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Oral Quercetin Supplementation Lowers Plasma sICAM-1 Concentrations in Female db/db Mice

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Author(s)

Silvia Wein, Eva Schrader, Gerald Rimbach, Siegfried Wolffram

ABSTRACT

Background: Flavonoids are documented for their potential anti-adipogenic, anti-inflammatory and anti-diabetic effects. Quercetin, one of the most abundant flavonoids in edible plants, was investigated for these effects in a diabetic mouse model (db/db, leptin receptor mutation) exerting early relevant clinical signs of non-insulin dependent diabetes mellitus, such as hyperglycemia, hyperinsulinemia, hypertriglyceridemia, hypoadiponectinemia and obesity. Materials & Methods: Female db/db mice (n = 24) were fed a flavonoid-poor maintenance diet without (C) or with the addition of quercetin (0.3 g/kg diet, Q) or rosiglitazone (4 mg/kg diet, TZD). Food and water were freely available during the 4 week feeding period. Thereafter, blood samples (fasted) were analyzed for glucose, insulin, triacylglycerols, non-esterified fatty acids, cholesterol, adiponectin and soluble intercellular adhesion molecule-1 (sICAM-1). Adiponectin mRNA levels were measured in adipose tissue. Furthermore, sICAM-1 release was investigated using tumor necrosis factor alpha stimulated EAhy926 cells. Results: Only TZD treatment reduced fasted plasma glucose, triacylglycerols and cholesterol and increased plasma adiponectin concentrations compared to groups C and Q. Adiponectin mRNA levels after quercetin treatment were not different from TZD-treatment or controls. Only quercetin treatment reduced sICAM-1 release *in vitro* and *in vivo*. Conclusions: Quercetin effectively reduced sICAM-1 release in the progressive diabetic state, revealing its anti-inflammatory potential *in vivo*.

KEYWORDS

Quercetin; Inflammation; Insulin Resistance; Obesity; Adiponectin

Cite this paper

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References

[1] V. Vachharajani and D. N. Granger, "Adipose Tissue: A Motor for the Inflammation Associated with Obesity," IUBMB Life, Vol. 61, No. 4, 2009, pp. 424-430. doi:10.1002/iub.169

[2] H. K. Vincent and A. G. Taylor, "Biomarkers and Potential Mechanisms of Obesity-Induced Oxidant Stress in Humans," International Journal of Obesity, Vol. 30, No. 3, 2006, pp. 400-418. doi:10.1038/sj.ijo.0803177

[3] J. Spranger, A. Kroke, M. Mohlig, M. M. Bergmann, M. Ristow, H. Boeing and A. F. Pfeiffer, "Adiponectin and Protection against Type 2 Diabetes Mellitus," Lancet, Vol. 361, No. 9353, 2003, pp. 226-228. doi:10.1016/S0140-6736(03)12255-6

[4] P. Dandona, A. Aljada and A. Bandyopadhyay, "Inflammation: The Link between Insulin Resistance, Obesity and Diabetes," Trends in Immunology, Vol. 25, No. 1, 2004, pp. 4-7. doi:10.1016/j.it.2003.10.013

[5] J. Constans and C. Conri, "Circulating Markers of Endothelial Function in Cardiovascular Disease," Clinica Chimica Acta, Vol. 368, No. 1-2, 2006, pp. 33-47. doi:10.1016/j.cca.2005.12.030

[6] A. J. H. Gearing, I. Hemingway, R. Pigott, J. Hughes, A. J. Rees and S. J. Cashman, "Soluble Forms of

Vascular Adhesion Molecules, E-Selectin, ICAM-1, and VCAM-1— Pathological Significance," Annals of the New York Academy of Sciences, Vol. 667, No. 1, 1992, pp. 324-331. doi:10.1111/j.1749-6632.1992.tb51633.x

[7] E. Hu, P. Liang and B. M. Spiegelman, "AdipoQ Is a Novel Adipose-Specific Gene Dysregulated in Obesity," Journal of Biological Chemistry, Vol. 271, No. 18, 1996, pp. 10697-10703. doi:10.1074/jbc.271.18.10697

[8] N. Maeda, M. Takahashi, T. Funahashi, S. Kihara, H. Nishizawa, K. Kishida, H. Nagaretani, M. Matsuda, R. Komuro, N. Ouchi, H. Kuriyama, K. Hotta, T. Nakamura, I. Shimomura and Y. Matsuzawa, "PPARgamma Ligands Increase Expression and Plasma Concentrations of Adi-ponectin, an Adipose-Derived Protein," Diabetes, Vol. 50, No. 9, 2001, pp. 2094-2099. doi:10.2337/diabetes.50.9.2094

[9] L. P. Qiao, P. S. MacLean, J. Schaack, D. J. Orlicky, C. Darimont, M. Pagliassotti, J. E. Friedman and J. H. Shao, "C/EBPa Regulates Human Adipo-nectin Gene Transcription through an Intronic Enhancer," Diabetes, Vol. 54, No. 6, 2005, pp. 1744-1754. doi:10.2337/diabetes.54.6.1744

[10] M. Guerre-Millo, "Adiponectin: An Update," Diabetes & Metabolism, Vol. 34, No. 1, 2008, pp. 12-18. doi:10.1016/j.diabet.2007.08.002

[11] Z. Bagi, A. Koller and G. Kaley, "PPAR{gamma} Activation, by Reducing Oxidative Stress, Increases NO Bioavailability in Coronary Arterioles of Mice with Type 2 Diabetes," AJP—Heart and Circulatory Physiology, Vol. 286, No. 2, 2004, pp. H742-H748.

[12] C. R. Benton, G. P. Holloway, S. E. Campbell, Y. Yoshida, N. N. Tandon, J. F. C. Glatz, J. J. J. F. Luiken, L. L. Spriet and A. Bonen, "Rosiglitazone Increases Fatty Acid Oxidation and Fatty Acid Translocase (FAT/CD36) but Not Carnitine Palmitoyltransferase I in Rat Muscle Mitochondria," Journal of Physiology-London, Vol. 586, No. 6, 2008, pp. 1755-1766. doi:10.1113/jphysiol.2007.146563

[13] J. Wilding, "Thiazoli-dinediones, Insulin Resistance and Obesity: Finding a Balance," International Journal of Clinical Practice, Vol. 60, No. 10, 2006, pp. 1272-1280. doi:10.1111/j.1742-1241.2006.01128.x

[14] R. M. Viner, Y. Hsia, T. Tomsic and I. C. K. Wong, "Efficacy and Safety of Anti-Obesity Drugs in Children and Adolescents: Systematic Review and Meta-Analysis," Obesity Reviews, Vol. 11, No. 8, 2010, pp. 593-602. doi:10.1111/j.1467-789X.2009.00651.x

[15] J. Kennedy, "Herb and Supplement Use in the US Adult Population," Clinical Therapeutics, Vol. 27, No. 11, 2005, pp. 1847-1858. doi:10.1016/j.clinthera.2005.11.004

[16] E. Middleton, C. Kandaswami and T. C. Theoharides, "The Effects of Plant Flavonoids on Mammalian Cells: Implications for Inflammation, Heart Disease, and Cancer," Pharmacological Reviews, Vol. 52, No. 4, 2000, pp. 673-751.

[17] G. Williamson and C. Manach,. "Bioavailability and Bioefficacy of Polyphenols in Humans. II. Review of 93 Intervention Studies," American Journal of Clinical Nutrition, Vol. 81, Suppl. 1, 2005, pp. 243S-255S.

[18] O. Kwon, P. Eck, S. Chen, C. P. Corpe, J. H. Lee, M. Kruhlak and M. Levine, "Inhibition of the Intestinal Glucose Transporter GLUT2 by Flavonoids," FASEB Journal, Vol. 21, No. 2, 2007, pp. 366-377. doi:10.1096/fj.06-6620com

[19] X. K. Fang, J. Gao and D. N. Zhu, "Kaempferol and Quercetin Isolated from Euonymus alatus Improve Glucose Uptake of 3T3-L1 Cells without Adipo-genesis Activity," Life Sciences, Vol. 82, No. 11-12, 2008, pp. 615-622. doi:10.1016/j.lfs.2007.12.021

[20] Y. Kumazawa, K. Kawaguchi and H. Takimoto, "Immunomodulating Effects of Flavonoids on Acute and Chronic Inflammatory Responses Caused by Tumor Necrosis Factor Alpha," Current Pharmaceutical Design, Vol. 12, No. 32, 2006, pp. 4271-4279. doi:10.2174/138161206778743565

[21] S. Wein, N. Behm, R. K. Petersen, K. Kristiansen and S. Wolffram, "Quercetin Enhances Adiponectin Secretion by a PPAR-Gamma Independent Mechanism," European Journal of Pharmaceutical Sciences, Vol. 41, No. 1, 2010, pp. 16-22. doi:10.1016/j.ejps.2010.05.004

[22] B. A. Graf, P. E. Milbury and J. B. Blumberg, "Flavonols, Flavones, Flavanones, and Human Health: Epidemiological Evidence," Journal of Medicinal Food, Vol. 8, No. 3, 2005, pp. 281-290. doi:10.1089/jmf.2005.8.281

[23] P. R. Johnson, M. R. C. Greenwood, B. A. Horwitz and J. S. Stern, "Animal-Models of Obesity—Genetic-Aspects," Annual Review of Nutrition, Vol. 11, 1991, pp. 325-353.

doi:10.1146/annurev.nu.11.070191.001545

[24] C. J. Edgell, C. C. McDonald and J. B. Graham, "Permanent Cell Line Ex-pressing Human Factor VIII-Related Antigen Established by Hybridization," Proceedings of the National Academy of Sciences of the USA, Vol. 80, No. 12, 1983, pp. 3734-3737. doi:10.1073/pnas.80.12.3734

[25] K. Srinivasan and P. Rama-rao, "Animal Models in Type 2 Diabetes Research: An Overview," Indian Journal of Medical Research, Vol. 125, No. 3, 2007, pp. 451-472.

[26] J. Ahn, H. Lee, S. Kim, J. Park and T. Ha, "The Anti-Obesity Effect of Quercetin Is Mediated by the AMPK and MAPK Signaling Pathways," Biochemical and Bio-physical Research Communications, Vol. 373, No. 4, 2008, pp. 545-549. doi:10.1016/j.bbrc.2008.06.077

[27] P. J. Chien, Y. C. Chen, S. C. Lu and F. Sheu, "Dietary Flavonoids Suppress Adipogenesis in 3T3-L1 Preadipocytes," Journal of Food and Drug Analysis, Vol. 13, No. 2, 2005, pp. 168-175.

[28] M. Kobori, S. Masumoto, Y. Akimoto and H. Oike, "Chronic Dietary Intake of Quercetin Alleviates Hepatic Fat Accumulation Associated with Consumption of a Western-Style Diet in C57/BL6J Mice," Molecular Nutrition & Food Research, Vol. 55, No. 4, 2011, pp. 530-540. doi:10.1002/mnfr.201000392

[29] L. Rivera, R. Moron, M. Sanchez, A. Zarzuelo and M. Galisteo, "Quercetin Ameliorates Metabolic Syndrome and Improves the Inflammatory Status in Obese Zucker Rats," Obesity, Vol. 16, No. 9, 2008, pp. 2081-2087. doi:10.1038/oby.2008.315

[30] J. Barrenetxe, P. Aranguren, A. Grijalba, J. M. MartinezPenuela, F. Marzo and E. Urdaneta, "Effect of Dietary Quercetin and Sphingomyelin on Intestinal Nutrient Absorption and Animal Growth," British Journal of Nutrition, Vol. 95, No. 3, 2006, pp. 455-461. doi:10.1079/BJN20051651

[31] T. Mahesh and V. P. Menon, "Quercetin Allievates Oxidative Stress in Streptozotocin-Induced Diabetic Rats," Phytotherapy Research, Vol. 18, No. 2, 2004, pp. 123-127. doi:10.1002/ptr.1374

[32] A. K. Shetty, R. Rashmi, M. G. R Rajan, K. Sambaia and P. V. Salimath, "Antidiabetic Influence of Quercetin in Streptozotocin-Induced Diabetic Rats," Nutrition Research, Vol. 24, No. 5, 2004, pp. 373-381.

[33] J. K. Dunnick and J. R. Hailey, "Toxicity and Carcinogenicity Studies of Quercetin, a Natural Component of Foods," Funda-mental and Applied Toxicology, Vol. 19, No. 3, 1992, pp. 423-431. doi:10.1016/0272-0590(92)90181-G

[34] J. Wilding, "Thiazolidinediones, Insulin Resistance and Obesity: Finding a Balance," International Journal of Clinical Practice, Vol. 60, No. 10, 2006, pp. 1272-1280. doi:10.1111/j.1742-1241.2006.01128.x