



# Cardiopreventive effect of ethanolic extract of Date Palm Pollen against isoproterenol induced myocardial infarction in rats through the inhibition of the angiotensin-converting enzyme



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## ABSTRACT

The present study aimed to examine the putative preventive effect of the ethanolic extract Date Palm Pollen (DPP, *Phoenix dactylifera* L., family Arecaceae) on isoproterenol-induced myocardial infarction (MI) in rats. Twenty four rats were randomly divided into four groups including control. They were treated with DPP extract (400 mg/kg) and clopidogrel (0.2 mg/kg) for 7 days followed by myocardial injury induction using subcutaneous isoproterenol (100 mg/kg) with an interval of 24 h for two days (6th and 7th day). Administration of isoproterenol exhibited indicative changes in the ECG pattern evidenced by significant elevation of ST-segment and cardiac injury markers viz.; troponin-T, creatine phosphokinase (CPK), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) by 315%, 71%, 64% and 170%, respectively as compared to control. Additionally, the angiotensin-converting enzyme (ACE) activity in plasma was increased by 33% associated to histological myocardial necrosis. However, pre-co-treatment with DPP extract improved the cardiac biomarkers injury, normalized cardiac function indices and prevented the ventricular remodeling process through inhibition of ACE activity by 34% and the inhibition of the generation of radical oxygen species. Extensive characterization of this DPP extract using LC-HRMS revealed numerous flavonoids and phenols compounds which could be endowed with cardiopreventive actions. Overall, these results proved that DPP extract has preventive effects on cardiac remodeling process.

## 1. Introduction

Cardiovascular diseases remain the most important cause of mortality in both developed and developing countries, accounting approximately 20% of all annual deaths worldwide (Ittagi et al., 2014). The cardiovascular system is susceptible to many chronic diseases such as hypertension and myocardial infarction. The myocardial infarction (MI) reflects the death of cardiac myocytes due to prolonged ischemia.

It is considered an acute coronary syndrome that may happen during the natural path of coronary atherosclerosis. This pathology could be mediated to several factors affecting the arterial wall (Boersma et al., 2003). Hence, it is a result of imbalance between coronary blood supply and cardiac demand (Mnafigui et al., 2016a,b). It increases myocardial necrosis which causes cardiac dysfunction including blood pressure, heart rate and electrocardiographic (ECG) changes and left ventricular (LV) dysfunction associated with an alteration in activities of cardiac

**Abbreviations:** DPP, date palm pollen; MI, myocardial infarction; HRESIMS, high resolution electrospray ionization mass spectrometry; ECG, electrocardiographic; LV, left ventricular; CPK, creatine phosphokinase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; ACE, angiotensin-converting enzyme; TC, total cholesterol; TG, triglycerides; ECL, electrochemiluminescence; ROS, reactive oxygen species

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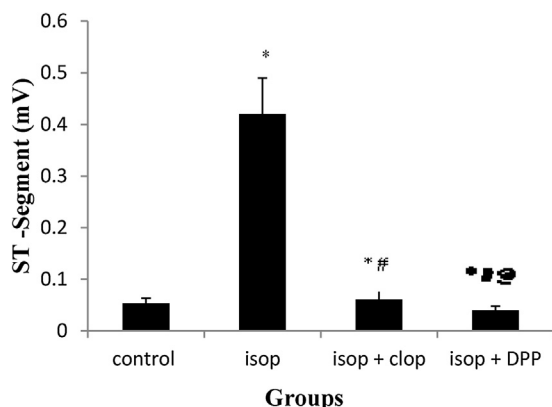
**Table 1**

Effect of DPP ethanolic extract on body weight, heart weight and heart weight/body weight ratio in isoproterenol induced myocardial infarction in rats.

Parameters	Control	Isop	Isop + Clop	Isop + DPP
Body weight (g)	176.66 ± 10.44	173.66 ± 13.41	174.5 ± 13.18	199.88 ± 3.06 <sup>##@</sup>
Heart weight (g)	0.82 ± 0.16	1.14 ± 0.17 <sup>*</sup>	0.92 ± 0.09 <sup>#</sup>	1.02 ± 0.14 <sup>##</sup>
Heart weight/body weight ratio	0.46 ± 0.08	0.65 ± 0.05 <sup>*</sup>	0.54 ± 0.04 <sup>#</sup>	0.51 ± 0.06 <sup>#</sup>

Values are given as mean ± SD for groups of six animals each.

Statistically, values are presented as follows: \* P < 0.05 significant differences compared to controls. # P < 0.05 significant differences compared to isoproterenol group @ P < 0.05 significant differences to rats treated with clopidogrel.



**Fig. 1.** Effect of DPP ethanolic extract on ST-segment elevation (mV) in the ECG (recorded from limb lead II) in normal control, isoproterenol alone injected and treated rats. Values are given as mean ± SD for group of six rats. Statistically, values are represented as follows: \* P < 0.05 significant differences compared to controls. # P < 0.05 significant differences compared to isoproterenol group. @ P < 0.05 significant differences compared to isoproterenol-treated group with clopidogrel.

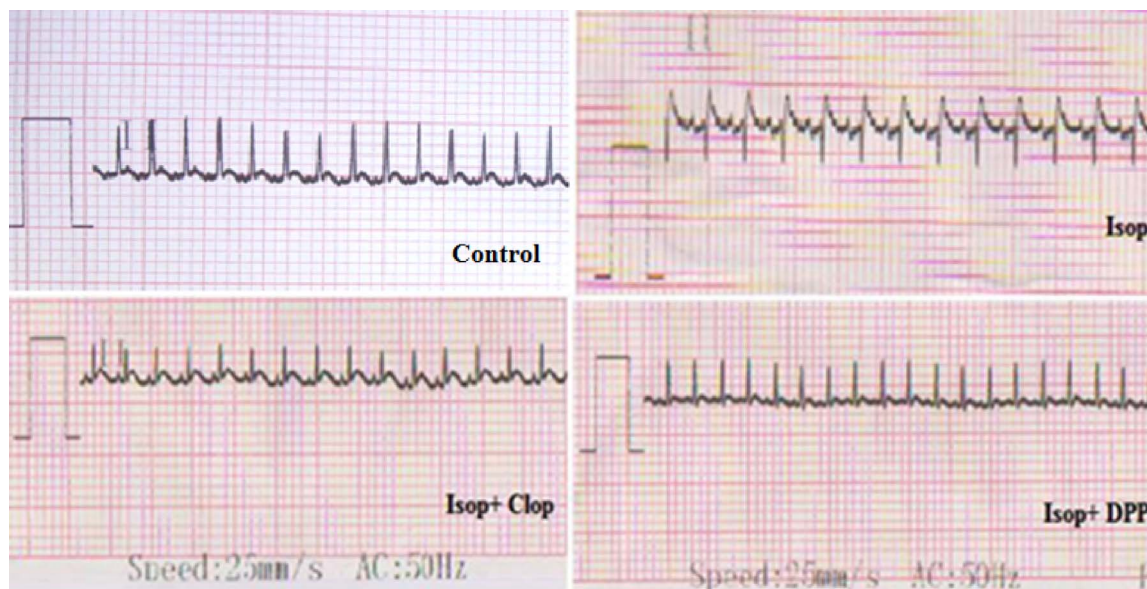
specific enzymes. Cardiac troponins are frequently accompanied with inflammation-related proteins and myocardial infarction in case of severe heart damage (Mnafgui et al., 2016a,b).

Isoproterenol [1-(3,4-dihydroxyphenyl)-2-isopropylaminoethanol HCl] is a synthetic catecholamine with β-adrenergic agonist effect which shown to cause severe stress in the myocardium resulting in infarction-like necrosis of the heart muscles (Upaganlawar et al., 2011). However, the administration of isoproterenol in supra-maximal doses could stimulate subendocardial ischemia, necrosis, hypoxia followed by fibroblastic hyperplasia with decreased myocardial compliance and

inhibition of diastolic and systolic function (Mehdizadeh et al., 2013). In veterinary and human medicine, numerous synthetic drugs were designed for the management of heart attack but exhibit many side effects. Hence, several attempts have been taken for the identification of new therapeutic approaches to prevent myocardial infarction. A great attention has been given to the polyphenols as effective bioactive compounds that protect cells from myocardial damage. Naturally-occurring polyphenolic compounds with antioxidant properties are widely in vegetables, fruits, tea, etc (Hertog et al., 1993).

Historically, date palm trees (*Phoenix dactylifera* L.) belonging to family Areaceae were extensively used in folk medicine as potential source for treatment of many human diseases. Date Palm Pollen (DPP) has been reported as rich source of diverse secondary metabolites that elucidate its potential uses in several disorders. Antioxidants play a significant action as preventive agents via neutralization or inhibition of reactive oxygen species (ROS) that suppress the development and progression of many diseases. Recent investigations reported that date palm possesses a potent ability to neutralize free radical (Rahmani et al., 2014; Al-Farsi et al., 2005). Accordingly, the DPP proved effective in many biological proprieties such as aphrodisiac, anti-inflammatory, anti-coccidial, anti-apoptotic (Elberry et al., 2011; Metwaly et al., 2014), anti-toxicant (Eraslan et al., 2008), and hepatoprotective (Uzbekova et al., 2003) activities.

Despite this large flow of data on the promising properties and attributes of DPP, no studies have been performed to explore the preventive effect of DPP against experimentally-induced myocardial infarction in rats. This encouraged us in the current study to explore this effect with scientific evidence.



**Fig. 2.** Effect of DPP ethanolic extract on electrocardiographic (ECG) pattern in normal and experimental rats.

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