Baicalein decreases uric acid and prevents hyperuricemic nephropathy in mice

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background: Hyperuricemia is an independent risk factor for kidney diseases, metabolic syndrome, diabetes, hypertension and cardiovascular diseases. Because approximately 70% of uric acid(UA)is excreted from the kidney. Hyperuricemia occurs when kidney function declines. However, the role of elevated UA on chronic kidney diseases(CKD)remains controversial. At present, urate lowering therapy in asymptomatic hyperuricemia is also conservative. Thus, further experimental and clinical studies are still needed to identify the association between hyperuricemia and CKD.As a natural flavonoid extracted from the Chinese herb *Scutellariae radix*, baicalein has many biochemical and pharmacological benefits, including antioxidant, anti inflammation, anti tumor anti fibrosis and cardiovascular protective effects. Aim: the purpose of this study is to determine whether baicalein executed a kidney protection action in hyperuricemia and mechanisms involved. Methods:Molecular docking analysis and surface plasmon resonance(SPR)were conducted to reveal the direct interaction between baicalein and xanthine oxidoreductase(XOR) 50mg/kg/d baicalein was orally administrated into ICR male mice for 21 days, including 7 days pretreatment. Serum UA, creatinine, BUN and urine UA were determined by commercial kits, and microalbuminuria as tested with ELISA kit. Masson trichrome staining was performed to evaluate renal fibrosis. The expressions of Nox4, FN, MMP 7, E cadherin and α SMA were detected by Western blot analysis. Results:in this paper, we firstly indentified baicalein as an effective XOR inhibitor in vitro and in vivo. Molecular docking analysis and SPR revealed a direct interaction between baicalein and XOR.Moreover, 50mg/kg/d baicalein treatment significantly suppressed the viability of xanthine oxidoreductase in hyperuricemia mouse model. Baicalein may block both of the XOR dependent and NADPH oxidase dependent production of ROS and enhance ROS elimination, This normalizes the imbalance between the oxidative and anti oxidative status after hyperuricemia. The data showed that baicalein remarkably prevented renal dysfunction, ameliorated kidney fibrosis, alleviated EMT and oxidative stress in hyperuricemia mice. Conclusion: Baicalein can attenuate the development of hyperuricemia induced nephropathy through XOR inhibition, NADPH oxidase dependent and XOR dependent ROS elimination, EMT moderation and fibrosis alleviation. Our studies highlight that baicalein can alleviate fibrosis and EMT possibly through MMP 9 signaling and MMP7 in hyperuricemic nephropathy