Effect of alpha-lipoic acid on hepatic insulin signaling-related proteins expression in high fat diet plus streptozotocin-induced diabetic rats

Szu-Chuan Shen[1]*, Cho-Hua Yang[1], Wen-Chang Chang[2], Shih-Xiang Lin[1], Rong-Shiuan Tu[1], James Swi-Bea Wu[3] Yu-Wen Ting[3]

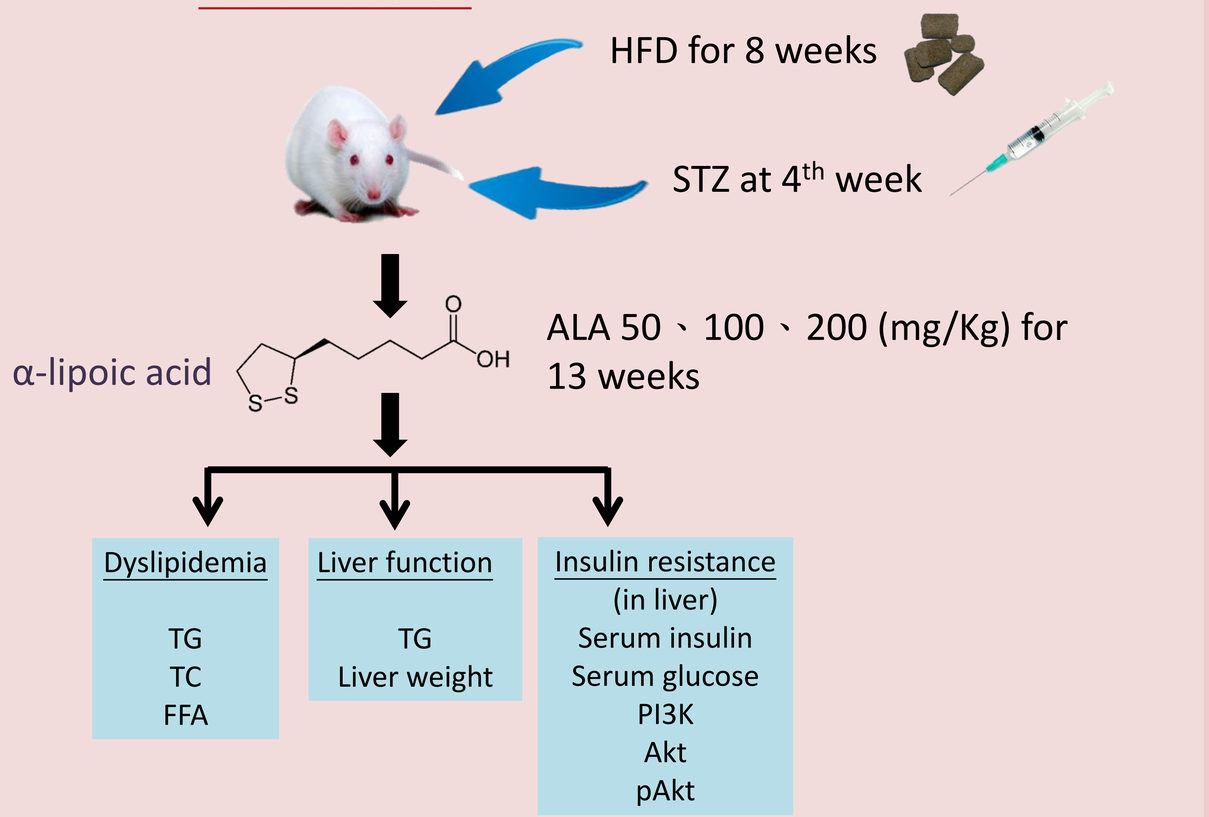
國立臺灣師範大學

[1]Graduate Program of Nutrition Science, National Taiwan Normal University, No. 162, Sec. 1, Heping E.Rd. 10610, Taiwan.
[2]Department of Food Science, National Chiayi University, No.300, Syuefu Rd., Chiayi City, 60004, Taiwan.
[3]Graduate Institute of Food Science and Technology, National Taiwan University, P.O. Box 23-14, Taipei 10672, Taiwan.
*Corresponding author's E-mail address: scs@ntnu.edu.tw

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a metabolic disorder disease and characterized as insulin resistance. Alpha-lipoic acid (ALA) which acts as a cofactor for pyruvate dehydrogenase and α-keto-glutamate dehydrogenase in TCA cycle is a potent biological antioxidant. This study aims to investigate the effect of ALA on ameliorating insulin signaling pathway in high fat diet (HFD) plus streptozotocin (STZ) induced diabetic rats. Male Wistar rats fed HFD (60% fat of calorie) for 4 weeks were intraperitoneally (ip) injected STZ (30mg/kg B.W.) and then served HFD for 8 weeks continuously to induce diabetes. The diabetic rats were orally administered with ALA (200mg/kg B.W.) once a day for 13 weeks. The serum biochemistries values of rat were measured using ELISA method. The hepatic insulin signaling-related protein expressions were analyzed by western blotting. The results show that the treatment of ALA for 13 weeks significantly reduced fasting serum glucose level in HFD/STZ induced diabetic rats ($p<0.05$). Futhermore, the fasting serum lipid profiles such as triglyceride and total cholesterol values were decreased, whearas, the high density lipoprotein value was increased significantly in ALA treated diabetic rats ($p<0.05$). Moreover, western blotting analysis indicates that ALA significantly increased hepatic insulin signaling-related proteins such as insulin receptor, PI3K and Akt/PAkt expressions in diabetic rats. The above observations demonstrate that ALA may ameliorate hepatic insulin resistance via enhancing PI3K/Akt pathway-related protein expressions and has potential on preventing progression of T2DM.

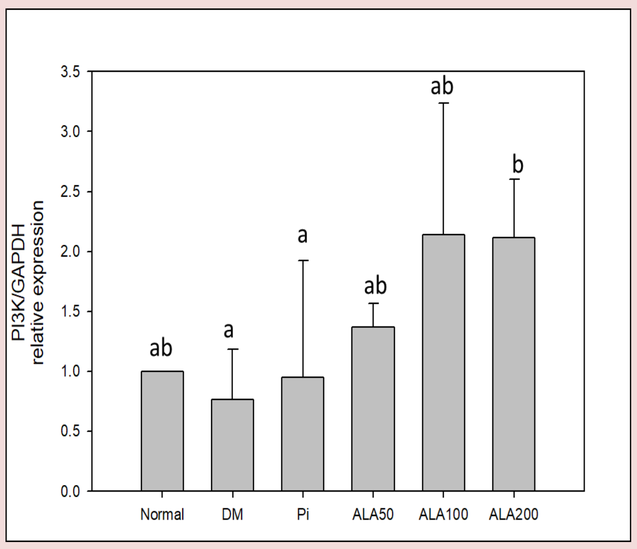
EXPERIMENTAL FRAMEWORK



RESULTS

Table 1. Serum lipid profile in HFD/STZ induced T2DM rats treated with alpha-lipoic acid for 13 weeks

	Normal	DM	Pio	ALA50	ALA100	ALA200
TC(mg/dL)	77.33±6.90 [a]	124.70±12.49 [b]	73.00±4.70 [a]	80.50±4.97 [a]	77.33±4.95 [a]	76.17±2.23 [a]
TG(mg/dL)	70.00±8.55 [a]	250.7±12.2 [b]	118.7±19.54 [a]	165.7±15.16 [ab]	215.7±17.41 [b]	104.0±7.72 [a]
HDL-C(mg/dL)	73.83±6.03 [a]	61.50±1.91 [a]	71.00±5.43 [a]	73.33±2.55 [a]	84.83±12.97 [a]	103.7±11.1 [b]
FFA(mmol/L)	0.65±0.05 [a]	1.17±0.07 [b]	0.77±0.06 [a]	0.89±0.03 [ab]	0.86±0.04 [b]	0.57±0.02 [a]



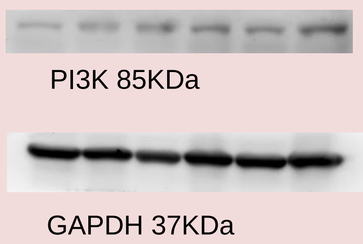


Fig 3. Hepatic PI3K expression in HFD/STZ induced T2DM rats treated with alpha-lipoic acid for 13 weeks.

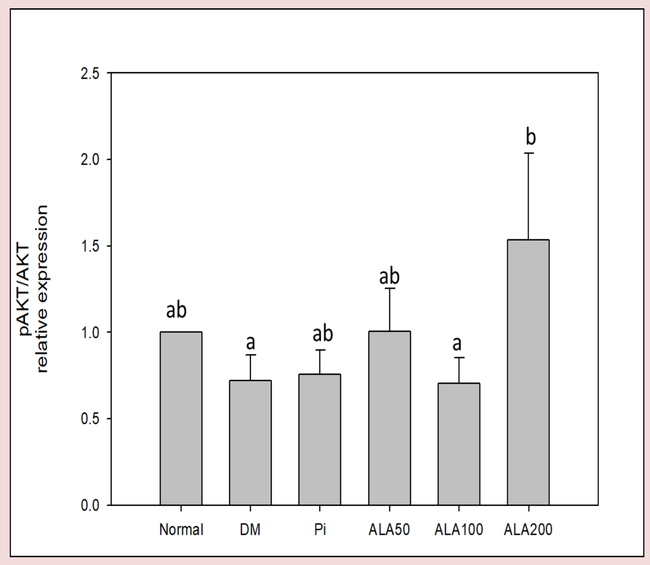




Fig 4. Hepatic pAkt/Akt expression in HFD/STZ induced T2DM rats treated with alpha-lipoic acid for 13 weeks.

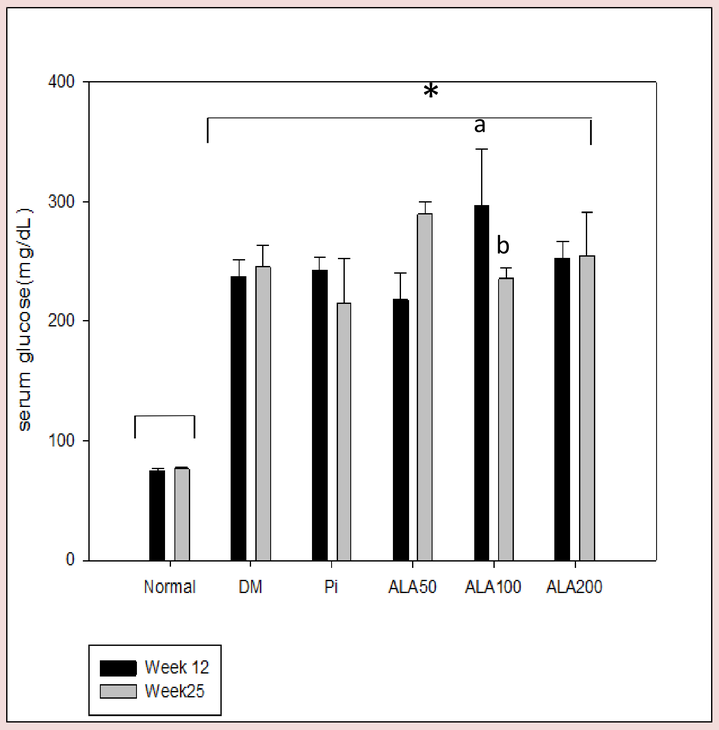


Fig 1. Serum fasting glucose in HFD/STZ induced T2DM rats treated with alpha-lipoic acid for 13 weeks and 25week.

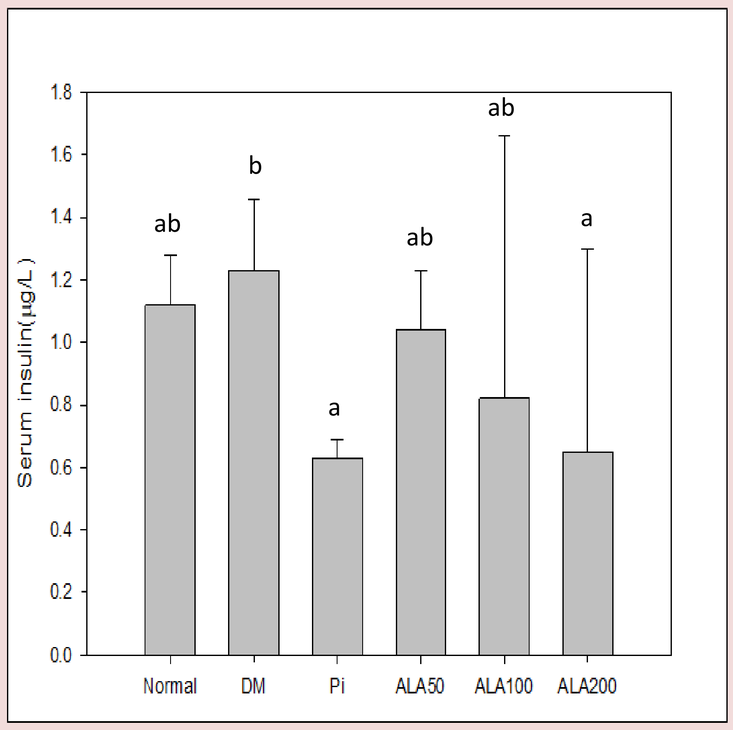


Fig 2. Serum insulin in HFD/STZ induced T2DM rats treated with alpha-lipoic acid for 13 weeks.

CONCLUSION

