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LETTER

Forsythoside B Mitigates Monocrotaline-Induced Pulmonary Arterial Hypertension via Blocking the NF-κB Signaling Pathway to Attenuate Vascular Remodeling [LETTER]

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Dear editor

We have read the article by Liu et al about Forsythoside B Mitigates Monocrotaline-Induced Pulmonary Arterial Hypertension via Blocking the NF-κB Signaling Pathway to Attenuate Vascular Remodeling. The purpose of this study was to identify the inhibitory effect of Forsythoside B (FTS•B) on the NF-κB signaling pathway. Pulmonary arterial hypertension (PAH) is a serious pathological disease with limited effective treatment options. The proliferation of pulmonary artery smooth muscle cells (PASMCs) is induced by the activation of the nuclear factor-κB (NF-κB) signaling pathway which plays a crucial role in the pathogenesis of PAH.[1] Forsythoside B (FTS•B) is a phenylethanoid glycoside known for its effect to effectively activate nuclear factor erythroid 2-related factor 2 (Nrf2) to exert antioxidant and anti-inflammatory effects, it serves as a means of alleviating myocardial ischemia-reperfusion injury and suppressing the activation of endogenous inflammatory factors by inhibition of nuclear factor-kappa B (NF-κB) signaling.[2]

Based on the methodological details given, they induced PAH condition with monocrotaline (MCT) intraperitoneal injection and measured the right ventricular hypertrophy using echocardiography and right heart catheterization.[1] Jasenovec et al confirmed the well-known effects of monocrotaline administration on the lungs and the right ventricle, as well as pulmonary arterial pressure. Additionally, they also discovered the activation of the alternative pathway of the renin-angiotensin system, specifically an increase in angiotensin (Ang) 1–7 and Ang 1–5, along with an increase in Ang I, but without any change in Ang II levels. Furthermore, there was a downregulation of aldosterone observed 4 weeks after monocrotaline administration.[3] Phorbol 12-myristate 13-acetate (PMA) is a potent phorbol ester known for its effect on activating NF-κB. It is a specific activator of Protein Kinase C (PKC) and hence activates nuclear factor-kappa B (NF-κB). The nuclear factor kappa B (NF-κB) is responsible for regulating genes involved in inflammation and immune responses. NF-κB might be important in cardiovascular diseases (CVDs), atherosclerosis, and diabetes. It is reported that several therapeutic agents such as pimobendan and sodium–glucose cotransporter 2 inhibitors used for CVDs and diabetes, have anti-inflammatory effects by inhibiting NF-κB activation; anti-inflammatory therapy may have beneficial effects in CVDs and diabetes.[4]

Based on the results, the FTS•B decreased the effect of MCT in vascular remodeling and pulmonary artery pressure and also improved right ventricular hypertrophy and survival. Moreover, FTS•B reversed PDGF-BB-induced PASMC proliferation and migration, decreased PCNA and CyclinD1 expression, and decreased levels of IL-1β, IL-6, and phosphorylation of p65 caused by MCT.[1] In addition, FTS•B exerts neuroprotective effects by modulating various pathways, including oxidative stress, anti-inflammation, NF-κB signaling, 2-AG, Nrf2 signaling, acetylcholinesterase,

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PI3K-Akt signaling, ferroptosis, gut-brain axis, TLR4 signaling, endoplasmic reticulum stress, PI3K/Akt/mTOR signaling, and PPARγ signaling pathway.[5]

We acknowledge and appreciate the findings obtained from the research. This study could serve as a model for better understanding the effect of FTS•B on impaired PAH by suppressing the NF-κB signaling pathway to attenuate vascular remodeling. They also show that FTS•B might serve as an alternative medicine for PAH treatment.

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Disclosure

The authors report no conflicts of interest in this communication.

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