口服玫瑰純露之大鼠急性毒性評估[1]

張隆仁[2]、洪梅珠[2]、郭肇凱[2]、廖俊旺[3]

摘　要

玫瑰純露又稱爲玫瑰花水，係以水蒸氣蒸餾法萃取玫瑰花瓣所得之產品，可作爲香精、化妝品原料或飲料等多樣用途。爲瞭解以健康安全的栽培方式，所生產出符合我國「食用花卉規範」的玫瑰花瓣原料所研製之玫瑰純露其食用之安全性，直接以水蒸氣蒸餾法萃取玫瑰花瓣所得之4:1 (W/V)純露樣品，對大鼠進行口服急性毒性試驗，測試劑量爲5 g/kg，投予後連續觀察14天。結果顯示，試驗期間全部鼠隻均無中毒症狀或死亡；在體重及增重方面，「玫瑰純露」處理組及對照組間並無顯著差異。血液學及血清生化學檢測結果，並未顯示有與試驗物質有關之影響。大鼠體內重要臟器，亦均無明顯因試驗物質引起之肉眼及組織病理變化。綜合試驗結果顯示，「玫瑰純露」對大鼠之口服急性毒性LD_{50}值爲大於5 g/kg，適量口服玫瑰純露，應無急性毒性副作用並具安全性。本項試驗研究，爲我國臺灣地區首度以香藥草作物進行蒸餾萃取所得之純露產品爲目標進行之急性毒性評估試驗，結果具有參考價值，並可供未來相關產品進行安全性評估之參考依據。

關鍵字：玫瑰純露、口服急性毒性、50%致死劑量(LD_{50})。

前　言

純露的英文名稱爲「hydrosols」，意指「水溶液」，以往它是植物精油萃取過程的副產品，著名的僅有「玫瑰水」與「柑桔水」兩項產品，如今由於其相較於植物精油，屬於安全性較高，且兼具植物精油之功用，目前國際市場已有上百項的香藥草植物被開發出純露產品上市，成爲新興的天然美容保養品，國際與國內市場均呈現逐漸熱絡之趨勢(14)。玫瑰純露即消費市場習稱「玫瑰水」的產品，具溫和的保濕與收斂性功用，可作爲開發調理肌膚的美容保養產品之原料，亦可直接利用爲化妝水或泡澡，達到放鬆及恢復活力之功能。玫瑰純露也適宜將之開發飲料、甜點、冰類或酒類製品，作爲增添香氣之使用。國內約有300公頃的玫瑰切花生產面積，其中面積最大的屬埔里鎮已達50餘公頃，爲協助當地農會輔導農民擴大國產玫瑰之栽培面積與多樣化利用，乃積極地除原來玫瑰的切花生產導向外，開創以美容、保養、

[1] 行政院農業委員會臺中區農業改良場研究報告第 0731 號。
[2] 行政院農業委員會臺中區農業改良場副研究員、研究員兼秘書、助理研究員。
[3] 國立中興大學獸醫病理學研究所副教授。

食用等高附加價值之用途。本計畫研究目的為測試行政院農業委員會臺中區農業改良場研製之「玫瑰純露」對哺乳動物之安全性，藉以建立產品安全資料 (Material Safety Data Sheet)，提供使用時安全評估之參考。試驗於國立中興大學動物疾病診斷中心進行，試驗依據衛生署健康食品安全性評估-口服急毒性試驗規範[(1)]，並符合美國環保署(USEPA) (*Health Effects Test Guidelines*, OPPTS 870.1100, *Acute oral toxicity*, US EPA 712–C–98–190. In: OPPTS *Harmonized Test Guidelines*, Series 870.3050, EPA712–C–00–366, 1998)及經濟合作暨開發組織(*OECD Guidelines for the Testing of Chemicals*. Section 4: Health Effects. *No. 420: Acute Oral Toxicity-Fixed Dose Procedure, No. 423: Acute Oral Toxicity-Acute Toxic Class Method, No. 425: Acute Oral Toxicity-Up and Down Method*, 2001)等試驗規範進行口服急性毒性試驗。

圖一、食用玫瑰花瓣原料與純露產品。

Fig. 1. Rose hydrosols products and the raw materials of edible rose petals.

材料與方法

樣品製備

「玫瑰純露」樣品為行政院農業委員會臺中區農業改良場試驗田所栽培之玫瑰(*Rosa* spp.)品種，該品種係自市售佳娜紅(Grand Gala)選育出的品系。採用符合衛生署頒訂之「食用花卉規範」，所生產的新鮮花瓣(圖一)為原料，經清洗後，以水蒸氣蒸餾設備進行蒸餾萃取，入料量為2公斤之玫瑰花瓣，取其5:1 (W/V；鮮花重：萃取液體積)比例的萃取液(即玫瑰純露)為試驗材料。樣品外觀呈透明無色液體，比重約為1。保存於4℃冰箱中，試驗純度視為100%。水蒸氣蒸餾法是應用高熱的水蒸氣將植物體中的揮發性成分或稱香氣分子之化學鍵結打斷後隨同水蒸氣帶出來，再利用冷凝管將水蒸氣與香氣分子冷凝為液態，隨後再經過油水分離程序即可獲得植物精油，而萃取過程中所蒐集水溶性的部份即稱為純露。本試驗所使用材料僅有2公斤，故僅能搜集到純露。

供試動物

5週齡大鼠(SD品系)，購自樂斯科生技園區實驗動物培育及研發中心(宜蘭，臺灣)，動物房溫度設定為20~22℃及12小時光/12小時暗之光照週期。以鼠專用粒狀飼料(LabDiet® 5001

Rodent diet, Purina Mills LLC, St. Louis, MO, USA)及逆滲透水供應，經1週適應期後進行試驗。動物試驗之進行經中興大學動物實驗委員會審核通過(IACUC: 97-052)，實驗動物之使用與操作，均依據中華實驗動物學會之『實驗動物管理與使用指南』規範進行[15]。

試驗步驟

口服急性毒性試驗分爲5 g/kg劑量組及餵食蒸餾水之對照組，每組10隻大鼠(雌、雄各半)，以飽和苦味酸染劑於背部作編號標識。口服急性毒性試驗之試驗樣品純度視爲100%，試驗時以逆滲透水稀釋玫瑰純露；配置試驗濃度爲0.5 g/ml。以不鏽鋼胃管，依體重經口餵食投予體積量爲10 ml/kg。處理後每日觀察並每週稱體重1次，至處理後第14天止。試驗結束時，大鼠以氣體麻醉(2% Isoflurane, Halocarbon Laboratories, South Carolina, USA)後經腹主動脈採血，並達完全放血後犧牲，進行大體解剖，檢查體內臟器之肉眼及組織病理變化。

血液學檢查

試驗結束後，大鼠以Isoflurane麻醉，自腹主動脈採集全血放入含EDTA抗凝血劑之試管(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)。包括紅血球數(red blood cell count, RBC count)、血紅素(hemoglobin, Hb)、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)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400倍下，計算白血球中，淋巴球、嗜中性球、單核球、嗜酸性球及嗜鹼性球等百分率(%)等。

血清生化檢查

試驗結束後，大鼠以Isoflurane麻醉，自腹主動脈採集全血放入含EDTA抗凝血劑之試管，復以離心機(Kubota 2010, Tokyo, Japan)，於3,000 rpm離心15分鐘，取上清液血清(serum)，以血清生化儀(Chiron Diagnostics Corporation, Oberlin, OH, USA)檢測肝及腎血清酵素值，包括天門冬胺酸轉胺酶(aspartate aminotransferase, AST)、丙胺酸轉胺酶(alanine aminotransferase, ALT)、尿素氮(blood urea nitrogen, BUN)、肌酸酐(creatinine)等項目。

臟器病理檢查

以 2% Isoflurane 麻醉後經腹主動脈放血後犧牲及解剖，秤腦、心、肝、腎、脾、胸腺、腎上腺，睪丸及卵巢等臟器重量(g)，並以最後一週之最終體重(g)，作爲體內臟器重量比率(%)之計算。觀察肉眼病理變化，取臟器浸泡於10%中性福馬林溶液固定1週，經組織粗修與石臘包埋後，以石臘組織切片機(Leica RM 2145, Nussloch, Germany)製成2 μm厚度之組織切片，經Hematoxylin & Eosin (H&E)染色，於光學顯微鏡觀察組織病理變化。並依據Shackelford等人之方法進行組織病理變化描述及病理評估，標準爲5等級：1 = 極微(minimal, < 1%); 2 = 輕微(slight, 1~25%); 3 = 中度 (moderate, 26~50%); 4 = 中度嚴重(moderate/severe, 51~75%); 5 = 極度嚴重(severe/high, 76~100%)。

結果分析

試驗期間各組之體重變化，依體重(g)或增重(g或%)變化，以統計分析軟體Microsoft Excel進行Pair Students *t*-test進行組間比較分析，其組間顯著差異水準爲$p<0.05$。試驗結束後，若處理組動物死亡數超過處理動物數半數(50%)，以統計方式求取藥劑量與死亡率之迴歸方程式，計算動物半數致死劑量(LD_{50}值)及其95%可信賴區間(confidence limit)。

結果與討論

結果顯示，以「玫瑰純露」口服投予大鼠後，全部鼠隻無中毒症狀或死亡(表一)，顯示測試樣品對大鼠之口服急性毒性LD_{50}值大於5 g/kg。「玫瑰純露」處理組雄、雌鼠第0、7及14天時體重及增重亦無明顯影響($p>0.05$) (表二)。

表一、「玫瑰純露」口服急性毒性試驗之大鼠臨床症狀及死亡率

Table 1. Clinical observation and time course of death of rats in the rose hydrosols acute oral toxicity test

Sex/Dose (g/kg)	Animal No. [2]	Clinical sign	Day after treatment								Mortality (%)[1]
			1	2	3	4	5	6	7	14	
Male											
0	5	Normal	5	5	5	5	5	5	5	5	0
5	5	Normal	5	5	5	5	5	5	5	5	0
Female											
0	5	Normal	5	5	5	5	5	5	5	5	0
5	5	Normal	5	5	5	5	5	5	5	5	0

[1] Mortality (%)=(Dead no./Treated no.)×100.

[2] Number of rats were observed.

表二、「玫瑰純露」口服急性毒性試驗之大鼠體重及增重變化

Table 2. Changes of body weight and weight gain of rats after gavaged with rose hydrosols at 0, 7, and 14 days in the acute oral toxicity test

Dose (g/kg)	Animal No.	Means of body weight (g)/gain (%) [5]		
		0-day	7-day[1, 2]	14-day[3, 4]
Male				
0	5	190.7± 5.8[5]	230.3± 6.7(20.8±3.3)	270.3±11.3(41.7±4.6)
5	5	190.6± 7.8	240.1±11.4(26.1±6.9)	285.6±11.0(50.0±5.7)
Female				
0	5	162.3±16.4	189.6±11.6(17.3±4.5)	209.0±20.3(29.0±6.8)
5	5	162.3± 9.9	195.2±7.8(20.5±5.3)	210.0±6.5(29.9±9.3)

[1] Means of body weight (BW) on the 7^{th} day (g)=($7^{th}-0^{th}$)BW (g).

[2] Body weight (BW) gain on the 7^{th} day (%)=($7^{th}-0^{th}$)BW (g)/(0^{th})BW (g)×100.

[3] Means of body weight (BW) on the 14^{th} day (g)=($14^{th}-0^{th}$)BW (g).

[4] Body weight (BW) gain on the 14^{th} day (%)=($14^{th}-0^{th}$)BW (g) /(0^{th})BW (g)×100.

[5] Means of body weight (g)/gain (%) are expressed as the mean±SD (n =5).

血液學檢查(complete blood count, CBC)方面，雌鼠白血球總數(WBC count)、紅血球總數(RBC count)、血紅素(Hb)、血球容積比(Hct)、平均紅血球體積(MCV)、平均血紅素(MCH) 、平均血紅素濃度(MCHC)、血小板總數(PLT)及白血球分類等均無明顯差異(表三及四)。而雄鼠僅在紅血球總數(RBC count)、血球容積比(Hct)及血小板總數(PLT)項目於對照組(6.8±0.3 10^6/μl、41.4±2.4%及895.8±1 66.3 10^3/μl)與處理組間(7.2±0.2 10^6/μl、45.9±0.8%及1132±117.8 10^3/μl)雖具顯著性差異(p<0.05)，但已知雄鼠紅血球總數(RBC count)正常生理值範圍爲6.76~7.45 10^6/μl，血球容積比(Hct) 正常生理值範圍爲36~48%，血小板總數(PLT)正常生理值範圍爲500~1300 10^3/μl[5]。上述數值皆於正常生理值範圍內，同時並無出血或貧血等相關毒性症狀出現，顯示並無臨床病理學上之意義，均無與試驗物質有關之影響。

表三、「玫瑰純露」口服急性毒性試驗之大鼠血液學變化

Table 3. Changes of hematological parameters of rats after gavaged with rose hydrosols in the acute oral toxicity test

Dose (g/kg)	WBC[1] (10^3/μl)	RBC (10^6/μl)	HGB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	PLT (10^3/μl)
Male								
0	9.4±2.8[2]	6.8±0.3	13.3±0.6	41.4±2.4	61.3±1.8	19.7±0.8	32.1±1.6	895.8±166.3
5	9.9±2.7	7.2±0.2*	13.9±0.3	45.9±0.8*	64.0±2.4	19.4±0.7	30.3±0.9	1132.0±117.8*
Female								
0	4.8±1.2	6.9±0.5	13.8±0.9	42.0±3.7	60.6±3.2	19.9±0.8	32.9±1.8	975.0±425.1
5	7.1±3.3	6.8±0.2	13.7±0.8	42.4±1.5	62.5±1.2	20.2±0.5	32.3±1.0	1128.0±160.7

[1] WBC, white blood count; RBC, red blood cell; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; PLT, platelets.

[2] Data are expressed as the mean ± SD (n = 5).

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

表四、「玫瑰純露」口服急性毒性試驗之大鼠白血球分類變化

Table 4. Changes of white blood cells differentiation of rats after gavaged with rose hydrosols in the acute oral toxicity test

Dose	WBC	Lymph	Neutrophil (%)		Monocyte	Eosinophil	Basophil
(g/kg)	(10^3/μl)	(%)	Band	Segment	(%)	(%)	(%)
Male							
0	9.4±2.8	79.4±3.1[1]	0.0±0.0	19.2±3.6	1.4±0.8	0.0±0.0	0.0±0.0
5	9.9±2.4	78.0±4.9	0.0±0.0	20.8±5.0	1.2±0.7	0.0±0.0	0.0±0.0
Female							
0	4.8±1.2	80.2±5.7	0.0±0.0	18.6±6.2	1.2±1.0	0.0±0.0	0.0±0.0
5	7.1±3.0	81.6±2.1	0.0±0.0	17.2±2.9	1.2±1.5	0.0±0.0	0.0±0.0

[1] Data are expressed as the mean ± SD (n = 5).

在肝及腎血清酵素值(表五)方面，尿素氮(BUN)及肌酸酐(creatinine)項目在對照組雄鼠(17.1±1.9 mg/dl及0.5±0.0 mg/dl)及處理組雄鼠(12.3±2.3 mg/dl及0.4±0.1 mg/dl)間具顯著性差異(p<0.05)；而天門冬胺酸轉胺酶(AST)在對照組雌鼠(144.8±12.8 U/l)及處理組雌鼠(89.6±19.4 U/l)間具顯著性差異(p<0.05)。其餘肝腎血清酵素指標，如丙胺酸轉胺酶(alanine aminotransferase, ALT)組間則無差異(p>0.05)。已知雄鼠尿素氮(BUN)及肌酸酐(creatinine)正常生理值範圍分別爲16±3 mg/dl及0.4±0.1 mg/dl，而雌鼠天門冬胺酸轉胺酶(AST) 正常生理值範圍爲104±16 U/l(Harkness and Wagner, 1989)。因此上述數值皆於正常生理值，顯示並無臨床病理學上之意義，均無與試驗物質有關之影響。

表五、「玫瑰純露」口服急性毒性試驗之大鼠血清肝及腎臟功能指數變化

Table 5. Serum biochemistry changes in liver and renal function of rats treated with rose hydrosols in the acute oral toxicity test

Dose (g/kg)	AST (U/l)[1]	ALT (U/l)	BUN (mg/dl)	Creatinine (mg/dl)
Male				
0	126.4±16.7[2]	49.5±31.1	17.1±1.9	0.5±0.0
5	106.6±21.1	28.0±7.1	12.3±2.3*	0.4±0.1*
Female				
0	144.8±12.8	30.8±4.7	18.4±1.8	0.5±0.1
5	89.6±19.4*	26.2±10.1	18.3±3.3	0.5±0.1

[1] AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen.

[2] Data are expressed as the mean±SD (n =5).

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

體內臟器重量包括腦、心、肝、腎臟、脾臟、胸腺、腎上腺、睪丸及卵巢重量及百分比與對照組比較均無明顯差異(表六)。檢查體內臟器，結果顯示對照組與處理組之腦、心、肝、腎臟、脾臟、胸腺、腎上腺、睪丸及卵巢等重要臟器均無因試驗物質引起之肉眼病理變化(圖二及三；表七)。

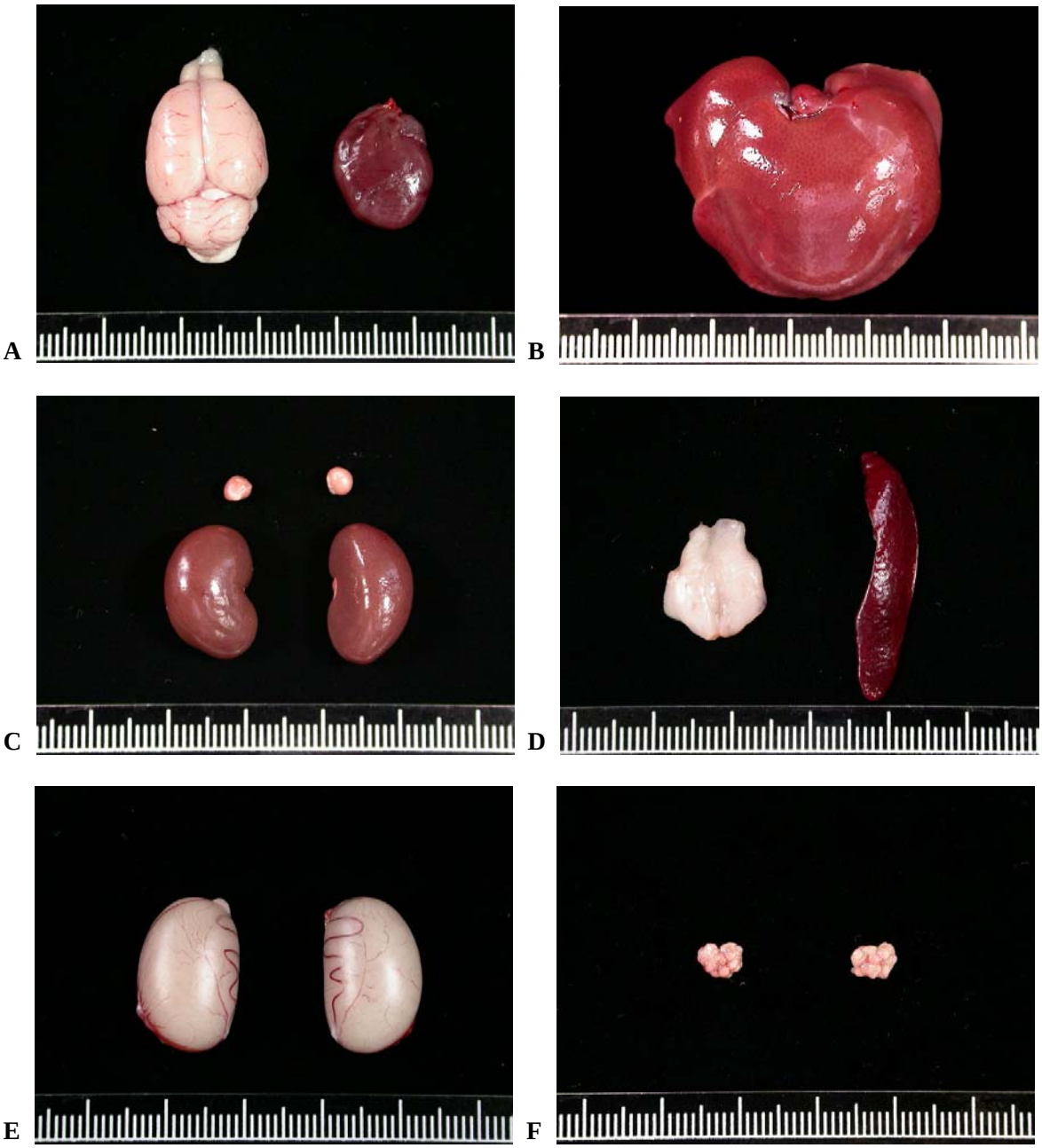
表六、「玫瑰純露」口服急性毒性試驗之大鼠臟器重量變化

Table 6. Relative organ weight changes of rats treated with rose hydrosols in the acute oral toxicity

Dose (g/kg)	Brain (%)[1]	Heart (%)	Liver (%)	Kidney (%)	Spleen (%)	Thymus (%)	Adrenal gland (%)	Testis/Ovary (%)
Male								
0	0.69±0.03[2]	0.32±0.01	2.73±0.07	0.71±0.04	0.20±0.02	0.14±0.02	0.01±0.00	0.97±0.08
5	0.67±0.04	0.31±0.03	2.79±0.13	0.72±0.03	0.19±0.03	0.14±0.02	0.01±0.00	0.93±0.07
Female								
0	0.90±0.09	0.37±0.06	3.06±0.57	0.81±0.13	0.20±0.05	0.22±0.06	0.03±0.00	0.04±0.01
5	0.89±0.03	0.36±0.02	2.93±0.17	0.78±0.05	0.21±0.02	0.20±0.03	0.02±0.01	0.03±0.00

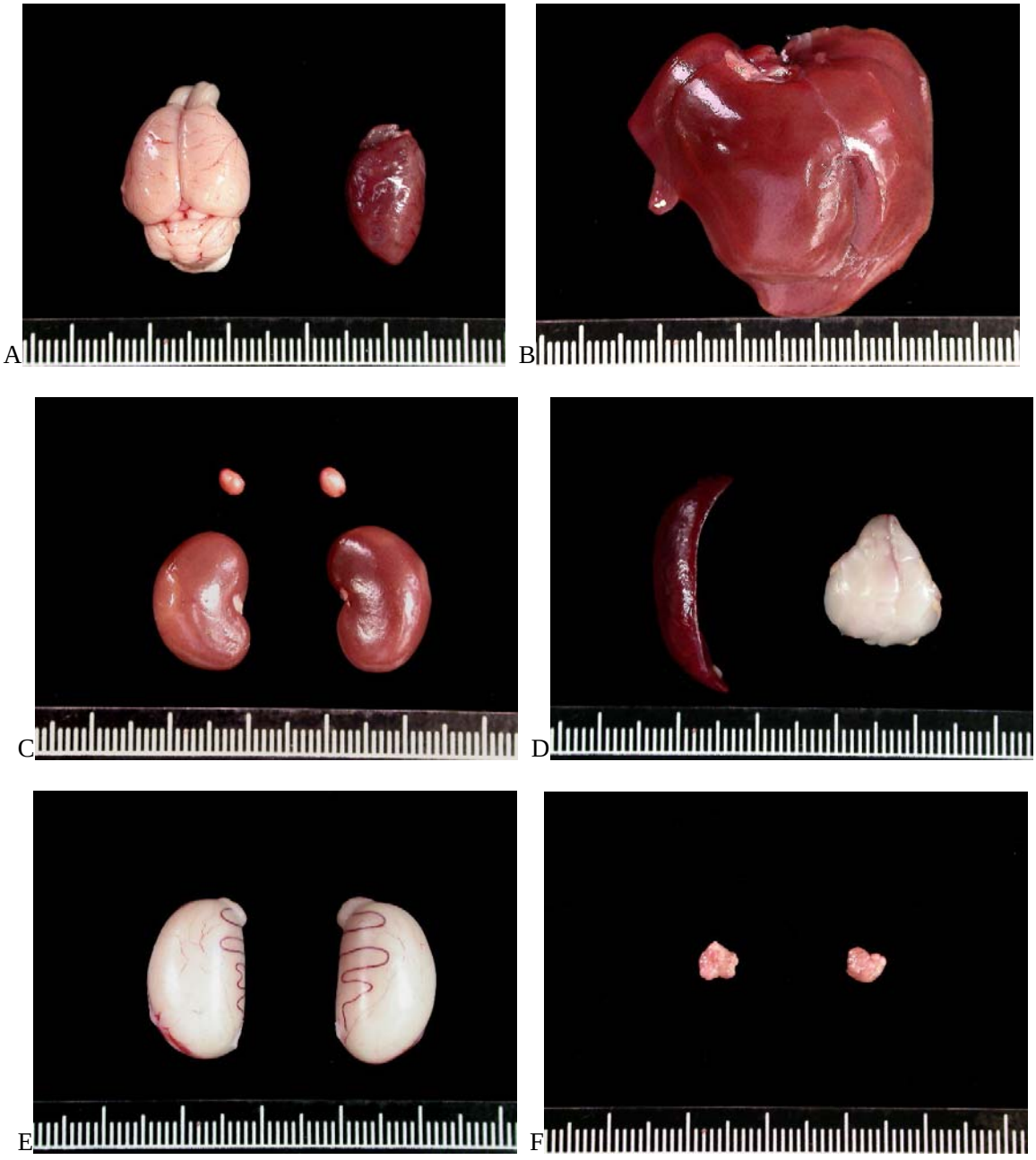
[1] Organ weight (%) = [organ weight (g)/ final body weight (g)] × 100.

[2] Data are expressed as the mean±SD (n = 5).



圖二、「玫瑰純露」口服急性毒性試驗對照組大鼠體內臟器之肉眼病理觀察。對照組大鼠之腦及心臟(A)、 肝(B)、腎及腎上腺(C)、胸腺及脾 (D)、睪丸(E)、卵巢(F)等重要臟器均無明顯肉眼病理變化。

Fig. 2. Gross findings of rats in the rose hydrosols acute oral toxicity test. No significant gross lesions of brain and heart (A), liver (B), kidney and adrenal (C), thymus and spleen (D), testis (E) and ovary (F) were found in the control group.



圖三、「玫瑰純露」口服急性毒性試驗處理組大鼠體內臟器之肉眼病理觀察。處理組之腦及心(A)、肝(B)、腎及腎上腺(C)、胸腺及脾(D)、睪丸(E)及卵巢(F)等重要臟器均無明顯肉眼病理變化。

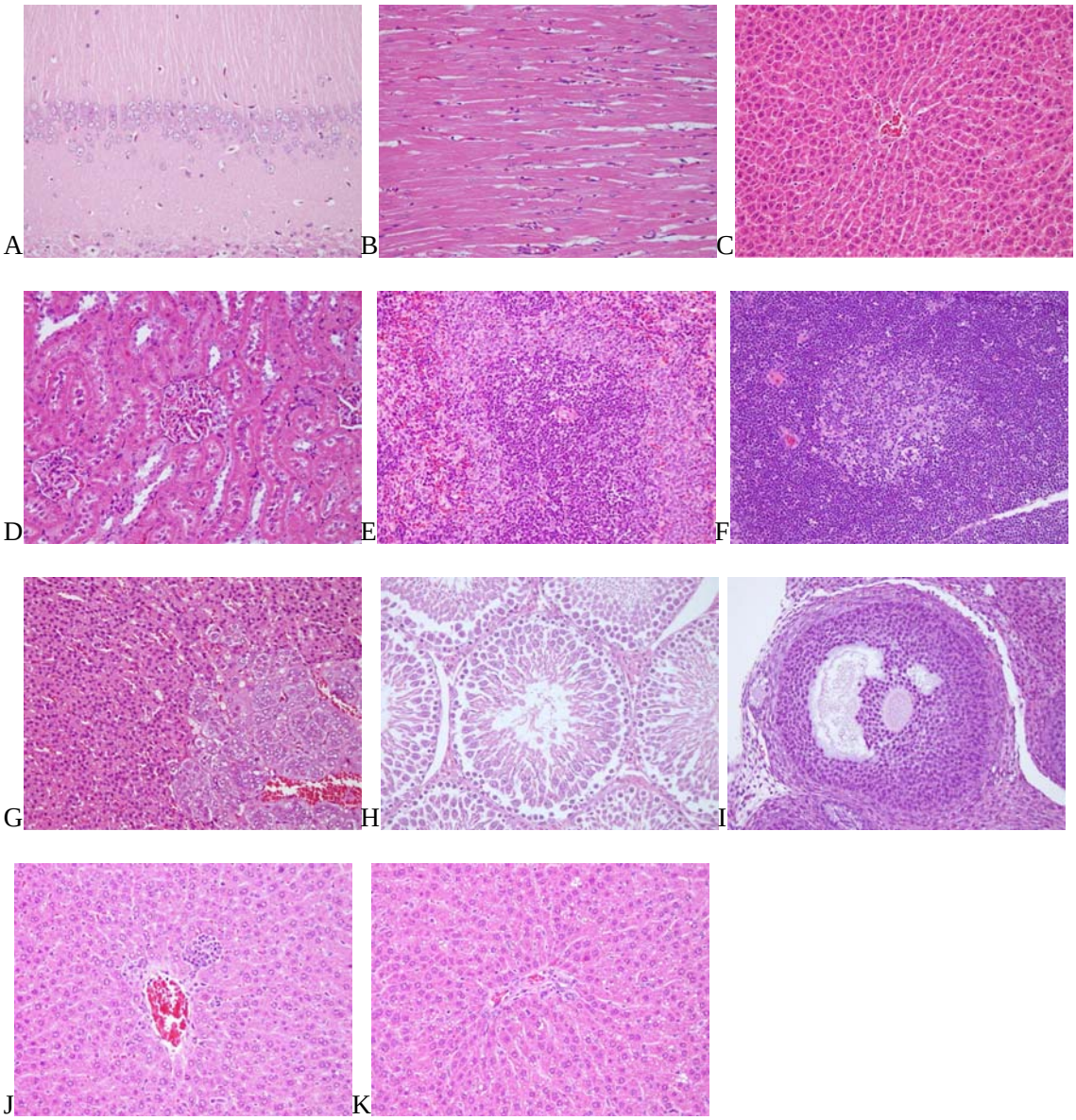
Fig. 3. Gross findings of rats in the rose hydrosols acute oral toxicity test. No significant gross lesions of brain and heart (A), liver (B), kidney and adrenal (C), thymus and spleen (D), testis (E) and ovary (F) were found in the treated group.

表七、「玫瑰純露」口服急性毒性試驗之大鼠肉眼病理變化綜合評估
Table 7. Summary of gross findings of rats treated with rose hydrosols in the acute oral toxicity test

Organ	Gross findings	Dose (g/kg) /Sex			
		Control (0 g/kg)		Rose Hydrosols (5 g/kg)	
		Male	Female	Male	Female
Total of rats		5	5	5	5
Adrenal	NA[1]	-	-	-	-
Brain	NA	-	-	-	-
Heart	NA	-	-	-	-
Liver	NA	-	-	-	-
Kidney	NA	-	-	-	-
Spleen	NA	-	-	-	-
Thymus	NA	-	-	-	-
Testis	NA	-		-	
Ovary	NA		-		-

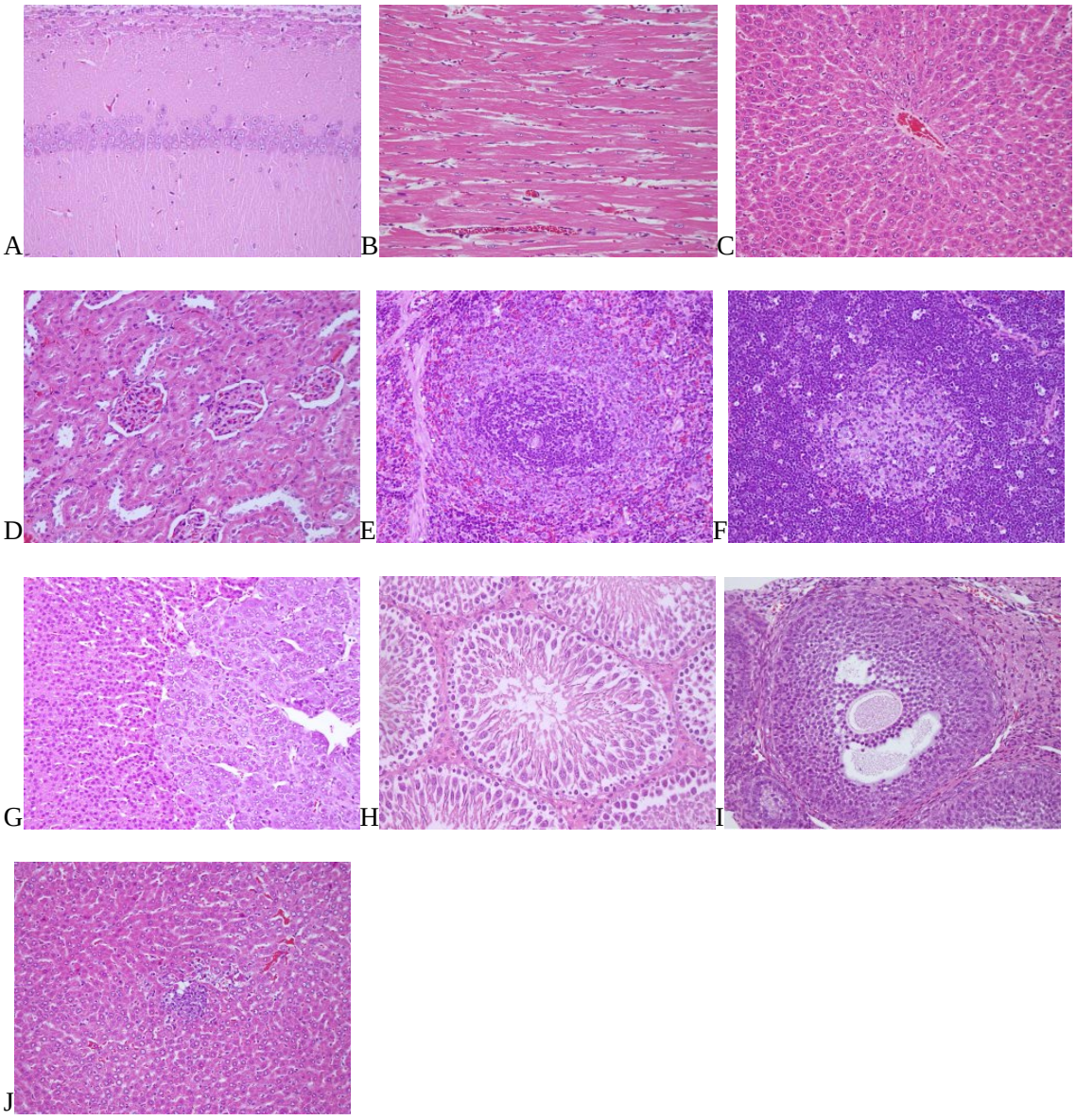
[1] -: NA, No abnormalities.

組織病理檢查在對照組與處理組均出現肝臟局部、輕微至輕度單核細胞浸潤(mononuclear cell infiltration)病變，對照組雄雌鼠發生率爲0/5及1/5，處理組雄雌鼠發生率則爲1/5及2/5。此外，僅對照組雌鼠肝臟細胞出現極微脂肪滴浸潤，發生率爲2/5，對照組雄鼠及處理組雌雄鼠則無(圖四及五、表八)。以上病變在對照組與處理組間並無劑量相關性，爲自發性病變，與試驗物質無關。



圖四、「玫瑰純露」口服急性毒性試驗對照組大鼠體內臟器之組織病理觀察。對照組大鼠腦(A)、心臟(B)、肝臟 (C)、 腎臟(D)、脾臟(E)、胸腺(F)、腎上腺(G)、睪丸(H)、卵巢(I)等重要臟器均無明顯組織病理變化(H&E stain, 200×)。僅少量雄雌鼠出現極輕微肝臟單核細胞浸潤(J)及極微脂肪滴浸潤(K)，爲自發性及非特異性發生(H&E stain, 400×)。

Fig. 4. Histopathological findings of control rats in the rose hydrosols acute oral toxicity test. No significant lesions of brain (A), heart (B), liver (C), kidney (D), spleen (E), thymus (F), adrenal gland (G), testis (H) and ovary (I) were found in the control group (H&E stain, 200×). Only few rats showed minimal mononuclear cell infiltration (J) and fat droplets (K) in livers, and were considered as spontaneous and non-specific incidences (H&E stain, 400×).



圖五、「玫瑰純露」口服急性毒性試驗對照組大鼠體內臟器之組織病理觀察。處理組之大鼠腦(A)、心臟(B)、肝臟 (C)、 腎臟(D)、脾臟(E)、胸腺(F)、腎上腺(G)、睪丸(H)、卵巢(I)等重要臟器均無明顯組織病理變化。處理組少數鼠隻出現肝臟輕微單核細胞浸潤(J)，爲自發性及非特異性病變 (H&E stain, 400×)。

Fig. 5. Histopathological findings of rose hydrosols-treated rats in the acute oral toxicity test. No significant lesions of brain (A), heart (B), liver (C), kidney (D), spleen (E), thymus (F), adrenal gland (G), testis (H), and ovary (I) were found in the control group. Few rats showed focal minimal mononuclear cell infiltration in livers (J). The lesions above were considered as spontaneous and non-specific incidences and were not related to the test substance. (H&E stain, 400×).

表八、「玫瑰純露」口服急性毒性試驗之大鼠組織病理變化綜合評估

Table 8. Summary of histopathological findings of rats treated with rose hydrosols in the acute toxicity test

Organ	Lesions	Male		Female	
		Control	Treatment	Control	Treatment
Adrenal	Significant lesion	-[1]	-	-	-
Heart	Significant lesion	-	-	-	-
Kidney	Significant lesion	-	-	-	-
Liver					
	Infiltration, mononuclear cell, focal, minimal	0/5[2]	1/5	1/5	2/5
	Infiltration, fat droplet, minimal	0/5	0/5	2/5	0/5
Ovary	Significant lesion			-	-
Spleen	Significant lesion	-	-	-	-
Testis	Significant lesion	-	-		
Thymus	Significant lesion	-	-	-	-

[1] -: No significant lesions.

[2] Incidence: No. affected rats/ no. rats were examined.

綜合以上試驗結果，玫瑰純露對大鼠之口服急性毒性半致死劑量(LD_{50})每公斤體重大於5公克，符合依據世界衛生組織(WHO)對毒性之等級分類(7)，是屬於「正常使用時無毒性(unlikely to present hazard in normal use)」物質。據此，針對本試驗所製備之玫瑰純露，經換算人體口服食用後所產生的急性毒性危害的評估應是安全無虞的。

參考文獻

1. 衛生署 1999 口服急毒性及28天餵食毒性試驗 「健康食品安全及功效評估方法」 衛署食字第8803780號 臺北。
2. Chan, P. K. and A. W. Hayes. 1994. Acute toxicity and eye irritancy, In: Principles and Methods of Toxicology, A. Wallace Hayes (ed.), 3rd Edition, pp. 579-648. Raven Press, New York.
3. Copplestone, J. F. 1988. The development of the WHO Recommended Classification of Pesticides by Hazard. Bull. W.H.O. 66: 545-551.
4. Environmental Protection Agency (EPA), Office of Prevention, Pesticides and Toxic Substances. 1998. Acute oral toxicity. In: OPPTS Harmonized Test Guidelines, Series 870.1100, EPA 712–C–98–190, 10 pp. Washington, DC.
5. Giknis, M. L. and C. B. Clifford. 2006. Clinical laboratory parameters for Crl:CD (SD) rats. Charles river laboratories inc.

6. Gosselin, R. E., R. P. Smith and H. C. Hodge. 1984. Ingredient Index. In: Clinical Toxicology of Commercial Products, Acute Poisoning, Section II: A, 5th Edition, pp. 1-5. Baltimore: Williams and Wilkins Company, USA.
7. Harkness, J. E. and J. E. Wagner. 1989. The biology and medicine of rabbits and rodents, 3rd Edition. Lea & Febiger, Philadelphia.
8. Japanese Ministry of Health and Welfare. 1997. Guidelines for toxicity studies of drugs. In: Japanese Technical Requirements for New Drug Registration, with Relevant Japanese and ICH Guidelines Collected in Appendix, Appendix (21) S4 (ICH). pp. 272-290, Yakuji Nippo, Ltd., Tokyo.
9. Liang, C. T., M. H. Chang, C. C. Hong and K. J. Huang. 1999. Established the blood chemistry reference values for SPF rats and mice. J. Chin. Soc. Sci. 25: 55-68
10. Organization for Economic Cooperation and Development. 2001. Acute Oral Toxicity-Fixed Dose Procedure. In: OECD Guideline for the Testing of Chemicals. Section 4: Health Effects, No: 420, 14 pp., Adopted: 17th December, 2001.
11. Organization for Economic Cooperation and Development. 2001. Acute Oral Toxicity-Acute Toxic Class Method. In: OECD Guideline for the Testing of Chemicals. Section 4: Health Effects, No: 423, 14 pp. Adopted: 17th December, 2001.
12. Organization for Economic Cooperation and Development. 2001. Acute Oral Toxicity-Up and Down Method. In: *OECD Guideline for the Testing of Chemicals.* Section 4: Health Effects, No: 425, 26 pp., Adopted: 17th December, 2001.
13. Shackelford, C., G. Long, J. Wolf, C. Okerberg and R. Herbert. 2002. Qualitative and quantitative analysis of nonneoplastic lesions in toxicology studies. Toxicol. Pathol. 30: 93-96.
14. Suzanne, Catty. 2001. Hydrosols: The next aromatherapy, Healing Art Press (ed.). Rochester, Vermont, Canada.
15. Yu, J. Y. L., C. K. Cheng, B. J. Chen, M. J. Cheng, H. H. Cheng, W. J. Chang, H. H. C. Chen, C. C. Hong, P. J. Lee, S. C. Liang, K. S. Sheu, Y. Y. Sung, C. N. Weng, C. W. Tsai, C. S., Wang, M. H. Wang, L. S. Yen, C. K. Yu and J. Y. L. Yu. 2005. A Guideline for the Care and Use of Laboratory Animals. Published by the Chinese Society for the Laboratory Animal Science, 3rd Edition, Taipei, Taiwan, ROC (in Chinese).

Acute Oral Toxicity Study of Rose Hydrosols in Rats[1]

Long-Zen Chang[2], Mei-Chu Hong[2], Xhao-Kai Kuo[2] and Jiunn-Wang Liao[3]

ABSTRACT

Rose Hydrosols is also called rose water, mainly comes from extracting rose petals by steam distillation, has been widely used in essence flavor, cosmetic and drink industry. This study was performed to assess the acute oral toxicity of rose hydrosols in Sprague Dawely (SD) rats. Rose hydrosols were single administrated orally with dosages of 5000 mg/kg body weight by feeding needle and then observed for 14 days. Mortality, signs of toxicity, mean body weights, mean body weights gains, and gross necropsy findings were recorded for 14 days post treatment of rose hydrosols. No animal death was found during the study period. In male and female rats, there were no statistical differences in the mean body weights and mean body weights gains between control and rose hydrosols groups. There were no rose hydrosols treatment- related findings in hematological, serum biochemical parameters, gross necropsy and histopathology evaluation. The results show that no acute adverse toxic affects of rose hydrosols for rats of either sex and the LD_{50} of feeding rose hydrosols in rats is over 5,000 mg/kg body weight. This is the first time that using hydrosol coming from herbs by steam distillation as the tested material for acute oral toxicity test in Taiwan, the results is valuable and could be considered when evaluating safety of the other hydrosol-related products.

Key words: rose hydrosols, acute oral toxicity, 50% lethal dosage.

---

[1]Contribution No. 0731 from Taichung DARES, COA.

[2]Associate Agronomist , Senior Researcher and Secretary, Assistant Researcher of Taichung DARES, COA.

[3]Professor, Graduate Institute of Veterinary Pathobiology, National Chung Hsing University.