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Sujet de Thèse :

The Adverse Effects of Type 1 Diabetes and Chronic Mild Stress on Affective, Cognitive and Physiological Disorders: Application of Phenolic Fractions from Date (Phoenix dactylifera L.) Seeds as a promising Antioxidant and Nutraceutical Glucose Regulator

Abstract:

The concurrence of Type-1 Diabetes Mellitus (T1DM), psychiatric disorders and cognitive decline constitutes a major health problem. Living with a chronic illness such as T1DM is challenging as it interferes with social, mental, and physical functions, which affect the quality of life of these patients. The current work aimed: (1) to explore the influences of T1DM and stress on affective, cognitive and physiological disorders in patients with T1DM, and (2) to characterize the effects of Phenolic Fraction Concentrates (PFC) extracted from date seed as a promising antioxidant and glucose regulator in the regulation of physiological, behavioral and cognitive changes related to hyperglycemia in chronically stressed diabetic rats.

In this regard, a cross-sectional analysis was carried out in adult patients with T1DM (N=140). The Rey-Osterrieth complex figure test was used to evaluate the cognitive functions. In addition, patients also completed the 21-item Depression, Anxiety, and Stress Scale to assess their mental health state. The findings revealed that the risk factors including long diabetes duration, lipid parameters, dieting, and bulimia were the strongest predictors of visual perception (VP) and working memory (WM) impairments. In addition, a negative correlation between psych-emotional symptoms and cognitive functions was obtained. Furthermore, our findings revealed that the more the level of diabetes-related stress increases, VP and WM scores significantly decrease.

On the other hand, experimental rat models of T1DM (induced by a single dose of Streptozotocin, 65 mg/kg) and stress (induced by a chronic mild stress paradigm (two unpredictable mild stressors/day, 6 days/week for 12 weeks)) were used to investigate if PFC improves chronic hyperglycemia-related behavioral changes and cognitive impairment by mitigating oxidative stress and neuro-inflammation in chronically stressed diabetic rats. In fact, PFC showed powerful antioxidant activity as determined by scavenging and reducing assays. PFC significantly inhibited digestive enzymes in a dose-dependent manner. In addition, our product possesses a powerful anti-inflammatory effect through their ability to inhibit protein denaturation. Furthermore, a PFC dose of 50 mg/kg was considered the optimal healthy dose for rats. In this regard, PFC supplementation decreased significantly oxidative stress and attenuated neuro-inflammation, especially in brain regions in chronically stressed diabetic rats compared to Insulin monotherapy. This combination was also linked with a significant effect in modeling the corticosterone level as well as glucose homeostasis and lipid parameters, which are markedly altered in T1DM associated with stress. Besides, our findings showed that the associated treatment possesses important anxiolytic and antidepressant-like proprieties in this rat model. This supplementation protected also these rats against learning and memory impairment, which can be mainly mediated by its capacity to protect brain cells against oxidative stress and neuro-inflammation triggered by diabetes and chronic stress.

Keywords: Diabetes, Stress, Phenolic fraction concentrates, Oxidative stress, Inflammation.