

## Curcumin Attenuates Angiogenesis in Liver Fibrosis and Inhibits Angiogenic Properties of Hepatic Stellate Cells

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**Abstract :** Sinusoidal pathological angiogenesis is a novel therapeutic target for liver fibrosis. We demonstrated that curcumin ameliorated fibrotic injury and sinusoidal angiogenesis in rat liver with fibrosis caused by carbon tetrachloride. Curcumin reduced the expression of angiogenic markers in fibrotic liver. Experiments in vitro showed that the viability and vascularization of rat liver sinusoidal endothelial cells (LSECs) were not impaired by curcumin. Further investigations showed that curcumin inhibited VEGF expression in hepatic stellate cells (HSCs) by disrupting PDGF- $\beta$ R/ERK and mTOR pathways. HSC motility and vascularization were also suppressed by curcumin via blocking PDGF- $\beta$ R/FAK/RhoA cascade. Gain- or loss-of-function analyses revealed that activation of PPAR $\gamma$  was required for curcumin to inhibit angiogenic properties of HSCs. We concluded that curcumin attenuated sinusoidal angiogenesis in liver fibrosis possibly by targeting HSCs via a PPAR $\gamma$  activation-dependent mechanism. PPAR $\gamma$  could be a target molecule for reducing pathological angiogenesis during liver fibrosis.

**Keywords :** angiogenesis, hepatic stellate cell, curcumin, peroxisome proliferator-activated receptor- $\gamma$

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