

薑黃對大鼠 28 天餵飼之安全性

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1 臺中縣霧峰鄉 農委會農業藥物毒物試驗所應用科理組

2 臺中縣霧峰鄉 農委會農業試驗所農化組

(接受日期：中華民國 92 年 7 月 28 日)

摘 要

廖俊旺、蔡淑珍、王順成、黃振聲* 2003 薑黃對大鼠 28 天餵飼之安全性 植保會刊 45 : 237 - 255

薑黃 (Turmeric, *Curcuma longa* Linn.) 含薑黃素 (curcumin)，經動物試驗得知薑黃素具抗腫瘤及護胃等多種功效，唯世界衛生組織與農糧組織 (WHO/FAO) 對長期食用薑黃之安全性仍有疑慮。本研究為探討國內薑黃之食用安全性，進行薑黃對大鼠 (Sprague-Dawley, SD) 之口服急性及 28 天餵飼急性試驗。口服急性試驗以藥物之最高測試劑量 5,000 mg/kg bw 薑黃粉經胃管餵飼大鼠後，薑黃粉並未造成大鼠中毒或死亡。28 天餵飼急性試驗則以 100 (低)、500 (中) 及 1,000 (高) mg/kg bw 薑黃粉為試驗組，另以 1,000 mg/kg bw 薑黃素 (65 - 70 % 純度, Sigma) 為藥劑對照組，經胃管連續餵飼大鼠 28 天，結果顯示，薑黃粉及薑黃素亦未造成大鼠中毒或死亡。各組體重、每日飼料消耗量、血液相及白血球分類與對照組比較均無明顯差異。唯薑黃粉中及高劑量組血漿中之纖維蛋白原 (fibrinogen, Fbg) 含量則較對照組減少及凝固時間延長，前凝血酶時間 (prothrombin time, PT) 及活化部份凝血激素時間 (activated partial thromboplastin time, APTT) 均有縮短 ($p < 0.05$)。血清生化檢查各處理組用功能指標，如麩氨酸氨基轉氨酶 (aspartate aminotransferase, AST)、總膽紅素 (total bilirubin)、膽固醇 (cholesterol)、三酸甘油酯 (triglyceride) 均有不同程度升高；腎功能指標，如尿素氮 (blood urine nitrogen, BUN)、肌氨酸 (creatinine) 及血清離子含量亦有顯著性上升 ($p < 0.05$)。尿液含白血球、上皮細胞及圓柱體數目則減少。薑黃粉高劑量組及薑黃素組雄鼠之肝及腎臟重量 (%) 有顯著性增重 ($p < 0.05$)；病理檢查各處理組臟器雖無明顯肉眼病理變化，但雄鼠用臟器細胞空泡及腎臟絲球體含濾液之數目均有輕微增加。綜合以上結果，薑黃對大鼠並無口服急性，且經 28 天餵飼高劑量 (1,000 mg/kg) 薑黃對大鼠亦無明顯急性傷害。然而，薑黃對大鼠血漿 Fbg 及 PT 之影響，是否與傳統

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中藥使用薑黃為『活血化癥』之藥理作用有關，仍有待進一步探討。

(關鍵詞：薑黃、28 天餵飼安全性、大鼠)

緒 言

保健食品一般源於傳統中醫食藥同源的理念，目前國內開發與研究保健食品日益增多⁽⁴⁾。鬱金 (*Curcuma Longa* Linn.) 俗名為薑黃 (turmeric) 或秋鬱金，為薑科植物 (Zingiberaceae)，原產於印度⁽³⁾，分佈中國大陸及南亞各地。中藥用薑黃根莖，性狀為不規則卵圓、圓柱或紡錘形，彎曲，叉狀分枝，表面深黃棕色，粗糙，具縱皺紋，有明顯環狀之環節、圓形分枝痕及鬚根痕 (圖 A)，質堅實不易折，切面呈棕黃色角質狀 (圖 B)，有蠟樣光澤，內皮層明顯，維管束呈點狀。薑黃含有薑黃素 (curcumin) (圖 D)、葡萄糖、果糖、菜油酯醇 (campesterol)、麥甾固醇 (β -sitosterol)、類脂質化合物及揮發油等物質。氣芳香，味苦辛，官能鑑別檢查以質堅實，斷面色赤

黃，氣味濃為佳。古中醫分類別，屬於行氣降氣藥⁽¹⁾，具有祛風熱，清肝明目，除痰結及『活血化癥』⁽³⁾等功用。

薑黃外觀呈黃色，為咖喱的主要原料之一，廣泛作為增加風味著色劑之食品添加。古印度人每日攝取量約為 4 g，該產地薑黃根部含有較高成份之薑黃素 (1-5%)⁽⁹⁾。薑黃素具有抗發炎，可治療創傷、抗氧化、抑制多種腫瘤及護用等功能^(1, 9, 14, 17, 18)，亦為傳統中醫藥⁽¹⁾。雖然食用薑黃被認為是安全的 (general recognized as safety, GRAS) 食品添加物，唯美國國家毒理計畫 (National Toxicology Program, NTP, 1993) 曾進行 Turmeric oleoresin (含 79-85% 類薑黃素, curcumoid) 餵飼動物之慢性試驗，發現高劑量組 (1%) 大鼠 (F344/N rats) 陰道腺體癌 (clitoral gland adenomas) 及小鼠 (B6C3F1 mice) 肝癌 (hepatocellular

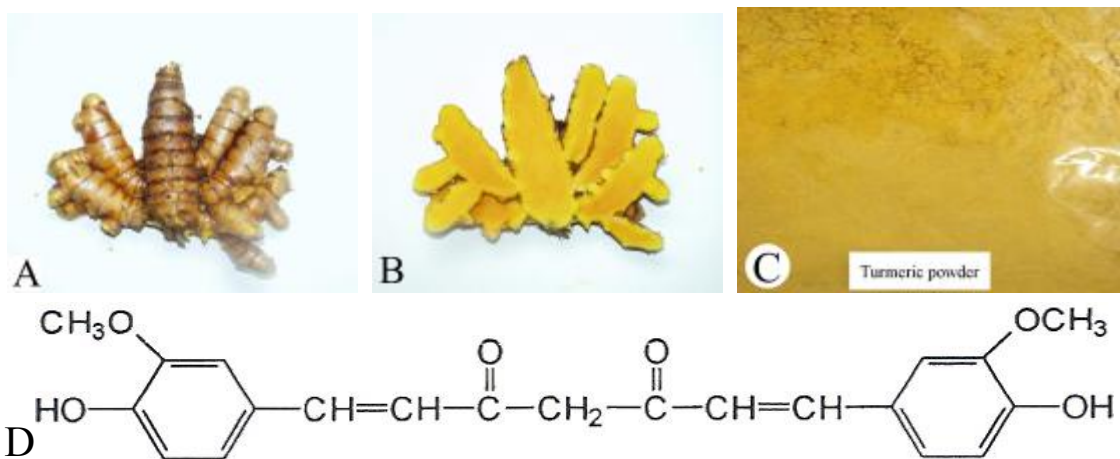


圖 1、薑黃新鮮塊根(A)及縱切面(B)，經烘乾磨粉之薑黃粉(C)及薑黃素化學結構式(D，分子量：368.4，引用自 CBADC, 1996, J. Cellular Biochem. 265: 72-85.)。

Fig. 1. Fresh tubers (A), cross section (B), ground powder of turmeric (C), and the chemical structure of curcumin (D, MW: 368.4, cited from CBADC, 1996, J. Cell. Biochem. 265: 72-85.)

adenoma) 發生率增加⁽¹⁵⁾，因而引起世界衛生組織/農糧組織 (WHO/FAO) 對薑黃長期食用之疑慮，建議薑黃作為食品添加物時，所含薑黃素之每日可攝取劑量 (ADI) 暫時限制為 0.1 mg/kg bw⁽⁹⁾。

一般植物性保健食品雖被認為是安全的，且部份確有保健功效，但因種類及數量眾多，成份亦複雜多變，若含有內生性毒物質 (inherent plant toxicants)，長期食用是否可能造成其他不良影響，唯部份保健食品之安全性，仍缺乏動物試驗加以印證。本研究為探討國內種植薑黃之食用安全性，以大黃品系薑黃根莖經乾燥研磨成乾燥粉，測試對大鼠口服急毒性及 28 天餵飼毒性，評估薑黃高劑量及重複食用後對哺乳動物之影響，藉以作為人體食用之安全性參考。

材料與方法

供試藥劑

薑黃 (大黃種) 約兩斗塊根乾燥粉由農試所提供，其製作過程係將新鮮樣本洗淨切片，60°C 烘乾及磨粉，經 60 mesh 篩網過篩所得。薑黃乾燥粉外觀呈黃色粉狀 (圖 1-C)，組成分含有薑黃素 0.31–0.55 % 乾物重⁽²⁾、水分 9.08 %、粗蛋白質 12.62 %、粗脂肪 4.65 %、粗纖維 5.97 %、灰分 7.32 %、碳水化合物 60.36 %、水溶性醣 (glucose) 11.54 % 及酸鹼值 (pH) 6.35。薑黃含有豐富鉀、磷、鎂等礦物質，其含量 (mg/100g) 為：鉀 (K) 2419.2、磷 (P) 544.2、鎂 (Mg) 353.0、鈣 (Ca) 114.8 及鐵 (Fe) 9.68 等。另以薑黃素 (curcumin 65–70 %, from *Curcuma longa*, Sigma, MO, USA) 作為對照藥劑。

供試動物

五週齡大鼠 (Sprague-Dawley, SD 品系) 購自財團法人國家實驗研究院國家實

驗動物中心，在動物飼育室觀察一週後，取體重相近之健康成鼠進行試驗。試驗動物給予充足之飼料 (Rodent Laboratory Chow 5001, Purina, MO, USA) 及飲水。動物飼育室控制狀況為溫度 22±1°C、相對濕度 50–70 % 及 12 小時光/12 小時暗之光照週期。實驗動物使用與操作均依據『實驗動物管理與使用指南』規範進行⁽²⁴⁾。

試驗步驟及觀察

薑黃對大鼠之口服急毒性及 28 天餵飼安全性試驗，主要依據衛生署公告之「健康食品安全及功效評估方法」⁽⁵⁾ 測試規範，該規範並符合美國環保署 (USEPA) 及歐洲經濟合作開發組織 (Organization for Economic Cooperation and Development, OECD) 之藥物毒物試驗準則規範^(11,23)。

口服急性毒性試驗

口服急性毒性試驗以最高劑量 5,000 mg/kg bw 薑黃粉作為試驗組及對照組，每組 10 隻大鼠 (雌雄各半)。薑黃粉並不完全溶於水，以逆滲透分離水 (Ultrapure, reverse osmosis system, Iowa, USA) 稀釋配成懸浮液體，將薑黃粉以胃管強迫餵飼大鼠，每隻餵飼量為 10 ml/kg。處理後每日觀察並每週稱體重，直至處理後第 14 天為止。試驗結束後，鼠隻以 CO₂ 犧牲後進行大體解剖，檢查體內臟器之內眼病理變化並檢查體內臟器之相對重量 (%)、血液相、尿及腎血清酵素等項目。

28 天餵飼安全性試驗

薑黃粉之劑量選擇依據衛生署公告「健康食品 28 天餵飼毒性」方法，以 1,000 mg/kg bw 為試驗最高劑量，其次中劑量為 500 mg/kg bw 及低劑量為 100 mg/kg bw，另以薑黃素 1,000 mg/kg bw 作為藥劑對照組，每組處理 20 隻大鼠 (雌雄各半)，以胃管連續餵飼薑黃粉 28 天，對照組則僅餵

飼逆滲透法離子水。

臨床症狀及眼球觀察

每日觀察臨床症狀，記錄中毒症狀、症狀發覺、復原或死亡時間，每週並詳細檢查一次。於試驗前及試驗結束時以眼底鏡 (Genesis, Kowa, Tokyo, Japan)，檢查對照組及高劑量組大鼠之眼球眼底變化。

體重、飼料消耗量及飼料利用率

每週以秤重天平 (Mettler, PM3000, Switzerland) 稱取大鼠體重及飼料消耗量，並每週更換新鮮粉狀飼料 (250 g)，飼料消耗量之計算以每週飼料添加總量 (250 g)，減去剩餘飼料量 (g)，再除以每週 7 日，所得即為每日消耗量 (g)。飼料利用率 (%) 之計算，即每日體重增重 (g) 除以每日飼料消耗量 (g)，再乘以 100 %。

血液學檢查

試驗結束後，以乙醚麻醉大鼠並自腹部大動脈放血，採集 1 ml 全血放入含 EDTA 抗凝血劑試管 (K3 EDTA syringes, Vacutainer, NJ, USA)，於血球計數儀 (Sysmex K-4500, Toa Medical Electronics Co., Ltd., Kobe, Japan) 檢測血液相 (complete blood count, CBC)，包括：白血球數 (white blood cell count, WBC count)、紅血球數 (red blood cell count, RBC count)、血球容積比 (hematocrit, Hct)、平均紅血球體積 (mean corpuscular volume, MCV)、平均血紅素 (mean corpuscular hemoglobin, MCH)、平均血紅素濃度 (mean corpuscular hemoglobin concentration, MCHC)、血紅素 (hemoglobin, Hb) 及血小板 (platelet) 等項目。白血球分類 (differential leukocyte count) 以血液抹片，經 Weigert's Iron Hematoxylin Stain Kit (A.J.P. Scientific Inc., NJ, USA) 染色後，於光學顯微鏡 (Nikon Optic-2, Tokyo,

Japan) 400 倍下，計算 100 個白血球中，淋巴球 (lymphocyte)、嗜中性球 (neutrophil)、單核球 (monocyte)、嗜酸性球 (eosinophil) 及嗜鹼性球 (basophil) 等各佔百分率 (%) 等。

血液凝固檢查

採集 2 ml 全血加入 3.8 % Buffered sodium citrate 之抗凝管 (9:1, Vacutainer, Becton Dickson, NJ, USA)，以離心機 (Sigma 2K-15, Osterode am Harz, Germany) 於 4 °C，3,000 xg 離心 10 分鐘，取血漿 (plasma) 以血液凝固分析儀 (automated coagulated analyzer, CA-550, Sysmex Corporation, Kobe, Japan) 檢測纖維蛋白原 (Fibrinogen, Fbg) 時間 (s) 及含量 (mg/dl)、前凝血酵素時間 (prothrombin time, PT) 及活化部份前凝血酵素原時間 (activated partial thromboplastin time, APTT) 等。

血清生化檢查

採集 5 ml 全血裝入血清分離管 (Vacutainer, Franklin Lakes, NJ, USA)，於離心機 (Kubota 2010, Tokyo, Japan)，以 775 xg 離心 15 分鐘。取血清液血清 (serum)，以血清生化儀 (Chiron Diagnostics Corporation, Oberlin, OH, USA) 檢測血液生化值，包括麩氨酸氨基轉氨酶 (aspartate aminotransferase, AST)、麩氨酸丙酸轉氨酶 (alanine aminotransferase, ALT)、總膽紅素 (total bilirubin)、膽固醇 (cholesterol)、三酸甘油酯 (triglyceride)、尿素氮 (blood urea nitrogen, BUN)、肌氨酸 (creatinine)、肌酸激酶 (creatine kinase)、乳酸脫氫酶 (lactate dehydrogenase, LDH)、總蛋白 (total protein, TP)、白蛋白 (albumin)、鹼性磷酸酶 (alkaline phosphatase, ALP)、麩氨酸轉氨酶 (γ -glutamyltranspeptidase, GGT)、葡萄糖 (glucose)、澱粉酶 (amylase) 及磷 (inorganic phosphorus)、鉀 (potassium)、

氯(chloride)、鈣(calcium)及鎂(magnesium)等離子濃度。

尿液學檢查

實驗結束前日，將大鼠放入代謝籠(Nalgene, Techniplast Co., Italy) 18 小時後，收集每隻尿量(volume)並記錄顏色(color)。取條狀試紙(AMES Reagent Strips)沾濕尿液，置於尿液分析儀(Clinitek 100 Urine Chemistry Analyzer, Miles Inc. Diagnostic Division Ellchart, IN, USA)檢測尿液比重(specific gravity)、膽紅素(bilirubin)、尿膽紅素原(urobilinogen)、酸鹼值(pH)、蛋白質(protein)、葡萄糖(glucose)、酮體(ketones)、硝基鹽(nitrite)、潛血反應(occult blood)；另尿液以 775 xg 離心 15 分鐘，取沉渣滴入血球計數盤(Digisystem Laboratory Instruments Inc. Taipei, ROC)於光學顯微鏡 400 倍下，計數尿中白血球(leukocyte)、紅血球(red blood cell)、上皮細胞(epithelial cell)、圓柱體(cast)、結晶體(crystal)及寄生蟲(parasite)等。

臟器重、肉眼及病理觀察

大鼠經乙醚麻醉後解剖，稱腦、胸腺、心、肝、腎、脾、腎丸或卵巢等臟器重量(g)並以最後一週之最終體重(g)，作為體內臟器重量比率(%)之計算基準。觀察肉眼病理變化，取臟器浸泡於 10% 中性福馬林溶液中固定一週，經組織粗修與石臘包埋，以石臘組織切片機(Leica RM 2145, Nussloch, Germany)製成 4-6 μm 厚度之組織切片，經 Hematoxylin & Eosin (H&E) (6)染色後，於光學顯微鏡觀察組織病理變化。以肝細胞空泡數目(vacuoles)分四等級：-：0；±：1-5；+：6-10；++：11-50；+++：51-100 個；腎絲球體內含均質液(glomerular homogeneous exudate)分四等級：-：0；±：1-2；+：3-5；++：6-10 個進行評估。

結果分析

各組數據以平均值及標準差值(mean±SD)表示，各處理組與對照組以 Student's *t*-test 進行統計分析，以 *p* 值小於 0.05 者即為具顯著性差異。

結 果

薑黃對大鼠之口服急性毒性

大鼠以胃管單次口服餵飼薑黃粉 5,000 mg/kg bw 劑量並連續觀察 14 天，結果薑黃粉並未引起大鼠急性中毒或死亡。薑黃粉組雄鼠第 7 天之平均增重(2.1%)比對照組(11.5%)顯著性下降($p < 0.05$)，第 14 天時則恢復。試驗結束後經人體解剖檢查，薑黃粉組雄鼠之肝臟表面顏色稍黃，其他臟器並無明顯肉眼病變。薑黃粉組臟器與體重之相對重量(%)、血液相、肝及腎血清酶素等項目與對照組者比較均無統計學顯著性差異。薑黃粉對大鼠之口服急性毒性 LD₅₀ 大於 5,000 mg/kg bw，為『正常使用時無急性毒性(unlikely to present hazard in normal use)』物質⁽¹⁰⁾。唯薑黃粉組的血漿 Fbg 凝固時間及含量(30.8 s 及 167.2 mg/dl)，明顯比對照組(28.2 s 及 180.5 mg/dl)凝固時間延長及含量減少($p < 0.05$)。

薑黃粉及薑黃素對大鼠 28 天餵飼之安全性評估 臨床症狀、飼料攝取量及體重之影響

28 天餵飼試驗期間，薑黃粉各劑量組及薑黃素處理組之大鼠均無中毒症狀，各處理組之體重、飼料消耗量及飼料利用率(%)均與對照組無明顯差異(圖 1 及表 1)。唯在第二週時，因操作不慎，胃管誤插入食道將薑黃粉注入胸腔內，造成薑黃低劑量組雄鼠、中及高劑量組雌鼠各有 1 隻大鼠，引起異物性急性纖維性胸膜炎及心包膜炎(acute fibrinoid pleuropericarditis)而死亡，該組數據均以 $n=9$ 作統計分析。

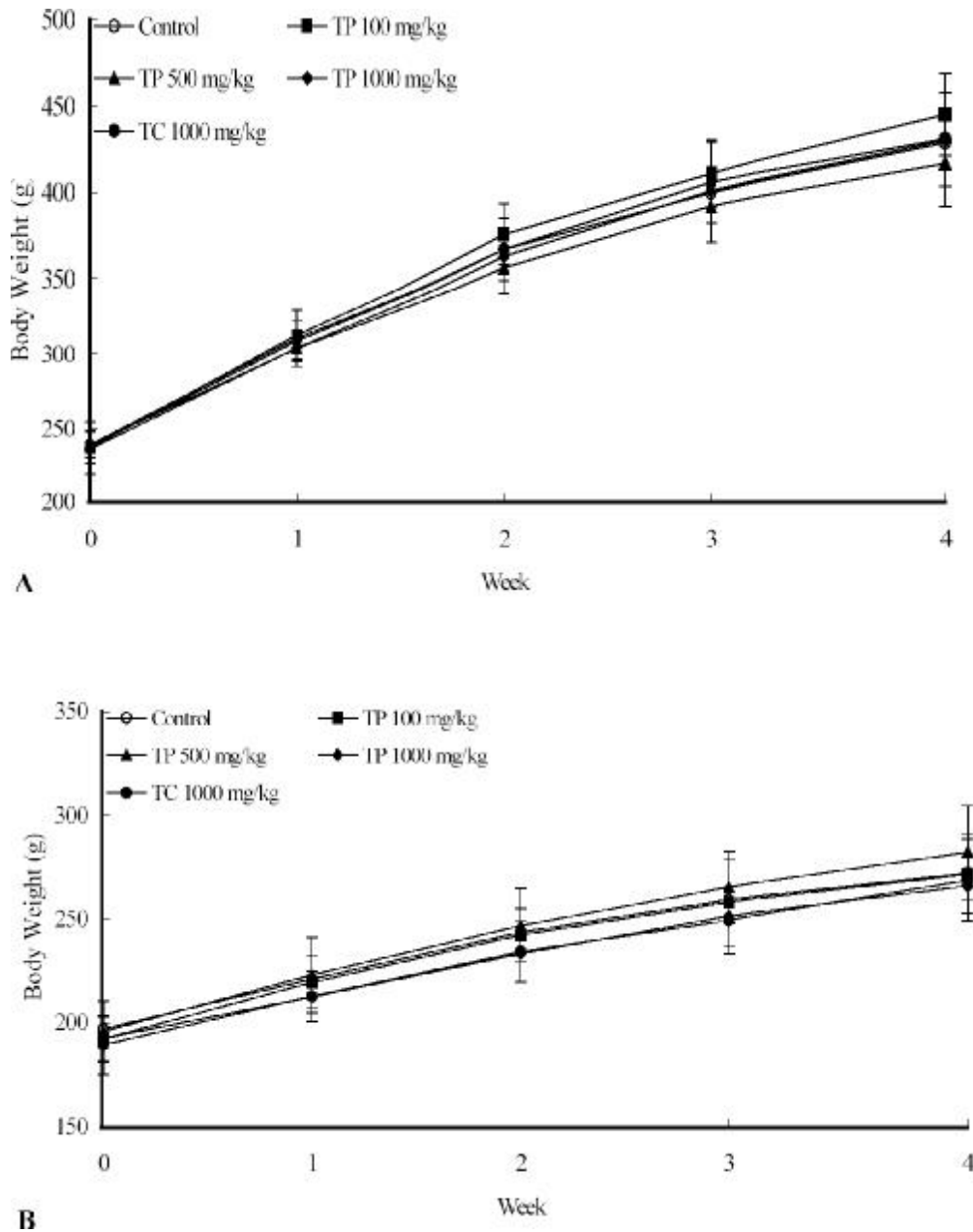


圖 2、薑黃粉及薑黃素經胃管餵飼大鼠 28 天之後體重變化。試驗組雄鼠(A)及雌鼠(B)之體重與對照組比較均無顯著性差異。

Fig. 2. Body weight changes of rats treated with turmeric powder and curcumin by daily gavage for 28 days. No significant changes in body weight (g) were found in treated male (A) and female (B) rats. TP: turmeric powder; TC: 65%–70% curcumin.

表一、薑黃粉經胃管餵飼大鼠 28 天之每日飼料消耗量變化

Table 1. Changes in feed consumption and efficiency of rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | Feed consumption (g) | | | | Feed efficiency (%) ²⁾ |
|-------------------------------|------------------------|----------|----------|----------|--------------------------------------|
| | 1 | 2 | 3 | 4 week | |
| Male | | | | | |
| Control | 31.0±1.3 ³⁾ | 30.2±1.5 | 30.4±2.1 | 28.5±2.0 | 29.9±1.2 |
| TP 100 | 29.8±2.9 | 31.1±2.4 | 29.7±3.7 | 28.5±2.3 | 33.0±9.7 |
| TP 500 | 29.4±1.3* | 29.1±1.4 | 29.4±1.8 | 26.8±1.7 | 28.7±1.3 |
| TP 1,000 | 29.7±2.6 | 30.4±1.9 | 30.3±2.0 | 28.6±1.6 | 29.7±1.8 |
| TC 1,000 | 30.6±2.0 | 32.5±2.1 | 32.6±2.5 | 29.6±2.9 | 31.3±2.2 |
| Female | | | | | |
| Control | 21.5±1.5 | 21.2±2.4 | 22.8±4.2 | 20.8±1.3 | 12.4±1.6 |
| TP 100 | 22.0±1.3 | 20.7±1.5 | 21.1±1.4 | 20.8±1.2 | 13.3±1.6 |
| TP 500 | 21.0±1.9 | 22.4±4.6 | 22.5±1.4 | 22.0±1.1 | 13.8±1.8 |
| TP 1,000 | 20.1±1.0 | 20.6±1.6 | 21.6±3.0 | 20.1±2.5 | 12.4±2.2 |
| TC 1,000 | 20.1±3.3 | 19.9±1.6 | 20.8±1.7 | 20.2±2.4 | 14.0±5.2 |

1) TP, turmeric powder; TC, 65 %–70 % curcumin.

2) Feed efficiency (%) = [daily body weight gain (g)/daily food intake (g)] × 100%.

3) Data are expressed as the mean±SD ($n = 9-10$).

* Significant difference between the control and treated groups at $p < 0.05$.

血液學之影響

血液學檢查 (RBC 等項) 在各處理組與對照組均無明顯差異, 薑黃粉組低及高劑量之雄鼠及高劑量組雌鼠之白血球總數有降低; 薑黃粉低劑量組及薑黃素組之雌、雄鼠帶狀白血球 (band neutrophil) 減少。其他各組雌、雄鼠之血液學檢查, 仍在正常大鼠生理參考值範圍內⁽¹³⁾, 不具劑量與毒性傷害相關性 (表二)。

血漿凝固之影響

在薑黃粉中及高劑量組雌鼠與中及低劑量組雌鼠之 Fbg 凝固時間 (s), 較對照組有明顯延長及含量 (mg/dl) 減少 ($p < 0.05$)。薑黃粉中及高劑量組雌鼠之 PT 及 APTT 反應時間縮短 ($p < 0.05$)。薑黃素組雌鼠之 Fbg 凝固時間減短及含量 (mg/dl) 增加, PT 時間縮短及 APTT 時間延長 ($p < 0.05$), 雌鼠則無明顯差異 (表三)。

血清生化值之影響

薑黃粉各劑量組及薑黃素組雌、雄鼠之血清麩氨酸氨基轉氨酶、總膽紅素、膽固醇、三酸甘油脂、總蛋白質、白蛋白、尿素氮、肌氨酸及離子 (P^{3-} 、 Ca^{2+} 、 Mg^{2+} 及 Cl^{-}) 均比對照組顯著性上升 ($p < 0.05$); 另外, 薑黃粉各劑量組及薑黃素組雌鼠之澱粉酶亦有增加 ($p < 0.05$) (表四及五)。

尿液學之影響

在薑黃粉及薑黃素各組雌、雄鼠之尿量、顏色、比重、膽紅素、尿膽紅素原、酸鹼值、蛋白質、葡萄糖、酮體、硝基鹽、潛血反應及寄生蟲等, 除部份有差異外, 各處理組間未呈現劑量與毒性反應之正相關性 (表六)。薑黃粉及薑黃素各組雌、雄鼠之尿沉渣白血球、上皮細胞、圓柱體、結晶體等則比對照組減少 ($p < 0.05$) (表七)。

表 2、薑黃粉經胃管餵飼大鼠 28 天之血液學變化

Table 2. Changes in hematological parameters in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | RBC (10 ⁶ /μl) ²⁾ | HGB (g/dl) | HCT (%) | MCV (fl) | MCH (pg) | MCHC (g/dl) |
|----------------------------|---|------------|----------|----------|----------|-------------|
| Male | | | | | | |
| Control | 7.5±0.1 ³⁾ | 16.2±0.1 | 46.9±1.0 | 61.8±0.4 | 21.4±0.3 | 34.7±0.5 |
| TP 100 | 7.5±0.1 | 16.0±0.1 | 46.5±0.6 | 62.0±0.6 | 21.3±0.2 | 34.4±0.2 |
| TP 500 | 7.3±0.1 | 15.5±0.1 | 46.2±0.6 | 62.5±0.6 | 21.1±0.2 | 33.7±0.3 |
| TP 1,000 | 7.4±0.1 | 15.8±0.1 | 47.2±0.7 | 63.2±0.2 | 21.2±0.1 | 33.5±0.2 |
| TC 1,000 | 8.0±0.1 | 16.8±0.1 | 49.4±0.5 | 61.7±0.4 | 21.0±0.2 | 34.0±0.2 |
| Female | | | | | | |
| Control | 6.7±0.7 | 15.3±0.1 | 41.5±0.3 | 61.7±0.3 | 22.7±0.1 | 36.8±0.1 |
| TP 100 | 6.9±0.1 | 15.2±0.2 | 42.2±0.6 | 60.4±0.5 | 21.7±0.2 | 36.0±0.1 |
| TP 500 | 6.6±0.1 | 15.0±0.2 | 42.9±0.9 | 65.0±0.5 | 22.7±0.3 | 35.0±0.3 |
| TP 1,000 | 7.0±0.1 | 15.7±0.1 | 43.7±0.2 | 61.9±0.7 | 22.2±0.2 | 35.9±0.3 |
| TC 1,000 | 6.9±0.1 | 15.4±0.2 | 42.0±0.5 | 60.6±0.6 | 22.3±0.2 | 36.8±0.2 |

| | WBC (10 ³ /μl) | Lymph (%) | Neutrophil (%) | | Monocyte (%) | Eosinophil (%) | Basophil (%) |
|---------------|---------------------------|-----------|----------------|----------|--------------|----------------|--------------|
| | | | Band | Segment | | | |
| Male | | | | | | | |
| Control | 11.6±1.2 | 83.2±1.4 | 1.2±0.2 | 13.0±1.5 | 3.3±0.4 | 0 | 0 |
| TP 100 | 7.0±0.7* | 85.0±1.5 | 0.8±0.3 | 10.4±1.0 | 3.1±0.4 | 0.2±0.2 | 0 |
| TP 500 | 12.2±1.1 | 85.4±0.9 | 0.4±1.6* | 9.3±0.9 | 5.0±0.5* | 0 | 0 |
| TP 1,000 | 7.5±0.5* | 82.3±1.1 | 0.6±0.1 | 13.2±0.9 | 3.9±0.6 | 0 | 0 |
| TC 1,000 | 9.7±0.9 | 83.3±1.5 | 0.3±0.1* | 13.3±1.4 | 3.7±0.4 | 0.1±0.1 | 0 |
| Female | | | | | | | |
| Control | 5.7±0.4 | 83.6±1.5 | 0.8±0.2 | 12.2±1.3 | 3.2±0.3 | 0 | 0 |
| TP 100 | 5.5±0.5 | 84.2±0.6 | 1.3±0.2 | 10.8±0.4 | 3.3±0.5 | 0 | 0 |
| TP 500 | 6.4±0.7 | 83.5±1.3 | 0.6±0.2 | 11.5±1.2 | 3.8±0.4 | 0 | 0 |
| TP 1,000 | 8.7±0.9* | 84.1±1.1 | 0.7±0.3 | 12.0±1.0 | 2.7±0.5 | 0.1±0.1 | 0 |
| TC 1,000 | 7.5±0.9 | 85.2±1.3 | 0.1±0.1* | 10.6±1.3 | 3.9±0.5 | 0 | 0 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood count; Lymph, lymphocytes.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

* Significant difference between the control and treated groups at $p < 0.05$.

表三、薑黃粉經胃管餵飼大鼠 28 天血液凝固變化

Table 3. Changes in blood coagulation parameters in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | PLT (10 ³ /μl) ²⁾ | Fbg | | PT (s) | APTT (s) |
|-------------------------------|--|-----------|------------|-----------|-------------|
| | | (s) | (mg/dl) | | |
| Male | | | | | |
| Control | 1161±29 ³⁾ | 19.9±0.2 | 245.3±2.8 | 33.6±0.2 | 25.9±1.0 |
| TP 100 | 1108±30 | 19.8±0.2 | 246.3±3.5 | 34.3±0.5 | 27.7±2.3 |
| TP 500 | 1083±31 | 23.3±1.0* | 213.6±8.9 | 29.3±0.5* | 22.5±1.0* |
| TP 1,000 | 1004±28* | 23.0±0.9* | 216.0±8.0* | 15.3±0.1* | 25.5±0.7 |
| TC 1,000 | 1073±35 | 17.3±0.2* | 281.2±4.4* | 15.2±0.1* | 41.3±2.8* |
| Female | | | | | |
| Control | 1049±36 | 24.5±1.0 | 202.7±8.1 | 15.0±0.2 | 30.7±1.9 |
| TP 100 | 1145±38 | 30.4±1.6* | 167.0±8.8* | 15.0±0.1 | 40.9±1.7* |
| TP 500 | 1065±28 | 30.1±1.4* | 166.8±7.5* | 15.5±0.1 | 34.6±0.7 |
| TP 1,000 | 1095±43 | 26.8±1.4 | 188.1±10.2 | 15.6±0.1 | 33.4±1.7 |
| TC 1,000 | 1159±80 | 25.9±1.6 | 195.6±10.7 | 15.2±0.3 | 25.4±1.6 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ PLT, platelets; Fbg, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

* Significant difference between the control and treated groups at $p < 0.05$.

表四、薑黃粉經胃管餵飼大鼠 28 天血清肝及腎臟功能指數變化

Table 4. Serum biochemistry changes in liver function in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | ALT (U/l) ²⁾ | AST (U/l) | T. bilirubin (mg/dl) | Cholesterol (mg/dl) | Triglyceride (mg/dl) | BUN (mg/dl) | Creatinine (mg/dl) |
|-------------------------------|----------------------------|--------------|-------------------------|------------------------|-------------------------|----------------|-----------------------|
| Male | | | | | | | |
| Control | 23.8±2.8 ³⁾ | 70.7±7.9 | 0.12±0.01 | 35.4±4.6 | 29.8±3.0 | 12.9±1.4 | 0.33±0.03 |
| TP 100 | 32.7±2.3* | 90.1±3.8* | 0.20±0.01* | 46.4±5.0 | 36.3±4.2 | 18.3±1.7* | 0.44±0.04* |
| TP 500 | 28.9±1.8 | 89.5±3.2* | 0.19±0.01* | 47.3±2.8* | 45.2±5.0* | 17.2±1.1* | 0.41±0.02* |
| TP1,000 | 27.6±0.8 | 102.4±7.1* | 0.20±0.01* | 44.3±1.4* | 44.3±5.6* | 16.4±1.0* | 0.44±0.01* |
| TC 1,000 | 30.6±1.4 | 103.7±6.0* | 0.30±0.01* | 40.6±2.1 | 34.7±3.4 | 19.4±1.4* | 0.44±0.02* |
| Female | | | | | | | |
| Control | 21.4±1.5 | 75.1±7.3 | 0.17±0.01 | 62.2±4.9 | 27.7±1.0 | 17.1±1.1 | 0.45±0.03 |
| TP 100 | 26.6±1.5* | 82.9±4.7 | 0.17±0.01 | 74.1±6.1 | 30.4±3.4 | 23.4±1.5* | 0.52±0.02 |
| TP 500 | 27.7±3.0 | 103.7±7.1* | 0.20±0.01 | 79.3±4.6* | 48.7±6.5* | 17.5±0.7 | 0.47±0.01 |
| TP1,000 | 26.7±1.1* | 92.6±3.3* | 0.26±0.01* | 85.8±3.0* | 37.2±3.8* | 24.1±1.0* | 0.57±0.02* |
| TC 1,000 | 23.2±0.9 | 94.3±5.3* | 0.31±0.01* | 73.7±4.1 | 42.1±3.0* | 30.5±1.9* | 0.64±0.04* |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ ALT, alanine aminotransferase; AST, aspartate aminotransferase; T. bilirubin, total bilirubin; BUN, blood urea nitrogen.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

* Significant difference between the control and treated groups at $p < 0.05$.

姜黄粉、薑黄粉經胃管餵飼大鼠 28 天其他血清生化值變化

Table 5. Serum biochemistry changes in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | CK (U/l) ²⁾ | LDH (U/l) | T. protein (g/dl) | Albumin (g/dl) | ALP (g/dl) | GGT (U/l) |
|----------------------------|--------------------------|---------------|-------------------------|--------------------------|---------------------------|--------------------------|
| Male | | | | | | |
| Control | 281.6±52.8 ³⁾ | 610.6±102.5 | 3.3±0.3 | 2.5±0.2 | 169.4±25.6 | 0.7±0.2 |
| TP 100 | 203.0±20.9 | 605.5±35.8 | 4.6±0.2* ⁴⁾ | 3.3±0.1* | 174.3±8.1 | 0.6±0.2 |
| TP 500 | 326.7±24.2 | 639.8±40.4 | 4.9±0.3* | 3.4±0.1* | 183.4±8.3 | 0.8±0.2 |
| TP1,000 | 253.2±40.4 | 694.7±107.4 | 5.0±0.1* | 3.6±0.1* | 187.2±8.5 | 0.5±0.2 |
| TC 1,000 | 332.7±51.4 | 775.1±73.6 | 5.2±0.1* | 3.7±0.1* | 192.6±14.0 | 1.1±0.2 |
| Female | | | | | | |
| Control | 223.8±41.6 | 483.7±96.3 | 4.4±0.1 | 3.2±0.1 | 122.2±9.2 | 1.2±0.2 |
| TP 100 | 115.7±21.7* | 335.8±64.1 | 5.5±0.1* | 3.9±0.1* | 94.2±8.4 | 1.6±0.1 |
| TP 500 | 372.4±60.2 | 867.8±124.2* | 5.4±0.1* | 3.9±0.1* | 118.6±4.4 | 1.4±0.2 |
| TP1,000 | 192.2±29.4 | 568.4±53.7 | 5.5±0.1* | 3.9±0.1* | 129.4±10.0 | 0.8±0.1 |
| TC 1,000 | 322.4±61.7 | 627.0±93.8 | 5.5±0.1* | 3.9±0.1* | 104.2±8.5 | 1.3±0.2 |
| | Glucose (mg/dl) | Amylase (U/l) | P ³⁻ (mg/dl) | Ca ²⁺ (mg/dl) | Mg ²⁺ (mEq/dl) | Cl ⁻ (mEq/dl) |
| Male | | | | | | |
| Control | 98.5±7.6 | 590.8±49.2 | 5.9±0.5 | 6.2±0.7 | 1.07±0.18 | 79.8±6.5 |
| TP 100 | 129.1±13.3 | 780.3±57.0* | 7.3±0.3 | 8.1±0.4* | 1.10±0.06 | 97.8±3.7* |
| TP 500 | 117.5±8.5 | 765.8±49.4* | 8.1±0.3* | 8.2±0.4* | 1.98±0.07* | 90.8±3.7 |
| TP1,000 | 117.3±7.4 | 851.5±46.9* | 7.6±0.1* | 8.2±0.1* | 2.16±0.16* | 101.0±1.2* |
| TC 1,000 | 115.2±6.3 | 823.3±32.2* | 8.6±0.1* | 8.2±0.1* | 1.75±0.16* | 104.3±1.4* |
| Female | | | | | | |
| Control | 109.4±6.3 | 427.6±25.1 | 5.6±0.3 | 7.4±0.3 | 1.11±0.07 | 91.7±3.2 |
| TP 100 | 108.6±6.4 | 486.5±19.7 | 7.4±0.2* | 8.6±0.2* | 1.34±0.08 | 93.2±1.8 |
| TP 500 | 103.7±7.0 | 472.4±23.3 | 7.2±0.1* | 8.4±0.1* | 1.92±0.07* | 95.2±0.7 |
| TP1,000 | 106.1±6.0 | 363.5±71.7 | 7.4±0.3* | 8.6±0.1* | 1.90±0.05* | 108.0±1.2* |
| TC 1,000 | 101.4±7.6 | 472.5±22.5 | 7.8±0.1* | 8.2±0.1* | 1.69±0.05* | 106.1±0.4* |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ CK, creatine kinase; LDH, lactate dehydrogenase; T. protein, total protein; ALP, alkaline phosphatase; GGT, gamma glutamyl-transferase.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

* Significant difference between the control and treated groups at $p < 0.05$.

表六、薑黃粉經胃管餵飼大鼠 28 天之尿液學變化

Table 6. Changes in urinary analyses in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | Volume (ml) | Appear. | S. Gravity ²⁾ | pH | Protein (mg/dl) | Urobilinogen (EU/dl) |
|----------------------------|------------------------|---------|--------------------------|-----------|-----------------|----------------------|
| Male | | | | | | |
| Control | 12.6±0.7 ³⁾ | PY | 1.025±0.001 | 7.10±0.12 | 32.5±8.1 | 0.20±0.01 |
| TP 100 | 11.7±1.1 | PY | 1.025±0.001 | 7.33±0.11 | 31.1±8.8 | 0.20±0.01 |
| TP 500 | 12.8±0.7 | PY | 1.025±0.001 | 7.25±0.11 | 27.0±2.0 | 0.20±0.01 |
| TP1,000 | 12.6±1.0 | PY | 1.028±0.001 | 7.20±0.13 | 35.5±7.3 | 0.20±0.01 |
| TC 1,000 | 13.4±0.8 | PY~Y | 1.050±0.027 | 7.40±0.14 | 51.0±10.6 | 0.20±0.01 |
| Female | | | | | | |
| Control | 7.5±0.6 | PY | 1.024±0.001 | 6.95±0.13 | 15.0±2.2 | 0.20±0.01 |
| TP 100 | 10.7±0.6 | PY | 1.023±0.001 | 7.15±0.10 | 10.5±3.9 | 0.20±0.01 |
| TP 500 | 8.5±0.4 | PY | 1.024±0.001 | 7.05±0.05 | 20.0±4.1 | 0.20±0.01 |
| TP1,000 | 8.5±0.4 | PY | 1.020±0.001 | 7.38±0.24 | 15.0±3.3 | 0.20±0.01 |
| TC 1,000 | 10.3±0.8 | PY~Y | 1.024±0.001 | 7.05±0.15 | 19.5±3.2* | 0.20±0.01 |

| | Glucose | | Bilirubin | | Ketone | | | Nitrite | | Oc. Blood | | | Leukocyte | | | |
|---------------|-----------------|---|-----------|---|--------|---|---|---------|---|-----------|---|---|-----------|---|---|----|
| | - | ± | - | ± | - | ± | + | - | + | - | ± | + | - | ± | + | ++ |
| Male | | | | | | | | | | | | | | | | |
| Control | 3 ⁴⁾ | 7 | 1 | 9 | 0 | 4 | 6 | 10 | 0 | 9 | 1 | 0 | 8 | 2 | 0 | 0 |
| TP 100 | 8 | 1 | 8 | 1 | 0 | 8 | 1 | 5 | 4 | 9 | 0 | 0 | 6 | 2 | 0 | 1 |
| TP 500 | 7 | 3 | 7 | 3 | 0 | 6 | 4 | 5 | 5 | 10 | 0 | 0 | 9 | 1 | 0 | 0 |
| TP1,000 | 8 | 2 | 9 | 1 | 0 | 7 | 3 | 9 | 1 | 10 | 0 | 0 | 9 | 1 | 0 | 0 |
| TC 1,000 | 6 | 4 | 9 | 1 | 0 | 4 | 6 | 5 | 5 | 10 | 0 | 0 | 8 | 2 | 0 | 0 |
| Female | | | | | | | | | | | | | | | | |
| Control | 6 | 4 | 10 | 0 | 4 | 6 | 0 | 9 | 1 | 6 | 0 | 4 | 9 | 1 | 0 | 0 |
| TP 100 | 8 | 2 | 10 | 0 | 5 | 4 | 1 | 6 | 4 | 10 | 0 | 0 | 9 | 0 | 0 | 1 |
| TP 500 | 9 | 0 | 8 | 1 | 3 | 6 | 0 | 6 | 3 | 9 | 0 | 0 | 9 | 0 | 0 | 0 |
| TP1,000 | 8 | 1 | 9 | 0 | 3 | 6 | 0 | 7 | 2 | 9 | 0 | 0 | 9 | 0 | 0 | 0 |
| TC 1,000 | 8 | 2 | 10 | 0 | 5 | 4 | 1 | 7 | 3 | 10 | 0 | 0 | 10 | 0 | 0 | 0 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ S. gravity, specific gravity; Oc. blood, occult blood; PY, pale yellow; Y, yellow; Grades for each value. Glucose (mg/dl): -, nil; ±, 0.1; bilirubin (mg/dl) -, nil; ±, 0.4; ketone (mg/dl): -, nil; ±, 5; +, 15; nitrite: -, normal; +, positive; occult blood and leukocyte: -, negative; ±, trace; +, mild; ++, moderate.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

⁴⁾ Affected rat number.[change the number in the table too]

* Significant difference between the control and treated groups at $p < 0.05$.

表七、薑黃粉經胃管餵飼大鼠 28 天之尿液沉渣變化

Table 7. Urinary sediment changes in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | Urinary sediments (10 ³) ²⁾ | | | | Parasite | | Crystal | | | | |
|-------------------------------|--|----------|-----------|----------|------------------|---|---------|---|---|----|-----|
| | RBC | WBC | Epithelia | Cast | - | + | - | ± | + | ++ | +++ |
| Male | | | | | | | | | | | |
| Control | 1.6±0.4 ³⁾ | 1.0±0.2 | 10.7±2.0 | 7.9±0.6 | 10 ⁴⁾ | 0 | 0 | 2 | 2 | 4 | 2 |
| TP 100 | 0.6±0.2* | 0.3±0.1* | 5.2±1.3* | 7.6±1.4 | 9 | 0 | 0 | 0 | 5 | 3 | 1 |
| TP 500 | 1.4±0.4 | 1.8±1.6 | 5.7±0.6* | 5.1±0.6* | 10 | 0 | 0 | 0 | 5 | 2 | 3 |
| TP1,000 | 1.2±0.3 | 0.8±0.3 | 6.2±0.8* | 2.3±0.3* | 10 | 0 | 0 | 1 | 4 | 2 | 3 |
| TC 1,000 | 0.9±0.3 | 0.1±0.1* | 4.0±0.4* | 2.4±0.1* | 10 | 0 | 0 | 0 | 7 | 2 | 1 |
| Female | | | | | | | | | | | |
| Control | 0.4±0.8 | 1.4±0.2 | 8.0±1.4 | 10.6±1.4 | 10 | 0 | 0 | 6 | 3 | 1 | 0 |
| TP 100 | 1.4±0.6 | 0.6±0.1* | 6.3±0.8 | 5.6±0.7* | 10 | 0 | 0 | 4 | 4 | 2 | 0 |
| TP 500 | 3.3±2.1 | 1.0±0.5 | 2.7±0.4* | 3.7±0.3* | 9 | 0 | 0 | 5 | 2 | 0 | 2 |
| TP1,000 | 0.8±0.3 | 0.3±0.1* | 5.2±0.8 | 3.2±0.3* | 9 | 0 | 0 | 0 | 6 | 3 | 0 |
| TC 1,000 | 1.5±0.8 | 0.7±0.1 | 3.7±0.7* | 2.4±0.4* | 10 | 0 | 0 | 3 | 7 | 0 | 0 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ Urinary sediments: RBC, red blood cells; WBC, white blood cells. Grades for observation: Parasite: non, -; Positive, +; Crystal: -: Nil; ±: a few in a few fields examined; +: a few in some fields examined; ++: a few in all fields examined; +++: many in all fields examined.

³⁾ Data are expressed as the mean±SD ($n = 9-10$).

⁴⁾ Examined rat number.[change the number in the table too]

* Significant difference between the control and treated groups at $p < 0.05$.

臟器重量、尿尿及組織病理學之影響

古薑黃粉中及高劑量組雄鼠之用臟重量 (%) 雖有增加, 但無顯著性差異; 薑黃素組雄鼠之用臟重量 (%) 則有顯著增重。薑黃粉高劑量組及薑黃素組之腎臟重量 (%) 亦有增加 ($p < 0.05$), 其他各組之腦、心、胸腺、脾臟、睪丸及卵巢之重量均與對照組無明顯差異 (表八)。體內各臟器無明顯的肉眼病理變化; 組織病理檢查, 古薑黃粉中、高劑量組及薑黃素組雄鼠用細胞空泡數及腎絲球體內含均質樣濾液 (圖三) 出現數較對照組有輕微增多 (表九), 雌鼠則無影響。各處理組之其他器官均無明顯組織病理學變化。

討 論

薑黃常用於食品添加, 以增加食品風味及色澤變化, 並有長期食用之歷史淵源, 因而被認為是相當安全⁽⁹⁾, 另一方面, 自薑黃所萃取出之薑黃素具有多項功能: 抗發炎及抗氧化等作用^(16, 17, 18)。本 28 天餵飼試驗結果亦顯示, 古薑黃粉及薑黃素處理組雌、雄鼠之尿沉渣白血球、上皮細胞、圓柱體、結晶體數目均比對照組顯著減少, 推測與薑黃具有抗菌及抗發炎作用有關。植物性食品組成多樣性, 且各產地所含有有效成份含量亦不同, 例如, 印度薑黃根部含有 1-5% 薑黃素⁽⁹⁾, 而國內產製大黃

表八、薑黃粉經胃管餵飼大鼠 28 天之臟器重量變化

Table 8. Organ weight changes of rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | Brain (%) ²⁾ | Heart (%) | Thymus (%) | Spleen (%) |
|----------------------------|---------------------------|--------------|-------------|-------------|
| Male | | | | |
| Control | 0.486±0.004 ³⁾ | 0.287±0.005 | 0.120±0.005 | 0.184±0.006 |
| TP 100 | 0.474±0.008 | 0.284±0.006 | 0.112±0.007 | 0.176±0.008 |
| TP 500 | 0.501±0.008 | 0.311±0.009* | 0.114±0.004 | 0.196±0.009 |
| TP1,000 | 0.477±0.009 | 0.297±0.014 | 0.112±0.006 | 0.208±0.006 |
| TC 1,000 | 0.471±0.013 | 0.251±0.009 | 0.105±0.005 | 0.182±0.008 |
| Female | | | | |
| Control | 0.714±0.013 | 0.316±0.008 | 0.165±0.009 | 0.217±0.010 |
| TP 100 | 0.700±0.013 | 0.313±0.006 | 0.177±0.012 | 0.212±0.006 |
| TP 500 | 0.707±0.020 | 0.324±0.006 | 0.145±0.011 | 0.218±0.009 |
| TP1,000 | 0.726±0.014 | 0.329±0.010 | 0.180±0.006 | 0.214±0.008 |
| TC 1,000 | 0.710±0.016 | 0.326±0.011 | 0.162±0.008 | 0.221±0.012 |
| | Liver (%) | Kidney (%) | Testis (%) | Ovary (%) |
| Male | | | | |
| Control | 2.827±0.035 | 0.668±0.018 | 0.852±0.028 | - |
| TP 100 | 2.697±0.023* | 0.618±0.012* | 0.872±0.078 | - |
| TP 500 | 2.872±0.035 | 0.682±0.016 | 0.861±0.024 | - |
| TP1,000 | 2.875±0.060 | 0.721±0.010* | 0.835±0.016 | - |
| TC 1,000 | 2.984±0.058* | 0.709±0.011 | 0.841±0.031 | - |
| Female | | | | |
| Control | 3.105±0.048 | 0.642±0.014 | - | 0.046±0.003 |
| TP 100 | 3.019±0.071 | 0.661±0.014 | - | 0.048±0.002 |
| TP 500 | 3.220±0.094 | 0.664±0.021 | - | 0.050±0.004 |
| TP1,000 | 3.020±0.063 | 0.656±0.011 | - | 0.046±0.002 |
| TC 1,000 | 3.148±0.042 | 0.679±0.020 | - | 0.045±0.003 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ Organ weight (%) = [organ weight (g)/ final body weight (g)] × 100.

³⁾ Data are expressed as the mean±SD (n = 9–10).

* Significant difference between the control and treated groups at $p < 0.05$.

種薑黃僅含有薑黃 0.31–0.55 % 乾物重⁽²⁾。薑黃可再經萃取出類薑黃素，經以 HPLC 儀器分析主要成份，含有 Curcumin、Demethoxycurcumin 及 Bisdemethoxycurcumin

等 3 種。目前類薑黃素成品純度較高者，有 97 % 薑黃素 (Merck, Germany)，3 種主要成份中各有 77、17 及 3 % 之比率；其次為 Turmeric oleoresin (Natural Yellow

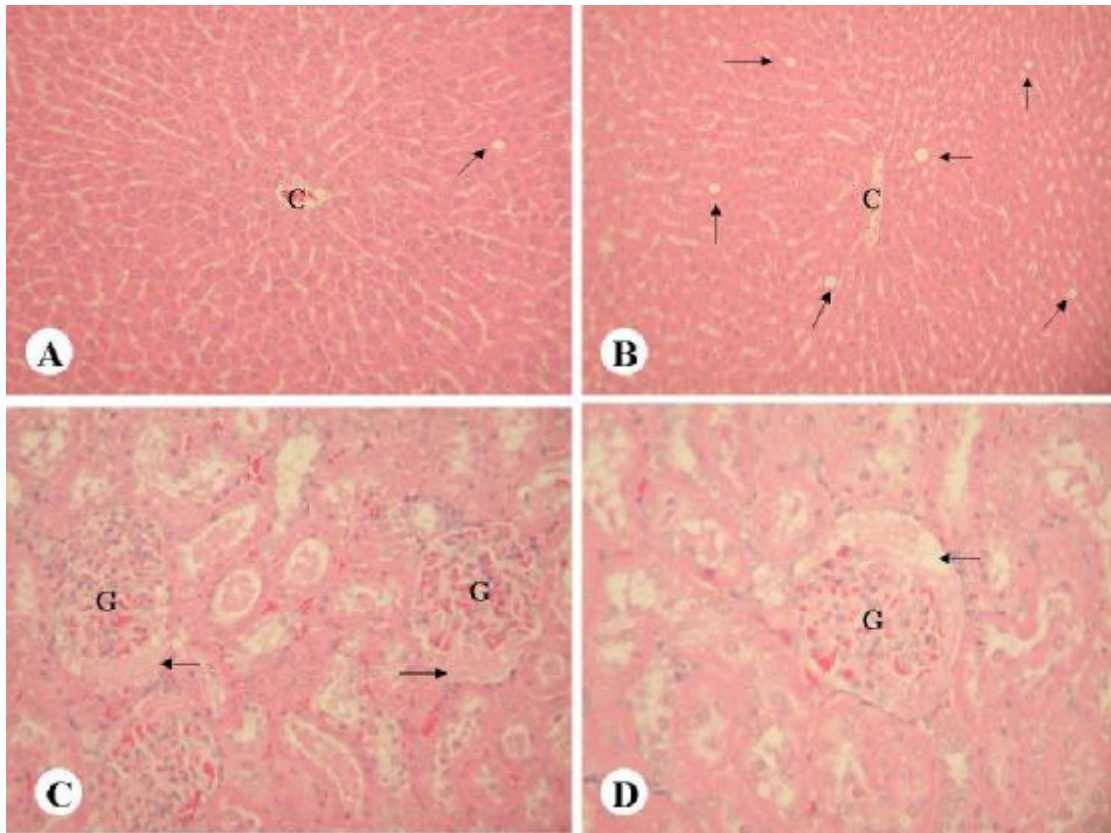


圖3、薑黃粉經胃管餵飼大鼠28天之用肝臟組織病理變化。肝臟用細胞空泡變化(箭頭)，A.對照組；B. 薑黃粉 1,000 mg/kg bw 組；腎臟絲球體鮑氏囊腔濾液(箭頭)，C 對照組；D 薑黃粉 1,000 mg/kg bw 組。C：中心靜脈區；G：腎絲球體 (H&E stain, 200x)。

Fig. 3. Histopathological findings in the liver and kidney of rats treated with turmeric powder (TP) for 28 days. Hepatic vacuoles (arrow), (A) control; (B) 1000 mg/kg bw TP group. Eosinophilic transudate (arrow), (C) control; (D) 1000 mg/kg bw TP group. C, central vein; G, glomerulus (H&E stain, 200x).

3)，含 75 - 89 % 類薑黃素⁽⁹⁾；另一為 65-70 % (curcumin, Sigma, MO, USA)。薑黃素本身並不具致變異性，且可抑制致癌物所引起之變異性⁽⁹⁾，唯自 1993 年美國國家毒理計畫 (NTP) 曾以純度較低之 Turmeric oleoresin 類薑黃素餵飼動物二週後，發現高劑量 (1%) 處理組小鼠 (B6C3F1 mice) 肝腫瘤 (hepatocellular adenoma) 比率增加⁽¹⁵⁾，乃建議薑黃作為食品添加劑，薑黃所含薑黃素對人每日可攝取劑量 (ADI) 暫時限制為 0.1 mg/kg bw⁽⁹⁾。但該

毒理試驗結果仍受質疑，因該試驗所使用試驗物質 (turmeric oleoresin) 之純度較低，含有較多未知 (unknown) 物質，是否為誘發癌症之主要因素，而非薑黃素所造成，仍有待釐清⁽⁹⁾。

本實驗為評估國內所栽種薑黃之安全性，選用大黃種薑黃塊根乾燥磨粉後之成品，為一天然植物性食品，含薑黃素 0.31-0.55 %⁽²⁾，在單一高劑量餵飼大鼠並未造成急性大鼠中毒或死亡，口服急毒性等級為『正常使用時無急性毒性』^(10, 22)。

表九、薑黃粉經胃管餵飼大鼠 28 天之臟器組織病理變化評估

Table 9. Incidences of liver and kidney changes in rats treated with turmeric powder and curcumin by daily gavage for 28 days

| Dose (mg/kg) ¹⁾ | Animal No. | Liver | | | | | Kidney | | | |
|-------------------------------|---------------|------------------------|---|---|----|-----|------------------------------------|---|---|----|
| | | Vacuoles ²⁾ | | | | | Glomerular exudation ³⁾ | | | |
| | | - | ± | + | ++ | +++ | - | ± | + | ++ |
| Male | | | | | | | | | | |
| Control | 10 | 3 ⁴⁾ | 7 | 0 | 0 | 0 | 7 | 2 | 1 | 0 |
| TP 100 | 9 | 0 | 1 | 5 | 3 | 0 | 8 | 1 | 0 | 0 |
| TP 500 | 10 | 4 | 5 | 0 | 0 | 1 | 10 | 0 | 0 | 0 |
| TP1,000 | 10 | 3 | 3 | 2 | 0 | 2 | 6 | 1 | 1 | 2 |
| TC 1,000 | 10 | 1 | 4 | 4 | 1 | 0 | 6 | 4 | 0 | 0 |
| Female | | | | | | | | | | |
| Control | 10 | 10 | 0 | 0 | 0 | 0 | 6 | 4 | 0 | 0 |
| TP 100 | 10 | 7 | 2 | 1 | 0 | 0 | 10 | 0 | 0 | 0 |
| TP 500 | 9 | 7 | 2 | 0 | 0 | 0 | 6 | 4 | 0 | 0 |
| TP1,000 | 9 | 8 | 1 | 0 | 0 | 0 | 6 | 3 | 0 | 0 |
| TC 1,000 | 10 | 8 | 2 | 0 | 0 | 0 | 3 | 7 | 0 | 0 |

¹⁾ TP, turmeric powder; TC, 65%–70% curcumin.

²⁾ Vacuoles: -: 0; ±: 1–5; +: 6–10; ++: 11–50; +++: 51–100 were found in the full section of liver.

³⁾ Glomerular exudate: -: 0; ±: 1–2; +: 3–5; ++: 6–10 glomeruli were found in the full section of the kidney.

⁴⁾ Affected rat number ($n = 9-10$).

但薑黃經高劑量食用後，大鼠初期體重有明顯降低，可能因薑黃具有苦辛味，導致食慾暫時性降低而後恢復。體內臟器之相對重量(%)、血液相、肝及腎血清酶素等項目與對照組者比較均無統計學顯著性差異；肝臟外觀稍黃，但並無明顯組織病理學變化，推測可能為薑黃本身之色素沉積現象，以上結果顯示食用薑黃口服急性毒性之安全性高。

根據調查薑黃對人每日取食量為 4 g⁽⁹⁾，以成人體重 60 公斤換算每日薑黃取食量為 66.6 mg/kg/day。雖然 Sambaiah 等人(1982)曾以市售薑黃經磨粉(0.1–10%)與薑黃素(0.1–2%)等濃度，添加於飼料

中連續餵飼大鼠 8 週後，僅在薑黃粉高劑量組(10%)飼料攝取量有降低，但對血液及肝功能(GOT及GPT)及組織病理學均無影響。本實驗中薑黃粉 28 天餵飼試驗劑量之選擇，乃依據急性毒性及衛生署公告「健康食品 28 天餵飼毒性」方法，以 1,000 mg/kg bw 為試驗最高劑量，此劑量亦高於正常人每日食用之 15 倍，經 28 天連續餵飼大鼠後，發現薑黃粉與薑黃素二者均會引起大鼠 AST 及總膽紅素值升高，而薑黃素具有促進膽汁之快速代謝與排泄作用^(19, 22)，推測高量攝取時，導致總膽紅素及 AST 上升。同時，血清中澱粉酶、總蛋白及白蛋白亦有升高，應與薑黃本身含有較

多粗蛋白質 (12.62%) 及粗脂肪 (4.65%) 並有促進膽汁快速代謝, 增加食物脂質消化吸收, 以致大鼠肝臟脂肪較度脂肪用有關。Sambaiah 等人 (1982) 曾指出薑黃對正常大鼠之膽固醇並無影響, 唯仍有報告指出, 薑黃所含之薑黃素會降低高膽固醇飲食所誘發大鼠之高膽固醇⁽²¹⁾及抑制四氯化碳傷害所引起用細胞脂質過氧化作用^(16, 17, 18)。日本實驗則發現薑黃與薑黃素均有提高正常大鼠膽固醇及三酸甘油酯含量之作用, 可能與前人⁽²¹⁾以高膽固醇飲食誘發高膽固醇產生病態動物不同所致, 兩者差異之原因, 仍有待進一步探討。又本次實驗亦發現, 大鼠經薑黃粉與薑黃素餵飼後之雄鼠肝及腎臟重量有增加, 並引起輕度脂肪用及腎臟絲球體鮑氏囊腔 (Bowman's capsule) 均質樣濾液及血中離子濃度明顯增加, 推測與薑黃本身含有豐富鉀、磷及鎂等礦物質有關, 經腸內吸收後, 促使體內離子濃度增加, 因而血中尿素氮、肌氨酸及離子濃度亦隨之上升, 但薑黃粉經高劑量 (1000 mg/kg) 連續餵飼 28 天後, 仍未對大鼠之肝及腎臟有明顯病理性傷害。

抗凝血物質, 如肝素 (heparin) 在血漿中具有抗前凝血酶原 (antiprothrombin) 作用, 引起凝血時間延長。臨床上, 肝素經常作為心血管阻塞治療藥物⁽⁸⁾, 而薑黃在口服急性及 28 天餵飼試驗中, 亦顯示薑黃會降低大鼠血漿之 Fbg 含量及產生凝血時間延長作用及 PT 作用時間縮短現象, 但薑黃素組則反而有 Fbg 凝固及 PT 縮短及 APTT 時間增長作用。唯在試驗期間, 均未發現大鼠有出血及凝血不全之毒性, 其差異可能與薑黃屬天然植物性食品, 所含未知物質, 可能影響血液凝固值變化。血液凝固因子, 除血小板外, 尚牽涉許多複雜機制⁽⁸⁾, 例如, 嚴重肝及腎臟等疾病可能會抑制 Fbg 及前凝血酶 (prothrombin) 之合成, 進而影響血液凝

固; 殺鼠劑 (Warfarin) 中藥會抑制用臟前凝血酶原合成及 VII、IX、X 凝血因子, 降低 PT、APTT 及 Fbg; 阿斯匹林 (aspirin) 中藥則干擾血小板釋出 ADP⁽⁸⁾; 飲食中魚油因含有高量長鏈脂肪酸 (long chain n-3 fatty acid), 過多會抑制 Vit. K, 進而影響前凝血酶素之合成, 凝血時間延長⁽¹²⁾。然而, 薑黃降低大鼠血漿之 Fbg 含量及凝固時間延長作用, 是否與傳統中藥使用薑黃作為『活血化癥』⁽²⁾之藥理作用有關, 目前並無相關研究報告, 其作用機制仍有待進一步探討。

雖然有許多研究指出, 薑黃及薑黃素具有抑制用纖維化及抗腫瘤作用^(7, 16, 20), 唯世界衛生組織與農糧組織 (WHO/FAO) 對食用薑黃仍有疑慮, 並推測若高劑量長期食用後可能對人體造成慢性傷害⁽¹⁵⁾。然而, 本實驗結果顯示, 食用薑黃之口服急性毒性安全, 同時 28 天餵飼安全結果亦可知, 高劑量薑黃及薑黃素僅對大鼠引起輕度脂肪用與腎絲球體濾液增加, 並無其他明顯病理傷害, 唯此現象是否可能成為誘發慢性肝及腎損傷之前兆因子, 仍有待進一步探討。

謝 辭

本試驗由行政院農業委員會藥物毒物試驗所科技計畫 91 農科-4.1.3-藥-P1(2)經費補助, 試驗期間蒙本所劉清標、彭明霞、湯秀枝、邱秀英、高鳳鳳及陳怡慈等諸位協助, 謹此誌謝。

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ABSTRACT

Liao, J. W.¹, Tsai, S, J.², Wang, S. C.¹, and Hwang, J. S.^{1*} Safety evaluation of turmeric (*Curcuma longa* L.) powder via oral gavage for 28 days in rats. Plant Prot. Bull. 45: 237-255. (¹Division of Applied Toxicology, Taiwan Agricultural Chemicals and Toxic Substances Research Institute, Wufeng, Taiwan 413, ROC; ²Division of Agricultural Chemistry, Taiwan Agricultural Research Institute, Wufeng, Taiwan 413, ROC)

Turmeric (*Curcuma longa* Linn.) contains curcumin that has antioxidative effects on inflammatory and hepatic disorders, and inhibits carcinogen-induced cancers in animal models. However, the chronic effect of turmeric is a concern of the WHO/FAO. The objective of this study was to evaluate the oral acute and 28-day feeding toxicity of turmeric powder (TP) in Sprague-Dawley (SD) rats. Results revealed that the acute oral LD₅₀ of TP was greater than 5000 mg/kg body weight (bw) in rats. In addition, the TP was administered by daily gavage in rats at doses of 0, 100, 500, and 1000 mg/kg bw for 28 days. The positive control was 1000 mg/kg bw of curcumin (65 %–70 %, Sigma). No toxic effects were found by evaluating clinical signs, body weight, feed consumption and efficiency, hematology, and autopsy in the TP- and curcumin-treated groups. TP but not curcumin decreased the content of fibrinogen, shortened the prothrombin time (PT), and activated the partial thromboplastin time (APTT) in plasma ($p < 0.05$). Turmeric powder treatment increased organ weights of the liver and kidney in male rats ($p < 0.05$) and elevated the levels of serum aspartate aminotransferase (AST), total bilirubin, cholesterol, triglyceride, blood urine nitrogen (BUN), creatinine, and ions (P^{3-} , Ca^{2+} , Mg^{2+} , and Cl^-) in both sexes ($p < 0.05$). Although, slight increases in hepatocytic vacuoles and glomerular exudate were found in the liver and kidney, however, no significant toxic effects were observed in treated male rats. These findings indicate that no acute oral toxicity was observed, and the higher daily intake (1000 mg/kg) of TP for 28 days also showed no significant toxic effects in rats. The changes in fibrinogen and PT in plasma after TP treatment might relate to the use of turmeric for anticoagulation in Chinese medicine; this effect needs to be illustrated by further studies.

(Key words: turmeric tuber, 28-day feeding toxicity, rats)

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