丁豎朽藉活化肝中之 HCG、IGF-1 及 uPA 訊息途徑來促進部分肝切除大鼠之肝再生能力

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背景:此報告中我們探討中草藥對肝臟再生的訊息途徑影響，中草藥共包含有丹參、高氏柴胡、黨參和丁豎朽四種。同時探討四種訊息途徑含有肝細胞生長因子增生途徑 (HGF pathway)和類胰島素生長因子存活途徑(IGF-1 pathway)，抗纖維化的纖維母細胞生長因子及 uPA 途徑(uPA pathway)，以及與結痂形成有關之 TGFβ1 途徑。

方法:將大白公鼠分為十二組，以 silymarin(1g/kg/day)為正控制組；saline 為負控制組。分別以酒精誘導大白公鼠肝損傷 7 天,並各別餵食四種中草藥(1g/kg/day)，緊接著在 3 天及 7 天後進行肝臟切除手術。並以西方墨點法偵測蛋白質含量變化，同時以 RT-PCR 偵測 mRNA 基因表現之改變。

結果: 丁豎朽和 silymarin 餵食大白公鼠在 3 天肝臟切除手術中，其 HGF，IGF-1 signaling pathway 及 uPA pathway 的上下游訊息因子，其蛋白質表現量和基因表現量均有增加。再者，在 7 天的大白公鼠肝臟部份切除中，我們發現除 Silymarin 和丁豎朽餵食之大白鼠外，以高氏柴胡和丹參餵食的大白公鼠，其 HGF、IGF-1 及 UPA pathway 亦均有被活化之現象。況且，結果顯示長期肝臟部份切除 7 天後，促纖維化因子 TGFβ1 及 pro-collagen 之 mRNA 基因表現量亦有減少，除此之外，增生指標 α-SMA 之蛋白質表現量在 3 天及 7 天的部份肝切除中亦有上升現象。

總結:我們發現丁豎朽與 Silymarin 餵食後在 3 天肝切除大白鼠肝臟中具有很強的促增生效用，均強活化 HGF 增生途徑，IGF 細胞存活途徑及 uPA 抗纖維化途徑。而在 7 天的肝切除大白鼠中，發現除丁豎朽與 Silymarin 外，並且高氏柴胡和丹參顯現活化這些途徑之能力。所以，除保肝藥(silymarin)外，丁豎朽亦為一強而有效枝促肝損傷再生的中草藥。

Elephantopus Scaber acts as a strong proliferating agent on the hepatic-regeneration by activating HGF, IGF-1 pathways and uPA system in partial hepatectomized rats

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Background: In this report, we study the hepatic-regeneration effects in partial hepatectomy rats of four types of Chinese herbal medicines, including *Condonopsis pilosula*, *Salvia miltorrhiza* Bung, *Bupleurum Kasi*, and *Elephantopus Scaber* L. Four signaling pathways have been investigated, the proliferate and survival pathways of hepatocyte growth factor (HGF) and insulin like growth factor -1 (IGF-I), the anti-fibrosis of fibroblast growth factor(FGF)-uPA pathway and the scar formation of TGF pathway. **Method:**Liver injury was induced in male Spraque-Dawley rats by ethanol. Male Wistar rats, separated into groups randomly, were fed four Chinese herbals (1g/kg/day) and silymarin (25mg/kg) for 7 days. Then 70% partial hepatectomy was conducted and the effects of hepatic-regeneration were estimated on the following 3rd and 7th day. Western blotting was performed to measure the protein levels, RT-PCR were used to measure the gene expression levels. **Result:** The results showed that extract of *Elephantopus scaber* L, and Silymarin increased the component protein and mRNA levels of HGF pathway, IGF-1 signaling pathway and uPA ststem on 3rd day. On day 7th, the HGF, IGF-1 and uPA signal pathways were activated not only by Silymarin and *Elephantopus scaber* L but also *Bupleurum Kai* and *Salviamiltorrhiza* Bunge. It also showed that TGFβ1 and pro-collagen, the fibrosis factors, mRNA expression were decreased on 7 days after partial hepatectomy. Besides, the proliferate markers, α-SMA protein expression and mRNA expression level is increased. **Conclution:** It came to the conclusion that the extract of *Elephantopus scabe* L possessed the strongest proliferating effects in this study. We find that *Elephantopus scaber* L and Silymarin have more stronger proliferation, activation HGF proliferation pathway, IGF cell survival pathway and UPA anti-fibrosis pathway after partial hepatectomy on 3 days.. However, we find besides *Elephantopus scaber* L and Silymarin after partial heptectomy on 7 days, *Salvia miltorrhiza* Bung and *Condonopsis pilosula* have actived these pathway. Therefore, in addition to silymarin, *Elephantopus scaber* L was also stronger enhance liver regeneration Chinese medicine.