

Pharmacological study of therapeutic outcomes of carvedilol and co enzyme Q10 combination in isoprenaline-induced myocardial infarction in rats

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿ قالوا سبحانك لا علم لنا الا ما علمتنا

إنك انت العليم الحكيم ﴾

صدق الله العظيم
الآيه (32) سورة البقره

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ABSTRACT

Abstract:

The present study was designed to elucidate the potential pharmacological outcomes of carvedilol combination with co enzyme Q10 in isoprenaline-induced myocardial infarction in rats.

Method: Carvedilol and/or co enzyme Q10 was given once daily for 14 consecutive days at doses of 10 mg/kg orally after administration of two doses of ISP (85 mg/kg; s.c.). **Results:** ISP induced significant myocardial damage in rats, which was characterized by significant tachycardia, ECG changes, increased absolute and relative heart weight, increased serum CK-MB, myofibrillar disarrangement and several histological changes. ISP induced lipid profile alteration expressed as elevation in triglyceride, cholesterol and LDL with reduction in HDL. These lipid alterations were modified by treatment with Carvedilol and/or co enzyme Q10. As indicators of oxidative stress, ISP increased cardiac lipid peroxide levels and decreased the levels of cardiac GSH and serum total antioxidant capacity. Moreover, ISP increased the expression of TNF- α and NF- κ B which further promote apoptotic cell death and increases caspases 3 and 9 activities. Adding Carvedilol and/or co enzyme Q10 treatment ameliorated all parameters the ECG changes and normalized CK-MB level additional improvement in all parameters as compared to both alone therapy. **Conclusion:** The present study provides the evidence that carvedilol and co enzyme Q10 treatment could reduce the myocardial injury and improves cardiac function in ISP-induced MI. These effects are mostly via its hypolipidemic, antioxidant, and anti-inflammatory effects that suppress caspase mediated apoptotic pathway. Co enzyme Q10 has additional effects if combined with carvedilol.

Keywords: Carvedilol; co enzyme Q10; isoproterenol; myocardial infarction; oxidative stress; apoptosis.

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List of Abbreviations

ACCF	American College of Cardiology Foundation
ACS	Acute Coronary Syndromes
ADP	Adenosine diphosphate
AHA	American Heart Association
ALT	alanine aminotransferase
AMI	Acute myocardial infarction
Apaf-1	apoptosis protease activation factor-1
ATP	Adenosine triphosphate
Bcl-2	B-cell lymphoma 2
Bcl-xl	B-cell lymphoma-extra large
bFGF	Fibroblast growth factor basic
BMI	Body mass index
CAT	Catalase
CHD	Coronary heart disease
CHF	Congestive heart failure
c-IAP-1	Cellular inhibitor of apoptosis protein 1
CK-MB	Creatine kinase MB
COX-1	Cyclooxygenase-1
CRP	C-reactive protein
cTnT	Cardiac troponin T
CVD	Cardiovascular diseases

LIST OF ABBREVIATIONS

DMSO	Dimethyl sulphoxide
DNA	Deoxyribonucleic acid
DOX	Doxorubicin
DTI	Direct thrombin inhibitors
DTNB	5,5' dithiobis-2-nitrobenzoic acid
ECG	Electrocardiography
EDTA	Ethylene-diamine tetraacetic acid
EM	Electron microscope
ESC	European Society of Cardiology
G6PDH	Glucose-6-phosphate Dehydrogenase
GABA	Gamma-aminobutyric acid
GP	Glycoprotein
GSH	Reduced glutathione
H & E	Hematoxylin and Eosin
HDL	High-density lipoprotein
HF	Heart failure
HHcy	Hyper-homocysteinemia
HRP	Horseradish Peroxidase
IUPAC	International Union of Pure and Applied Chemistry
i.p.	Intraperitoneal
I/R	Ischemic Reperfusion
IL	interleukin
iNOS	Induced Nitric oxide
ISP	Isoprenaline

LIST OF ABBREVIATIONS

IκB	inhibitor of κB proteins
LAD	Left anterior descending coronary artery
LDH	lactate dehydrogenase
LDL	Low-density lipoprotein
LOX-1	Lectin-like Ox-LDL receptor-1
LPA	lipoprotein –A
LPL	lipoprotein lipase
LTC4	leukotrienes C4
LV	Left ventricular
LWMH	low molecular weight heparin
MDA	Malondialdehyde
MI	Myocardial infarction
MPO	Myeloperoxidase
MMP 1	Matrix metalloproteinase 1
MMP9	Matrix metalloproteinase 9
NADH	Nicotinamide adenine dinucleotide hydrogen
NADP	Nicotinamide adenine dinucleotide phosphate
NF-κB	Nuclear Factor kappa-B
NO	Nitric oxide
NSTEMI	Non-ST-Elevation myocardial infarction
NYHA	New York Heart Association
Ox-LDLs	Oxidized Low-density lipoprotein
PDGF	Platelet derived growth factor
PGE2	prostaglandin E2