杜牛膝萃取物對腎纖維化抑制之研究

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摘 要

根據行政院衛生署新聞稿公告之民國98年度國人主要十大死因，其中糖尿病及腎炎、腎徵候群及腎性病變致死排行分別為第五名及第十名。糖尿病型的腎臟疾病將導致終末期的腎臟病產生，而終末期的腎臟病的特徵是腎臟的纖維化，因此對於抑制腎臟纖維化的建議已是被作為治療終末期腎臟病的一項策略。 杜牛膝 (Radix Achyranthis Bidentatae)是一種具促進血液循環功效的中藥，已被廣泛的用來治療肝臟及腎臟疾病。在此一研究中探討杜牛膝萃取物對於腎臟纖維化抑制的角色，杜牛膝萃取物經由酒精熱萃取方式取得，利用乙型轉型生長因子(transforming growth factor-β 簡稱TGF-β)誘導刺激大鼠之腎纖維母細胞NRK -49F纖維化，並於TGF-β刺激24小時後，再分別添加入不同劑量之杜牛膝(RAB)萃取液並持續培養24小時，以此研究杜牛膝萃取物對抑制腎臟纖維化之角色與效果。TGF-β為一種細胞纖維化激素，其訊息傳遞乃經由第一型乙型轉型生長因子受器(TGF-β RI)與受器後之訊息分子(如:Smad2、Smad3與Smad4蛋白)，進一步刺激細胞纖維化，此一路徑可藉由Smad7蛋白產生抑制化效果，阻斷纖維化訊息之傳遞。 實驗於添加杜牛膝萃取液後發現，不會影響細胞存活率，可依添加劑量的增加而降低了纖維連結蛋白(fibronectin)的產生，並且抑制了受器TGF-β RI與TGF-β結合的活性。在訊息傳遞路徑中，具抑制傳遞纖維化效果的訊息分子-Smad7也隨著添加劑量的上升而增加，進而有效抑制細胞纖維化。本研究發現杜牛膝萃取液可透過抑制纖維連結蛋白產生及TGF-β 之Smad纖維化訊息路徑控制腎臟細胞纖維化，因此，杜牛膝具有臨床上抗腎纖維化之應用潛力。

關鍵詞 : 杜牛膝、腎纖維化、乙型轉型生長因子、纖維連結蛋白、Smad訊息路徑

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