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Evaluating Cross Talk Between Insulin Resistance, Inflammation and Fibrosis Along with Exploring Therapeutic Potential of *Beta Vulgaris* in Experimentally Induced Diabetic Cardiomyopathy in Rat Model.

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Abstract

Diabetic cardiomyopathy often manifests as inflammation, insulin resistance, reduced myocardial contractility, and eventually myocardial fibrosis. Most of the drugs lower hyperglycemia but there is lack of drugs protecting against myocardial insults. In this context, one of research domains explores natural compounds having medicinal properties. Thus, our aim was to explore cross talk between insulin resistance, inflammation and fibrosis along with exploring efficacy of *Beta vulgaris* in diabetic cardiomyopathy. Firstly *in vitro* analyses (antioxidant/antihyperglycemic) was conducted before incorporating extract in *in vivo* experiment. For diabetes induction, *Wistar* albino rats (age 1-3 weeks; n=24) fed with high fat diet for 2 months followed by nicotinamide and streptozotocin administration. Diabetic rats were equally divided into positive control, standard control, treatment group (*Beta vulgaris*@500mg/kg/bw), with comparison to negative controls fed on normal diet. Fasting blood glucose and ECG, were monitored. After decapitation (30 days), metabolic profile (serum glucose, insulin, lipid profile, oxidative stress markers, myocardial enzymes) was assessed. Expression levels of genes and transcriptional factors of insulin signaling pathway (INS-I, INS-II, PDX-1, MAFA, GLUT-2), proinflammatory genes (TNF-α, NF-κb), and profibrotic gene (TGF-β), were analyzed. After statistical analyses, significant ($P \leq 0.05$) lowering of serum glucose, lipid profile, and eventually myocardial enzymes was seen in treatment group in addition to upregulated insulin pathway genes and downregulated TNF-α, NF-κb and TGF-β. Afterwards, we extended study to explore direct effect on cardiac fibroblasts and western blot revealed decreased α-SMA in treated group, confirming therapeutic efficacy of *Beta vulgaris* extract in protecting myocardial insults followed by insulin resistance and fibrosis.

Keywords: Diabetic cardiomyopathy, insulin resistance, fibrosis, *Beta vulgaris*

Abbreviation: TGF-β: Transforming growth factor; ECG: Electrocardiograph