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About your manuscript (Minor Revision) - TJPS-44712

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Turkish Journal of Pharmaceutical Sciences

Ref.: Ms. No. TJPS-44712, "Ferulic Acid Prevents Angiogenesis Through COX-2 and VEGF on The Chick Embryo Chorioallantoic Membrane Model"

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Ferulic Acid Prevents Angiogenesis Through Cyclooxygenase-2 and Vascular... https://doi.org/10.4274/tjps.galenos.2019.44712 (doi: 10.4274/tjps.galenos.2019.44712)

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TJPS-44712: Research Article

Ferulic Acid Prevents Angiogenesis Through Cyclooxygenase-2 and Vascular Endothelial Growth Factor on The Chick Embryo Chorioallantoic Membrane Model

Juni Ekowati[1], Iwan Sahrial Hamid[2], Nuzul Wahyuning Diyah[1], S Siswandono[1]
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INTRODUCTION: This study designed to verify the antiangiogenic activity of ferulic acid (FA) and its potency to inhibit COX-2 and VEGF expression on CAM model. Moreover besides, we verified its mechanism of action by docking the molecule on COX-2, tyrosine kinase and VEGF-2 proteins in silico
METHODS: Anti-angiogenesis assay of FA at the doses of 30, 60 and 90 µg were performed using CAM of chicken eggs with nine-day old which were stimulated by 60 ng basic fibroblast growth factor (b-FGF). Celecoxib 60 µg was used as reference drug. The inhibitory activity on VEGF and COX-2 expressions were conducted by immunohistochemistry assay (IHC). Molecular docking of FA were accomplished by Molegro Virtual Docker program ver. 5.5. on COX-2 enzyme (PDB ID 1CX2), tyrosine kinase receptor (PDB ID 1XKK) and VEGF-2 receptor (PDB ID 4ASD).
RESULTS: FA at doses 30, 60, 90 µg significantly prevented angiogenesis on CAM model ($p<0.05$), which were represented as inhibitory activities against endothelial cell of blood vessels (42.6-70.7%) and neovascularization (43.0-86.6%). Inhibitory activities of FA against VEGF expression were stronger than its action on COX-2 expression. Molecular docking on VEGF-2 receptor result in RS value of FA was -73,844 kcal/mol, and celecoxib was -94.557 kcal/mol. RS value on tyrosine kinase of FA was -84.954 kcal/mol, while celecoxib was -93.163 kcal/mol. Docking on COX-2 receptor denoted RS value of FA was -73,416 kcal/mol, while celecoxib was -118,107 kcal/mol.
DISCUSSION AND CONCLUSION: Reduction of VEGF-2 & COX-2 expression due to treatment with FA at dose range 30–90 µg seem to be related to angiogenesis inhibition, which is presented by two parameters, namely inhibition of neovascularization and endothelial cell growth in blood vessels It was concluded that FA is promising anti-angiogenic therapeutic agent especially at early stage, and this activity can be resulted from inhibitory action on COX-2 and VEGF-2 proteins.

Keywords: ferulic acid, COX-2, VEGF, tyrosine kinase, angiogenesis, chorio allantoic membrane

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