



AMELORATION OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)/NON-ALCOHOLIC STEATOHEPATITIS (NASH) BY CHICORY SEED EXTRACT VIA MODULATION OF PPARa AND **SREBP-1**

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Chicory (Cichorium intybus L.) is known for having antidiabetic and lipid lowering effects [1]. We evaluated the effect of chicory seed extract (CI) on hepatic steatosis induced by BSA-oleic acid complex (OA) in HepG2 cells (in vitro) [2] and by early and late stage diabetes in rats (in vivo). Different dosages of CI (1.25, 2.5 and 5 mg/ml) were applied along with OA (1mM) to HepG2 cells, simultaneously and nonsimultaneously, and without OA to ordinary non-steatotic cells. Cellular lipid accumulation and glycerol release were measured, and the expression levels of sterol regulatory element-binding protein-1c (SREBP-1c) and peroxisome proliferatoractivated receptor alpha (PPAR α) were determined. Liver samples, from our previous study [3], were stained with Hematoxylin and Eosin (H&E). Significant histological damage (steatosis-inflammation-fibrosis) to cells and tissues and down-regulation of SREBP-1c and PPAR α genes that accrued from steatosis induction were prevented by CI in simultaneous treatment. In non-simultaneous treatment, CI up-regulated the expression of both genes to restored normal levels of the corresponding protein. However, CI seemed to act as a PPARa agonist as its stimulating effect on PPARa was more noticeable [4, 5]. CI released glycerol from HepG2 cells, and seemed to target the first and second hit phases of hepatic steatosis. A preliminary attempt to characterize CI showed caffeic acid, chlorogenic acid, and chicoric acid, among the constituents [6].

References

[1] Kim, M.; Shin, H. K. J. Nutr. 1998, 128, 1731-1736.

[2] Cui, W.; Chen, S. L.; Hu, K. Q. Am. J. Transl. Res. 2009, 2, 95-104.

[3] Ghamarian, A.; Abdollahi, M.; Su, X.; Amiri, A.; Ahadi, A.; Nowrouzi, A. DARU 2012, 20, 56.

[4] Oosterveer, M. H.; Grefhorst, A;, van Dijk, T.H.; Havinga, R.; Staels, B.; Kuipers,

F.; Groen, A. K.; Reijngoud, D. J. J. Biol. Chem. 2009, 284, 34036-34044.

[5] Llorach, R.; Tomas-Barberan, F.A.; Ferreres, F. J. Agric. Food. Chem. 2004, 52, 5109-5116.