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# Eplerenone pretreatment protects the myocardium against ischaemia/reperfusion injury through the phosphatidylinositol 3-kinase/Akt-dependent pathway in diabetic rats

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## Abstract

We investigated the eplerenone-induced, PI3K/Akt- and GSK-3β-mediated cardioprotection against ischemia/reperfusion (I/R) injury in diabetic rats. The study groups comprising diabetic rats were treated for 14 days with 150 mg/kg/day eplerenone orally and 1 mg/kg wortmannin (PI3K/Akt antagonist) intraperitoneally with eplerenone. On the 15th day, the rats were exposed to I/R injury by 20-min occlusion of the left anterior descending coronary artery followed by 30 min of reperfusion. The hearts were processed for biochemical, molecular, and histological investigations. The I/R injury in diabetic rats inflicted a significant rise in the oxidative stress and apoptosis along with a decrease in the arterial and ventricular function and the expressions of PI3K/Akt and GSK-3β proteins. Eplerenone pretreatment reduced the arterial pressure, cardiac inotropy, and lusitropy. It significantly reduced apoptosis and cardiac injury markers. The histology revealed cardioprotection in eplerenone-treated rats. Eplerenone up-regulated the PI3K/Akt and reduced the GSK-3β expression. The group receiving wortmannin with eplerenone was deprived eplerenone-induced cardioprotection. Our results reveal the eplerenone-induced cardioprotection against I/R injury in diabetic rats and substantiate the involvement of PI3K/Akt and GSK-3β pathways in its efficacy.

**Keywords** Ischemia–reperfusion injury · Eplerenone · PI3K/Akt pathway · GSK-3β · Diabetes

## Abbreviations

| | |
|---|---|
| I/R | Ischemia/reperfusion |
| PI3K | Phosphatidylinositol 3-kinase |
| GSK-3β | Glycogen synthase kinase-3β |
| ROS | Reactive oxygen species |
| STZ | Streptozotocin |
| LAD | Left anterior descending coronary |

## Introduction

An imbalance between the demand and supply of blood to the myocardium results in ischemia, and a persistent deprivation of the myocardium from oxygen supply leads to myocardial infarction (MI). MI is associated with an irreversible necrosis of the myocardial tissue [1]. MI represents one of the global health challenges and contributes to a huge socioeconomic and healthcare burden [2]. The treatments for myocardial ischemia and MI include the reinstatement of blood supply to the ischemic tissue and maximum salvage of the functional myocardium [3]. Diabetes mellitus is

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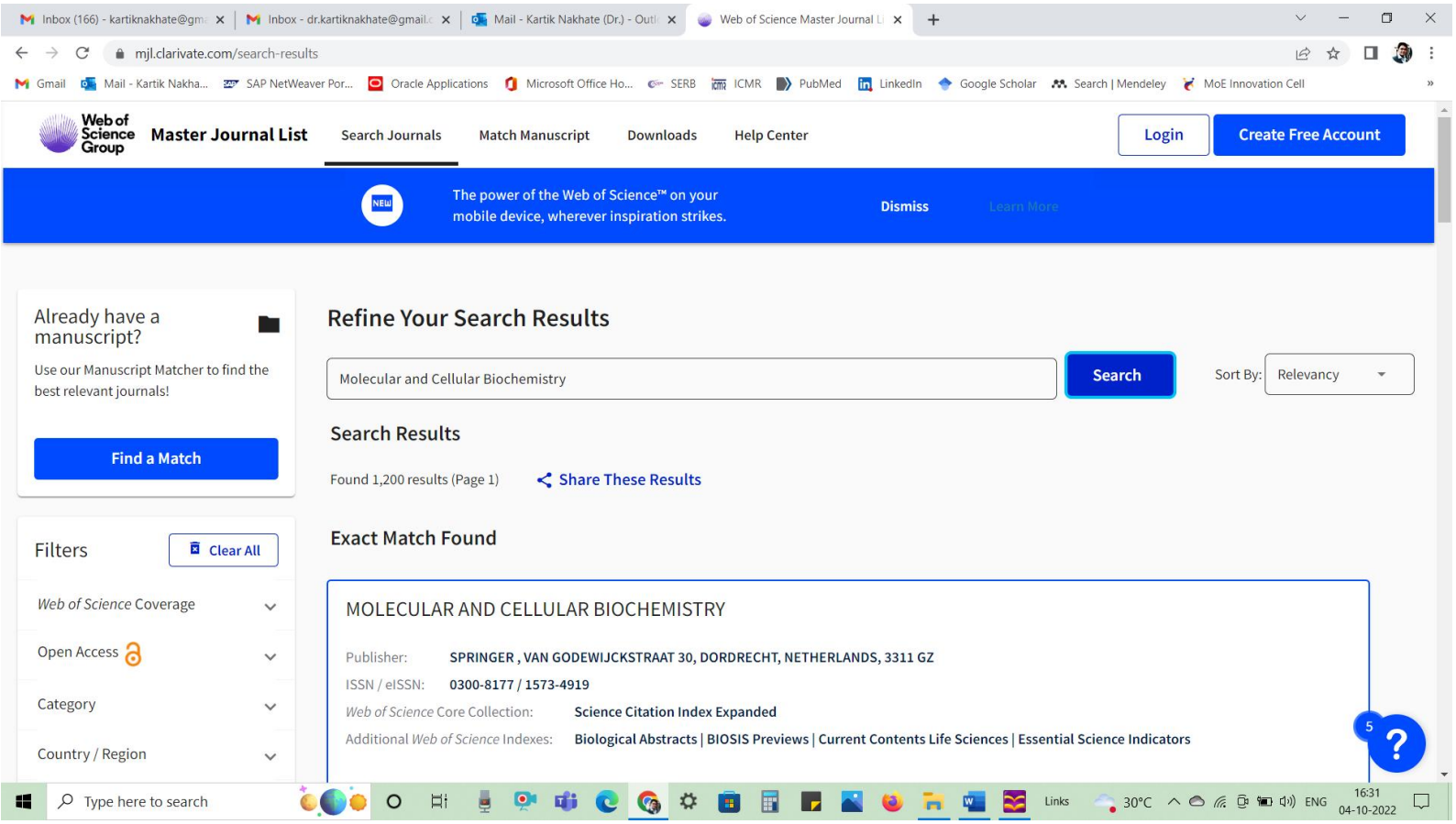
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