

The effect of *Carum carvi* oil on the level of heat shock proteins 70 and 72 in the liver and skeletal muscle tissues in diabetic rats

Faranak Moradi¹, Nasrin Kazemipour², Foad Noorbakhsh³ and Saeed Nazifi^{4*}

¹ MSc Student of Biochemistry, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

² Associate Professor, Department of Basic Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

³ Assistant Professor, Department of Basic Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

⁴ Professor, Department of Clinical Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran

Received: 25.03.2021

Accepted: 31.07.2021

Abstract

The metabolic abnormalities of diabetes lead to superoxide overproduction in vessels and myocardium resulting in diabetes complications. *Carum carvi* oil probably reduces oxidative stress and increases heat shock protein by hypoglycemic, hypolipidemic, and antioxidant effects. We aimed to study the effect of *Carum carvi* oil on HSP in the liver and skeletal muscle in diabetic rats. 50 male Sprague Dawley rats were randomly divided into 5 groups (control, drug control, drug carrier negative control, negative control, and treatment). Diabetes was induced in the negative controls and treatment groups with streptozotocin (40mg/kg body weight, single dose, IP). Control and negative control groups did not receive any therapy but treatment and drug control rats were gavaged with 10 mg/kg of *Carum carvi* oil daily during 30 days of the study. The weight of rats was measured on 3,7,21,30 days and fasting blood sugar was measured on 3 and 30 days. The liver and skeletal muscle tissues were removed at the end of the experiment. The level of HSP 70 and 72 was determined by an ELISA kit. The findings of HSP measurement demonstrated an increase in level of these protein in the treatment group but in the drug carrier negative control and negative control groups. HSP was decreased significantly due to the injection of STZ. Our results showed that the compounds in this oil (*Carum carvi*) can increase the concentration of HSP 70 and 72 in the liver and skeletal muscle tissues.

Key words: Diabetes mellitus, *Carum carvi* oil, Heat shock proteins 72 and 70, Liver, Skeletal muscle

* Corresponding Author: Saeed Nazifi, Clinical Pathology Division, Department of Clinical Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran, E-mail: nazifi@shirazu.ac.ir



© 2020 by the authors. Licensee SCU, Ahvaz, Iran. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0 license) (<http://creativecommons.org/licenses/by-nc/4.0/>).

References

- Adeyemi, D. O., Ukwanya, V. O., Obuotor, E. M., Adewole, S. O. 2014. Anti-hepatotoxic activities of *Hibiscus sabdariffa* L. in animal model of streptozotocin diabetes-induced liver damage. BMC Complementary and Alternative Medicine 14(1), 277.
- American Diabetes Association. 2018. Classification and diagnosis of diabetes: standards of medical care in diabetes. Diabetes Care, 41(Supplement 1), S13-S27.
- Atalay, M., Oksala, N. K., Laaksonen, D. E., Khanna, S., Nakao, C., Lappalainen, J., Sen, C. K. 2004. Exercise training modulates heat shock protein response in diabetic rats. Journal of Applied Physiology 97(2), 605-611
- Atalay, M., Oksala, N., Lappalainen, J., Laaksonen, D. E., Sen, C. K., Roy, S. 2009. Heat shock proteins in diabetes and wound healing. Current Protein and Peptide Science 10(1), 85-95.
- Awasthi, N., Wagner, B. J. 2005. Upregulation of heat shock protein expression by proteasome inhibition: an antiapoptotic mechanism in the lens. Investigative Ophthalmology and Visual Science 46(6), 2082-2091.
- Bamosa, A. O., Kaatabi, H., Lebdaa, F. M., Elq, A., Al-Sultant, A. 2010. Effect of *Nigella sativa* seeds on the glycemic control of patients with type 2 diabetes mellitus. Indian Journal of Physiology and Pharmacology 54(4), 344-354.
- Baynes, J. W. 1991. Role of oxidative stress in development of complications in diabetes. Diabetes 40(4), 405-412.
- Bellini, S., Barutta, F., Mastrocola, R., Imperatore, L., Bruno, G., Gruden, G. 2017. Heat shock proteins in vascular diabetic complications: review and future perspective. International Journal of Molecular Sciences 18(12), 2709.
- Bitar, M. S., Farook, T., John, B., Francis, I. M. 1999. Heat-shock protein 72/73 and impaired wound healing in diabetic and hypercortisolemic states. Surgery 125(6), 594-601.
- Borcea, V., Nourooz-Zadeh, J., Wolff, S. P., Klevesath, M., Hofmann, M., Urich, H., Halliwell, B. 1999. α -Lipoic acid decreases oxidative stress even in diabetic patients with poor glycemic control and albuminuria. Free Radical Biology and Medicine 26(11-12), 1495-1500.
- Bruce, C.R., Carey, A.L., Hawley, J.A., Febbraio, M.A., 2003. Intramuscular heat shock protein 72 and heme oxygenase-1 mRNA are reduced in patients with type 2 diabetes: evidence that insulin resistance is associated with a disturbed antioxidant defense mechanism. Diabetes 52, 2338-2345.
- Craig, E. A., Gross, C. A. 1991. Is HSP70 the cellular thermometer? Trends in Biochemical Sciences 16, 135-140.
- Delogu, G., Bosco, L. L., Marandola, M., Famularo, G., Lenti, L., Ippoliti, F., Signore, L. 1997. Heat shock protein (HSP70) expression in septic patients. Journal of Critical Care 12(4), 188-192.
- Dhandapani, S., Subramanian, V. R., Rajagopal, S., Namasivayam, N. 2002. Hypolipidemic effect of *Cuminum cyminum* L. on alloxan-induced diabetic rats. Pharmacological Research 46(3), 251-255.
- Eddouks, M., Lemhadri, A., Michel, J. B. 2004. Caraway and caper: potential anti-hyperglycaemic plants in diabetic rats. Journal of Ethnopharmacology 94(1), 143-148.
- Ene, A., Bukbuk, D., Ogunmola, O. 2006. Effect of different doses of black caraway (*Carum carvi* L.) oil on the levels of serum creatinine in alloxan induced diabetic rats. Journal of Medical Sciences 6, 701-703.
- Furman, B. L. 2015. Streptozotocin-induced diabetic models in mice and rats. Current Protocols in Pharmacology 70(1), 5.47. 41-45.47. 20.
- Iacobellis, N. S., Lo Cantore, P., Capasso, F., Senatore, F. 2005. Antibacterial activity of *Cuminum cyminum* L. and *Carum carvi* L. essential oils. Journal of Agricultural and Food Chemistry 53(1), 57-61.
- Haidari, F., Seyed-Sadjadi, N., Taha-Jalali, M., Mohammed-Shahi, M. 2011. The effect of oral administration of *Carum carvi* on weight, serum glucose, and lipid profile in streptozotocin-induced diabetic rats. Saudi Medical Journal 32(7), 695-700.
- Hooper, P. L., Balogh, G., Rivas, E., Kavanagh, K., Vigh, L. 2014. The importance of the cellular stress response in the pathogenesis and treatment of type 2 diabetes. Cell Stress and Chaperones 19(4), 447-464.
- Hooper, P. L., Hooper, P. L. 2009. Inflammation, heat shock proteins, and type 2 diabetes. Cell Stress and Chaperones 14(2), 113-115.
- Hunter-Lavin, C., Hudson, P. R., Mukherjee, S., Davies, G. K., Williams, C. P., Harvey, J. N., Williams, J. H. 2004. Folate supplementation reduces serum HSP70 levels in patients with type 2 diabetes. Cell Stress & Chaperones 9(4), 344.

- Jafarnejad, A., Bathaie, S., Nakhjavani, M., Hassan, M., Banasadegh, S. 2008. The improvement effect of L-Lys as a chemical chaperone on STZ-induced diabetic rats, protein structure and function. *Diabetes/Metabolism Research and Reviews* 24(1), 64-73.
- Johri, R. 2011. *Cuminum cyminum* and *Carum carvi*: An update. *Pharmacognosy Reviews* 5(9), 63.
- Kiang, J. G., Tsokos, G. C. 1998. Heat shock protein 70 kDa: molecular biology, biochemistry, and physiology. *Pharmacology & Therapeutics* 80(2), 183-201.
- Kilgore, J. L., Musch, T. I., Ross, C. R. 1998. Physical activity, muscle, and the HSP70 response. *Canadian Journal of Applied Physiology* 23(3), 245-260.
- Kim, J. J., Choi, J., Lee, M. K., Kang, K. Y., Paik, M. J., Jo, S. K., Yee, S. T. 2014. Immunomodulatory and antidiabetic effects of a new herbal preparation (HemoHIM) on streptozotocin-induced diabetic mice. *Evidence-based Complementary and Alternative Medicine* 2014. Article ID 461685.
- Kumar, P., Singh, D. 2006. Molluscicidal activity of *Ferula asafoetida*, *Syzygium aromaticum* and *Carum carvi* and their active components against the snail *Lymnaea acuminata*. *Chemosphere* 63(9), 1568-1574.
- Kurucz, I., Morva, A., Vaag, A., Eriksson, K.-F., Huang, X., Groop, L., Koranyi, L. 2002. Decreased expression of heat shock protein 72 in skeletal muscle of patients with type 2 diabetes correlates with insulin resistance. *Diabetes* 51(4), 1102-1109.
- Macdonald, J. R., Bächinger, H. P. 2001. HSP47 binds cooperatively to triple helical type I collagen but has little effect on the thermal stability or rate of refolding. *Journal of Biological Chemistry* 276(27), 25399-25403.
- Madrigal-Matute, J., Martin-Ventura, J. L., Blanco-Colio, L. M., Egido, J., Michel, J. B., Meilhac, O. 2011. Heat-shock proteins in cardiovascular disease. *Advances in Clinical Chemistry* (54), 1-43.
- Misra, H., Soni, M., Silawat, N., Mehta, D., Mehta, B., Jain, D. 2011. Antidiabetic activity of medium-polar extract from the leaves of *Stevia rebaudiana* Bert. (Bertoni) on alloxan-induced diabetic rats. *Journal of Pharmacy and Bioallied Sciences* 3(2), 242.
- Modu, S., Gohla, K., Umar, I.A. 1997. Effect of black caraway oil on some Biochemical parameters in alloxan-induced diabetic rats. *International Journal of Biochemistry* 9, 28-36.
- Najda, A., Dyduch, J., & Brzozowski, N. 2008. Flavonoid content and antioxidant activity of caraway roots (*Carum carvi* L.). *Vegetable Crops Research Bulletin* 68, 127-133.
- Njemini, R., Demanet, C., Mets, T. 2004. Inflammatory status as an important determinant of heat shock protein 70 serum concentrations during aging. *Biogerontology* 5(1), 31-38.
- Oglesbee , M.J., Herdman, A. V., Passmore, G. G., Hoffman W.H. 2005. Diabetic ketoacidosis increases extracellular levels of the major inducible 70-kDa heat shock protein. *Clinical Biochemistry* 38, 900-904.
- Pockley, A. G. 2003. Heat shock proteins as regulators of the immune response. *The Lancet* 362(9382), 469-476.
- Porte, D., Kahn, S. E. 1991. Mechanisms for hyperglycemia in type II diabetes mellitus: therapeutic implications for sulfonylurea treatment—an update. *The American Journal of Medicine* 90(6), S8-S14.
- Shemshian, M., Mousavi, S. H., Norouzy, A., Kermani, T., Moghiman, T., Sadeghi, A., Ferns, G. A. 2014. Saffron in metabolic syndrome: its effects on antibody titers to heat-shock proteins 27, 60, 65 and 70. *Journal of Complementary and Integrative Medicine* 11(1), 43-49.
- Shirwaikar, A., Rajendran, K., Kumar, C. D., Bodla, R. 2004. Antidiabetic activity of aqueous leaf extract of *Annona squamosa* in streptozotocin-nicotinamide type 2 diabetic rats. *Journal of Ethnopharmacology* 91(1), 171-175.
- Simic A, Rancic A, Sokovic M.D. 2008. Essential oil composition of *Cymbopogon winterianus* and *Carum icarvi* and their antimicrobial activities. *Pharmaceutical Biology* 46: 437-441.
- Spruce, M.C., Potter, J and Coppini D.V. 2003. The pathogenesis and management of painful diabetic neuropathy: a review. *Diabetic Medicine* 20:88-98.
- Strokov, I., Manukhina, E., Bakhtina, L. Y., Malyshev, I. Y., Zoloev, G., Kazikhanova, S., Ametov, A. 2000. The function of endogenous protective systems in patients with insulin-dependent diabetes mellitus and polyneuropathy: effect of antioxidant therapy. *Bulletin of Experimental Biology and Medicine* 130(10), 986-990.
- Su, H. C., Hung, L. M., Chen, J.-K. 2006. Resveratrol, a red wine antioxidant, possesses an insulin-like effect in streptozotocin-induced diabetic rats. *American Journal of Physiology-Endocrinology and Metabolism* 290(6), E1339-E1346.
- Uusitupa, M. I., Mustonen, J. N., Juhani Airaksinen, K. 1990. Diabetic heart muscle disease. *Annals of Medicine* 22(6), 377-386.

- Zheng, G. q., Kenney, P. M., Lam, L. K. 1992. Anethofuran, carvone, and limonene: potential cancer chemoprotective agents from dill weed oil and caraway oil. *Planta Medica* 58(04), 338-341.
- Zilaee, M., Kermany, T., Tavalaee, S., Salehi, M., Ghayour-Mobarhan, M., Ferns, G. A. 2014. Barberry treatment reduces serum anti-heat shock protein 27 and 60 antibody titers and high-sensitivity c-reactive protein in patients with metabolic syndrome: A double-blind, randomized placebo-controlled trial. *Phytotherapy Research* 28(8), 1211-1215.