The effects of the novel IDPc inhibitor, DA-11004, on NADPH generation, insulin secretion, and glucose level in zucker rats

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The biological effects of NADPH-dependent isocitrate dehydrogenase (IDPc) inhibitor, DA-11004, was examined in obese zucker rats or streptozotocin-induced diabetic SD rats. Diabetes was induced by injection of streptozotocin (50mg/kg) dissolved in citrate buffer (pH 4.8) into the tail vein and induction of diabetes was confirmed by the measurement of the tail blood glucose level at 48h. DA-11004 (30mg/kg, po) was injected for successive 7days and significantly reduced the plasma glucose in streptozotocin-induced diabetic rats ($P<0.05$).
In obese zucker rats, DA-11004 (10mg/kg, ip) inhibited the increases of body weight and diet consumption when compared to control, but oxalomalate (30mg/kg, ip) had no effects. DA-11004 significantly reduced the weight of epididymal and retroperitoneal fats and NADPH generation in plasma ($P<0.01$). We measured the levels of free fatty acids (FFA) and insulin in plasma of zucker rats. DA-11004 reduced the level of FFA from 821.4 ± 229.6 to 587.2 ± 47.1 (μEq/L) and significantly decreased the plasma insulin responses when compared to control ($P<0.05$). Administration of DA-11004 into zucker rats significantly decreased the levels of glucose in liver and the levels of triglycerides, GOT, GPT, and LDH in plasma, but oxalomalate had no effects ($P<0.05$).
In summary, DA-11004 reduced the fat synthesis via inhibition of NADPH generation and inhibited the insulin secretion, FFA generation and declined the glucose and triglycerides levels in plasma and liver of zucker rats.

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KR-32158 protects heart-derived H9c2 cells from oxidative stress-induced cell death

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A benzopyranyl derivative, KR32158, synthesized as a plausible KATP opener, has been shown to exert cardioprotective effect in vivo myocardial infarction model. Myocardial ischemia, induced by oxidative stress, mental stress and fever, result in artheroscleosis, myocardial infarction and hypertrophy. In this study, we investigated in vitro effect of KR32158 by determining whether KR32158 produce cardioprotective effect against oxidative stress-induced death in heart-derived H9c2 cells. Oxidative stress was induced by buthionine sulfoximine (BSO) which inhibit GSH level and subsequently increase ROS level in H9c2. Cell death was determined by measuring lactate dehydrogenase(LDH) release. KR32158 significantly decreased LDH release from H9c2 induced by oxidative stress, in dose-dependent manner. And also, we measured BSO-induced ROS generation to confirm whether KR32158 had protective effect from ROS-induced cardiac injury. As the result, KR32158 significantly decreased BSO-induced ROS generation. We also observed cardioprotevtive effect of KR32158 morphologycally by using microscope. These results suggest that KR32158 has protective effects through inhibiting the production of ROS.