Multifaceted impact of caffeic acid phenethyl ester (CAPE) in experimental myocardial injuries

To the Editor,

We read with great interest the article by İlhan et al. (1) entitled "The effect of caffeic acid phenethyl ester on isoproterenol-induced myocardial injury in hypertensive rats published in Anatol J Cardiol 2014; 14: 576-82.". It is a well-designed and well-written manuscript and is original.

This work aimed to evaluate the potential of caffeic acid phenethyl ester (CAPE) to prevent damage after myocardial infarction induced by isoproterenol and hypertension produced by NG-nitro-L-arginine (L-NNA). They concluded that their findings confirm the therapeutic potential of CAPE against myocardial injury induced by isoproterenol via the inhibition of lipid peroxidation and induction of antioxidant enzymes in hypertensive rats.

We would like to contribute additional data for the mechanisms of the protective effect of CAPE on myocardial injury induced by various factors. We have shown that CAPE considerably depressed endogenous overproduction of nitric oxide (NO) in one of our experimental setups in spinal cord injury (2). The possible pathway is inducible nitric oxide synthase activity inhibition. The primary product of the interaction between NO and the superoxide radical (O2-) is peroxynitrite (-ONOO), which is capable of either oxidizing or nitrating various biological substrates where they produced. There is abundant evidence in literature that cellular death provoked by NO may be apoptotic (3). CAPE was found to exhibit profound inhibition of NFKB, a critical molecule in the apoptotic pathway (4). Although the authors administered L-NNA to the animals to induce hypertension, the promoting effect of CAPE in terms of the mitigation of NO production on cardiac tissue leading to hypertension should also be taken into account.

We also would like to draw attention to a specific point in the methodology of the above-mentioned study. In the experiments, the application procedure for CAPE is not obvious. It can be used either intravenously (5) or intraperitoneally. We wonder if the application path of CAPE was intraperitoneal or intravenous. If the path is one of them, then, CAPE was dissolved most probably in ethanol or other available solvents such as dimethyl sulfoxide (DMSO) and ethyl acetate [soluble in ethanol, DMSO, and ethyl acetate (50 mg mL-1)] (4) because it is a highly lipophilic (hydrophobic) compound. As a result, the control rats should also be given this solvent to get rid of adverse effect of ethanol or other solvents. We think that these methodologies should also be described in detail in the article.

In conclusion, the clinical significance of CAPE arises not only from antioxidants, free radical scavenging, and direct cardioprotective properties but also from the strong inhibition of NFKB and the production of endogenous NO as well as the inhibition of apoptosis.

Sümeyya Akyol, Ömer Akyol[1]
Department of Medical Biology, Faculty of Medicine, Turgut Özal University; Ankara-*Turkey*
[1]Department of Medical Biochemistry, Faculty of Medicine, Hacettepe University; Ankara-*Turkey*

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Address for Correspondence: Dr. Sümeyye Akyol,
Turgut Özal Üniversitesi Tıp Fakültesi, Tıbbi Biyoloji Bölümü,
Anadolu Bulvarı No: 16/A, Gimat Ankara-*Türkiye*
Mobile: +90 312 397 74 00
E-mail: sumeyyaak@gmail.com

DOI:10.5152/AnatolJCardiol.2015.6336

Author`s Reply

To the Editor,

Many thanks to the authors for their important contribution for paper entitled "The effect of caffeic acid phenethyl ester on isoproterenol-induced myocardial injury in hypertensive rats".

In our study, although the caffeic acid phenethyl ester (CAPE) application route was not defined in the main text, it was specified in the abstract section. The CAPE solvent used in our study is similar to that used in our earlier study (1). In this study, CAPE (Sigma, >97% pure) was dissolved in 95% ethanol (total 0.1 cc volume) and it was then diluted 10 times with saline. Consequently, 10% ethanol at 0.1 cc/day was administered to each rat. All groups received an equal volume of the ethanol/saline vehicle solution (2).

Selçuk İlhan
Department of Pharmacology, Faculty of Medicine, Fırat University; Elazığ-*Turkey*

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Address for Correspondence: Dr. Selçuk İlhan,
Fırat Üniversitesi Tıp Fakültesi,
Tıbbi Farmakoloji Anabilim Dalı, 23200, Elazığ-*Türkiye*
Phone: +90 424 237 00 00-4665
E-mail: selcukilhan52@gmail.com