Effects of extract F of red-rooted Salvia on mucosal lesions of gastric corpus and antrum induced by hemorrhagic shock-reperfusion in rats

Li-Hong Zhang¹, Chang-Bai Yao² and He-Quan Li³

¹Department of Anesthesiology, Second Clinical College, China Medical University, Shenyang 110003, Liaoning Province, China
²Department of General Surgery, Second Clinical College, China Medical University
³Department of Pathophysiology, China medical University

Supported by the National Natural Science Foundation of China, No. 3870890
Correspondence to: Li-Hong Zhang, Department of Anesthesiology, Second Clinical College, China Medical University, 36 Sanhao Street, Shenyang 110003, Liaoning Province, China. cumzhanglihong@163.net

INTRODUCTION

More and more stress has been put on gastric mucosal repair by reperfusion injury. Though scholars both at home and abroad have performed plenty of researches on it, there has been no satisfying method or drug yet[1-5]. Red-rooted Salvia is the traditional Chinese medicine for accelerating blood circulation and ameliorating congestion, and its pharmacological effect is very extensive. Resources of red-rooted Salvia in China is sufficient. It has been evidenced that the proportion of red-rooted Salvia dissolving in water can treat acute or chronic gastric mucosal lesions, and has protective effect on gastric mucosa. Extract F of red-rooted Salvia (EFRRS) is extracted from the proportion of red-rooted Salvia dissolving in water[6-11]. Because Prostaglandins (PGs) and oxygen free radical (OFR) play important roles in reperfusional injury[12-18], the present experiment was aimed at studying the endogen ous PGs and antioxidative ability in gastric corpus after administration of EFRRS.

METHODS

The rats were subject to hemorrhagic shock and followed by reperfusion, and were divided randomly into two groups. Group 1 received saline, and group 2 received EFRRS intravenously. The index of gastric mucosal lesions (IGML) was expressed as the percentage of lesional area in the corpus or antrum. The grade of gastric mucosal lesions (DGML) was catalogued grade 0, 1, 2 and 3. The concentrations of prostaglandins (PGs) were measured by radioimmunoassay. The concentration of MDA was measured according to the procedures of Asakawa. The activity of SOD was measured by the biochemical way. The growth rates or inhibitory rates of above-mentioned parametes were calculated.

RESULTS

As compared with IGML (%), grade 3 damage (%) and MDA content (nmol/g tissue) of gastric antrum which were respectively 79.6±0.59, 34.8±0.96 and 156.98±16.12, those of gastric corpus which were respectively 23.18±6.82, 58.4±9.07 and 230.56±19.37 increased markedly (P<0.01), whereas the grade 0 damage, grade 1 damage, the concentration of PGE₂ and PGI₂ (pg/mg tissue), the ratio of PGI₂/TXA₂, and the activity of SOD (U/g tissue) of corpus which were respectively 3.01±0.1, 8.35±1.95, 540.48±182.78, 714.38±123.74, 17.38±5.93 and 134.29±13.35 were markedly lower than those of antrum which were respectively 74.75, 92.29 and 122.25 were higher than those in antrum which were respectively 104.89, 58.40, 11.12, 56.58, 30.65 and 82.64, whereas the inhibitory rates (%) of IGML, grade 3 damage and MDA content of gastric corpus were 82.93, 65.32 and 59.09, being higher than those of gastric antrum which were 76.64, 53.18 and 42.37.

CONCLUSION

After hemorrhagic shock-reperfusion, the gastric mucosal lesions in the corpus were more severe than that in the antrum, which were related not only to the different distribution of endogenous PGs in the mucosa, but also to the different ability of antioxidation of the mucosa. The protective effect of EFRRS on the gastric mucosa in the corpus was more evident than that in the antrum, which was related to higher growth degree of PGs contents and antioxidative ability in gastric corpus after administration of EFRRS.

Subject headings

plant extracts/pharmacology; gastric mucosa/pathology; shock hemorrhagic; reperfusion; hydroxyl radical

Zhang LH, Yao CB, Li HQ. Effects of extract F of red-rooted Salvia on mucosal lesions of gastric corpus and antrum induced by hemorrhagic shock-reperfusion in rats. World J Gastroenterol, 2001; 7(4):672-677
Animal models
Male Wistar rats, weighing 260 g-300 g, were fasted overnight. The rats were anesthetized intraperitoneally with 5 mg·100g−1 of 20% Urethane. Tracheostomy was performed and PE-250 tubing was inserted into the trachea to maintain an open airway. Then open the abdomen and lavage the gastric lumen gently with warm saline. The right carotid artery was cannulated using a polyethylene tube to monitor the blood pressure. The femoral artery was canulated for withdrawing the blood and reinfused the shed blood. After the blood pressure was stabilized, normal saline or EFRRS (1 g·100g·wt−1) was administered for 25 min via a tail vein (0.03 mL·min−1). 1 mL of 0.1 mol/L HCl per 100 g body wt was then instilled into the stomach via the gastric tube, five min after the intragastric instillation of HCL, blood was withdrawn from the femoral artery. The mean arterial blood pressure fell to 2.67 kPa-4.0 kPa and was maintained at that level for 20 min. The shed blood was then reinfused, and 20 min later the rats were sacrificed. Rats were allocated into two groups. Group 1 (n = 9) received NS via the tail vein, and group 2 (n = 7) received EFRRS (1 g·100g·wt−1) via the tail vein.

Index of gastric mucosal lesions (IGML) and inhibitory rate (IR) of IGML
The corpus and antrum lesional areas were measured in square millimeters. IGML was expressed as the percentage of lesional area in the corpus or antrum20. IR was calculated by the following formula.

\[
\text{IR} = \frac{\text{IGML}_{\text{corpus or antrum}} - \text{IGML}_{\text{corpus or antrum}}}{\text{IGML}_{\text{corpus or antrum}}} \times 100\%
\]

Depth of gastric mucosal lesions (DGML), growth rate (GR) and IR of DGML
After measuring the lesional areas, the samples for light microscopy (LM) and scanning electron microscopy (SEM) were taken from the proximal anterior wall of the corpus or the middle of the antrum. The samples analyzed by LM were evaluated as follows21. The damage was graded as 0, 1, 2 and 3. Grade 0 was defined as normal intact surface mucous cells with intact gastric pits and glands. Grade 1: Surface mucous cells were vacuolated with pyknotic nuclei. Some exfoliation was present. Grade 2: In addition to the above changes, the cells lining the gastric pits were also disrupted and exfoliated. Grade 3: Cell destruction extended into the gastric glands (Figures 1-6). Samples analyzed by SEM were evaluated as follows22. Grade 0: The mucosa showed closely packed, polygonal surface mucous cells and narrow openings to the gastric pits. Grade 1: Surface cells were flattened with irregular shape, and gaps between individual cells. Grade 2: The basal lamina was exposed and was largely devoid of surface mucous cells, but still showed continuity, wide openings to the gastric pits were visible. The picture resembled that of a honeycomb. Grade 3: Most of the basal lamina were disrupted, and only a portion being still intact. Regular surface cells were no longer present (Figures 7-12). A close correlation between LM and SEM grading was found (r = 0.846, P < 0.01). The percentage of damage of each grade was calculated in each group. The METHODS to calculate the GR or IR of DGML were the same as that of IR of the lesional area.

PGs contents and GRs of PGs
Prostaglandin E2 (PGE2), 6-keto-PGF1α (6-keto-PGF1α; 6-keto is the metabolite of PGI2), and TXB2 (metabolite of TXA2) boxes were provided by Biochemistry Laboratory of Liberal Army General Hospital, and their concentrations were assayed by using radioimmunoassay. GRs of PGs were calculated in the same way as that of IR of the lesional area.

MDA content and IR of MDA
Malondialdehyde (MDA) is the final metabolism product of OFR. It can be measured by the way of Asakawa23. IR of MDA was calculated in the same way as that of IR of lesional area.

SOD activity and GR of SOD
Superoxide dimutase (SOD) was measured according to the biochemical method24. GR of SOD was calculated in the same way as that of IR of lesional area.

RESULTS
Comparison of IGML and its IRs between the gastric corpus and antrum
The results are shown in Table 1. After hemorrhagic shock-reperfusion, IGML in the corpus was much higher than that in the antrum (P<0.01). As compared with that in the corpus, IR in the antrum was lower after administration of EFRRS.

|                | Group 1 (n = 9) | Group 2 (n = 7) |
|----------------|----------------|----------------|
| Corpus         | 23.16±6.82     | 7.96±0.59      |
| Antrum         | 4.42±1.39      | 82.93          |

Table 1  IGML and its IR in gastric corpus and antrum (% ± s, x±s)

Comparison of DGML, and its IRs and GRs between the gastric corpus and antrum
The results are shown in Table 2. As compared with those in the corpus, grade 0 and 1 damages in the antrum were much increased (P<0.01), and grade 3 damage markedly decreased (P<0.01) after hemorrhagic shock-reperfusion. After administration of EFRRS, the GR of grade 0 and 1 damage and the IR of grade 3 damage in the antrum were much less than those in the corpus.

Comparison of the concentrations of PGE2, 6-keto- and TXB2, the ratio of 6-keto/TXB2 and their GRs between the gastric corpus and antrum
In Table 3, higher PGE2 and 6-keto levels and 6-keto/TXB2 ratio were found in the antrum compared with those in the corpus after hemorrhagic shock-reperfusion (P<0.01), and the GRs of PGE2, 6-keto and 6-keto/TXB2 in the corpus were higher than those in the antrum after administration of EFRRS.
Comparison of MDA content, IR of MDA, SOD activity and GR of SOD between the gastric corpus and antrum

In Table 4, higher SOD activity and lower MDA level were found in the antrum compared with those in the corpus after hemorrhagic shock-reperfusion ($P < 0.01$), and the GR of SOD and IR of MDA were higher in corpus than those in antrum after administration of EFRRS.

![Figures 1, 2 Grade 1 damage in gastric corpus and antrum. LM×330.](image1)
In grade 1 damage, surface mucous cells were damaged.

![Figures 3, 4 Grade 2 damage in gastric corpus and antrum. LM×330.](image2)
In grade 2 damage, the cells lining the gastric pits were also disrupted.

### Table 2
DGML and its IR or GR in the gastric corpus and antrum (%,$\bar{x}\pm s$)

| Group     | DGML | IR | SOD | GR |
|-----------|------|----|-----|----|
| Group 1 ($n=7$) |      |    |     |    |
| Corpus    | 3.01±1.01 | 8.35±1.95 | 31.32±4.49 | 58.44±9.07 |
| Antrum    | 13.92±2.25a | 26.78±5.06a | 25.98±8.32 | 34.86±4.96a |
| Group 2 ($n=6$) |      |    |     |    |
| Corpus    | 22.05±5.96b | 34.12±8.12b | 308.62 | 17.11 |
| Antrum    | 25.98±10.04 | 25.98±10.04 | 14.05±3.13b | 45.98 | 16.32±4.05b | 65.32 |

$P<0.01$, vs corpus; $^aP<0.01$, vs group 1.

### Table 3
PGs contents (pg/mg tissue), and their GRs in the gastric corpus and antrum (%,$\bar{x}\pm s$)

| Group     | PGE$_2$ | GR | 6-keto | GR | TXB$_2$ | 6-Keto/TXB$_2$ | GR |
|-----------|---------|----|--------|----|---------|----------------|----|
| Group 1 ($n=6$) |      |    |     |    |         |                |    |
| Corpus    | 540.48±182.78 | 714.38±123.74 | 58.28±6.74 | 17.38±5.93 |
| Antrum    | 2218.56±433.12b | 2531.76±492.35b | 62.49±9.51 | 43.46±8.51b |
| Group 2 ($n=6$) |      |    |     |    |         |                |    |
| Corpus    | 759.77±192.00a | 1248.32±158.54a | 74.75 | 45.37±7.54a | 33.42±9.24a | 92.29 |
| Antrum    | 2465.17±480.36 | 2698.31±526.71 | 56.58 | 50.02±7.50a | 56.78±5.45a | 30.65 |

$P<0.01$, vs corpus; $^aP<0.01$, vs group 1; $^aP<0.05$, vs group 1.

### Table 4
MDA content (nmol/g tissue), SOD activity (U/g tissue), IR of MDA and GR of SOD in the gastric corpus and antrum (%,$\bar{x}\pm s$)

| Group     | MDA | IR | SOD | GR |
|-----------|-----|----|-----|----|
| Group 1 ($n=6$) |      |    |     |    |
| Corpus    | 230.56±19.37 | 134.29±13.35 | 58.44±9.07 |
| Antrum    | 25.98±8.32 | 34.86±4.96 | 25.98±8.32 | 34.86±4.96 |
| Group 2 ($n=6$) |      |    |     |    |
| Corpus    | 94.32±11.32a | 63.256 | 260.32±52.67 | 56.38 | 50.02±7.50a | 56.78±5.45a | 30.65 |
| Antrum    | 90.46±12.45 | 104.89 | 42.42±8.58 | 34.86±4.96 | 16.32±4.05 | 65.32 |

$P<0.01$, vs corpus; $^aP<0.01$, vs group 1.

---

Comparison of MDA content, IR of MDA, SOD activity and GR of SOD between the gastric corpus and antrum

In Table 4, higher SOD activity and lower MDA level were found in the antrum compared with those in the corpus after hemorrhagic shock-reperfusion ($P<0.01$), and the GR of SOD and IR of MDA were higher in corpus than those in antrum after administration of EFRRS.
DISCUSSION

Reperfusion after hemorrhagic shock can lead to multiple organ damage, *i.e.*, reperfusion injury. The gastric lesions include stress ulcer, hemorrhage, necrosis, or perforation\(^{[25-28]}\). The present study showed that the area and depth of gastric mucosal lesions caused by hemorrhagic shock-reperfusion in the gastric corpus of rats were more severe than those in the antrum. This indicated that there were differences in resistance in gastric mucosa of the corpus and the antrum, which was probably related to differences in gastric mucosal blood flow, energy metabolism and the capacity to dispose the influxing hydrogen ion, but most probably was related with the different distribution of endogenous PGs and the different ability of anti-oxidation\(^{[29-33]}\). The present study also showed that the protective role of EFRRS was different in the gastric corpus and the antrum, EFRRS possessed more powerful capability to reduce the area of lesions and to lighten the extent of lesions in corpus than those in the antrum, indicating EFRRS had potential protective effect on the corpus mucosa, which was related to the higher changes of PGs and OFR in the corpus caused by EFRRS.

It was generally thought that gastric mucosa was affected by both injury factors as gastric acid and pepsin and protective factors as PGs and gastric mucus. Large quantities of PGs were

---

**Figures 5, 6** Grade 3 damage in gastric corpus and antrum. LM×330

In grade 3 damage, cell destruction extended into the gastric glands.

**Figures 7, 8, 9** Grade 1, 2 and 3 damage in gastric corpus. SEM×1500

**Figures 10, 11, 12** Grade 1, 2 and 3 damage in gastric antrum. SEM×1500

In grade 1 damage, surface cells were of irregular shape, and gaps between individual cells were present. In grade 2 damage, the basal lamina was exposed, but still showed continuity. Wide openings to the gastric pits were visible. In grade 3 damage, most of the basal lamina was disrupted, Regular surface cells were no longer present.
found in the gastric mucosa. Numerous studies have doc-
umented that PGs possessed potent cytoprotective action.
PGE₂ could obviously inhibit the secretion of basal gastric acid and
acid stimulated by histamine, p entagastrin and food in
dogs and humans. In addition, PGE₂ could increase the gastric
mucus layer. PGE₂ and PGI₂ could dilute the blood vessel,
increase the blood flow and carbohydrate secretion, and
enhance the resistibility of gastric mucosa to injury. PGs could
also lengthen the life span of epithelia and thick en the mucosa
layer[34,35,37]. In many physiological and pathophysiological
conditions, PGI₂ has protective effect on gastric mucosa.
On the contrary, TXA₂ may aggravate the gastric mucosal
injury[38,39]. The present findings showed the PGE₂ and PGI₂
contents and PGL/TXA₄ ratio in the antrum were markedly
higher than those in the corpus after hemorrhagic shock-
reperfusion, showing gastric antrum was more resistant than
gastric corpus. Arakawa[40] found PGE₂ levels in the gastric
corpus were significantly lower than that in the antrum, and
drug like indomethacin could easily damage the mucosa of
gastric corpus. He thought that the concentration of
endogenous PGE₂ decides the defensive ability of gastric
mucosa. The present study also showed that PGE₂ and 6-keto
levels and 6-keto/TX₂ ratio in the antrum and the corpus both
increased after administration of EFRRS, but the GRs of PGE₂,
6-keto and 6-keto/TX₂; in corpus were higher than t hose in
antrum, demonstrating the reinforcement of defensive ability
of gastric corpus was more powerful after administration of
EFRRS.

OFR played an important role in reperfusion injury. OFR
caus ed lipid peroxidation (LPO) of polyunsaturated fatty acid of
biomembrane, which resulted in the impairment of metabolism
and function of cells, even the death of cells. Plenty of OFRs
could lead to irreversible damage of gastric mucosa, because
they could cause intracellular calcium overload besides of
extensive LPO of tissues and cells[41-47]. OFR was produced by
the system of enzym e and no-enzyme. Malondialdehyde (MDA)
is the metabolite of LPO of OFR, and may reflect the degree of
cells attacked by OFR, therefore MDA is usually an marker
to monitor OFR. Superoxide dismutate (SOD) can clear superoxide
anion, and may reflect the ability of scavenging system of free
radical. Under normal conditions, OFR could be promptly
cleared by the body. Only when the production of OFR markedly
increased, or the ability of scavenging OFR much decreased,
tissues were injured[48,49]. The study showed that there were
higher SOD activity and lower MDA level in the antrum
compared with those in corpus after hemorrhagic shock-
reperfusion, so that the ability of anti-oxidation was more
powerful in gastric antrum, and the reperfusion injury was
easier in gastric corpus. This study also showed that the activity
of SOD and the concentration of MDA decreased in the antrum
and the corpus after administration of EFRRS, but the GR of
SOD and IR of MDA in corpus were higher than those in antrum,
demonstrating reinforcement of anti-oxidation of gastric corpus
was more powerful after administration of EFRRS. The increase
of SOD could accelerate the clearance of OFR to protect cell
from the attack of OFR, while the decrease of OFR made cells
produce more SOD, and clear more OFRs to form good cycle
possessing the role of protective gastric mucosa.

It had been demonstrated in our previous studies[50-54], that
EFRRS could increase the PGs contents, decrease the
production of OFRs, and had calcium block effect, which
resulted in some effects against gastric mucosal lesions induced
by hemorrhagic shock-reperfusion. The present study discussed
the mechanisms that the gastric injury in the corpus was easier
after hemorrhagic shock-reperfusion, and the causes that the
protective effects of EFRRS against gastric mucosal injury was
more powerful in the corpus through both PGs contents and
OFR system. This made the researches of reperfusion injury
of gastric mucosa and the protective effects of EFRRS perform
more profoundly and detailedly.

REFERENCES

1. Perry MA, Wadhwa S, Parks DA, Pickard W, Granger DN. Role of
oxide adics in ischemia-induced lesions in the cat stomach. Gastroenterology, 1986;90:62-67
2. Ekman T, Risberg B, Bagge U. Blocking of endothelial-leukocyte interaction (rolling) does not improve reflow in the rat gastric mucosa
after hemorrhagic shock and retransfusion. Shock, 1994;2:257-261
3. Ekman T, Risberg B, Bagge U. Ascorbate reduces gastric bleeding after hemor rhagic shock and retransfusion in rats. Eur Surg Res, 1995;27:39-48
4. Vasue N, Chan ET, Kaplowitz N, Guth PH. Effect of phorone and allopurinol on ischemia reperfusion injury in gastrointestinal mucosa of the rat. Pharmacology, 1992;44:334-343
5. Ekman T, Bagge U, Risberg B, Sossius B. Ascorbate preserves gastric mucosal metabolism and microcirculation after hemorrhagic shock
and retransfusion in rats. Eur Surg Res, 1995;27:39-48
6. Zhu QX. Treatment of Danshen tablet with 32 cases peptic ulcer. Xin Xue Rouxi Xue Za zhi, 1995;5:237-238
7. Liu RZ, Nie Q, Kong LF. Treatment of parenteral solution of compound Danshen with the disease of digestive system. Xin Xue Rouxi Xue Za zhi, 1995;3(Suppl) 4:74
8. Liu RJ, Wang YS, Li ZQ, Tang XK, Nie Q, Xia PJ, Guo Y, Zhang W. Experimental and clinical study of Danshen on treatment of peptic ulcer. World J Gastroenterol, 1998;4(Suppl 2):72-73
9. Wang GZ, Xu X, Ding LH, Li HQ. Effects of Danshen in prevention and treatment of rat acetic gastric ulcer. World J Gastroenterol, 1998;4:120
10. Liu H, Li QY, Zhan C. Clinical application of compound Danshen in the disease of digestive system. Shi jie Huaren Xiaohua Za zhi, 1999;7: 537-538
11. Gao MQ, Li HQ. Effect of Dan Shen extract F on ethanol-induced gastric mucosal lesion in rats and its mechanism. Zhongguo Bingli shengli Za zhi, 1999;9:644-647
12. Akger FM, Brown MF, Zibari GB, McDonald JC, Epstein CJ, Ross CR, Grang er DN. Role of superoxide in hemorrhagic shock-induced
P-selectin expression. Am J Physiol Heart Circ Physiol, 2000;279:H791-797
13. Smith SM, Grisham MB, Manci EA, Granger DN, Kvietys PR. Gastric mucosal injury in the rat. Role of iron and xanthine oxidase. Gastroenterology, 1987;92:950-956
14. Davis PK, Parascandola SA, Miller CA, Grotyohann LW, Martin LF. Arachnoiditis and macrophage infiltration in hemorrhagic shock-reperfusion injury. J Neurosurgery, 1995;82:1162-1168
15. Myers SJ, Bartula L. Circ Long-term hyperalimentation following hemorrhage/reperfusion injury induces intestinal proinflammatory responses. Shock, 1993;10:151-156
16. Itoh M, Guth PH. Role of oxygen derived free radicals in hemorrhagic shock-induced gastric lesions in the rat. Gastroenterology, 1985;88:1162-1168
17. Itoh M, Paulsen G, Guth PH. Hemorrhagic shock and acid-induced gastric injury in the rat. Gastroenterology, 1996;103:1103-1110
18. Lacy ER, Lto S. Microscopic analysis of ethanol damage to rat gastric mucosa after treatment with a prostanoid. Gastroenterology, 1992;103:809-825
19. Rutten CV, Hinder RA, Oosthuizen MMJ. Gastric mucosal lesions induced by hemorrhagic shock in baboons. Dig Dis Sci, 1994;39:819-823
20. Asakawa T. Thioarbitruricacid test for detecting lipid peroxides. Lipids, 1979;14:401-406
21. Yuan QS. The measurement of superoxide dimutase activity by pyrocatech in auto-oxidation. Yiyuan Congyi, 1983;16:19
22. Zollet l. Experimental study of hypovolemic shock-induced gastric mucosal lesions in the rat. Ann Acad Med Singapore, 1999;28:85-95
23. Jacinto SM, Chintala MS, Lokhandwala MF, Jandhyala BS. Efficacy and me chanisms of dopexamine in the prevention of ischemia-
reperfusion induced organ damage: role of oxygen free radicals. Clin Exp Hypertens, 1997;19:181-190
27 Kapoor R, Prasad K. Role of polymorphonuclear leukocytes in cardio-
vascular depression and cellular injury in hemorrhagic shock and reinfusion. Free Radic Biol Med, 1996;21:609-618
28 Tominaiga GT, Bailey S, Daughters K, Sarfeh IJ, Waxman K. The effect of Polyethylene Glycol-Superoxide Dismutase on gastric mu-
cosa and survival in shock with tissue injury. Am Surg, 1995;61:925-
29 Yasue N, Guth PH. Role of exogenous acid and retransfusion in
hemorrhagic shock-induced gastric lesions in the rat. Gastroenterolology, 1988;94(5 Pt 1):1135-1143
30 Brzozowski T, Konturek PC, Konturek SJ, Sliwowski Z, Drozdowicz
D, Sta chura J, Pajdo R, Meixner H, Hahn EG. Role of prostaglandins generated by cyclooxygenase-1 and cyclooxygenase-2 in healing of ischemia-
reperfusion-induced gastric lesions. Eur J Pharmacol, 1999;385:47-61
31 Maricic N, Ehrlich K, Gretzer B, Schuligoi R, Respondek M, Peskar
BM. Selective cyclo-oxygenase-2 inhibitors aggravate ischaemia-
reperfusion injury in the rat stomach. Br J Pharmacol, 1999;128:1659-
1666
32 Cabeza J, Motilva V, Martin MJ, de la Lastra CA. Mechanisms in-
volved in gastric protection of melatonin against oxidant stress by
ischemia-reperfusion in rats. Life Sci, 2001;68:1405-1415
33 Konturek PC, Duda A, Brzozowski T, Konturek SJ, Kwiecien S,
Drozdowicz D, Pajdo R, Hahn EG. Role of prostaglandins generated by
cyclooxygenase-1 and cyclooxygenase-2 in healing of ischemia-
reperfusion-induced gastric lesions. Scand J Gastroenterol, 2000;35:452-
463
34 Wada K, Kamisaki Y, Nakamoto K, Kishimoto Y, Ashida K, Itoh T.
Effect of plauanotol on gastric injury induced by ischemia-reperfusion in rats. J Pharm Pharmacol, 1997;49:903-907
35 Nakamoto K, Kamisaki Y, Wada K, Kawasaki H, Itoh T. Protective effect of acetaminophen against acute gastric mucosal lesions induced by ischemia-reperfusion in the rat. Pharmacology, 1997;54:203-210
36 Ishikawa T, Sarfeh IJ, Tarnawski A, Gushan H, Douglas T, Sugiyama
M. Epidermal growth factor protects portal hypertensive gastric mu-
cosa in ischemia/reperfusion: the role of capillary endothelia and
prostaglandins. Surgery, 1992;112:341-346
37 Wilson DE. Therapeutic aspects of prostaglandins in the treatment of
peptic ulcer disease. Dig Dis Sci, 1986;31:42S-46S
38 Miller TA. Protective effects of prostaglandins against gastric mucosa
l damage: current knowledge and proposed mechanisms. Am J Physiol,
1983;245(gastrointest. Liver physiol.8):601-623
39 Uribe A, Johansson C, Rubio C. Cell proliferation of the rat gastointest
inal mucosa after treatment with E2 prostaglandins and indomethacin. Digestion, 1987;36:238-329
40 Arakawa T, Nakamura H, Chono S. Prostaglandin E2 in the rat
gastric mucosa. Japan J Gastroenterol, 1980;77:1052-1058
41 Kurokawa T, Joh T, Ikar M, Seno K, Yokoyama Y, Itoh M. Rebamipide
protects against oxygen radical-mediated gastric mucosal injury in rats. Dig Dis Sci, 1998;43(Suppl 9):1135-117S
42 Wada K, Kamisaki Y, Nakamoto K, Kishimoto Y, Ashida K, Itoh T.
Effect of plauanotol on gastric injury induced by ischemia-reperfusion in rats. J Pharm Pharmacol, 1997;49:903-907
43 al-Swayeh OA, al-Humayyd MS, Mustafa AA, al-Tuwaijri AS, al-
Rashed RS, Ali AT. Sculpafat attenuates gastric mucosal lesions and
increased vascular permeability induced by ischaemia and
reperfusion in rats. J Gastroenterol Hepatol, 1997;12:481-489
44 Hahn KB, Park IS, Kim YS, Kim JH, Cho SW, Lee SI, Youn JK. Role of
reb amipide on induction of heat-shock proteins and protection against reactive oxygen metabolite-mediated cell damage in cul-
tured gastric mucosal cells. Free Radic Biol Med, 1997;22:711-716
45 Smith GS, Mercer DW, Cross JM, Barreto JC, Miller TA. Gastric injury
induced by ethanol and ischemia-reperfusion in the rat. Differing
roles for lipid peroxidation and oxygen radicals. Dig Dis Sci, 1996;41:
1157-1164
46 Tanaka J, Yuda Y. Role of lipid peroxidation in gastric mucosal lesions
induced by ischemia-reperfusion in the pylonus-ligated rat. Biol Pharm Bull, 1993;16:29-32
47 Yoshikawa T, Nakamura S, Takahashi S, Naito Y, Kondo M. Effect of
soda ion on gastric mucosal injury induced by ischemia-reperfusion and
its antioxidante d properties. J Clin Gastroenterol, 1993;17(Suppl 1):
S111-S115
48 Tan S, Yokoyama Y, Dickens E, Cash TG, Freeman BA, Parks DA.
Xanthine oxidase activity in the circulation of rats following hemor-
hagic shock. Free Radic Biol Med, 1993;15:407-414
49 Redl H, Gasser H, Schlag G, Marci I. Involvement of oxygen radicals in
shock related cell injury. Br Med Bull, 1993;49:556-565
50 Zhang LH, Yao CB, Zhang BJ. Variation of the prostaglandins con-
centra in rat gastric mucosa after reperfusion and the effects of Extract F of Red-Rooted Salvia (EFRS) on them. Zhonghua Mazuixue
Zazhi, 1995;15:415-417
51 Zhang LH, Yao CB, Zhang BJ. Variation of intracellular calcium
concentration of gastric mucosa in rat after ischemia-reperfusion and
the extract F of Red-Rooted Salvia on it. Zhonghua Mazuixue
Zazhi, 1995;15:500-502
52 Zhang LH, Zhang J, Yao CB, Li HQ, Zhang BJ. Comparison of effects of
Dan Shen Extract F and cimetidine on reperfusion injury in gastric
antrum. Zhonghua Mazuixue Zazhi, 2000;20:416-419
53 Zhang LH, Kong J, Yao CB, Cui JJ, Zhang BJ. Effect of Dan Shen
Extract F on anti-oxidation of gastric mucosa during reperfusion injury. Linchuang Ma zuixue Zazhi, 1999;15:30-31
54 Zhang LH, Li HQ, Yao CB. Effect of Dan Shen Extract F on reperfusion
injury in gastric antrum. Zhongguo Binglishengli Zazhi, 1999;15:395-
397

Edited by Wu XN