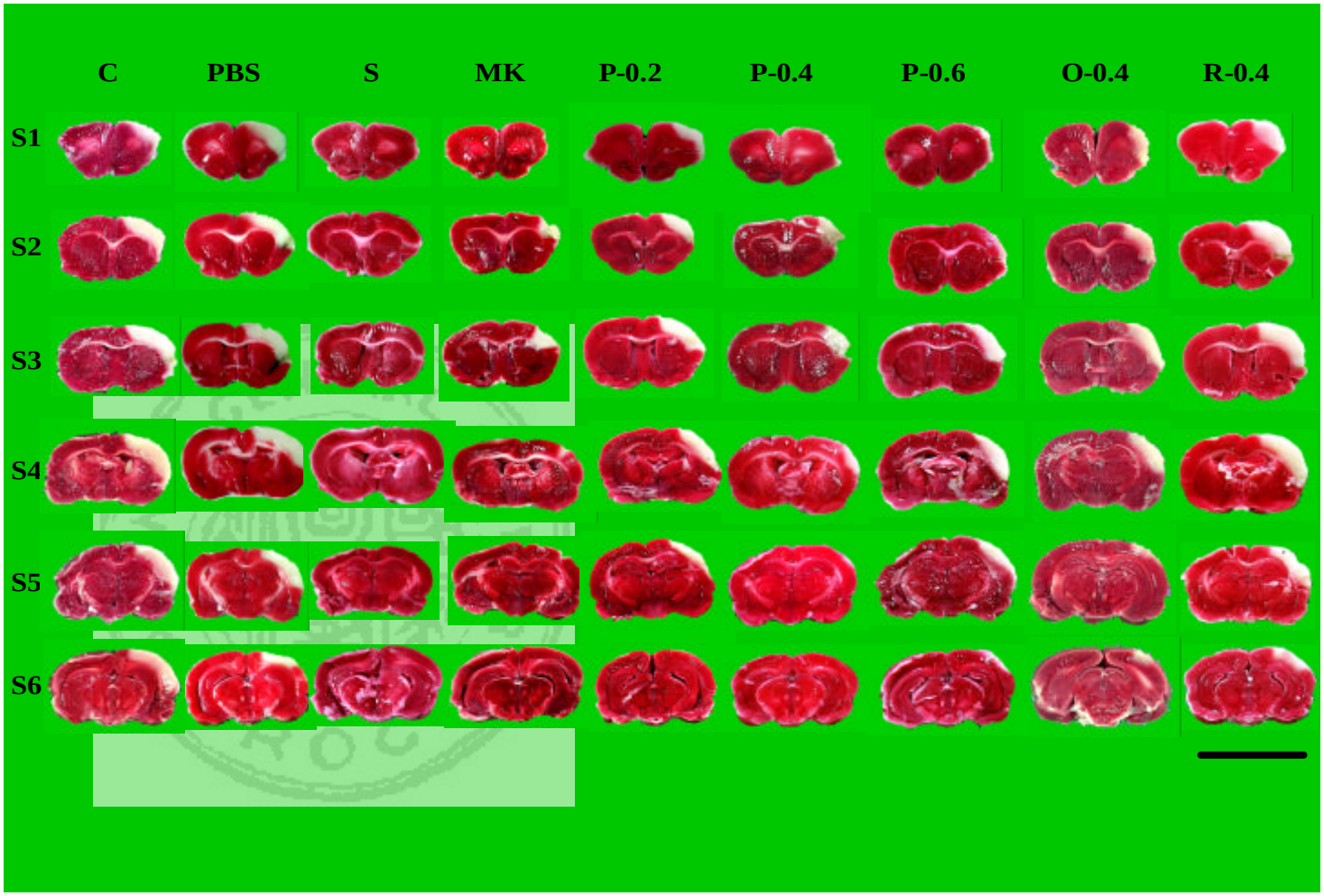

圖 4.1. 腦冠切片圖。各組大鼠經 24 小時缺血—再灌流後，取腦、染色、切片之大腦冠切圖. 在腦冠切片同側的白色區域代表腦梗塞區. 右圖下標示的比例尺＝1cm. C=control, MK=Mk801, S＝Sham, P-0.2=**紅花** 0.2 g/Kg **術前治療；**P-0.4=**紅花** 0.4 g/Kg**，術前治療；**P-0.6=**紅花** 0.6 g/Kg**，術前治療；**O-0.4=**紅花** 0.4 g/Kg ,**腦血流阻斷後** 30**分鐘術後治療;**R-0.4= **紅花** 0.4 g/Kg**再灌流後** 30**分鐘術後治療。以下各圖表組別代號說明與本圖相同。**。。.

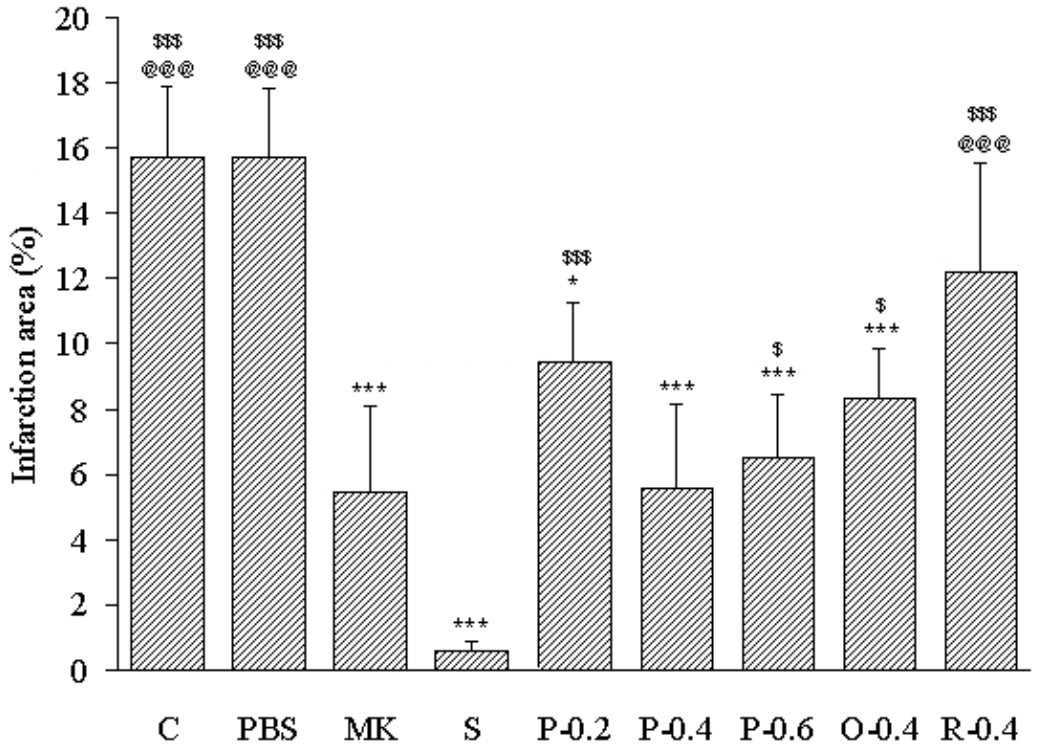

圖 4.2. 梗塞面積比率評估。各組大鼠經 24 **小時缺血—再灌流後之腦梗塞面積比率** (%)**。所有資料以** mean ± SD **表示，** *** p<0.001, *p<0.05 **表示與控制組之比較；**$$$P<0.001, $$p<0.01,$p<0.05 **表示與** Sham **組之比較；**@@@ p<0.01 **表示與** MK **組之比較**(n=6, Scheffe`s test)**。**

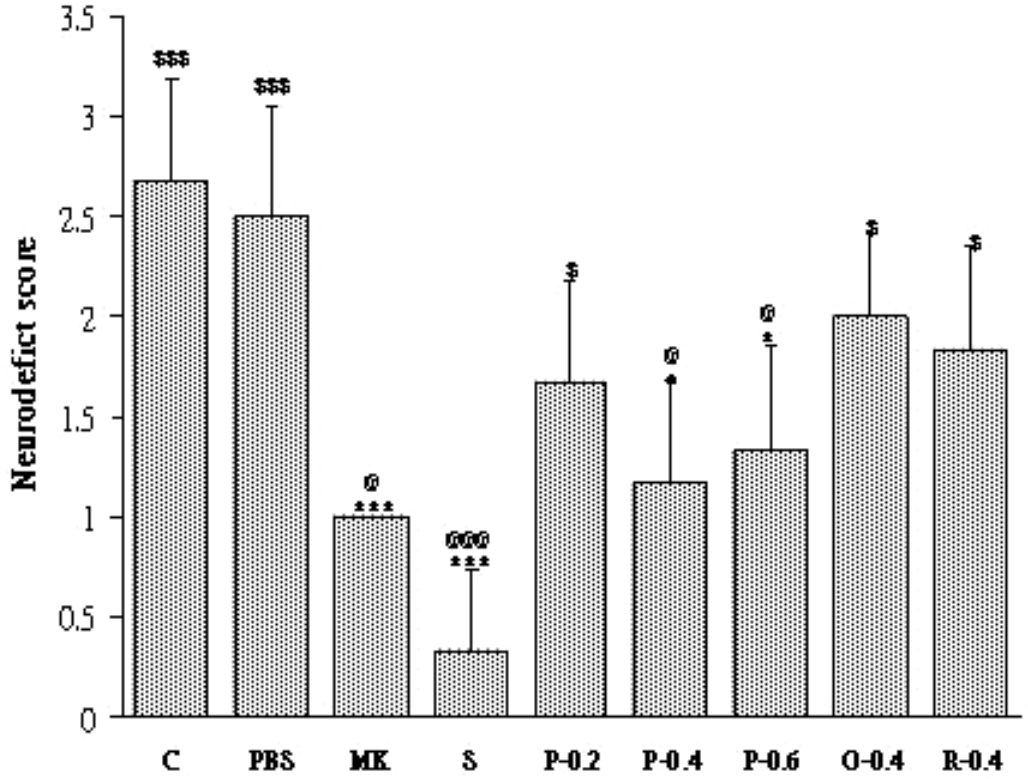

圖 4.3. 神經學缺陷級數評估。各組大鼠經 24 **小時缺血—再灌流後之神經學缺陷級數。所有資料以** mean ± SD **表示，** *** p<0.001,* p<0.05 **表示與控制組之比較；**$$$ p< 0.001,$ p< 0.05 **表示與** Sham **組之比較**. @@@ p< 0.01, @ p< 0.05 **表示與** PBS **組之比較**(n=6, Scheffe`s test)**。**

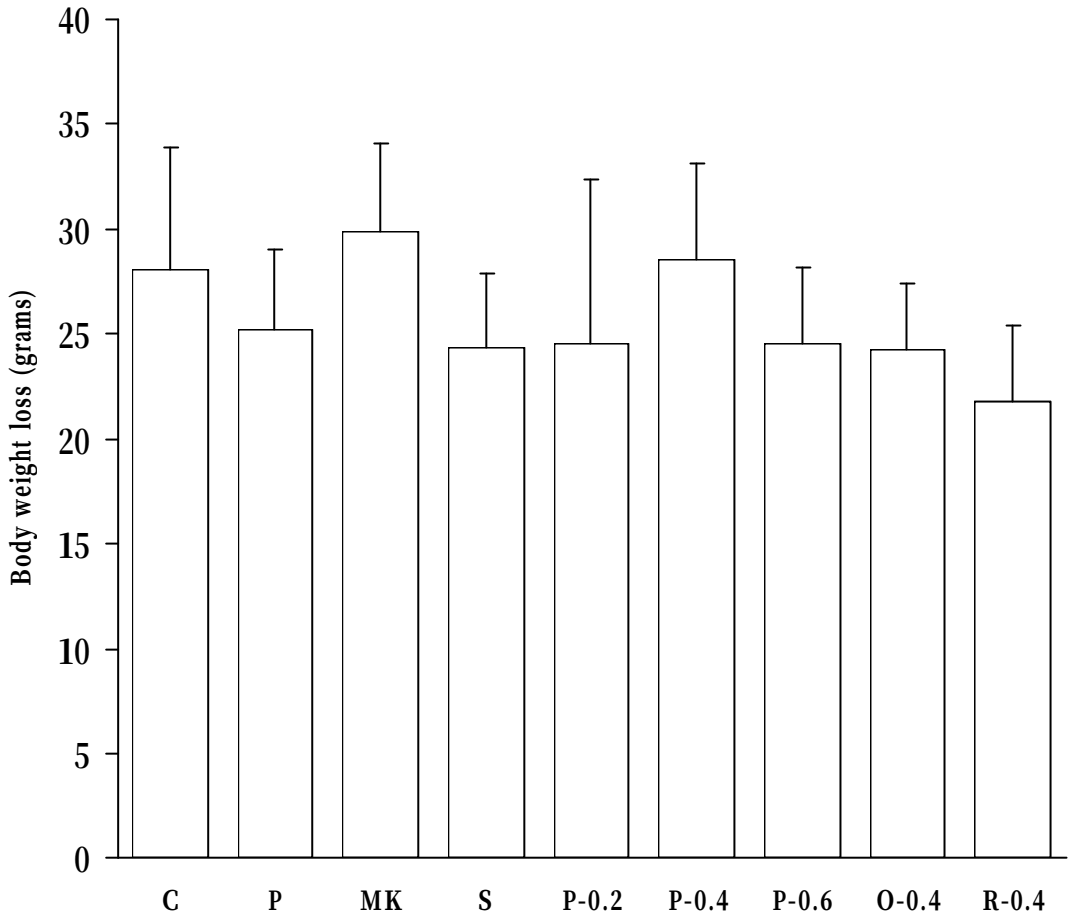

圖 4.4. 體重喪失評估。各組大鼠經 24 **小時缺血—再灌流後之體重下降**(g). **所有資料以** mean ± SD **表示。各組之間無統計學上顯著差異** (n=6, Scheffe`s test)

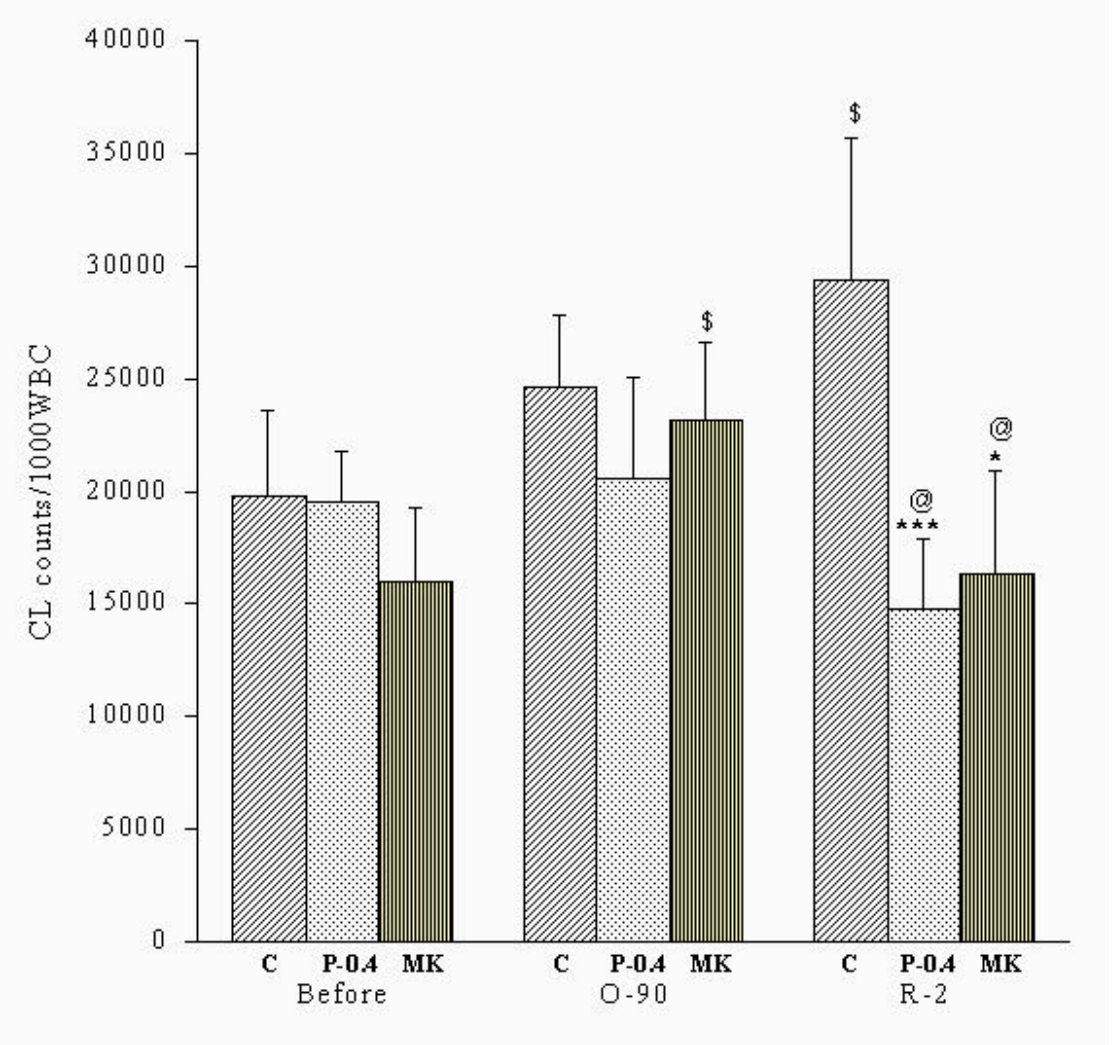

圖 4.5. 超氧陰離子之測量。以 chemiluminescence **方法在缺血—再灌流期間測量超氧陰離子。所有資料以** mean ± SD **表示。**Before= **在** MCAO **前** 15 **分鐘取血，**O-90=**缺血後** 90 **分鐘取血**, R-2= **再灌流後** 2 **小時取血**, CL=chemiluminescene. *** p<0.001,*p<0.05 **表示與控制組之比較；**$ p<0.05 **表示與時間點**-Before **之比較**, @ p<0.05 **表示與時間點** O-90 **之比較** (n=6, Scheffe`s test)**。**

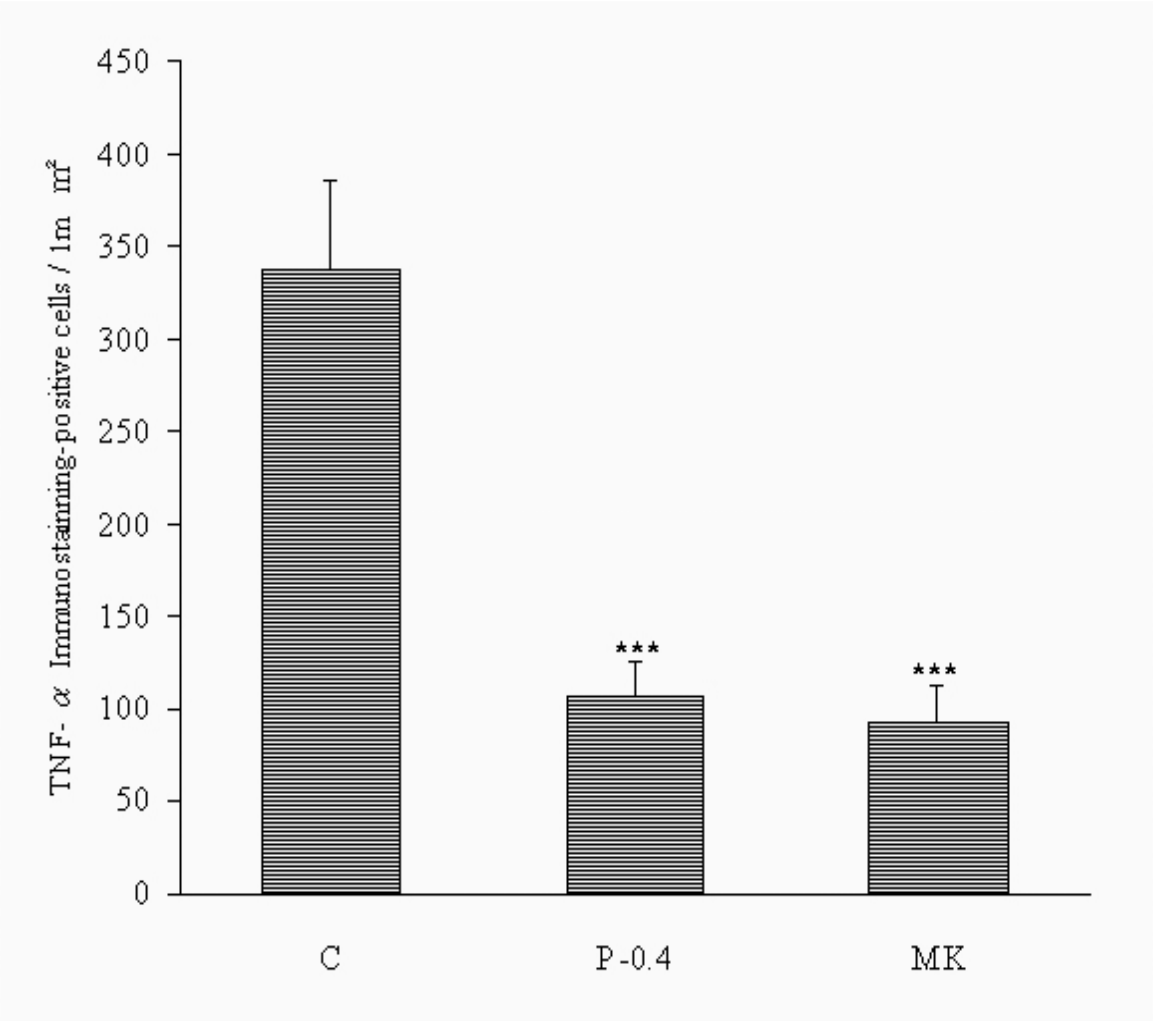

圖 4.6. TNF-a 免疫染色陽性細胞計數測量。各組大鼠經 24 **小時缺血—再灌流後，在梗塞皮質區** TNF-a **免疫染色陽性細胞之數量。所有資料以** mean ± SD **表示。** *** p<0.001 **表示與控制組之比較**(n=6, Scheffe`s test)。

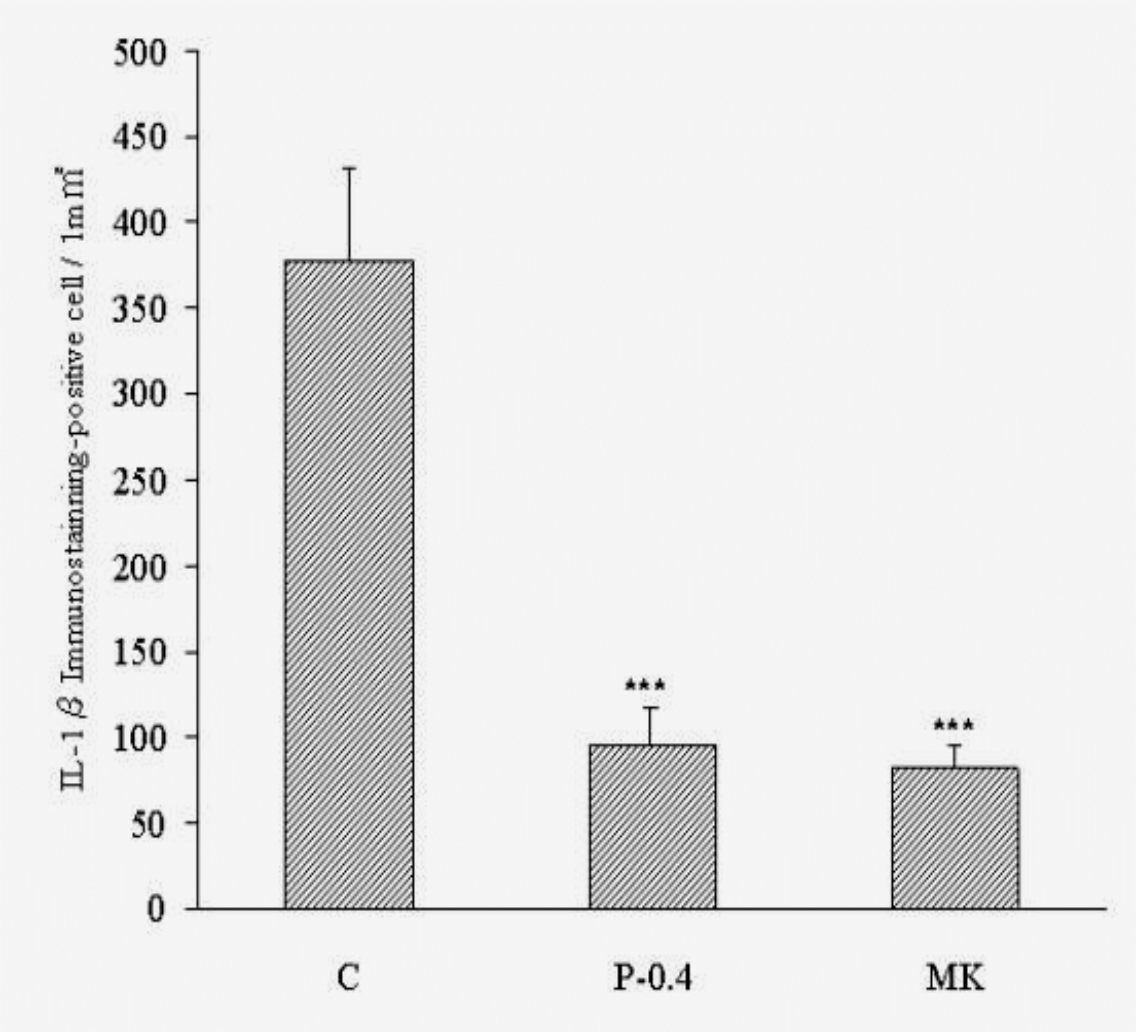

圖 4.7. IL-1ß 免疫染色陽性細胞計數測量。各組大鼠經 24 **小時缺血—再灌流後，在梗塞皮質區** IL-1ß **免疫染色陽性細胞之數量。所有資料以** mean ± SD **表示。** *** p<0.001 **表示與控制組之比較**(n=6, Scheffe`s test)。

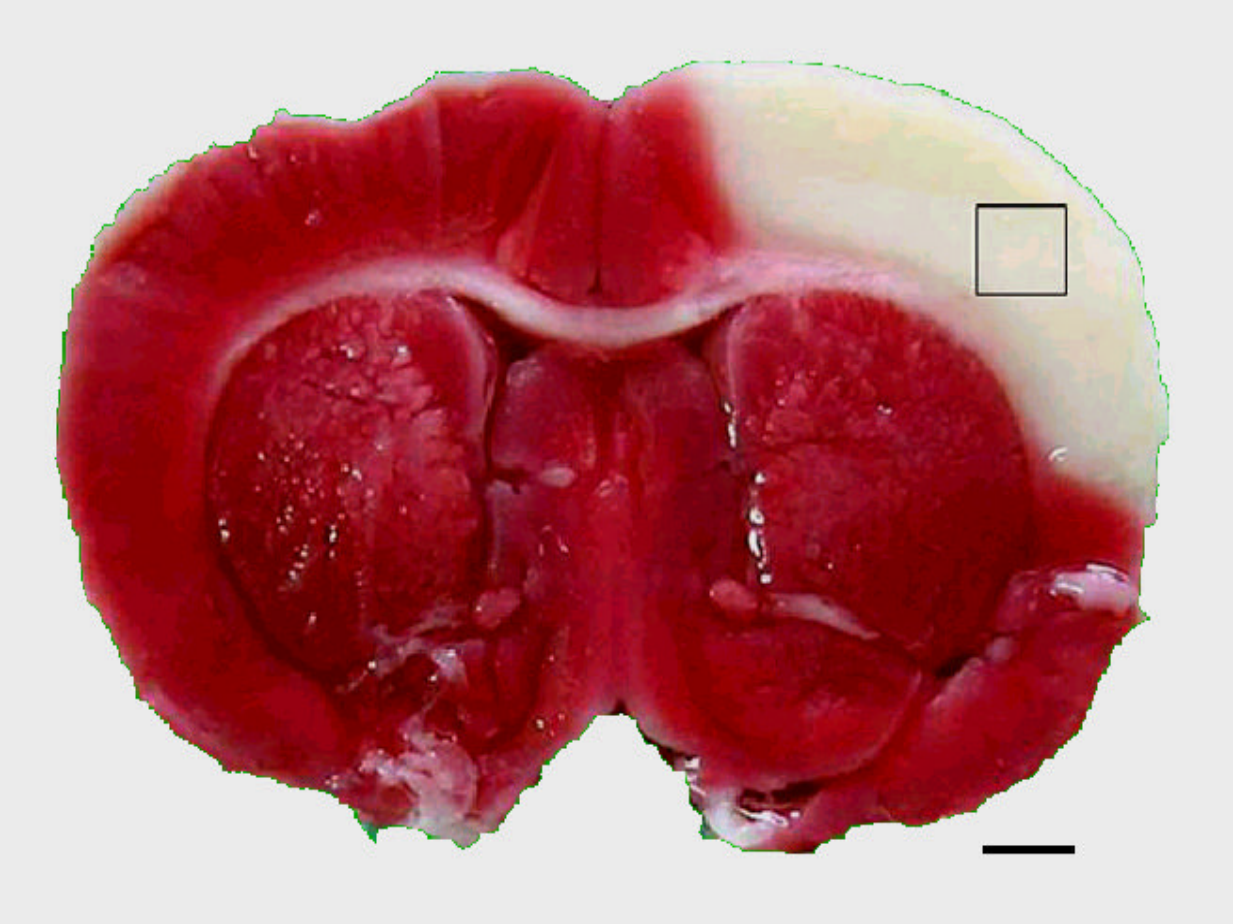

圖 4.8. TNF-a、IL-1ß 之計算面積位置標示圖。本片位置為從額業算起之大腦冠切片的第三片 (距離腦正中線 8.08 mm**、距前囟門** 0.92mm **). 圖中所標示的正方形區域為計算** TNF-a、IL-1ß **免疫染色陽性細胞數量的區域。圖中標示的比例尺** = 1mm^2**。**

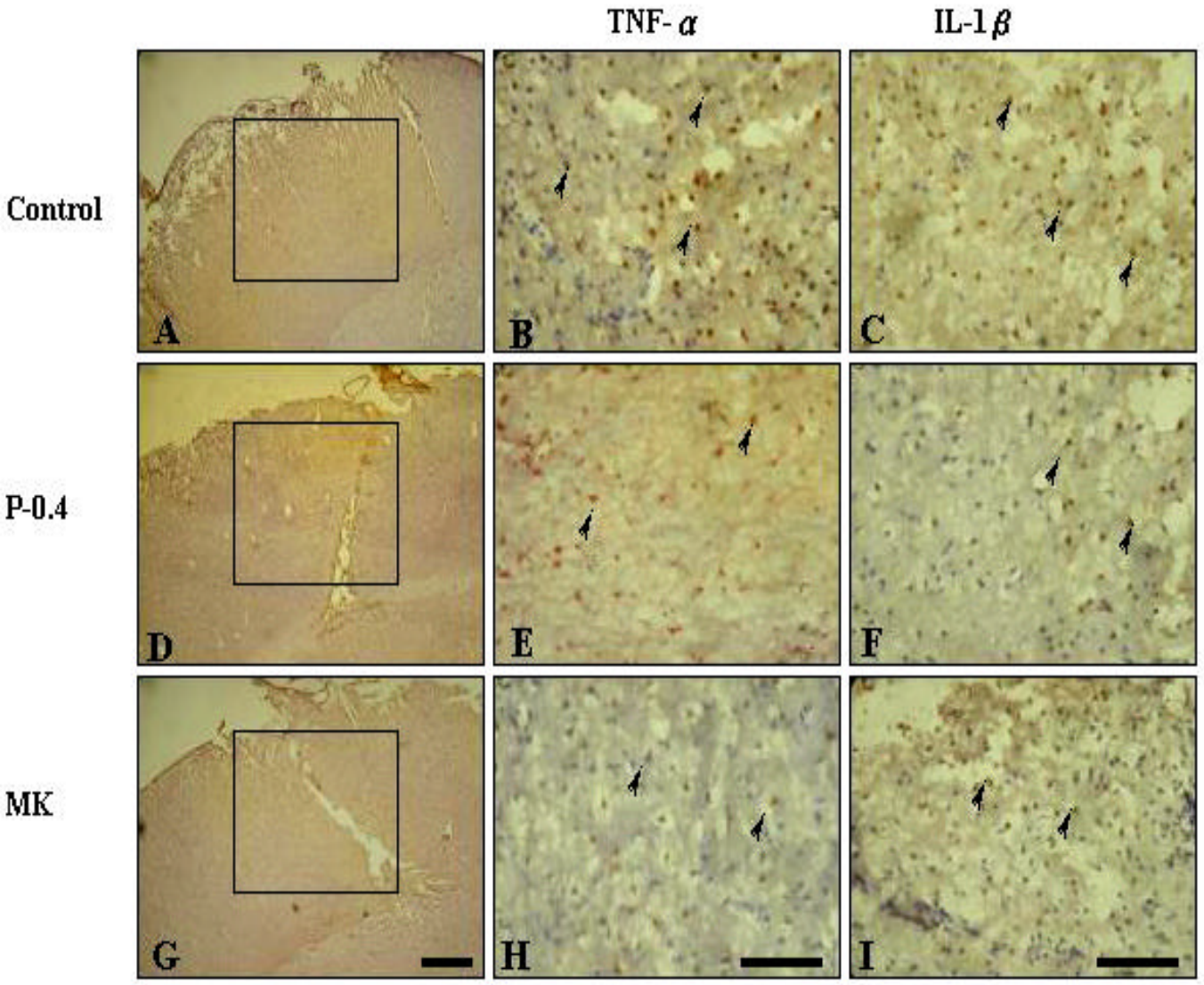

圖 4.9. TNF-a、IL-1ß 之免疫組織化學分析。各組大鼠經 24 **小時缺血—再灌流後，在梗塞皮質區中免疫染色陽性細胞圖。**TNF-a **免疫染色陽性細胞—控制組** (A.B)**、紅花** 0.4 g **術前治療組**(D.E)**、**MK **組**(GH)**；**IL-1ß **免疫染色陽性細胞—控制組**(C)**、紅花** 0.4 g**術前治療組**(F)**、**MK **組**(I)**。中間以及右側** 2 **行的圖，是最左側一行的圖中正方形區域的放大顯示圖**(10X)**。箭頭所指，表示為** TNF-a **以及** IL-1ß **免疫染色陽性細胞. 最左側** 1 **行圖中**(A.D and G)**標示的比例尺**=300 μm; **中間以及最右側** 2 **行圖中**(B.C.E.F.H.I) **標示的比例尺**=100 μm**。**

表 4.1. The effect of *Carthamus tinctorious* on rectal temperature in ischemia-reperfusion injured cerebral infarct rats

Time course / Groups	Pre-Ischemia	Ischemia	15	30	45	60	75	R	2H	24H
C	37.8±0.3	35.4±0.7	35.5±0.5	35.4±0.5	35.6±0.8	35.8±0.9	36.4±0.8	36.6±0.5	36.6±0.6	38.9±0.5
PBS	37.8±0.3	35.5±0.6	35.3±0.5	34.9±0.7	35.0±0.7	35.4±0.7	35.9±0.7	36.5±0.5	36.4±0.4	38.3±0.4
MK	37.8±0.2	35.4±0.5	34.3±1.0	33.7±0.7	33.6±0.8	33.8±0.7	34.2±0.8	35.0±0.7	35.8±0.6	38.4±0.4
S	38.0±0.3	35.4±0.7	35.3±0.3	35.2±0.4	35.0±0.4	35.2±0.2	35.6±0.4	35.8±0.6	35.9±0.3	38.3±0.5
P-0.2	37.9±0.3	35.3±0.3	35.0±0.4	34.9±0.4	34.8±0.5	34.9±1.1	34.9±1.1	35.4±0.5	36.3±0.4	38.2±0.5
P-0.4	37.9±0.3	35.3±0.6	35.0±0.7	34.9±0.9	34.8±1.1	34.9±1.2	34.9±1.3	35.4±0.7	35.8±0.4	38.2±0.3
P-0.6	38.0±0.3	35.2±0.8	34.1±1.0	34.1±1.0	34.0±0.7	34.1±0.5	34.3±0.4	34.9±0.6	35.7±0.5	37.6±0.3
O-0.4	38.0±0.2	35.0±0.5	34.6±0.6	34.3±0.7	34.3±0.6	34.5±0.7	34.3±0.6	35.0±0.5	35.9±0.3	37.8±0.7
R-0.4	37.9±0.4	34.9±0.5	34.5±0.5	34.0±0.3	34.0±0.6	34.1±0.5	34.4±0.4	35.0±0.8	35.8±0.4	37.3±0.9

所有資料以 mean ± SD **表示(℃)。本表以及下列各表中，**pre-ischemia **表示為兩側總頸動脈和右側中大腦動脈阻斷**

（BCA＋RMA）前之大鼠直腸溫度；ischemia 表示為阻斷 BCA＋RMA 腦血流時之大鼠直腸溫度；15、30、45、60、75 表示為阻斷 BCA＋RMA 腦血流後 15、30、45、60、75 分鐘之大鼠直腸溫度；R 表示為再灌流時之大鼠直腸溫度；2H、24H 表示為再灌流 2 小時、24 小時之大鼠直腸溫度。各組之間無顯著統計差異(n=6, Scheffe`s test)。

表 4.2. The effect of *Carthamus tinctorious* on mean arterial blood pressure in ischemia-reperfusion injured cerebral infarct rats.

Time course Groups	Ischemia	15	30	45	60	75	R
C	105.5±15.8	107.5±10.5	109.3±17.1	105.8±10.5	113.0±16.1	111.8±16.3	112.7±18.9
PBS	86.0±8.3	95.8±8.8	85.8±14.8	103.5±24.9	109.2±28.1	109.2±22.7	106.8±24.4
MK	91.7±25.8	93.8±31.0	88.2±25.2	82.7±22.3	108.0±27.2	101.3±26.1	111.7±30.2
S	109.8±16.1	118.3±16.1	103.5±26.9	121.2±14.9	123.3±18.5	113.0±14.8	112.2±13.8
P-0.2	94.3±18.0	93.0±13.4	93.5±18.9	105.2±8.6	115.5±18.7	112.7±16.7	101.7±13.2
P-0.4	87.2±10.0	94.5±15.1	106.5±12.2	103.8±16.7	115.2±17.5	117.8±16.9	100.7±17.0
P-0.6	94.8±25.4	96.7±27.6	87.0±30.3	101.2±25.3	90.7±27.7	101.3±26.1	107.0±28.1
O-0.4	96.5±17.1	107.0±13.1	101.2±21.4	92.5±12.7	98.5±18.4	104.3±11.6	109.7±14.4

R-0.4	93.2±9.2	117.3±6.4	113.3±9.6	108.7±18.9	111.3±16.9	117.8±16.9	100.7±17.0

所有資料以 mean ± SD **表示**(mmHg). **各組之間無顯著統計差異**(n=6, Scheffe`s test)。

表 4.3. The effect of *Carthamus tinctorious* on heart rate in ischemia-reperfusion injured cerebral infarct rats.

Time course Groups	Ischemia	15	30	45	60	75	R
C	395.7±70.0	367.0±29.1	400.2±29.3	389.2±67.3	352.2±55.8	369.3±63.9	380.7 ±33.2
PBS	302.3±72.1	291.2±70.8	297.7±19.8	352.8±83.3	343.2±78.2	360.3±80.5	388.8±117.6
MK	370.3±33.3	343.2±62.5	400.2±33.8	367.7±55.8	385.3±63.5	381.3±61.0	364.3 ±64.8
S	394.3±47.4	322.8±66.7	357.2±45.2	357.8±33.4	383.8±30.1	382.8±41.8	385.3 ±28.9
P-0.2	349.5±45.0	358.8±69.1	321.5±47.3	334.0±61.5	353.5±63.5	373.0±28.6	400.2 ±33.3
P-0.4	370.8±51.6	364.7±60.7	331.0±42.9	343.5±33.7	332.2±65.1	361.7±45.0	347.2 ±56.4
P-0.6	388.8±36.6	366.8±39.8	396.0±35.4	357.8±37.6	374.5±45.1	371.0±34.4	369.5 ±35.3
O-0.4	362.7±35.6	369.7±35.0	362.5±39.3	329.8±71.5	361.2±20.8	365.8±58.2	358.8 ±24.4
R-0.4	375.2±28.8	342.5±62.8	357.5±65.2	369.0±62.5	341.5±66.3	363.7±29.1	347.2 ±56.4

所有資料以 mean ± SD **表示**(beats/min)**。各組之間無顯著統計差異**(n=6, Scheffe`s test)**。**

表 4.4. The effect of *Carthamus tinctorious* on peripheral blood cells in ischemia-reperfusion injured cerebral infarct rats.

Groups	WBC X 10^3/μl	RBC X 10^6/μl	HGB (g/dl)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	PLT X 10^3/μl	LYM (%)	LYM X 1000/μl
C	7.9±2.9	7.8±1.3	16.4±2.8	49.9 ± 8.0	35.6±0.8	63.9±2.0	21.0±0.9	643.7±251.2	67.5±11.4	3.6±1.5
PBS	9.9±3.3	8.6±2.0	16.6±1.9	52.3±13.5	60.5±1.8	20.8±0.6	34.1±1.2	868.3±275.2	41.1±15.9	3.8±1.2
MK	5.2±1.6	8.5±1.0	18.0±2.1	51.5 ± 6.4	61.1±0.7	21.1±0.9	34.6±1.5	749.7±189.2	38.0 ± 9.7	2.0±0.9
S	7.0±3.3	7.6±0.7	15.5±1.7	46.7 ± 5.1	61.2±2.4	20.3±1.0	33.2±0.8	921.0±147.1	47.7±14.6	3.0±0.8
P-0.2	8.6±4.6	9.3±1.7	18.3±3.1	54.5 ± 8.5	60.8±2.6	20.1±1.2	33.9±1.8	749.8±207.9	37.2±14.7	3.2±1.7
P-0.4	8.2±3.1	7.4±1.5	15.9±1.8	46.2 ± 8.9	62.7±1.6	22.2±3.6	35.4±5.8	880.0±164.8	53.0 ± 7.4	4.4±1.9
P-0.6	7.1±2.9	7.7±0.8	16.3±1.6	48.1 ± 3.9	62.5±2.4	20.6±1.3	33.0±1.4	945.5±132.9	49.4±15.0	2.8±0.8
O-0.4	6.9±1.1	8.7±1.4	17.2±1.2	51.4 ± 8.7	61.6±1.2	20.8±1.5	33.7±2.0	865.8±265.1	42.8 ± 9.2	2.9±0.5
R-0.4	8.9±3.9	10.0±1.6	18.1±3.3	63.1 ±13.1	62.7±3.8	20.6±1.2	33.1±2.6	669.5±266.3	35.0±10.9	3.0±1.3

所有資料以 mean ± SD **表示**(beats/min)。 WBC= white blood cell; RBC= red blood cell; HGB= hemoglobin; HCT= hematocrit; MCV= mean corpuscular volume; MCH= mean corpuscular hemoglobin; MCHC= mean corpuscular hemoglobin concentration; PLT= platelet; LYM= lymphocyte. **各組之間無統計學差異**. (n=6, Scheffe`s test)。

表 4.5. The effect of *Carthamus tinctorious* on liver, renal and blood sugar in ischemia-reperfusion injured cerebral infarct rats.

Groups	AST (U/L)	ALT (U/L)	BUN (mg/dl)	Greatinine (mg/dl)	Blood Sugar (mg/dl)
C	425.9±215.9	76.3±37.9	31.1±15.2	0.6±0.2	144.2±30.9
PBS	336.2±111.7	65.4±27.5	23.7±10.1	0.4±0.1	160.4±31.2
MK	269.2 ± 81.9	50.5±13.7	25.4 ± 6.6	0.4±0.1	174.1±64.0
S	304.9±125.1	58.2±28.3	19.5 ± 2.9	0.4±0.	183.0±31.5
P-0.2	341.0±191.1	49.3±21.5	30.7±11.7	0.5±0.1	178.2±31.9
P-0.4	333.1 ± 83.8	48.5±13.1	35.1±12.2	0.6±0.1	174.6±36.1
P-0.6	388.3±122.7	66.7±17.8	26.9 ± 5.3	0.6±0.1	174.9±61.9
O-0.4	294.6 ± 98.7	49.1 ± 9.9	23.1 ± 5.4	0.5±0.1	171.2±68.5
R-0.4	400.0±102.9	80.1±53.4	37.1±23.4	0.6±0.1	162.2±33.4

所有資料以 mean ± SD **表示**. AST=aspartate aminotransferase,**舊稱** serum glutamic-oxaloacetic transaminase [SGOT]. ALT=alanine aminotransferase,**舊稱** serum glutamate-pyruvate transaminase [SGPT]. BUN= the levels of blood urea nitrogen. Cr= the levels of creatinines. BS= the levels of blood sugar。**各組之間無統計學差異**(n=6, Scheffe`s test)。

第五章 討論

5-1 本研究的設計是正確，而且結果值得信賴

根據中醫藥典籍的記載，紅花有活血化瘀的作用，而中醫的認為腦中風是由於血瘀所引起[85,86]，現代研究發現紅花所含有黃酮類，具有抗氧化[37,38]，和抗發炎的作用[40,87]。本研究是將 SD 大鼠兩側總頸動脈和右中大腦動脈的血流阻斷 90 分鐘，然後再灌流 24 小時，製造一個缺血- 再灌流損傷的腦梗塞動物模型，這個腦梗塞的動物模型可以造成局部腦梗塞和神經缺損，非常類似於人類的腦梗塞。MK801 屬於非鈣離子依賴性的 NMDA 受體拮抗劑[79]，一些研究已證實它能減少暫時性中大腦動脈阻塞的腦梗塞面積[79-82]。本研究的結果發現 MK801 前治療能減少腦梗塞面積，這個結果和較早期的一些研究報告一致，說明本研究的結果是值得信賴的。本研究根據預實驗（pilot study）的結果，分別採用紅花 0.2 g/Kg、0.4 g/Kg、0.6 g/Kg 於阻斷兩側總頸動脈和右大腦動脈腦血流前 10 分鐘施行腹腔注射給藥。另外，於腦血流阻斷後 30 分鐘，以及再灌流 30 分鐘分別腹腔注射紅花 0.4 g/kg，這種研究設計與人類發生腦梗塞後再施予治療相似，說明本研究的設計與人類的腦中風治療一致，結果也適用於人類。

5-2 紅花可以減少缺血—再灌流損傷腦梗塞大鼠的腦梗塞面積

本研究的結果顯示，紅花 0.2 g/kg，0.4 g/kg 和 0.6 g/kg 於阻斷兩側總頸動脈和右大腦動脈腦血流阻斷前 10 分鐘腹腔注射，以及紅花 0.4 g/kg 於腦血流阻斷後的 30 分鐘腹腔注射和 MK801 1.0 mg/Kg 相似，都能減少大鼠的腦梗塞面積，說明紅花能用來治療腦梗塞。

5-3 紅花能改善缺血—再灌流損傷腦梗塞大鼠的神經學狀態

本研究結果顯示，紅花治療 0.4 g/kg、0.6 g/kg 和 MK801 1.0 mg/kg 於腦血流阻斷前 10 分鐘腹腔注射，都能減少缺血- 再灌流損傷腦梗塞大鼠的神經缺損。一些研究已說明神經學缺損程度與梗塞面積大小呈正相關的關係[27,46]，而本研究也得到相似的結論。

5-4 紅花減少缺血—再灌流損傷腦梗塞大鼠的腦梗塞面積可能與氧化自由基有關

一些研究已知在缺血後的再灌流期，會產生大量的活性氧化自由基（reactive oxygen species，ROS），包括 superoxide anion (O_2．)、hydrogen peroxide (H_2O_2)、hydroxyl radicals（OH．）、nitric oxide（NO)、peroxynitrite anion ($OONO^-$) 等[49,51]。另一方面，也會耗損或破壞內生性抗氧化系統，因此推測缺血—再灌流後的神經細胞損傷是因內生性抗氧化系統與氧化自由基產生間平衡關係的破壞，導致細胞內大量 ROS 的生成，進而引發一連串的攻擊神經細胞所造成的結果。有研究發現 ROS 會對細胞內的大分子產生直接攻擊，造成細胞膜的 lipid peroxidation（脂質過氧化作用)、蛋白質的氧化作用（protein oxidation)、DNA 的氧化傷害（DNA oxidation)，而最後導致缺不可逆的腦神經細胞的損傷[52-54]。ROS 除了來自於粒腺體外，許多內生性氧化前驅酵素（prooxidant enzyme）如 nitric oxide synthases（NOS)、cyclooxygenases（Cox)、xanthine dehydrogenase（XDH)、xanthine oxidase（XO)、NADPH oxidase（NADPHO)、myeloperoxidase（MPO）以及 monoamine oxidase（MAO）等也有關係[49]。有些酵素對於發炎反

應扮演著重要的角色，當缺血後再灌流時，大量來自周邊的發炎細胞如 reactive microglia、leukocyte、monocyte/Macrophage 受發炎前驅細胞激素誘導、趨化，而不斷的湧向大腦血管、黏附、滲透進入梗塞區。這些發炎細胞會不斷的釋放出氧化自由基如 superoxide anion 等，進一步攻擊缺血後的神經細胞。

本研究的結果顯示紅花 0.4 g/kg 和 MK801 1.0 mg/kg 前治療能夠減少再灌流 2 小時的 lucigenin-CL counts，因此推測紅花可以抑制缺血- 再灌流超氧陰離子的生成或增加清除，由於一些研究已說明 lucigenin-CL counts 可代表由白血球所產生的超氧陰離子[27,83,84]。

5-5 紅花能減少缺血—再灌流損傷腦梗塞大鼠的發炎前驅細胞激素 (pro-inflammation cytokine)—TNF-a 染色陽性細胞

一些研究說明在大鼠缺血性中風發生後的 1-3 小時內，TNF-a mRNA 以及 protein 就會表現會升高[15-17]。但在梗塞皮質區內 TNF-a mRNA 的濃度，則在梗塞後 1 小時就升高，這是由於 TNF-a mRNA 表現的時間早於白血球穿透入梗塞區域的緣故，說明 TNF-a 的表現與白血球進入梗塞核心區的反應有關。局部缺血性中風發生後，於活化的微膠細胞（activated microglia）和巨噬細胞（macrophages）中的 TNF-a mRNA 快速上升，說明 TNF-a 屬於缺血性腦梗塞後內生性發炎反應的一環[62]。有報告認為 TNF-a 能誘導白血球黏附於大腦微循環的血管內皮細胞上，啟動腦中微血管的發炎反應[61]。

本研究的結果顯示紅花 0.4 g/kg 和 MK801 1.0 mg/kg 前治療能夠減少再灌流 24 小時後腦梗塞核心區的的 TNF-a 染色陽性細胞，

說明紅花有抑制腦梗塞後的發炎反應。

5-6 紅花能減少缺血—再灌流損傷腦梗塞大鼠發炎前驅細胞激素 (pro-inflammation cytokine)—IL-1ß 染色陽性細胞

當缺血性腦梗塞發生時，缺血區域的神經細胞、微膠細胞、星狀細胞或血管內皮細胞受到刺激，分泌出細胞激素如 TNF-a、IL-1ß 以及 interferon-a 等，這些細胞激素會促進神經膠細胞的活化，而釋出大量的細胞激素，其中最重要的就是發炎前驅激素 TNF-a 和 IL-1ß。一些研究已指出，在缺血發生時 IL-1 會被誘導而大量產生 [74,75]，這個現象在缺血後 6 小時達到顛峰，並持續數天。缺血發生後 IL-1 的產生主要來自於腦血管內皮細胞和微膠細胞，由於大量 IL-1 的產生使缺血性神經細胞損傷更加惡化，造成選擇性細胞的死亡以及腦水腫的發生 [76]。有研究認為若能阻斷 IL-1，就能減少因缺血所造成的神經細胞損傷，是由於抑制 IL-1 可以間接的減少細胞黏附因子（ICAM）的產生和減少其他發炎前驅因子的作用[75]。

本研究的結果顯示，紅花 0.4 g/kg 或 MK801 1.0 mg/kg 前治療， 能減少腦梗塞區域的 IL-1ß 染色陽性細胞，說明紅花減少缺血- 再灌流損傷腦梗塞面積可能與它抑制 IL-1ß 有關，由於 IL-1ß 會啟動一連串的後續發炎反應、誘導周邊發炎細胞黏附血管、滲透血管壁進而進入梗塞核心區，造成更大的腦損傷。

5-7 紅花不會影響缺血—再灌流損傷腦梗塞大鼠的生理功能

本研究的結果顯示紅花不影響缺血- 再灌流損傷腦梗塞大鼠的直腸溫度、平均動脈壓、心博速率和體重，因此推論紅花不會影響生理功能。這個結果也說明紅花對腦梗塞的效用和體溫無關

，由於一些研究已指出，體溫升高會使腦中風的病情更加惡化[86-89]

5-8 紅花不會影響缺血—再灌流損傷腦梗塞大鼠的肝、腎功能、周邊血液和血糖。

本研究的結果顯示紅花不影響缺血- 再灌流損傷腦梗塞大鼠的 GOT、GPT、BUN、Creatinine、WBC、RBC、HGB、HCT、MCV、MCHC、PLT、LYM（%）、LYM counts 以及血糖，因此推測紅花不會影響肝、腎和骨髓功能，以及周邊血液和血糖。這個結果也說明紅花對腦梗塞的效用與血糖無關，由於腦梗塞發生後血糖濃度的高低與梗塞面積的大小有關[27,88-90]。

第六章　結論

本研究的及結果說明紅花 0.4 g/kg、0.6 g/kg 於腦血流阻斷前 10 分鐘治療，以及 0.4 g/kg 於腦血流阻斷後 30 分鐘治療，都能減少缺血- 再灌流損傷腦梗塞大鼠的梗塞面積，推測紅花可以用來治療人類腦梗塞的急性期。

紅花能減少缺血發生後，再灌流期的超氧陰離子的濃度，以及減少腦梗塞核心區域的發炎前驅細胞激素 TNF-a、IL-1ß 染色陽性細胞，說明紅花對腦梗塞的效用與氧化自由基生成的抑制或清除，以及抑制因缺血而誘發一連串的發炎反應有關。

紅花不會改變缺血- 再灌流腦梗塞大鼠的生理功能包括直腸溫度、平均動脈壓、心博速率，以及肝、腎、骨髓、周邊血液和血糖等生化的值，因此推測紅花對腦梗塞的效用與體溫和血糖無關。

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The study in the relationship between effect of Carthamus tinctorious L. on Ischemia-Reperfusion cerebral infarct Rats, and tumor necrosis factor-a and interleukin-1ß

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Abstract

According to the theory of Traditional Chinese medicine, cerebrovascular accident mainly results from blood stasis. *Carthamus tinctorious L.* (CT) is considered that has the action of activate blood to eliminate stasis since long time ago. Several studies have known recently that CT has antioxidant, ant inflammation and inhibiting glutamate-mediated injury action, and also can protect neuronal cell in the brain. Therefore, the purpose of the present study is to investigate effect of CT on cerebral infarct. A total of 72 male Sprague-Dawley (SD) rats were studied. In experiment one (54 SD), an animal model of cerebral infarct was established by occluding bilateral common carotid arteries (CA) and the right middle cerebral artery (MCA) for 90 min, then reperfusion for 24 hrs. Intra- peritoneal (ip) administration of CT 0.2 g/kg, 0.4 g/kg, 0.6 g/kg and MK801 1.0 mg/kg 10 min before , and CT 0.4 g/kg 30 min after occluding the cerebral blood flow, respectively. In addition, CT 0.4 g/kg i.p. was done 30 min after reperfusion of 2 hrs. The cerebral infarct size and grade of neurological deficit were used as an index to evaluate the effect of CT on cerebral infarct. The superoxide anion was measured by lucigenin-Chemiluminescence (CL) counts before and 90 min after occluding the cerebral blood flow, and 2 hrs after reperfusion, respectively. The tumor necrosis factor- α (TNF-α) and interleukin-1 β (IL-1β) immunostaining in the core of cerebral infarct area, and the levels of blood sugar were also measured 24 hrs after reperfusion. The results indicated that pretreatment with CT 0.2 g/kg, 0.4 g/kg, 0.6 g/kg, MK801, and post-treatment with CT 0.4 g/kg all decreased the ratio of cerebral infarct area. Pretreatment with CT 0.4 g/kg or 0.6 g/kg also decreased the grade of neurological deficit. Pretreatment with CT 0.4 g/kg can decrease the lucigenin-CL counts at reperfusion of 2hrs, and it also can decreased the counts of both TNF-α and IL-1 β immunostaining positive cells in the cerebral infarct area, but the levels of blood sugar and rectal temperature were similar to the control.

In conclusion, CT can decrease both the ratio of cerebral infarct area and grade

of neurological deficit, suggesting can be used to treat acute stage of cerebral infarct in humans. This effect of CT has relationship to inhibit superoxide anion to reduce the generation of oxygen free radicals, and decreased proinflammatory cytokine TNF-α and IL-1β resulting to inhibit inflammatory response, but no relationship to blood sugar and rectal temperature were noted.

Keywords: Carthamus tinctorious L., Cerebral infarct, Neurological deficit, Superoxide anion, TNF-α 、IL-1β