

Curcumin: Another Potential Translational Candidate for Anti-Fibrosis on Heart Failure?

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Curcumin (diferuloylmethane), a polyphenol accounting for the yellow color of turmeric (a curry spice), is commonly used in Asian countries.¹ It has been reported to carry a diverse range of targeting molecules ranging from anti-inflammatory, antioxidant, and anti-fibrotic effects.^{2,3} In a pressure-overloaded rabbit model, curcumin improves left ventricle function by inhibiting the remodeling process.⁴ It also promotes cardiac repair and ameliorates cardiac dysfunction following myocardial infarction⁵ and can reduce angiotensin II-mediated cardiomyocyte growth via LOX-1 inhibition.⁶

Cardiac fibrosis plays a critical role in the pathophysiology of cardiovascular disease. Regarding its anti-fibrotic property, curcumin could also attenuate pulmonary fibrosis caused by amiodarone therapy,⁷ hepatic fibrosis by inhibiting hepatic stellate cell activation⁸ and also renal fibrosis.⁹ In an article by Chung et al.,¹⁰ it was found that curcumin can modify the antifibrotic process on cardiac fibroblasts through modulating transforming growth factor (TGF)- β and angiotensin (Ang) signaling.

In a more recent article by Chung et al.,¹⁰ several cellular functions were evaluated including: migration, proliferation, collagen production, and transcription signaling pathways in rat cardiac fibroblasts isolated from Sprague-Dawley rats with curcumin, co-administration of TGF- β 1 or Ang II. Most interestingly, the effects of curcumin on either TGF- β 1 or Ang II were different (Figure 1). Curcumin cannot affect the expression of receptor of TGF- β 1 both on control or co-administration of

TGF- β 1. On the other hand, curcumin can decrease the expression of Ang II type I receptor both on control or co-administration of Ang II concentration. In addition, the curcumin also decreased the suppressive effect of Ang II on matrix metalloproteinase-2 (MMP-2) activity in cardiac fibroblasts. As expected, with the remaining effect of MMP-2, the curcumin-treated cardiac fibroblasts can further digest the collagen contents as expressed by the greater diminished amount of collagen with stimulation of Ang II, especially compared with the condition stimulated by TGF- β 1. The effects on migratory, proliferative abilities were similar either at the baseline or after the co-administration of TGF- β 1 or Ang II. Not surprisingly, curcumin-treated cardiac fibroblasts down-regulated phosphorylated Akt and phosphorylated Smad2/3 expression irrespective of TGF- β 1 treatment. Curcumin also decreased phosphorylated extracellular signal-regulated kinase 1/2 levels in the presence of Ang II.

In the current study, curcumin has possible translational potentials. However, animal studies are mandatory to test these novel findings and some points still remain unanswered. First, because curcumin affects the Ang II pathway, the pleiotropic effect beyond the *in*

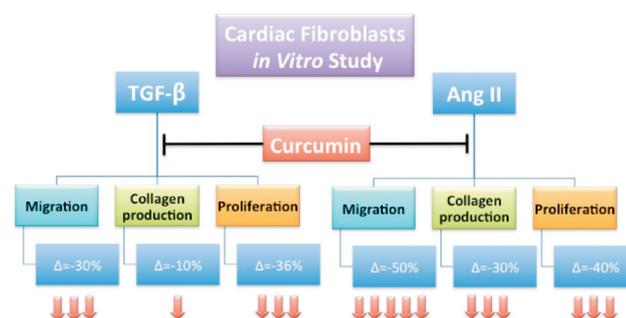


Figure 1. Curcumin prevents migration, collagen production and proliferation abilities on cardiac fibroblasts. With different effects on the receptor of TGF β and Ang II, the degree on the above abilities also varies between these 2 pathways. ANG, angiotensin; TGF, transforming growth factor.

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in vivo blood pressure lowering effect should be examined. Second, the appropriate *in vivo* dose effect of curcumin has yet to be established. In addition, it would be speculative at this point to conclude that, for antifibrotic consideration, the apoptosis effect may happen with higher dose treatment. Nevertheless, future clinical translational trials are expected.

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