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Therapeutic and preventive efficacy of mangiferin in an experimental model of schizophrenia

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The connection between inflammatory processes occurring during the pregnancy as well as the consequences of subsequent oxidative stress in the development of schizophrenia points to the potential efficacy of anti-inflammatory and antioxidant drugs as therapeutic approaches for schizophrenia. In this context, mangiferin, a natural polyphenolic compound abundant in the leaves of Mangifera indica L. with robust antioxidant and anti-inflammatory properties, could represent a potential candidate for schizophrenia treatment, particularly interesting as preventive or coadjuvant therapy in this disorder. Therefore, the aim of this study was to evaluate the therapeutic and preventive efficacy of mangiferin on behavioural and brain structural alterations induced by an experimental model of schizophrenia based on maternal immune activation.

PolyI:C administration in pregnant rats (4mg/kg, i.v. gestational day 15) was used as model of schizophrenia. Male offspring received daily mangiferin extract (50mg/kg, p.o.) (i) as a therapeutic treatment in young adults (postnatal day (PND) 60-70) or (ii) as a preventive therapy in adolescents (PND39-54). The preventive mangiferin effect was compared with those of preventive risperidone treatment (PND39-54, 0.3mg/kg, i.p.). Prepulse inhibition (PPI), novel object recognition (NOR), open field and amphetamine induced activity tests, were performed in the adult offspring (PND70). T2-weighted MRI brain images were acquired in the mangiferin preventive treatment (PND120). Data were analysed by repeated measure or two-way ANOVA, as appropriate, followed by post hoc test. $p<0.05$ was considered to be significant.

Results showed that mangiferin treatment in young adults significantly reversed the PPI deficit induced by the schizophrenia model. However, it failed to attenuate the sensitivity to amphetamine and the NOR deficit associated with this model. On the other hand, preventive mangiferin treatment during the adolescence also produced a significant reduction of PPI deficit presenting the same magnitude of improvement than risperidone showed. Additionally, the preventive mangiferin treatment showed a trend to improve both the NOR deficit and the time spent in the central zone in the open field test. MRI studies revealed that mangiferin treatment during adolescence partially prevented the morphometric alterations observed in the schizophrenia model, improving the cortical shrinkage and the cerebellum and the fourth ventricle enlargements. Nevertheless, the effect of mangiferin on MRI changes was weaker than after risperidone treatment.

These findings demonstrate that mangiferin was able to improve behavioural and morphometric abnormalities in the schizophrenia model. Therefore, these data suggest that mangiferin might be an alternative therapeutic or preventive strategy to improve clinical signs in the adulthood besides to modify the time course of this disease at the early stage of population with high-risk. Further studies would be necessary to demonstrate anti-inflammatory and antioxidant mechanisms involved in the efficacy of for schizophrenia treatment.

This work was supported by University of Cádiz (PR2019-046); CIBERSAM" (CB/07/09/0033); "INiBICA" (IN-C22), Ministerio de Ciencia, Innovación y Universidades, Instituto de Salud Carlos III (PI17/01766), co-financed by European Regional Development Fund (ERDF), "A way of making Europe", Delegación del Gobierno para el Plan Nacional sobre Drogas (2017/085), Fundación Alicia Koplowitz and "Consejería de Economía, Innovación, Ciencia y Empleo de la Junta de Andalucía" (CTS-510).

No conflict of interest

doi: 10.1016/j.euroneuro.2021.10.147

P.0151
NMDA receptor antagonists effects upon functional connectivity of glutamatergic system: a homer1a-based network approach

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