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EFFECTOF β-3 AGONIST, BRL 35 135, AND DIETARY FATS ON THEACCUMULATIONOF FATSIN RAT BODY FED WITH DIFFERENTDIETARY LIPIDS

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Background:

High prevalence of some fat-related metabolic, nutritional and endocrine diseases, such as obesity, diabetes, and some cardiovascular diseases has motivated many researchers to manipulate lipid metabolism with the hope of reducing excess fat accumulation in the body. Lipolysis must be one of the potential ways. Fat storage, mainly as triglycerides, in the body, is broken down through the lipolysis to fulfill the energy requirements. There are several mechanisms controlling lipolysis. Adrenergic system, especially β-adrenergic, is one of them. It has been believed that β-adrenergic receptors, mainly β-1, is involved in body thermogenesis. Currently, it is believed that another β-receptor, so-called β-3, is also involved in fat metabolism through the induction of lipolysis. Stimulation of β-3 adrenoceptors by using newly developed specific β-3 agonists, such as BRL 35 135 has induced lipolysis, both in vivo in rats and in vitro in adipocyte cell culture. On the other hand, the effects of different types of dietary lipids, specially animal fats, on health is considered recently. There are a lot of researches, some of them with controversial results regarding the effects of different dietary lipids on health. It has been observed that different dietary lipids show different pattern in fat accumulation in animal body. Some studies indicate that such difference is possibly due to interactions of lipids with β-adrenergic lipolytic activities. In addition it has been suggested that dietary lipids change the chemical composition of cell membrane, resulting in the alteration of the structure and fluidity of membrane. Then, such alteration affect adrenoceptor activity (For details refer to Fotovati A.& T. Ito, 1998).

Objective:

Previous studies of authors have shown some patterns of distribution and metabolism of different dietary intaked lipids rich in saturated fatty acid (SFA), polyunsaturated fatty acid (PUFA) and monounsaturated fatty acid (MUFA) in rats body. In this study, the possible interactions between the β-adrenergic activity and different dietary lipids have been studied by adding a specific β-3-agonist, BRL 35 135, in rats diets containing 4 different dietary lipids of animal and plant origins.

Materials and Methods:

Forty 7-weeks old male SD rats(purchased from Seac Co. Ltd., Japan) were raised on commercial diet for one week for adaptation. Then, they were divided into 2 groups, i.e. one group was fed agonist-free diets as control and the other, fed diets containing β-3 agonists; BRL 35135 {R*,R*-methyl-4-[2-[2-hydroxy-2-(3-chlorophenyl)methylamino]-propyl]-phenoxyacetate hydrobromide; developed and kindly donated by SmithKline Beecham Co.}. The pro-drug was dosed at 0.5 mg/kg body weight/day. Each group was further divided into 4 sub-groups fed diets containing 4 different fats; 12% of beef tallow, canola oil, olive oil or safflower oil. Other ingredients were the same for the four groups: 20% beef powder, 1% AIN-76 vitamin mixture, 3.5% AIN-76 mineral mixture, 0.3% DL-methionine, 0.2% choline bitartrate, 5% cellulose, 27.9% corn starch, 30% sucrose, 0.1% cholesterol. In beef tallow diet, 0.03% alpha-tocopherol (wt/wt) was added to beef tallow itself before mixing with other ingredients, as an antioxidant. All rats have been raised on these diets and under controlled condition (12 hr light/day, 20C temperature and 60% relative humidity) for 8 weeks in separated cages in animal raising facilities of Biotron Institute of Kyushu University. Weight gain and feed intake were measured every other day. Feces out-put was also measured weekly throughout the study. After eight weeks raising, the rats after anesthetization with ethyl ether were killed (carried out under the control of guideline for Animal Experiment in Faculty of Agriculture and the Graduate Course, Kyushu University and the Law[No.105]and Notification[No.6]of the Government)and their abdominal fat mass and liver were dissected out and weighted. Fat content of collected samples was extracted by Folch's method and their fatty acid composition was analyzed by gas chromatography (GC-14B, GAS CHROMATOGRAPH, SHIMADZU Co. Ltd., Japan)

Results:

There was no significant difference in daily feed intake between agonist-intaked and control rats in all dietary sub-groups. Daily weight gain was significantly lower in BRL35135-intaked (2.72 g/d) rats of canola sub-group compared to the control (4.52 g/d) rats of given sub-group ($P<0.05$). Daily feces out-put was lower in agonist-intaked rats than control, but the difference was not statistically significant. Amount of abdominal fat in BRL 35 135-intaked rats was significantly lower than control in all dietary sub-rats except beef tallow ($P<0.05$)[12.2, 8.33, 10.40 and 12.005 g in agonist-intaked and 13.68, 17.87, 17.76 and 20.6 g in control groups of beef tallow, canola oil, olive oil and safflower oil sub-groups respectively]. There was no significant difference in abdominal fat mass among control rats of all dietary sub-groups. Fatty acids composition of collected samples also showed no significant differences between agonist intaked and control dietary rats groups.

Discussion:

There are some evidences indicating that fatty acid composition of diet can affect adipocyte cell membrane composition. As described in one of the other papers beef tallow diet more efficiently promotes body fat accumulation than safflower oil by reducing lipolytic activities because of the lower β-receptor binding and sympathetic activity in adipose tissues and the binding affinities of β-receptors in adipose tissues were significantly lower in the beef tallow diet group (Matsuo et al, 1995). It is also believed that reduced β-adrenoceptor binding affinity correlated with reduced membrane fluidity in beef tallow-fed group (Matsuo et al, 1995).Our recent studies regarding the effect of dietary lipids on the growth of rats have shown that the increase of body weight of rats fed with a diet containing beef tallow (12% wt/wt) is lower than that of rats fed with a diet containing vegetable oils. In order to elucidate the reason for the difference between the results of above mentioned study and our results, we tried to investigate the effect of different dietary lipids on the accumulation of intaked lipids with and without BRL 35135 in the body. As a result, inclusion of BRL35 135 in the diet, as a β-adrenergic agonist reduced the fat accumulation in the body in all dietary fat groups, except beef tallow. It is suggested that lower fat accumulation in later groups is due to effective adrenergic-induced lipolysis of BRL35135 and in the beef tallow-fed group it was not effective.

Conclusion:

Dietary lipids containing different amounts of SFA, PUFA and MUFA show various pattern of accumulation in the animal body. Feeding diets rich in SFA, compared to diets rich in PUFA, MUFA, resulted in higher fat accumulation in the rat body in spite of inclusion of a specific β-3 agonist, BRL 35 135 as a adrenergic lipolysis-inducer. According to results of other studies, indicating a lower adrenegic induced lipolytic activities in rats fed beef tallow compared to other dietary lipids, and also results of present study, it can be occluded that feeding diets rich in SFA, such as beef tallow, reduce adrenergic activities possibly through the reduction in membrane fluidity due to changes in cell membrane fatty acid composition.

Reference:

Fotovati, A. and T. Ito (1998): Distribution and metabolism of dietary lipids in animal body. Rec. Res. Devel. in Nutrition Res.,2 pp.: 69-70

Kawahara S.,Inoue K.,Hayashi T., Masuda Y. and T. Ito :Lipids easy to accumulate in the liver and lipids hard to accumulate in it. *Nutrition Res* . 1997;17(6):1013-1023

Matsuo T., Sumida H. and M. Suzuki : Beef tallow diet decreases beta-adrenergic receptor binding and lipolytic activities in different adipose tissues of rat. *Metabolism* 1995 Oct.; 44(10):1271-1277.

Matsuo T., Sumida H. and M. Suzuki : Beef tallow diet decreases norepinephrine turnover rates in rat hypothalamus and cerebral cortex. Metabolism 1995 Nov.; 44(11):1377-1379.

Matsuo T. and M. Suzuki: Beef tallow diet decreases lipoprotein lipase activities in brown adipose tissue, heart and soleus muscle by reducing sympathetic activities in rats. *J. Nutr. Sci.Vitaminol.(Tokyo)* 1994 Dec.;40(6):569-581

Matsuo T. and M. Suzuki: Brain β-adrenergic receptor binding in rats with obesity induced by a beef tallow diet. *Metabolism* 1997 Jan 46(1):18-22.

Tajima A., Kawahara S., Shin K., Imaizumi K., Nakamura T. and T. Ito: Is beef tallow really hazardous to health?. *Nutrition Res.*, 1995; 15(10):1429-1436

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