MicroRNA-103 INHIBITOR *AS A POTENTIAL THERAPEUTIC TARGET* FOR MYOCARDIAL INFARCTION

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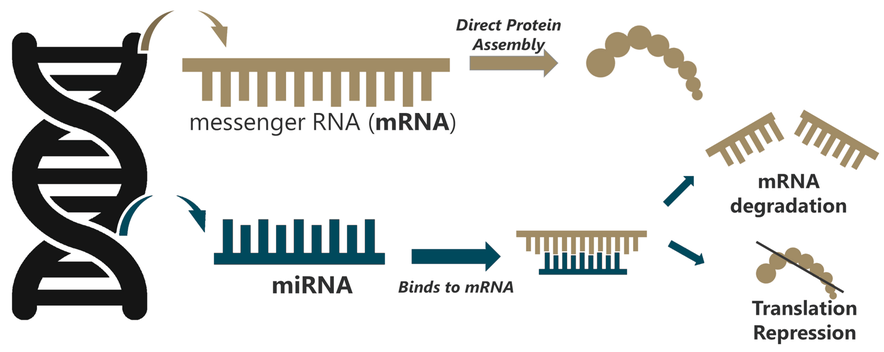
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INTRODUCTION

Myocardial infarction (**MI**) is myocardial cell death due to severe and prolonged ischemia produced from atherosclerosis-related coronary artery disease. MI triggers a cascade of inflammatory and reparative phases that end withcell necrosis [1].

MicroRNA (**miR**) is non-coding single stranded RNA that regulates protein expression [2].



miR-103 regulates expression of Fas-associated death domain (**FADD**) which decreases necroptosis of ischemic myocardium by targeting Receptor-interacting Protein Kinase (**RIPK**) [2, 3].

METHODS

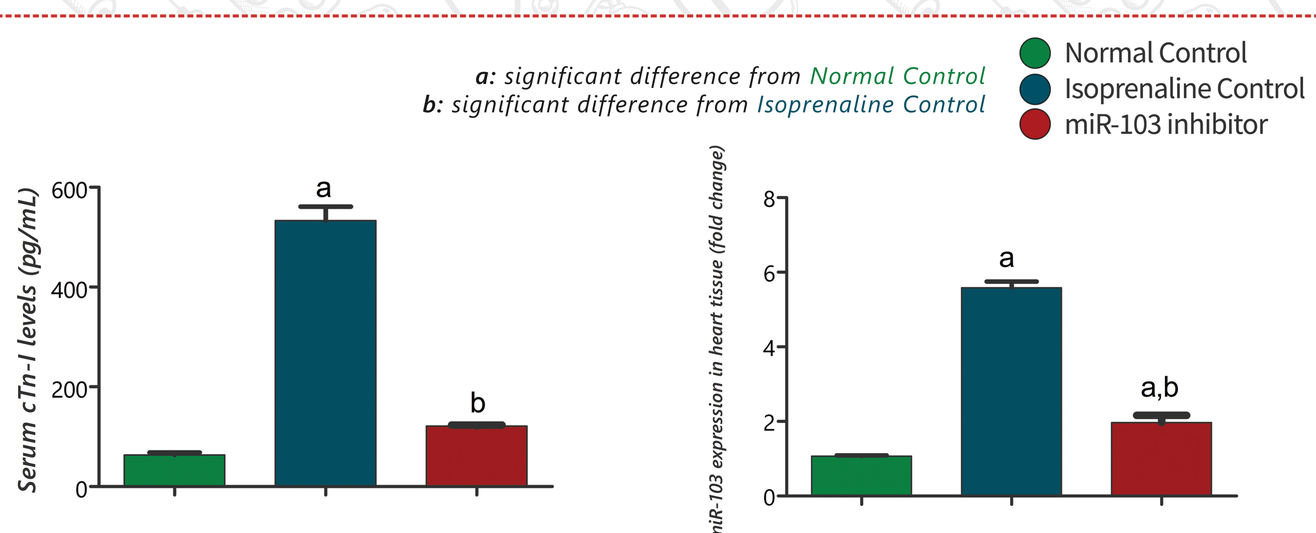
The study aims to investigate the modulatory effect of regulating mRNAs translation processes of myocardial infarction induced with Isoprenaline HCl 100 mg/kg (**ISO**)[4] by injecting miR-103 inhibitor.

Eighteen mice (15-25 gm) were allocated into three groups; Group A (control) received **normal saline**, Group B received **ISO only** and Group C received **ISO and miR-103 inhibitor.**

Mice were sacrificed by cervical dislocation under urethane anesthesia. Blood samples were collected for biochemical analysis of **Troponin-I** (**cTn-I**)**,** then the hearts were isolated and used for measuring mRNA expression levels of **miR-103**, **FADD**, **RIPK**, Interleukin-6 (**IL-6**)**,** in addition to **histopathological examination**.

RESULTS & DISCUSSION

a: *significant difference from Normal Control*
b: *significant difference from Isoprenaline Control*



Graph I *Serum cTn-I levels showed a significant* increase *in* ISO control group *when compared to* treatment group*, representing the decrease im MI biomarker in treatment group*

Graph II *Isoprenaline significantly increased miR-103 expression is in* ISO control group *in comparison to* treatment group*, indicating its importance in MI pathogenesis and the effectiveness of the antagomir on its expression.*

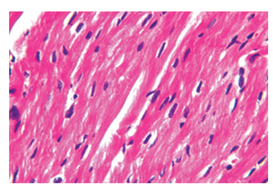


Figure I *Shows normal histological structure of the myocardium for* normal group *and no histopathological alteration recorded.*

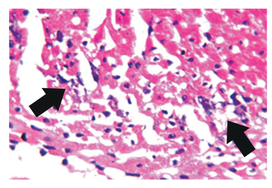


Figure II *Shows focal degeneration and inflammatory cells infiltration detected in the myocardium of* ISO control group*.*

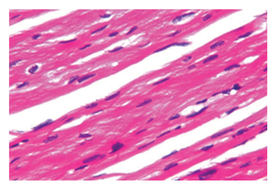
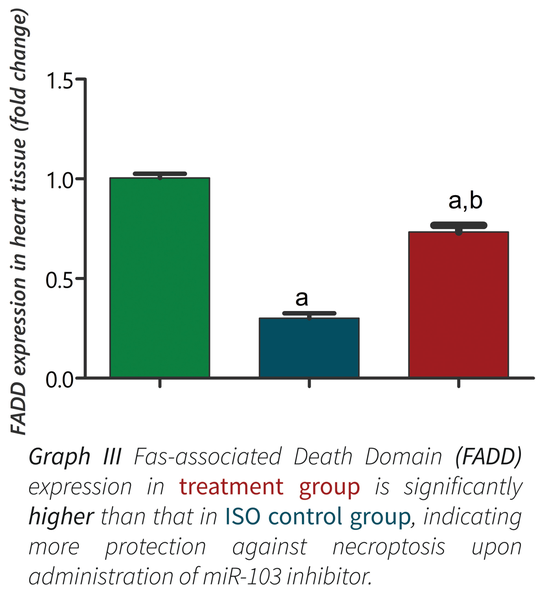
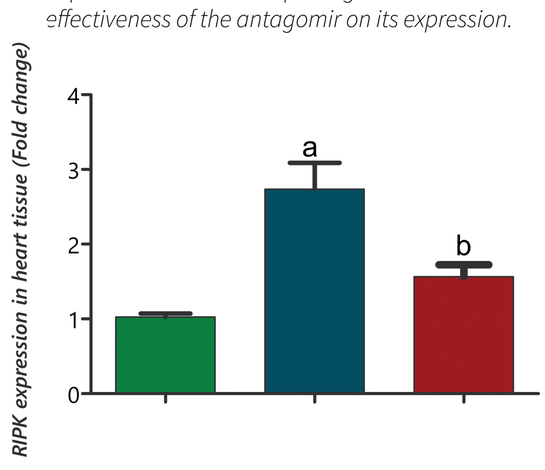


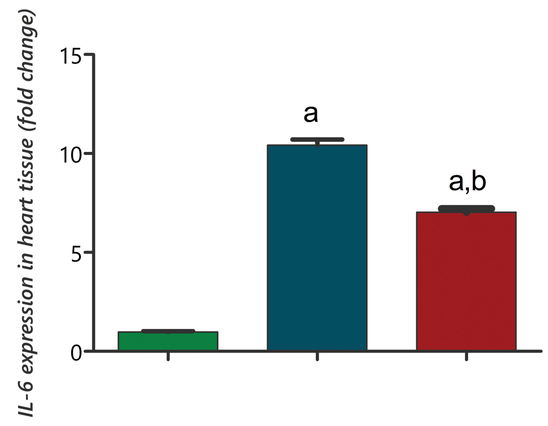
Figure III *Shows almost normal histological structure of the myocardium of* treated group*.*



Graph III *Fas-associated Death Domain* ***(FADD)*** *expression in* treatment group *is significantly* ***higher*** *than that in* ISO control group*, indicating more protection against necroptosis upon administration of miR-103 inhibitor.*

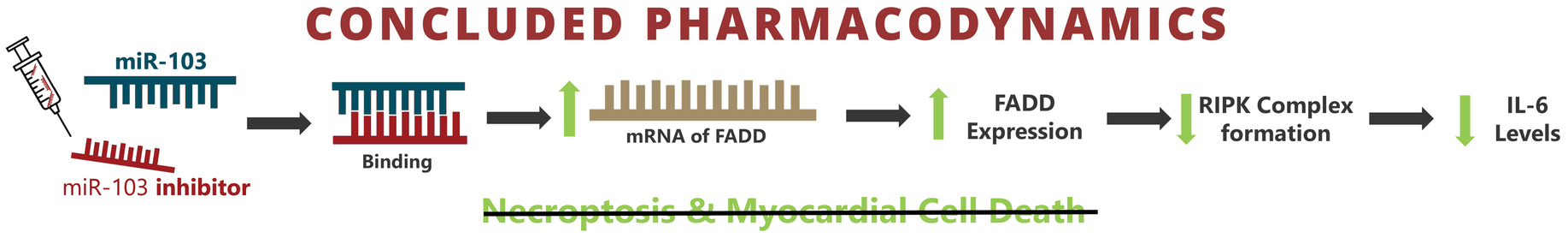


Graph IV *Receptor Interacting Protein Kinase (****RIPK****)* ***significantly reduced*** *in* treatment group *when compared to* ISO control group*, which indicates necroptosis atenuation.*



Graph V *IL-6 expression was significantly higher in* ISO control group *with obvious attenuation in* treatment group*, signifying the decrease in inflammation between the groups.*

CONCLUDED PHARMACODYNAMICS



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