https://doi.org/10.17952/38EPS.2026.P388

Assessing the Efficacy of Peptides on Acute Coronary Syndrome *In-vivo*

Offir Ertracht[1], Rani Wainer Shlomo[1,4,5], Mulate Zerihun[4], Shulamit Fluss Ben-Uliel[4], Shmuel Silitsky[4], Samar Gani[4], Liron Davis[4], Mona Shehadeh[3], Tali Reuveni[1], Shaul Atar[1,2,4], Nir Qvit[4]

[1]*The cardiovascular research laboratory,* [2]*Department of cardiology,* [3]*Clinical Laboratories Division, Galilee Medical Center, Naharyia,* [4]*The Azrieli Faculty of Medicine in the Galilee, Bar-Ilan university, Safed,* [5]*Cardiac rehabilitation, the Cardiovascular Department, Tzafon Medical Center, Poriya, Israel*

Introduction

- Cardiovascular disease (CVD), mainly myocardial infarction (MI) lead cause of morbidity and mortality worldwide.
- MI followed by reperfusion (ischemia/reperfusion – I/R) induces severe mitochondrial stress, characterized by calcium and reactive oxygen species overload, mitochondrial dysregulation - excessive fission, and attenuated fusion.
- All contributing the cardiomyocytes dysfunction, cardiac remodeling and death.
- Peptides are highly clinically relevant class of therapeutics in CVD.
- They offer high target specificity, favorable safety profiles, and the ability to modulate complex biological pathways.

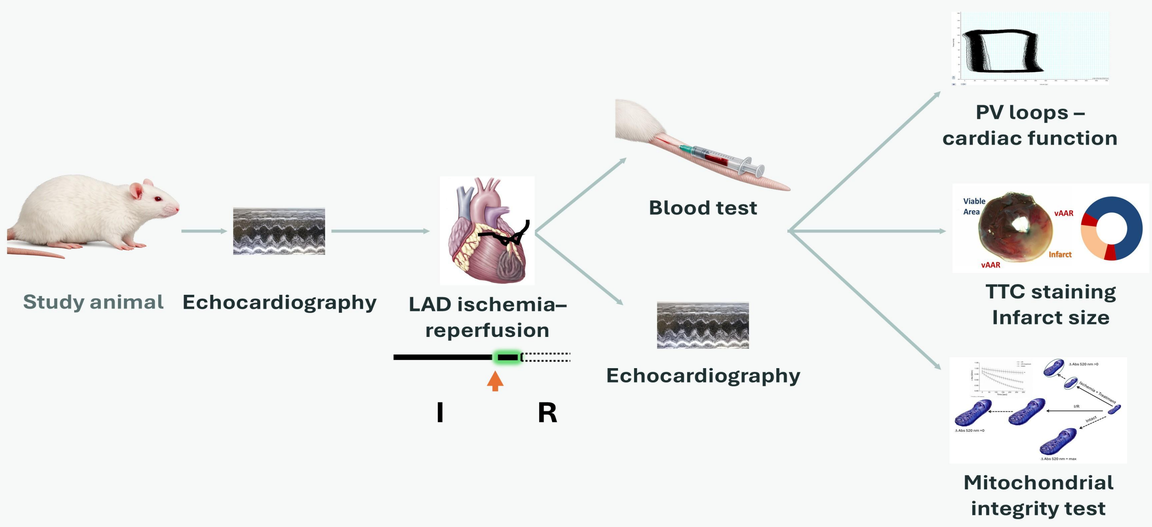
Hypothesis and aims

We hypothesized that CVP-350, a macrocyclic peptide specifically designed to inhibit the Drp1/Fis1 interaction, would preserve mitochondrial integrity and improve cardiac outcome following ischemia-reperfusion injury.

Methods

- Animal experiments were conducted according to ethical committee guidelines.
- A rat model of left anterior descending (LAD) coronary artery occlusion for 30 min, followed by reperfusion was applied. Five min prior to reperfusion, CVP-350 (2 mg/kg), was administered i.v. Infarct size was determined by triphenyl-tetrazolium chloride (TTC) staining, cardiac injury was evaluated using hematological biomarkers, and cardiac structure and function were assessed by echocardiography. Mitochondrial integrity was assessed by Ca^{2+}-induced swelling assay.

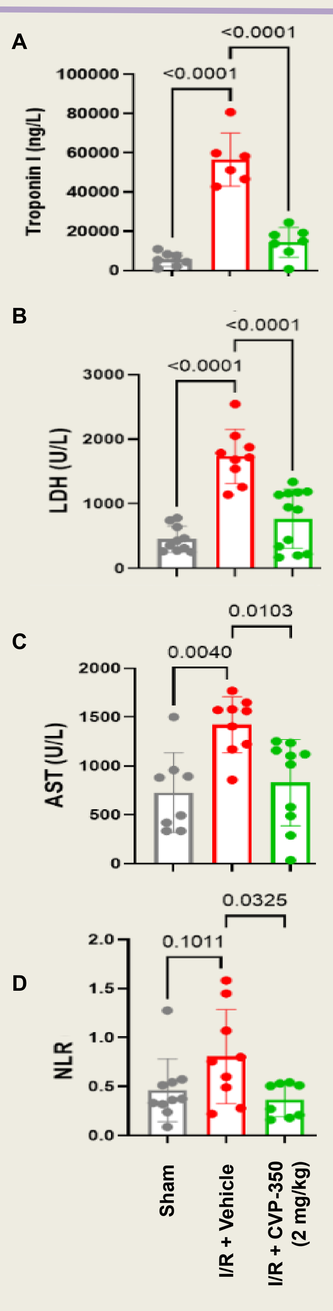
Rat LAD ischemia–reperfusion study design:

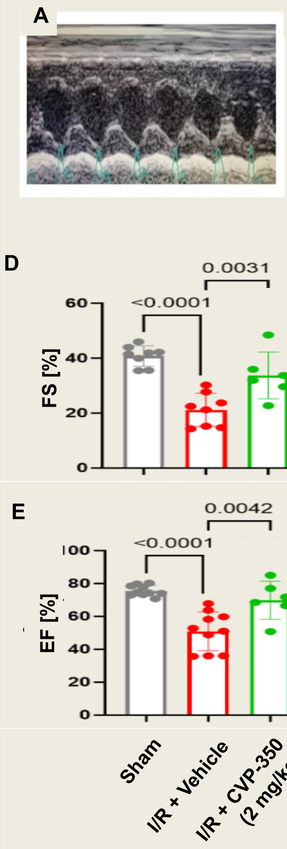


Results:

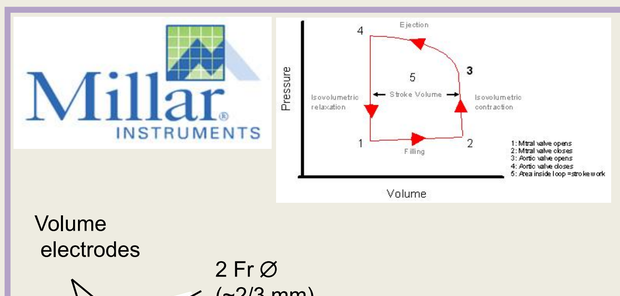
Blood samples results characterizing cardiac damage: **A.** Cardiac Troponin I, **B.** Lactate Dehydrogenase, **C.** Aminotransferase (AST), and **D.** Neutrophiles to Leucocytes ratio (NLR).

Results: Cardiac Troponin I show dramatic increase of over 50,000 ng/L, LDH increases to ~2000 u/l, AST and NLR to ~ 0.8, 24 hrs after I/R. ***CVP-350 decreases all these parameters significantly back to control (sham) level, indicating its cardiac protective efficacy.***

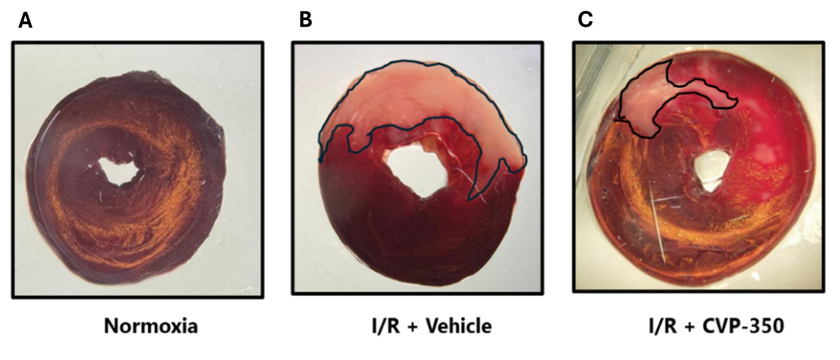




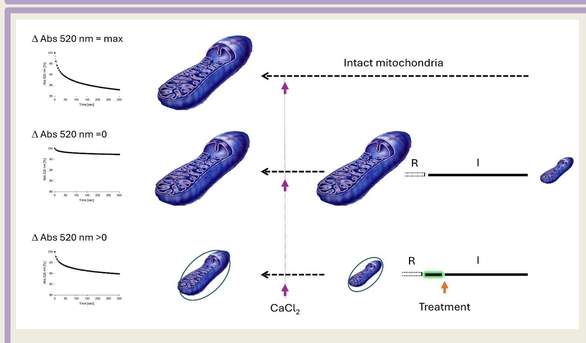
Echocardiography M-mode cines of: **A.** Sham **B.** I/R + Vehicle **C.** I/R + CVP-350 treatment. I/R attenuated wall motion seen as lack of waves in the upper side of the cine (**B**) preservation of function is seen in (**C**).
D. FS, and **E.** EF show summary of functional parameters.
CVP-350 efficacy is seen as preservation of FS and EF.

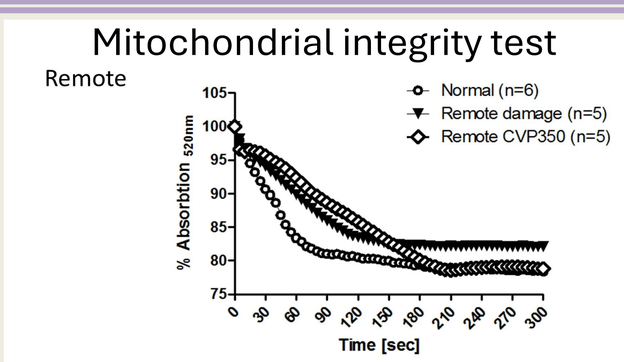


I/R decreases loop's size, i.e. attenuates SV, CO, SW and EF, further it moderates contraction and relaxation rates dp/dt_{max} and $_{min}$, respectively, and increases τ (relaxation time). ***CVP-350 treatment, preserved SV, CO, SW, EF and dp/dt_{max} and dp/dt_{min}.***

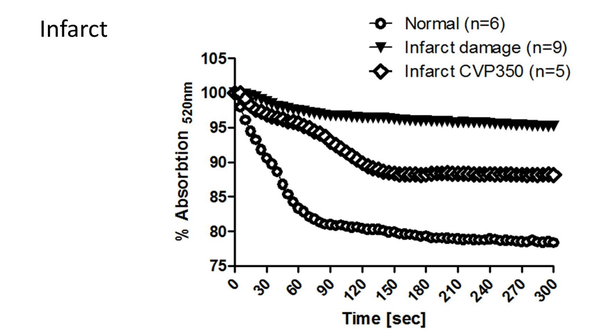


A-C representative mid cardiac level slices stained with TTC, for the **A.** sham operated rats (normoxia), **B.** I/R, and **C.** I/R + CVP-350, respectively. Infarct size assessments **D.** ***shows >50% reduction of infarct following CVP-350 administration.***





Mitochondria extracted from intact hearts or 4 h after I/R or 4 h after I/R + CVP-350 treatment were exposed to high (200 µM $CaCl_2$) calcium level, followed by 5 min of 520 nm inner mitochondrial cristae absorbance reading.



Ca^{2+} entrance to the mitochondria brings also water, causing membrane swelling, flattening of the cristae and reducing absorbance. As ***CVP-350 lowers the rate of 520 nm absorbance reduction, it possibly protects the mitochondria, preserving its ability to swell, during the ischemia period.***

Conclusions: ***CVP-350 prevents cardiac deterioration post I/R. It preserve mitochondrial integrity, reduced infarct size I/R, attenuates cardiac dysfunction seen by both echocardiography and direct cardiac performance measurements (PV-loop assessment). CVP-350 has the potential to become an adjacent treatment in a clinical scenario of MI and percutaneous intervention.***