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# Effects of Anti-obesity dietary supplement Dehydroepiandrosterone (DHEA) treatment on Serum methylation and oxidative stress biomarkers in DMBA-Induced Mammary Tumor Obese Zucker Rat Model

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## Abstract

Obesity has been epidemic in the US for over two decades and capable significantly affects the metabolic profile in animals and humans. As we reported earlier, obese rats have a significantly lower level of S-adenosylmethionine (SAM) in serum, a universal methyl group donor, and lower methylation ratio compare to lean animals. Also obesity has been linked with the risk of development of various cancers, including breast cancer. Dehydroepiandrosterone (DHEA) is an over-the-counter dietary supplement used as an anti-cancer agent and anti-obesity supplement. The objectives of this study were to investigate the long-term effects of DHEA treatment on serum concentration of methylation cycle and oxidative stress metabolites using 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumor model. Twenty (20) six-week-old obese female Zucker rats were used. Rats were randomly assigned and had *ad libitum* access to water and a diet of either chow (2016) as a control diet or chow with the addition of DHEA at a concentration of 6 g/kg of chow as a DHEA diet. All rats were orally gavaged at age 50 days with 65 mg DMBA/kg body weight and were sacrificed 155 days post-DMBA treatment and serums were collected. Serum concentration of SAM, Methionine, S-adenosylhomocysteine (SAH), reduced glutathione (GSH), oxidized glutathione (GSSG) and Cysteine were measured by HPLC method with electrochemical detection or LC-MS method. Obese rats fed the DHEA diet gained significantly less weight ($P<0.001$) than control fed rats. Fifty-five percent (55%) of the control diet group developed mammary tumors, while no tumors were detected in the DHEA diet group ($P<0.001$), despite control rats had significantly higher ($P<0.02$) GSH/GSSG ratio, known as “oxidative ratio”, and significantly ($P<0.001$) higher SAM/SAH ratio, known as “methylation ratio” compare to DHEA diet group. Serum concentration of methionine ($P<0.02$) and cysteine ($P<0.002$) were significantly lower in control group compare to DHEA diet group. Our results suggest that DHEA treatment can reduce body weight gain andtumors formation what is accompanied by increase in serum concentration of methionine and cysteine two critical amino acids involved in initiation of synthesis of methyl group donor (SAM) and antioxidative capacity (GSH). Lower methylation and oxidative ratios that we observed in DHEA diet group possibly reflect much higher turnover of GSH, GSSG, SAM and SAH in this group compare to control. Supported by ABI to RH.

## Biography

Reza Hakkak, Ph.D., is nutritionist and Professor and Chairman of the Department of Dietetics and Nutrition in the College of Health Professions, Professor of Pediatrics in the College of Medicine, and Professor of Department of Health Policy and Management in the College of Public Health at the University of Arkansas for Medical Sciences. Dr. Hakkak’s research includes Nutritional toxicology, Influence of diet and nutrition on cancer prevention or promotion, Obesity and Breast Cancer prevention or promotion, Animal modeling for Cancer Research. For past several years, his research interests have focused on links between obesity and breast cancer prevention or promotion. Dr. Hakkak has published more than 40 research articles and more than 150 abstracts and presentations.