行政院國家科學委員會專題研究計畫　成果報告

蔥科植物及其含硫成份抑制糖尿病老鼠抗藥性金黃葡萄球菌及克雷白氏菌感染之活體研究

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計畫主持人：曹世明
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一、計畫名稱: 蔥科植物及其含硫成份抑制糖尿病老鼠抗藥性金黃葡萄球菌及克雷白氏菌感染之活體研究

二、計畫編號: NSC-94-2314-B-040-013

三、主持人: 曹世明　中山醫學大學 醫學系

四、　計畫摘要: 以糖尿病老鼠為對象，確認蔥科植物及其抑菌成份在已罹患糖尿病的動物身上能有效的治療 MRSA 及克雷白氏菌引發的感染、氧化及或發炎的異常。

五、計畫成果: 證實大蒜、紅蔥頭的萃出液及其含硫成份在糖尿病活體內能夠有效抑制抗藥性病原菌誘發的血流感染。也證實大蒜、紅蔥頭的萃出液及含硫成份在糖尿病活體內能夠有效改善因感染而造成的氧化傷害及 cytokines 的異常。研究結果已投稿至 Journal of Antimicrobial Chemotherapy。摘要如下:

Objectives: Inhibitory effect of diallyl sulphide (DAS) and diallyl disulphide (DADS) against methicillin-resistant *Staphylococcus aureus* (MRSA) infection in diabetic mice was studied. The influence of these agents upon the plasma levels of fibronectin, c-reactive protein (CRP), fibrinogen, interleukin-6 (IL-6), tumour necrosis factor alpha (TNF-alpha); the activity of plasminogen activator inhibitor-1 (PAI-1), antithrombin III (AT-III) and protein C in MRSA-infected diabetic mice was examined.

Methods: To induce diabetes, mice were treated with streptozotocin i.p. for 5 consecutive days. Ten clinical MRSA isolates obtained from infected patients were used in this study (n=10). Diabetic mice were infected by injecting 200 μL MRSA-PBS solution, which contained 10^7 cfu, via the tail vein. At 4 d postinfection, 200 μL DAS or DADS was orally administrated twice at the interval of 12 h. Eight hr after each administration, mice were killed; blood and organs of each mouse were collected. Serial dilutions from kidney filtrate were used to determine colony count. Plasma levels of IL-6, TNF-alpha, CRP and fibrinogen; the activity of PAI-1, AT-III and protein C were determined by commercial kits. Plasma fibronectin level was determined by rabbit anti-rat fibronectin antibody and quantified by ELISA. Lipid oxidation of kidney and spleen was determined by measuring malondialdehyde level.

Results: DAS and DADS significantly decreased MRSA viability in kidney (P<0.05), in which each agent given twice showed greater inhibitory effect than given once (P<0.05). MRSA infection in diabetic mice significantly elevated plasma levels of IL-6 and TNF-alpha (P<0.05). DAS or DADS given once did not affect plasma levels of IL-6 and TNF-alpha (P>0.05); however, twice treatment of DAS or DADS significantly suppressed both IL-6 and TNF-alpha levels in plasma (P<0.05). DAS and DADS treatments also significantly reduced CRP, fibronectin and fibrinogen levels in plasma (P<0.05). DAS or DADS treatment did not affect PAI-1 activity (P>0.05), but twice treatment from DAS or DADS significantly increased AT-III activity (P<0.05). DADS

at twice treatment only could elevate protein C activity (P<0.05). MRSA infection significantly enhanced lipid oxidation in kidney and spleen, determined by malondialdehyde level (P<0.05), which were alleviated significantly by the treatments of DAS or DADS (P<0.05).

Conclusions: These data suggest that DAS and DADS could provide multiple protective functions against MRSA infection in diabetic individuals. In order to suppress pro-inflammatory cytokines and elevate AT-III activity in diabetic mice, twice administrations of DAS or DADS were needed. Therefore, the used dosage and administrative interval of DAS or DADS should be carefully considered for diabetic individuals.