• 系統編號	RG9701-0375
• 計畫中文名稱	植物萃取物(含中藥成分)化粧品安全性評估與檢驗方法之研究（二）
• 計畫英文名稱	--
• 主管機關	--
• 計畫編號	DOH96-FD-1004
• 執行機構	台北醫學大學生藥學研究所
• 本期期間	9601 ~ 9612
• 報告頁數	225 頁
• 使用語言	中文
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• 中文關鍵字	抗痘化粧品；安全性評估；中草藥；替代性動物實驗；茶樹精油
• 英文關鍵字	--
• 中文摘要	今年本計畫持續整理我國含植物萃取物(含中藥成分)成分安全性之法規，及各國相關規定。另收集目前市售品中添加於抗痘化粧品之植物萃取約有百餘種植物常被利用，前二十種最常使用具有抗痘功效的植物： 金縷梅、蘆薈、洋甘菊、茶樹、綠茶、薰衣草、迷迭香、甘草、檸檬、海藻、玫瑰、柳樹、金盞花、鼠尾草、黃瓜、葡萄、馬栗(七葉樹)、歐薄荷、薏仁、桑白皮、馬齒莧、酸橙、銀雪松樹。據此收集其相關文獻發現，大部分植物萃取物具有抗痘功能且其化學成分十分多元化，部分甚有毒性之報導，尤其以茶樹精油爲最主要抗痘成分且其具有的毒性也最多，因此如何做有效率的管理添加於抗痘化粧品十分困難。繼而收集各國之皮膚毒性評估實驗與替代性動物實驗。歐盟將於 2013 年全面禁止使用經動物實驗之化粧品，綜合參考文獻資料後，提出幾項可行的替代性動物實驗希望本研究將朝此方向建立一套可行且符合世界潮流之毒性評估方法。本研究選擇使用次數頻繁且具有潛在毒性之茶樹精油作爲本次抗痘化妝品安全性評估之物質。本實驗利用 ISO4730 做爲品質管制之標準，分析茶樹精油(TTO)及市售茶樹精油中主成分 terpinen-4-ol 其含量分布在 47.89 ~ 53.23 之間。而主要之毒性成分 1,8-Cineole 之含量分布於 1.73 ~ 5.28 之間。結果顯示 TTO 與市售茶樹精油皆符合標準。本研究利用單一劑量毒性試驗與皮膚刺激性試驗評估茶樹精油對於皮膚的傷害。實驗結果指出，茶樹精油在濃度低於 0.25%/site 時不具有皮膚刺激毒性，且在濃度 2% /site 對於磨損之大白兔皮膚沒有刺激作用。若長期 28 天塗抹時也不會對肝腎功能造成傷害。在細胞實驗時，我們利用 3T3 細胞株測試茶樹精油之毒性發現，對於細胞之半致死毒性約爲 0.047%~0.081%。此體外試驗之濃度較體內試驗低，可能的原因爲未考慮精油之吸收代謝的影響，因此建議未來利用體外細胞實驗評估是否可替代體內皮膚毒性時，應考慮進入體內之比例。
• 英文摘要	Purpose: Nowadays, essential oils are popularly used in cosmetics. Tea tree oil (TTO), the essential oil of Melaleuca alternifolia, is one of the most

widely used in aromatherapy and has been investigated as an antimicrobial, anti-inflammatory and anti-cancer agent. However, TTO can cause skin irritation at high concentrations. In this study, we will explore the safety dosage of TTO and discussed the mechanism of TTO induced skin irritation. Methods: The TTO was extracted from Melaleuca alternifolia (Taiwan Seed Improvement and Propagation Station as a standard) by hydrodistillation in a Clevenger-type apparatus for 7 hr. Five kinds of commercial TTO were purchased form Taiwan Market. The skin irritations of TTOs were evaluated by in vivo and in vitro assay. Two animal models were used to estimate the skin toxicity, i.e. acute systemic toxicity of rats and damaged skin of rabbit was used to evaluate skin irritation. Cytotoxicity effects of TTOs were evaluated by MTT assay in NIH-3T3 and HaCaT cell lines and measured the mechanisms. The toxic and active ingredients of TTOs were analyzed by GC-MS. Results and Conclusions: The ISO4730 guideline was employed to analyze the ingredients in TTOs. The results showed that the rang of major component content (terpinen-4-ol) and major toxic component content (1,8-Cineole) was 47.89 to 53.23 and 1.73 to 5.28, respectively. Furthermore, TTOs could induce apoptosis in NIH-3T3 cells and the IC50 values were 0.09%. In vivo studies, TTOs induced acute systemic toxicity in rats at 10% to 1% per site after 24 h treatment but no allergy at 0.25%. However, TTOs did not induce further skin irritation on the damaged skin of rabbit. However, rats were smeared with 2% TTOs for 28 days, the skin would be allergy, but the functions of liver and kidney did not be damaged. The current suggestions for the usage of different commercial TTOs are 1%-10%. However, according to the above results, only 0.25 % TTOs did not cause the skin irritation on rats. Therefore, we suggested that below 1% TTOs was the suitable and safety does for application in cosmetics.