

## Current studies on anti-endotoxic chemical components of traditional Chinese medicine in China

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### ABSTRACT

Endotoxin (ET) was found to have wide bioactivities and ET antagonists have become the pop research topic in life science. The chemical components of traditional Chinese medicine (TCM) were the substance basis of its pharmacology. This review demonstrated the study state of about 18 chemical components from TCM, eg, organic acids of Radix Isatidis, anisodamine, matrine, tetramethylpyrazine, colchicine, and glycine, etc, which showed anti-endotoxin effects through different routes. But now the most of them were limited to the laboratory. In the future, the trends of development should not only enlarge the range of research, but also strengthen the clinical study.

### INTRODUCTION

Endotoxin (ET) is consisted of lipopolysaccharide (LPS) and protein and its pathogenicity has attract common attention of doctors and scholars. Endotoxin antagonists have become the hot research topic in life science. Western medicines focus on antibody of ET and have achieved some success. But now natural medicine research starts to show its importance because antibody is expensive and specific. More than 20 years' traditional Chinese medicine (TCM) research showed that about 100 kinds of single TCM and complex of TCM have their chemical components that can be used against ET.

The chemical component of TCM is the substance

basis for its pharmacological action. There are a lot of factors that can influence the experiment results, so it is difficult to repeat. This review introduced the status quotation in the study of anti-endotoxin effect of TCM to instruct the future research and clinical application.

**Organic acids of Radix Isatidis** Radix Isatidis comes from *Isatis indigotica* Fort and can exert anti-endotoxin effect very well<sup>[1]</sup>. Wu *et al*<sup>[2]</sup> isolated 31 kinds of component from Radix Isatidis and each was made as 1 g/L aqueous solution. Limulus lysate test was made *in vitro* according to bacterial ET test. Results showed syringic acid, *o*-aminobenzoic acid, salicylic acid, and benzoic acid had anti-endotoxin effect. Among them, syringic acid had anti-endotoxin activity *in vivo*. Hou *et al*<sup>[3]</sup> found that salicylic acid can inhibit LPS-induced human leukemia-60 cells (HL-60) releasing interleukin-8 (IL-8). When its concentration reach 10  $\mu$ mol/L, the inhibitive rate of IL-8 production was 82.67%. Zhang *et al*<sup>[4]</sup> compared the active potency of Radix Isatidis organic acids by limulus lysate test and found that effective concentrations of anti-endotoxin were syringic acid 25 g/L, *o*-aminobenzoic acid 12.5 g/L, salicylic acid and benzoic acid 1.56 g/L, respectively. Therefore organic acids of Radix Isatidis may be suggested as quality control standard for these reagents.

**Anisodamine (Ani)** Ani, an alkaloid from *Scopolia tangutica*, belongs to a class of cholinceptor blocking drugs. It is an active LPS antagonist, and also can inhibit thromboxane A<sub>2</sub> (TXA<sub>2</sub>) and antagonize the platelet aggregation.

Li *et al*<sup>[5]</sup> analysed lipid peroxides (LPO) levels in serum and superoxide dismutase (SOD) and catalase (CAT) activity in erythrocyte in 4 groups of mice. Besides normal saline group and blank control group, another two groups were iv with *E Coli* O<sub>11</sub>B<sub>4</sub> ET (LD<sub>50</sub>), one of them pretreated with Ani. The SOD and CAT activity in 4 groups had no significant difference, while LPO levels in endotoxin-poisoned mice were

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significantly higher than those of Ani pretreated and control group ( $P < 0.01$ ). The increase of LPO level in poisoned mice showed the damage of cell membranes. The inhibitive effects of Ani on lipid peroxides may be resulted from improving the microcirculatory blood perfusion at ET challenge.

It suggested that  $\text{TNF}_\alpha$  gene expression increased obviously in ET shock and Ani strongly inhibited LPS-induced  $\text{TNF}_\alpha$  gene expression as well as had a beneficial anti-shock effect<sup>(6,7)</sup>. ET shock in rats was produced by iv injection of LPS (5 mg/kg).  $\text{TNF}_\alpha$  mRNA levels in rat liver at 2 h after LPS challenge was increased obviously ( $38 \pm 10$  vs saline control  $11 \pm 8$ ,  $P < 0.01$ ); the plasma  $\text{TNF}_\alpha$  contents was increased markedly [ $(21 \pm 3) \mu\text{g/L}$  vs  $(2.2 \pm 1.0) \mu\text{g/L}$ ,  $P < 0.01$ ]. Ani 10 mg/kg immediately injected after LPS injection markedly decreased the liver  $\text{TNF}_\alpha$  mRNA levels and plasma  $\text{TNF}_\alpha$  contents 2 h after iv LPS. Ani improved the mouse survival rate 24 h after LPS (20 mg/kg) challenge.

**Matrine (Mat)** Mat, an alkaloid found in species of *Sophora* plants in *Leguminosae*, has been used in treatment of chronic liver disease. Mat can reduce liver fibrosis in a rat hepatotoxic model. Antifibrotic effects of Mat on hepatic stellate cells may be related to reduction of fibrogenic cytokine production and blockade of their actions.

Lin *et al.*<sup>(8)</sup> studied the effect of Mat on LPS-induced  $\text{TNF}_\alpha$  and IL-6 production from rat Kupffer cell. Mat 125, 250, and 500 mg/L suppressed  $\text{TNF}_\alpha$  and IL-6 production from calcimycin-primed Kupffer cell in the presence of LPS (100  $\mu\text{g/L}$ ) in a concentration-dependent manner. Treatment with Mat 50 and 100 mg/kg before LPS injection (3.5 mg/kg) markedly decreased serum  $\text{TNF}_\alpha$  and IL-6 in mice. The results suggest that Mat may have protective effect on LPS-induced liver injury.

Hu *et al.*<sup>(9-11)</sup> investigated protective effect of Mat to liver; 1) The effect of Mat on LPS-induced fatal hepatitis and  $\text{TNF}_\alpha$  production in *Propionibacterium acnes* (PA)-primed mice were studied. Mice were injected ip LPS (10  $\mu\text{g}/\text{mouse}$ ) 7 d after ip PA (0.5 mL/mouse) to induce fatal hepatitis. After ip LPS, serum  $\text{TNF}_\alpha$  activity rose to  $(1657 \pm 406)$  kU/L at 1.5 h and plasma alanine aminotransferase (ALT) activity increased up to  $(1490 \pm 890)$  U/L at 5 h. Six of 8 mice died within 5 h and the massive hemorrhagic necrosis of the liver were observed in all mice. Administration of Mat (10, 50 mg/kg, ip, bid  $\times$  3 d) before the LPS injection markedly

reduced the elevation of serum  $\text{TNF}_\alpha$  and ALT activity in a dose-dependent manner, and diminished the mortality induced by LPS. Liver congestion and necrosis induced by LPS in PA-primed mice were ameliorated markedly by Mat pretreatment. Mat (62.5 – 250 mg/L) inhibited LPS-induced  $\text{TNF}_\alpha$  release from PA-primed mouse peritoneal macrophages (PM $\Phi$ ) *in vitro* in a concentration-dependent manner. These results suggest that Mat protected PA-primed mice from the development of fatal hepatitis induced by LPS due to inhibition of  $\text{TNF}_\alpha$  production. 2) The effects of Mat on LPS-induced fatal hepatitis in *D*-galactosamine (*D*-galN)-sensitized mice and  $\text{TNF}_\alpha$  release from PM $\Phi$  was studied. Mice were pretreated with Mat (10, 50 mg/kg, ip, bid  $\times$  3 d) and then injected ip LPS + *D*-galN. Liver injury was estimated by quantifying ALT and histopathologic examination. The  $\text{TNF}_\alpha$  activities in the supernatants of mouse PM $\Phi$  stimulated with LPS in the presence of Mat (32.5 – 500 mg/L) were monitored by the L929 target cells lytic assay. Mat markedly diminished hepatic injury induced by LPS in combination with *D*-GalN and inhibited LPS-induced  $\text{TNF}_\alpha$  release from mouse PM $\Phi$  *in vitro* in a concentration-dependent manner. 3) Mat (125 – 500 g/L) obviously inhibited LPS-induced splenocyte proliferation and release of IL-1 and IL-6 from mouse PM $\Phi$  *in vitro*. Splenocyte proliferation was assayed by [ $^3\text{H}$ ]TdR incorporation. IL-1 and IL-6 activities were measured by thymocyte proliferation assay and B9 cell proliferation methyl thiazolyl tetrazolium (MTT) colorimetric method, respectively.

Zhang *et al.*<sup>(12)</sup> studied the effect of Mat on production and actions of fibrogenic cytokines from mouse PM $\Phi$ . Mouse PM $\Phi$  were primed with calcimycin 1  $\mu\text{mol/L}$  for 8 h then elicited by LPS 100  $\mu\text{g/L}$  for 6 h to induce fibrogenic cytokines. Proliferative and collagen stimulating activity in the macrophage culture supernatants was determined by crystal violet staining assay and [ $^3\text{H}$ ]-proline incorporation assay using rat hepatic stellate HSC-T6 cell or mouse fibroblast NIH3T3 cell. Transforming growth factor  $\beta$  ( $\text{TGF}_\beta$ ) activity was measured by [ $^3\text{H}$ ]-thymidine incorporation assay using Mv-1-Lu mink lung epithelial cell. Results showed that Mat (0.5 – 2 mmol/L) significantly inhibit LPS-induced collagen stimulating activities and  $\text{TGF}_\beta$  production ( $P < 0.01$ ) whereas it did not inhibit proliferation activities induced by macrophages. Macrophage conditioned medium (MCM)-driven proliferation and collagen synthesis of HSC-T6 cells as well as NIH3T3 cells were

attenuated by Mat (0.5–2 mmol/L) in a concentration-dependent manner. In sum, anti-fibrotic effects of Mat on hepatic stellate cells may be related to reduction of fibrogenic cytokine production and blockade of their actions.

**Tetramethylpyrazine (TMP)** TMP is a important alkaloid from *Rhizoma Chuanxiong* and has vasodilator effect and anti-platelet aggregation effect. Fu *et al.*<sup>[13]</sup> studied the prophylactic effects of TMP on mice with endotoxemia and its relationship with platelet-activating factor (PAF). LD<sub>50</sub> of LPS (15 mg/kg) was injected into mice (iv) pretreated with TMP (ip) and PAF induced by LPS *in vivo* and *in vitro* in the experiment. Results showed that TMP obviously lowered the mortality of mice and also dose-dependently decreased the level of serum PAF (vs control). TMP dose-dependently decreased the release of PAF from PM $\Phi$  culture with LPS, reduced the PLA<sub>2</sub> activity and acetyl-CoA:lyso-PAF acetyltransferase activity of PM $\Phi$ . In conclusion, TMP protected the mice with endotoxemia from the death by decreasing the biosynthesis of PAF through the inhibition of the activities of PLA<sub>2</sub> and acetyl-CoA:lyso-PAF acetyltransferase.

The influence of TMP on LPS-induced TNF $\alpha$  gene expression was studied<sup>[14]</sup>. TNF $\alpha$  in supernatants of human whole blood were measured by ELISA; the TNF $\alpha$  mRNA was assessed by slot blot analysis. It was found that LPS-induced TNF $\alpha$  production was in dose-dependently manner. TNF $\alpha$  levels in the whole blood increased at 3 h and peaked at 6 h. The induction of TNF $\alpha$  mRNA was very rapid, peaking at 2 h after LPS challenge. TMP exerted inhibition on TNF $\alpha$  production in dose-dependently manner and had 2-phase effects on TNF $\alpha$  release. So it may be new approaches of anti-TNF $\alpha$  to treat with sepsis.

**Colchicine (Col)** Col is an alkaloid and a therapeutic drug for cirrhosis, hepaticosis, family's fever, anti-tumor, *etc.* The effect of Col on the changes of serum activity of TNF $\alpha$  induced by LPS was studied in rabbits iv administered with NS 0.2 mL/kg from 67 h before LPS injection or Col 0.5 mg/kg instead of NS<sup>[15]</sup>. Endotoxin shock was induced by iv injection of LPS 2 mg/kg after the challenge by *Bacillus Calmette-Guérin* (BCG). The results showed that pre-infusion Col decreased the peak levels of serum TNF $\alpha$  activity ( $P < 0.05$ ) and prevented the rabbits from decrease of mean arterial pressure (MAP) and white blood cell (WBC) count. The conclusion is Col can inhibit the synthesis or

secretion of TNF $\alpha$  *in vivo*.

Li *et al.*<sup>[16-18]</sup> found that microtubule polymerization inhibiting agent Col could depress dose-dependently the secretion of TNF $\alpha$  from rat macrophages (M $\Phi$ ) stimulated by LPS. As showed by indirect immunofluorescence and *in situ* hybridization, LPS was able to promote microtubule polymerization and markedly increase the intracellular TNF $\alpha$  mRNA as well as the expression of TNF $\alpha$  protein. Concomitant application of LPS and Col led to disruption of microtubules and a decrease in TNF $\alpha$  mRNA and TNF $\alpha$  protein expression. In cells treated with both LPS and Col, TNF $\alpha$  was found to have lost its normal cytoplasmic localization and disperse throughout the cytoplasm.

They further demonstrated that the inhibitory effect of Col was characterized by its delayed appearance, *ie.*, requiring 3 h to exert its full-blown depressive effect. In addition, this suppressive effect of Col was completely blocked by cycloheximide (CHX) known to inhibit the newly protein synthesis. Col alone showed no obvious effect on the LPS-induced TNF $\alpha$  mRNA stability. However, in the presence of CHX, Col did prolong the half life time of LPS-induced TNF $\alpha$  mRNA. These observations suggested that the effect of Col on TNF $\alpha$  gene expression may be the result of the dual action on the TNF $\alpha$  gene at the transcriptional and post-transcriptional level.

They also proved that when Col was added at various time intervals after LPS-stimulation, the inhibitory effect on TNF $\alpha$  synthesis by M $\Phi$  gradually disappeared between 2–8 h, but the suppressive effect of Col was significant when LPS and Col were simultaneously added, which indicated that Col acted at early stage of TNF $\alpha$  biosynthesis. On a molecular level, LPS-induced TNF $\alpha$  mRNA accumulation declined by addition of Col. It suggested that Col may reduce TNF $\alpha$  synthesis by inhibiting TNF $\alpha$  mRNA transcription.

**Taurine (Tau)** Tau is a main chemical ingredient from *Calculus Bovis seu Bubali*, *Scorpio*, *etc.* There are effects of detoxication, antioxidation, osmoregulation, and protecting cell membrane. Cheng *et al.*<sup>[19]</sup> studied the hypothermic effect of Tau on endotoxin-induced fever in rabbits and its relationship with some mediators (PGE<sub>2</sub> and cAMP). Tau (1.0 mg/kg) was icv infused 20 min after iv ET, followed by the slow infusion of Tau 0.06–0.22 mg·kg<sup>-1</sup>·min<sup>-1</sup> for about 20 min, caused sedation and peripheral vasodilation, and initially blocked the rise of rectal

temperature induced by ET (iv, 1 mg/kg). In ET + Tau group, the fluctuations in concentrations of PGE2 and cAMP parallel with the change of rectal temperature and the changes were similar to those of the control group, even though the fever was initially inhibited. There were no changes in the concentrations of these mediator in NS + Tau group.

In the experiment investigating the effect of Tau on the fever induced by ET after icv infusion of Tau and CaCl<sub>2</sub> into rabbits<sup>[20]</sup>, results showed that Tau perfusion could inhibit the initial febrile response to ET ( $P < 0.01$ ). When the perfusion of Tau was stopped, the rectal temperature continued to rise ( $P > 0.05$ ), which could be blocked by icv infusion of CaCl<sub>2</sub>. Therefore, Tau might increase the level of Ca<sup>2+</sup> in the hypothalamus and reduce Na<sup>+</sup>/Ca<sup>2+</sup> ratio, then lower the fever.

**Gypenoside (Gyp)** Gyp is a main chemical constitute from *Gynostemma pentaphyllum* (Thunb) Mak and has effects of against LPO, SOD, NO, triglyceride, total cholesterol, and oxygen free radicals damage. Its effect is similar with panaxadiol saponins while Gyp against endotoxin-induced disseminated intravascular coagulation (DIC) in rabbits. Lei *et al.*<sup>[21]</sup> found that Gyp obviously decreased endotoxin-induced positive rate of plasma protamine paracoagulation and consumption of fibrogen. Gyp also postponed the starting time of endotoxin-induced shock. Gyp can maintain prothrombin time in normal period and increase the platelet account in normal level. In conclusion, Gyp has a significant protective effect against endotoxic shock and prevent from subsequent DIC.

Huang *et al.*<sup>[22]</sup> studied the effects of Gyp on *c-sis* expression of bovine aortic endothelial cells (EC) and proliferation of vascular smooth muscle cells (VSMC) induced by LPS and oxygen free radical (OFR). Methods as follows: cultured bovine aortic endothelial cells were incubated with Gyp (10–20 mg/L) and LPS (16 mg/L) or xanthine (X) (100 μmol/L) plus xanthine oxidase (XO) (100 U/L). Gene *c-sis* expression was determined by *in situ* hybridization. Nitrite, metabolic product of NO, was measured according to a modified Griess' method, and the proliferation of EC and VSMC was estimated by MTT assay. Results showed that LPS promoted *c-sis* gene expression and inhibited NO release; X-XO inhibited EC proliferation and NO release. Both LPS and X-XO stimulated SMC proliferation. Gyp significantly decreased *c-sis* gene expression and increased NO synthe-

sis and EC proliferation. Furthermore, Gyp indirectly inhibited SMC proliferation by blocking the effects of LPS and X-XO. The effects of Gyp were against partial by NO synthase inhibitor, N<sup>G</sup>-L-Arg. In conclusion, Gyp inhibited LPS and X-XO stimulated SMC proliferation by attenuating *c-sis* gene expression and promoting NO synthesis or release of EC.

#### Ginkgolide B (GB) and ginkgolide A (GA)

Ginkgolides, extracted from *Ginkgo biloba* leaves, are natural and specific platelet activating factor (PAF) receptor antagonist. Du *et al.*<sup>[23]</sup> observed that PAF in liver was increased gradually after LPS 10 mg/kg was injected, and reached the peak at 8 h. Level of malondialdehyde (MDA) was decreased and adenosine triphosphate (ATP) was increased by GB 5 mg/kg ip 15 min before LPS. It suggested that GB may be one of the important anti-endotoxic shock agent.

Du *et al.*<sup>[24,25]</sup> also showed the increase of PAF, TNF<sub>α</sub>, and NO<sub>2</sub><sup>-</sup>/NO<sub>3</sub><sup>-</sup> after iv injection of LPS 200 and 300 μg/kg. When GB were injected ip 10 min before LPS, PAF and TNF<sub>α</sub> did not change markedly vs LPS group but NO<sub>2</sub><sup>-</sup>/NO<sub>3</sub><sup>-</sup> was reduced. GB increased the survival rate of rabbits. GB pretreatment before LPS 200 μg/kg iv could prevent MAP, LVSP, dp/dt<sub>max</sub>, and IP against decrease and reverse cardiac function disorder.

Du *et al.*<sup>[26]</sup> studied the effects of GA and GB on nitric oxide (NO) production in cultured neonatal rat microglia. No inhibitory effects of GA and GB on NO production were observed in resting microglia, but in LPS-stimulated microglia NO production was inhibited by GA and GB 1–10 μmol/L with IC<sub>50</sub> values of 5.7 and 1.1 μmol/L, respectively. It indicated that GA and GB inhibited NO production in LPS-stimulated microglia.

Zhang *et al.*<sup>[27]</sup> studied the effect of GA on ET-induced small intestinal motility dysfunction in rabbits. Thirsty rabbits were randomly assigned to control, LPS, and ginkgolides group. Conscious rabbits were fasted for 18 h. Two pairs of electrodes were implanted in the duodena-jejunum, and after seven days intestinal myoelectric activity was continuously recorded. GA 5 mg/kg iv greatly ameliorated disorder of intestinal motility but had no effects on normal myoelectricity.

#### Panaxadiol saponins (PS)

PS have wide pharmacological actions. Liu *et al.*<sup>[28–30]</sup> studied anti-endotoxic shock property of PS. PS was administrated to rats 5–10 min before LPS 0.8 mg/kg were given. The results showed that 16-h survival rate was higher and the level of 5-HT and norepinephrine in lung, brain stem,

and serum were lower in PS-pretreated group than that in the endotoxic shock group induced by LPS alone ( $P < 0.05$ ); lipid peroxidation in lung, kidney, heart, and brain tissues were inhibited by PS pretreatment. It indicated that PS had anti-endotoxic shock effect.

**Kintop** Kintop is considered as a slimming and hypolipemia herbicidal medicine and its main component is *Rheum* extracts. Jin *et al.*<sup>[31]</sup> investigated kintop's effect on endotoxemia at different time points after administration. MAP did not obviously decline in Kintop group (15 mg/kg), but declined in endotoxemia group. LPS began to rise at 2 h after injection of LPS and declined at 4 h; however it began to decline at 1 h and reached the bottom at 2 h in Kintop group.  $\text{TNF}_\alpha$  concentrations in endotoxemia group was 42 % higher than that in Kintop group ( $P < 0.05$ ). The moving distances of intestinal contents was longer ( $P < 0.05$ ), which was negatively correlated with LPS concentration ( $r = -0.94$ ,  $P < 0.05$ ). In conclusion, Kintop may ameliorate endotoxemia by lowering the serum  $\text{TNF}_\alpha$  level, sustaining the MAP, and increasing intestinal peristalsis.

#### **Kallji dehydrographolidi succinus (KDS)**

Zhang *et al.*<sup>[32]</sup> observed that scattered or destroyed net-shape and short-belt shape of LPS was induced by KDS. Its effect on LPS is similar with polymyxin B. KDS 5 and 20 g/L inactivated LPS by 83.6 % and 94.0 %, respectively. Meanwhile, KDS 0.625 - 5 g/L could slightly increase the production of inflammatory cytokines ( $\text{TNF}_\alpha$ , IL-1, and IL-2) secreted by the normal PM $\Phi$  and greatly inhibit their activities in a concentration-dependent manner.

**Glycine (Gly)** Gly widely exists in traditional Chinese medicine. LU *et al.*<sup>[33]</sup> studied inhibitory effect of Gly on LPS pyrogenicity in rabbits. The results showed that biphasic fever induced by LPS 100 U was changed into monophasic fever by Gly 10 mg, and monophasic peak was further reduced by Gly 50 mg and almost inhibited completely when Gly was increased to 200 mg. It has no effects when Gly was administrated 5 min after ET injection. The results indicates that Gly inhibit the pyrogenic action of ET directly and dose-dependently but have no effects if being injected after ET.

Qi *et al.*<sup>[34]</sup> modified Limulus Amebocyte Lysate (LAL) test by ultraviolet spectrometry to investigate interaction between LPS and polymyxin B or Gly *in vitro*. Gly/polymyxin B, polymyxin B alone, and Gly alone lowered LPS level greatly after LPS was injected

( $P < 0.01$ ). And effects of Gly/polymyxin B was stronger than polymyxin or Gly alone ( $P < 0.01$ ). In ultraviolet spectrometry graph, there were difference between action of Gly and polymyxin to neutralize LPS; polymyxin B decreased absorption peak value of LPS at 206 nm and 257nm, however, absorption peak values of Gly and LPS can be added up at 212 nm and 257 nm. It suggested that 1) phosphoric acid unit and amino-bioglucose of lipid A were changed and activating C factor in LAL was lost after LPS was neutralized by Gly and polymyxin B. 2) Gly and polymyxin B affected different parts of ET molecule. 3) Gly/polymyxin B mixture might be better than any one of single antagonist.

Sun *et al.*<sup>[35]</sup> observed the effects of Gly on the binding rate of LPS to monocytes by flow cytometry. The percentage of fluorescein-iso-thiocyanate-labeled LPS bound to monocytes was  $(85.2 \pm 1.6)$  % and the mean fluorescein intensity was  $3.03 \pm 0.19$ . After Gly was added to 0.027 mol/L, the binding percentage was decreased to  $(22.5 \pm 1.8)$  % and mean fluorescein intensity to  $1.04 \pm 0.08$ . These results demonstrated that Gly interfered with the binding of LPS to monocyte.

#### **Ammonium glycyrrhizate (GL)**

GL is a chemical constituent from Radix Glycyrrhizae with ability of detoxication and anti-allergy. Chen *et al.*<sup>[36]</sup> studied the effect of GL on LPS-induced bronchial hyper-reactivity. Latency periods was prolonged by 47.8 %; the levels of histamine and isoproterenol in smooth muscle tissue were decreased; cAMP in plasma was increased greatly in GL-treated group (1 mg/kg,  $\times 4$  d) compared with control group.

**Tetrandrine (Tet)** Tet is a dibenzylisoquinoline alkaloid from *Stephania tetrandra* S Moore which has immunosuppressive and calcium antagonistic properties. In clinical, it is mainly used for slight-hypertension, heavy or serious-hypertension, and hypertension crisis. Tet can concentration-dependently decrease the release of PAF from rat PM $\Phi$  stimulated by LPS<sup>[37]</sup>.

In summary, study of anti-endotoxic components in traditional Chinese medicine has achieved some progress and established a strong basis for discovering the new anti-endotoxin agents. But the kinds involved are still small in number. Especially, cooling and detoxicating agents should be paid more attention.

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**关键词** 中草药; 内毒素类; 脂多糖; 板蓝根; 山萆薢碱; 苦参碱; 川芎嗪; 秋水仙碱; 甘氨酸

细菌内毒素 (Endotoxin) 是迄今发现的生物活性最为广泛的物质之一。内毒素拮抗剂的研究已成为生命科学的热门话题。中药化学成分是中药药理作用的物质基础。板蓝根有机酸; 山萆薢碱; 苦参碱; 川芎嗪; 秋水仙碱及甘氨酸等 18 个中药化学成分分别从破坏内毒素分子结构、抑制内毒素诱导的炎性介质的合成和释放及降低内毒素的致热性和致死性等不同途径呈现其抗内毒素作用。但大多数仍局限于实验室, 今后不仅应扩大研究范围, 还应加强临床应用研究。

### 国内中药化学成分抗内毒素研究现状

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