Volume : 3 | Issue : 11 | November 2014 • ISSN No 2277 - 8179

Protective Effect of Hesperidin Agains Neurobehavioral Disorders And oxidative Stress in The Diabetic Ratte Gestante Strain Wistar

Biology

KEYWORDS : Diabete, Behavioral, Anxiety, Hesperidin, GSH hepatic, GST hepatic

Chouba Ibtissem *	Laboratory of Neuro- endocrinology Applied Biology Department; Badji Mokhtar University Annaba , 23000 , Algeria .
Nessaibia Issam	Laboratory of Neuro- endocrinology Applied Biology Department; Badji Mokhtar University Annaba , 23000 , Algeria .
Haloui Meriem	Laboratory of Neuro- endocrinology Applied Biology Department; Badji Mokhtar University Annaba , 23000 , Algeria .
Tahraoui Abdelkrim	Laboratory of Neuro- endocrinology Applied Biology Department; Badji Mokhtar University Annaba , 23000 , Algeria .

ABSTRACT

Our problem is to evaluate the behavioral effects of infection and combination diabetes - infection in pregnant rats and the protective effect of an antioxidant on neurobehavioral alterations and complications. Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 60 mg / kg . The hesperidins, a natural flavonoid was administered orally (gavages) at a dose of 100 mg / kg. This administration reduces anxiety and reduces damage due to hyperglycemia associated with a significant decrease in the rates of reduced glutathione (GSH) and maternal liver on the other hand, by increasing the activity of glutathione S- transferase (GST) hepatic mother, biomarkers of oxidative stress. The results indicate the ability of hesperidin to prevent changes induced by experimental diabetes.

1. Introduction

Diabetes mellitus type 1 is a common disease that affects individuals predisposed to develop at an early age an autoimmune reaction against pancreatic islet B cells [1]. It is one of the inevitable consequences, a disorder in the regulation of carbohydrate metabolism to a possibility of screening for psychiatric disorders such as depression, anxiety and behavioral problems [2]. Streptozotocin induces diabetes mellitus and diabetic causes installation syndrome characterized by polyphagia, polyuria, polydipsia, and glucosuria [3, 4] .STZ is a reference substance for the experimental study of diabetes [5, 3]. This endocrine disorder is characterized by the destruction of β cells Langerhans responsible for insulin deficiency [6]. Diabetologists have obviously deduced that a complementary therapy consisting of plant extracts is required to optimize the treatment of diabetes [7, 8, 9]. Flavonoids are powerful antioxidants that may inhibit the formation of free radicals and oxidation oppose macromolecules realizing the effectiveness of several herbs as natural diabetes [10]. In this context, we have developed an experimental approach that aims to study the antioxidant power of hesperidin on oxidative stress applied to pregnant rats by assessing the ability of detoxification kindergarten through the assay of reduced glutathione (GSH) and measuring the activity of glutathione S- transferase (GST) and its impact on the emotional state during the gestational period announced by the
(Open Field) behavioral test.

2 Materials and Methods

2.1 Animals

The biological material base that we have chosen is the rat Rattus rattus of the Wistar strain from Pasteur Institute in Algiers. The rats are nocturnal mammals of the order of rodents. Upon their arrival, the rats weighed an average of 180 grams, and at the time of the experiment, they weighed on average 250 ± 20 grams. The rats were acclimated under standardized conditions of natural photoperiod, an average temperature of 22 ± 4 º C and humidity of 50-70%. After an adaptation period of three weeks , we have selected 25 females based on weight which we separated into five experimental groups each include five rats control group T, vehicle control CV lot , lot control treated hesperidin CH Lot diabetic vehicle DV lot diabetic treated hesperidin DH .

2.2 Treatment of Animals

2.2.1 Administration of streptozotocin

Streptozotocin (STZ) is a chemical commonly used in animal models for the study of diabetes [11]. Diabetes was induced in rats by intraperitoneal injection of STZ (Sigma Lowis ST, Mo) at a dose of 60 mg / kg body weight [12] dissolved in a 0.1M sodium citrate buffer pH 4.5.

2.2.2 Administration of hesperidin

Administration is by gastric gavages of rats to a high dose of 100 mg / kg body weight. Treatment with vehicle or the antioxidant Nacl for controls begin 72 hours after the induction of diabetes and it is for three days (15th , 17th and 18th day gestational).

2.3 The test of open field (Open Field, OF)

The OF test, first described by Hall in 1934 [13], the device is a Plexiglas platform (70cm x 70cm x 40cm) divided into central and peripheral area. Each rat was placed individually in the center of the floor for 5 minutes and allowed exploration

[14]. An animal considered anxiety will tend to prefer the peripheral zone Parameters measured the time spent in the center , time spent in the periphery and the distance traveled.

2.4 Determination of reduced glutathione (GSH) Liver

The assay of GSH is based on the colorimetric method of Ellman (1959)

[15]. The principle is based on the oxidation reaction of GSH with acid 5, 5'- dithiobis - 2 nitrobenzoic acids (DTNB) and releasing the absorbent at 412 nm thionitrobenzoic acid (TNB).For this assay , one gram of liver was homogenized in three volumes of 5 % TCA using a mill and then centrifuged at 1000 revs / min . 50 mu.l of supernatant are diluted in 10 ml of phosphate buffer (0.1 M, pH 8). To 3 ml of the dilution mixture, 20 .mu.l DTNB (0.01 M) are added, the absorbance measurement is obtained at a wavelength of 412 nm.

2.5 Determination of glutathione S - transferase (GST) Liver

The measurement of the overall GST acivité is to provide to the various isoenzymes CDNB chlorodinitrobenzene. The

CDNB readily reacts with GSH to form an enzymatically light at 340 nm absorbing conjugate. The value of the optical density is proportional to the bound GST activity [16] .son procedure is to mix 840 mu.l phosphate buffer (100 mM , pH 6.5) , 50 mu.l CDNB , 10 .mu.l sample then add 100 µ GSH. The measurement of the enzymatic activity was performed for 5 minutes. The concentration of proteins in each organ was determined by the method of Bradford M (1976) [17] by using a calibration curve previously made by means of bovine serum albumin (BSA).

2.6 Statistical analysis of results

Results are presented as mean ± SEM and shown in histograms. A comparison test was used medium . The test T of Student with the MINITAB program for comparing two averages.

3 Results

3.1 Variation of the open Field Test parameters

The results in Figure 1A shows that the group of diabetic and diabetic rats treated spends less time in the central part of the device by providing groups of rats control , vehicle control and treated with hesperidin (W: 36 ± 12,28 vs DV:10.4 ± 2.05), (W: 36 ± 12.28 vs DH: 13.4 ± 5.23), (CV : 22.8 ± 7.46 vs. DV : 10.4 ± 2,059)

Figure 1B shows that the distance traveled by the control and diabetic rats treated with hesperidin was significant (P < 0.05) than that traversed by the vehicle control rats (CV : 33 ± 8.23 vs CH : 60 ± 1.69), (CV : 33 ± 8.23 vs DH: 45 ± 6.5) and a significant decrease (P < 0.01) in diabetic vehicle (CV : 33 ± 8.23 vs DV : 18 ± 4) and highly significant increase in the diabetic treated hesperidin (P < 0.001) by supplying the diabetic rats vehicle (DV :18 ± 4 vs DH: 45 ± 6.5)

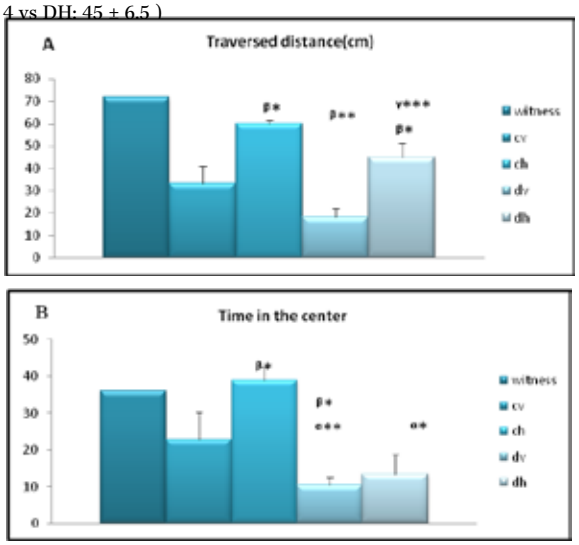

Figure 1: Behavior of pregnant rats in the control and treated open Field. The distance traveled (A), time spent in the center (B), (α) comparison with rats witness (β) compared with diabetic rats and vehicle (γ) compared with diabetic rats treated

Ns : Non significant difference P > 0.05 ; * P < 0.05 ; ** P <0.01 ; *** P < 0.001

3.2 Hepatic content of reduced glutathione (GST) in pregnant rats

The results showed a highly significant (P < 0.001) in liver glutathione content in diabetic rats vehicle and a very significant increase (P < 0.01) contribution to the controls (W: 55 ± 4.87 vs. DV: 24 ± 2.64), (W: 55 ± 4.87 vs DH: 33 ± 9.74).

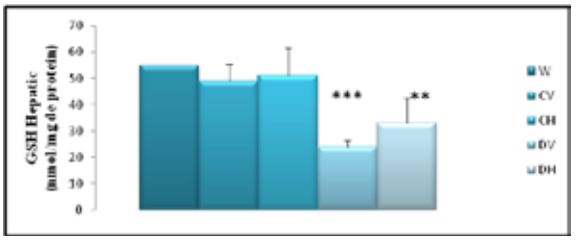

Figure 2. Variation of the concentration of hepatic GSH nmol / mg protein

Ns. : non significant difference P > 0.05 ; *P < 0.05 ; **P < 0.01; ***P < 0.001

3.3 Measuring the hepatic activity of glutathione S- transferase (GST) in pregnant rats

The results indicate a highly significant increase (P < 0.001) in liver GST concentration in diabetic rats treated with vehicle and hesperidin by contribution to controls (W: 117.2 ± 6.14 vs DV: 214.4 ± 5.59), (W: 117.2 ± 6, 14 vs DH: 161, 2 ± 4, 81).

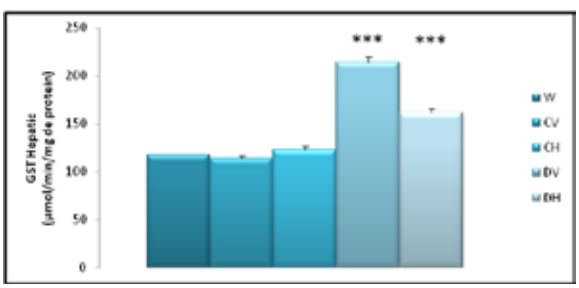

Figure 3: Hepatic activity variation of GST in µmol/min/mg of proteins

Ns: Non significant difference P > 0.05 ; *P < 0.05 ; **P < 0.01; ***P < 0.001

4. Discussion

Our experimental study focused on properties that potentiate hesperidin fight against neurobehavioral alterations in rats of Wistar diabetic pregnant. Recently, hypoglycemic agents products derived from plants have attracted the attention of researchers since natural plant sources are usually considered less toxic by contribution to synthetic sources [18]. The experimental streptozotocin-induced diabetes is characterized by hyperglycemia [11] which is linked by several studies to defects in insulin secretion by reducing the mass of β cells of Langerhans islets [19,20,21,22]. It activates the expression of protein kinase C, protein responsible for the dephosphorylation of the insulin receptor [23]. These complications associated with diabetes status seem to negatively affect the browser behavior and anxious state of diabetic rats at OF whose comparison with the control group reported persistent and acute locomotor hypoactivity represented by a decrease in the distance [24]. The results of our work mention a hierarchical efficiency of hesperidin against different levels of disorders caused by the disease, and it will intervene at the molecular and cellular level by correcting the hyperglycemic diabetic rats treated status because it has anti-diabetogenic property, insulin-like [25]. The relationship between DHC complications and pro status / maternal antioxidant in recent years was a journey of extensive research [26]. Our results have showed a highly significant decrease in hepatic reduced glutathione (GSH) in diabetic pregnant rats. It is ubiquitous tripeptide core network of the cellular antioxidant which includes a series of enzymatic systems scavengers, such as that of glutathione S-transferase (GST) [27]. The increase in total activity of hepatic GST in the untreated diabetic lot reflects the mobilization of an-

ti-radical defenses dependent GSH in response to intense oxidative stress, indicating that chronic hyperglycemia generalize the production of free radicals in the body. Supplementation of hesperidin partially restores the hepatic GSH levels while simultaneously attenuates hyperactivity S-transferase in the liver. What prompts us to consider our results as positive for the administration of flavonoids was largely due to a decrease in oxidative phenomena via mechanisms involving the interference of these polyphenols with GSH-dependent enzyme system [28]. In this sense, the antioxidant power of hesperidin has been evaluated in several scientific contexts in which it protected the liver mesenchymal against oxidative stress induced by toxic molecules [29].

5. Conclusion

The crucial problem is summarized in the fact that the induction of experimental diabetes mellitus streptozotocin causes complications and neurobehavioral disruption maternal plasma biochemical metabolism and causes a state of oxidative stress. The administration of hesperidin with a protective effect against anxiety and depressive disorders in rats Wistar diabetic. Treatment with hesperidin seems to restore the levels of maternal hepatic GSH; this suggests that it also has an antioxidant effect.

REFERENCE

1. Bresson,D.,von Herrath,M. (2007).Moving towards efficient therapies in type 1 diabetes : to combine or not to combine ? Autoimmunity Reviews.,6,315-322 | | 2. Oldroyd,J., Banerjee,M.,Heald, A. (2005). Diabetes and ethnic minorities. Postegrad Med J., 81,486-490. | | | 3. Omari, N., Dahmani-aït akli,Y., Labrousse.F and Hadj bekkouche , F .(2011). Influence of the streptozotocin on the corticotrope axis of the Wistar rat (Rattus norvegicus).,80,907- 938 | | 4. Calop,J., Limat,S and Frnandez,C.(2008). clinical pharmacology and therapeutic. Masson, Elsevier Masson, Paris. pp.417-427. | | 5. Portha, B.(1974). In: noninsulin-dependent diabetes mellitus. Dr Fatalis CR. Raynal AFP. Paris. | | 6. Bendayan,M., Malide,D and Ziv,E.(1995). Immuno-cytochemical investigation of insulin secretion by pancreatic beta-cells in control and diabetic sand rats (Psammomys obesus). J. Histochem. Cytochem., 43, 771-784. | | 7. Jin, H., Ogino, K., Fujioka,T., Yoshida, M and Ishimaru,K.(2008). new acylphloroglucinol glycocide from solidago altissima L.J Nat Med Apr .,62(2),199-201. | | 8. Bagchi,D., Garg, A., Krohn, R., Bagchi,M., Tran,M and Stohs,S. (1997). Oxygen free radical scavenging abilities of vitamins C and E, and a grape seed proanthocyanidin extract in vitro. Res Commun Mol Pathol Pharmacol., 95,179–90. | | 9. Kim, S. H., Hyun, S., H and Choung, S. Y. (2006). Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. Journal of Ethnopharmacology., 104(1–2) ,119–123. | | 10. Toumi, M.L., Merzoug, S., Boutefnouchet , A ., Tahraoui,A., Ouali, K and Guellati, M.A.(2009). Hesperidine, a natural citrus flavanone, alleviates hyperglycaemic state and attenuates embryopathies in pregnant diabetic mice. Journal of Medicinal Plans Research Vol. 3(11), pp. 862-869 | | 11. Frode, T.S and Medeiros, Y. S. (2008). Animal models o test drugs with potential antidiabetic activity Journal of Ethnopharmacology., 155 , 173-183. | | 12. Akbarzadeh, D., Norouzian,M., Mehrabi,R., Sh, Jamshidi., Farhangi,A., Allah Verdi,A., S. M. A. Mofidian and B. Lame Rad. (2007). Induction of diabetes by Streptozotocin in rats Indian J Clin Biochem., 22(2), 60–64. | | | 13. CS, Hall.(1934) Emotional behavior in the rat. J Comp Physical., 18, 385-403. | | 14. Sáenz, JCB., Villagro, OR and Trias, JF. (2006). Factor analysis of Forced Swimming test, Sucrose Preference test and Open Field test on enriched, social and isolated reared rats. Behav Brain Res., 169,57-65 | | 15. Ellman, G. L.(1959). Plasma antioxidants. Arch. Biochemistry and Biophyisics., 82, 70-77. | | 16. Habig , W H., Pabs, M J and Jacobi, W B.(1974). The first enzymatic step in mercapturic acid formation J Biol Chem., 249 , 137-143. | | 17. Bradford, M . (1979). A rapid and sensitive method for the quantification of microgram quantities of protein utilizing the principle of protein-dye binding Anal Biochemn.,72,248-254 | | 18. Sabu, M C., Smitha , K and Ramadasan, K.(2002). Anti-diabetic activity of green tea polyphenols and their role in reducing oxidative stress in experimental diabetes Journal of Ethnopharmacology., 83, 109-116 | | 19. Georg, P and Ludvik , B. (2000). Lipids and diabetes Journal of Clinical and Basic Cardiology., 3 ,159-162. | | 20. Aughsteen , A.A. (2000). Ultrastructural study on the effect of streptozotocin on the islets of Langerhans inmice J of Electron Microscopy., 49(5), 681-690. | | 21. Szkudelski , T and Szkudelska, K.(2002). Streptozotocin induces lipolysis in rat adiposytes in vitro. Phys Res., 51, 255-259. | | 22. Chen, V and Ianuzza, CD.(1981). Dosage effect of streptozotocin on rat tissue enzyme activities and glycogen concentration. Can J Physiol Pharmacol., 60, 1251-1256. | | 23. Davidoff ,AJ., Davidson, MB ., Carmody , MW., David, ME and Ren, J.(2004). Diabetic cardiomyocyte dysfonction and myocyte insulin resistance : role of glucose-induced PKC activity. Molecular and Cellular Biochemistry., 262, 155-163. | | 24. Wuarin-Bierman, L., Zahnd, GR ., Kaufman, F., Burcklen,L ., Adler, J ., hyperalgesia in spontaneous and experimental animal models of diabetic neuropathy. | | 25. Akiyama, S., Katsumata, S ., Suzuki, K., Ishimi,Y ., Wu,J and Uehara, M. (2010). Dietary hesperidin exerts hypoglycemic and hypolipidimic effects in streptozotocin-induced marginal type 1 diabetic rats. J Clin Biochem Nutr., 46 (1), 87-92 | | 26. Valko, M., Leibfritz, D., Moncola, J., Cronin, M .T. D ., Mazura, M and Telser, J. (2007). Free radicals and antioxidant in normal physiological functions and human disease The International Journal of Biochemistry & Cell Biology., 39, 44-84 | | 27. Abidi, P., Aaqq ,F., Arif, J .M., Lohani, M and Rahman, Q.(1999). Chrysotile-mediated imbalance in the glutathione redox system in the developement of pulmonary injury Toxicol Lett., 106, 31-39 | | 28. Dastmalchi, K ., Dormana, H. J. D ., Oinonena,P.P ., Darwis, Y ., Laakso, I and Hiltunen, R . (2008). Chemical composition and in vitro antioxidative activity of lemon balm(Melissa officinalis L) extract LWT., 41, 391-400 | | 29. Tirkey, N., Pilkhwal, S., Kuhad, A and Chopra, K. (2005). Hesperidin, a citrus bioflavonoid, decreases the oxidative stress produced by carbon tetrachloride in rat liver and kidney BMC Pharmacol., 5(1) , 2 |