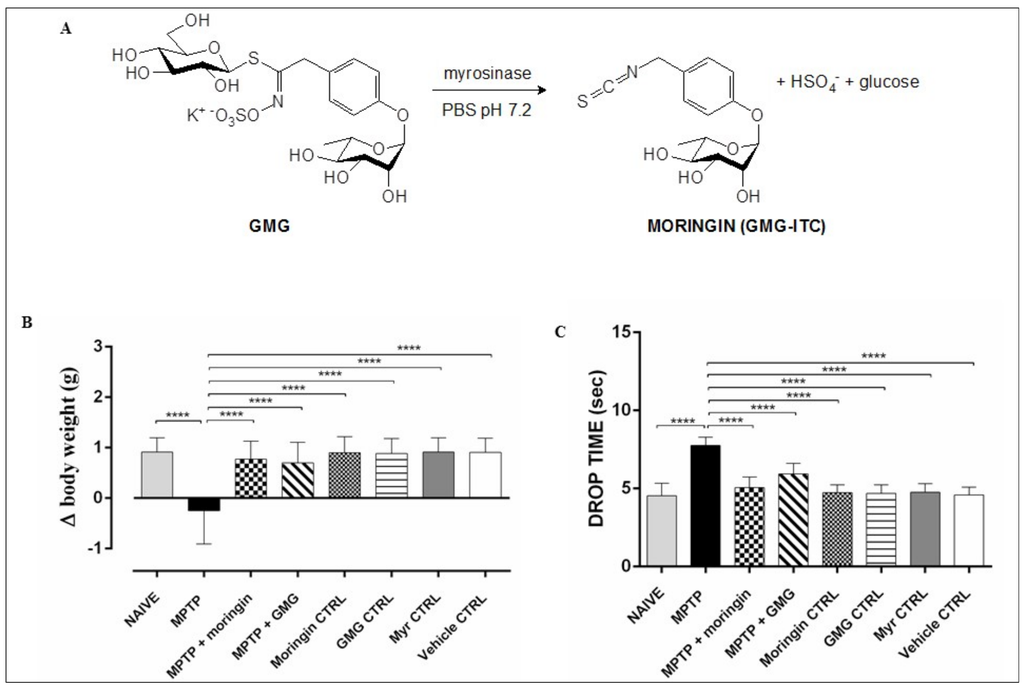
INTRODUCTION: The present study was aimed at estimating a possible neuroprotective effect of glucomoringin (4-(α-L-rhamnopyranosyloxy)benzyl glucosinolate;) bioactivated with the enzyme myrosinase to form the corresponding isothiocyanate (4-(α-L-rhamnopyranosyloxy)benzyl C; moringin) in the treatment or prevention of Parkinson's disease (PD). Here, the beneficial effects of moringin were compared to those of pure glucomoringin, not enzymatically activated, *in vivo* experimental mouse model of sub-acute PD.

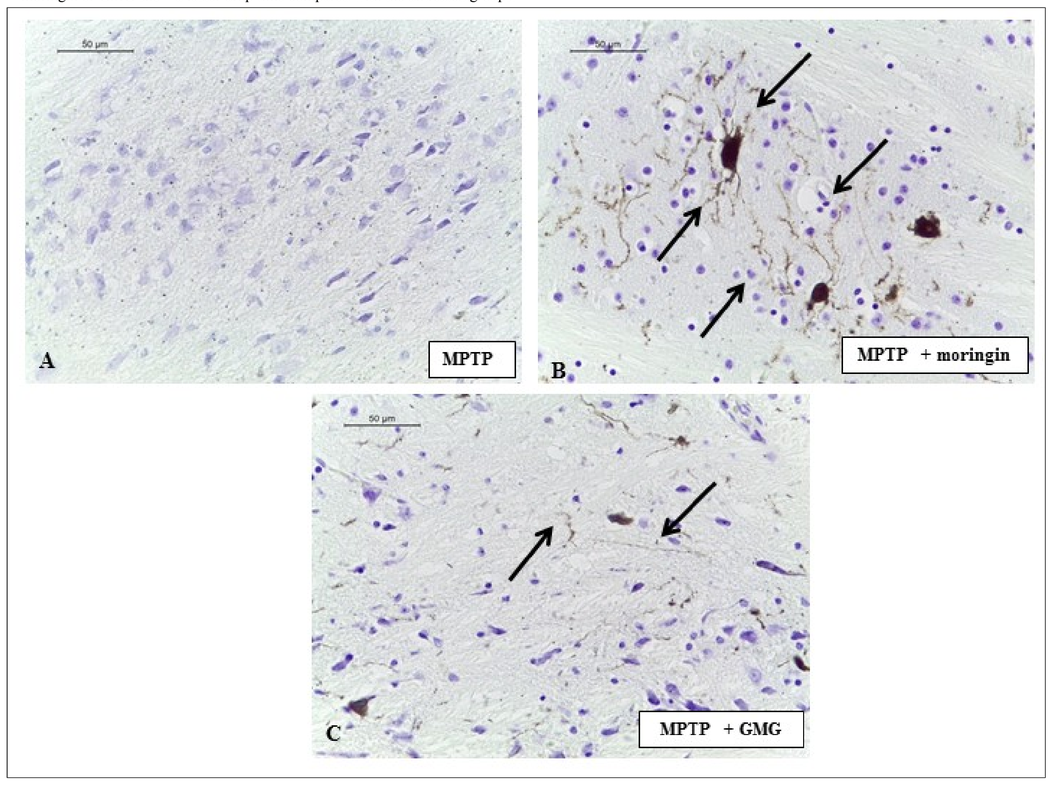
MATERIAL and METHODS: Sub-acute PD was induced in C57BL/6 mice by administration of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) according to Langston et al (1). Mice were daily pretreated for 1 week with moringin (10mg/kg + 5µl myrosinase/mouse) and with glucomoringin (10mg/kg). Behavioural evaluations were also performed in order to assess motor deficits and bradykinesia in MPTP-mice. Besides, assuming that pre-treatment with moringin could modulate the triggering of inflammatory cascade and the response to it correlated, we tested its *in vitro* anti-inflammatory activity by using a model of RAW 264.7 macrophages stimulated with lipopolysaccharide (LPS).

RESULTS: Achieved results in vivo showed a higher efficacy of moringin compared to glucomoringin not only to modulate inflammatory pathway, but also oxidative stress and apoptotic pathways. In addition, the greater effectiveness of moringin in countering mainly the inflammatory pathway has been corroborated by the results obtained in vitro.

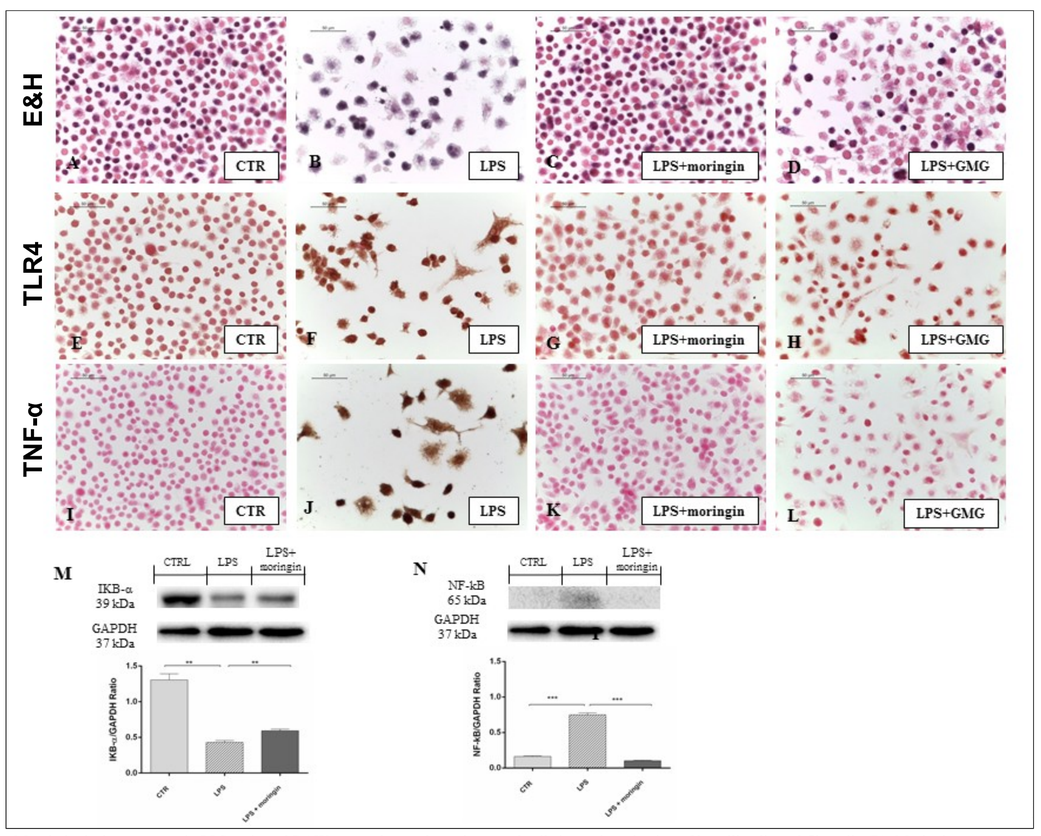
CONCLUSION: According to our findings, moringin is a good and effective candidate in the treatment or prevention of experimental PD, as it is able to modulate different molecular pathways underlying the progression of this disease.
We believe that identifying a phytochemical that can be easily extracted, at low cost, from *M. oleifera* seeds, followed by simple enzyme bio-activation may bring about an important backdrop, not only therapeutic for patients with already full-blown PD but, if considered as a regular dietary supplement, may helpful for preventive purposes.



(A) Production of 4-(a-L-rhamnopyranosyloxy)benzyl isothiocyanate (moringin; GMG-ITC) by myrosinase-catalyzed hydrolysis of GMG, purified from Moringa oleifera seeds, in PBS solution (pH 7.2) (B) MPTP-injected mice show a significant body weight loss. Moringin or GMG pretreatment significantly prevents MPTP-induced weight loss. (C) The same experimental group examined in a pole test gives significant results. MPTP-administrated mice pretreated with moringin or GMG show a faster drop time compared with the untreated groups.



Golgi stain. Compared with GMG, moringin significantly improves the neuronal dendrites and prevents the decreasing of TH expression in MPTP mice. A severe loss of termination at the level of the dendrite tree is marked in brain samples taken from untreated MPTP mice (A). Nigral DA neurons are preserved significantly by moringin-pretreated MPTP mice (B) (showed in black arrows) than GMG-treated MPTP mice (C).



Morphological assessment in LPS-activated RAW macrophages shows increased cell size and production of lamellipodia and filopodia (B). Moringin pretreatment significantly reduced these LPS-triggered morphological features (C). Control cells show normal morphological appearance (A). GMG pretreatment reduced partially LPS-triggered morphological features (D). Immunocytochemistry results show that in LPS-activated macrophages, proinflammatory markers, TLR4 (F) and TNF-a (J), show enhanced expression, while moringin pretreatment shows basal level staining for TLR4 (G) similar to that of control cells (E) and negative staining for TNF-a (K) expression. Control cells show negative staining for TNF-a (I). GMG pretreatment displayed partial but significant reduction of positive staining for TLR4 (H) as well as for TNF-a (L) when compared with the LPS-moringin group. Western blot results show reduced expression of IkB-a (M) and enhanced expression of NF-kB (N) in LPS-stimulated macrophages, moringin pretreatment significantly increased the IkB-a level and decreased the NF-kB level in LPS-activated macrophages.

1. Langston JW, Ballard P. et al. Chronic Parkinsonism in humans due to a product of meperidine-analog synthesis. Science. 1983;219:979-980.

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