



# Analysis of the Improving Effect of Shenlian Granules on Rats with Chronic Atrophic Gastritis Based on Antioxidant and Liver and Kidney Protection Mechanisms

Wenchong Xiao<sup>1</sup>, Sufang Zhou<sup>2,3\*</sup>, Xiangyu Tian<sup>4</sup>, Lili Bai<sup>1</sup>

<sup>1</sup>The First Clinical Medical College of Guizhou University of Traditional Chinese Medicine, Guiyang 550025, Guizhou, China

<sup>2</sup>The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang 550001, Guizhou, China

<sup>3</sup>Wu Wenyao National Famous Traditional Chinese Medicine Expert Inheritance Studio, Guiyang 550001, Guizhou, China

<sup>4</sup>Department of Laboratory Medicine, Chongqing Yongchuan District Jimai Hospital (Chongqing Yongchuan District Children's Hospital), Chongqing 402100, China

\*Corresponding author: Sufang Zhou, zhsfang2669@126.com

**Copyright:** © 2025 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited

## Abstract

**Objective:** To investigate the ameliorative effects of Shenlian Granules on rats with chronic atrophic gastritis from the perspectives of antioxidant and liver and kidney protection. **Methods:** A rat model of chronic atrophic gastritis was established using three combined methods, and then selected the best modeling method for this experiment. That is, chemical method (alternating free access to 0.1% ammonia solution and 20 mmol/L sodium deoxycholate solution) + hunger and satiety method (alternating one day of satiety followed by one day of hunger) + physical stimulation (30-minute tail clamping with a plastic clip on the satiety day). The model was maintained for 10 consecutive weeks. After confirming successful modeling by observing changes in the intrinsic glands of the gastric mucosa of SD rats, the rats were randomly divided into six groups: a model group, a control group, and groups receiving Shenlian Granules at low, medium, and high concentrations. Treatment and observation began at week 11. The treatment groups (low, medium, and high concentration groups) were gavaged with Shenlian Granules (1.65 g/kg, 3.3 g/kg, and 6.6 g/kg, respectively). The control group was gavaged with Morodan (2.43 g/kg). The model and blank groups were gavaged with purified water (2 mL per rat) once daily for 10 weeks. During modeling and treatment, the rats' general condition was observed, and post-treatment weight changes were recorded. Sixteen hours after the last gavage, blood was collected from the abdominal aorta under anesthesia. Serum ALT, AST, BUN, and Cre levels were measured by an automated biochemical analyzer, and serum MDA, T-SOD, and GSH levels were measured by ELISA. **Results:** Shenlian Granules effectively improved the mental activity and body weight of rats with chronic atrophic gastritis. Shenlian Granules reduced serum ALT, AST, BUN, Cre and MDA levels, and increased T-SOD and GSH-Px levels in rats with chronic atrophic gastritis ( $p < 0.01$ ). The differences were statistically significant and concentration-dependent. **Conclusion:** Shenlian granules may restore chronic atrophic gastritis by enhancing antioxidant capacity. It also plays a protective role in liver and kidney function during the drug action process, which further provides a reliable experimental basis for the clinical use of this prescription in the treatment of patients with chronic atrophic gastritis.

## Keywords

Shenlian granules  
Chronic atrophic gastritis  
Antioxidant effect  
Liver and kidney  
function

## 1. Introduction

Chronic atrophic gastritis (CAG) belongs to the category of “stomach pain”, “fullness” and “noise” in traditional Chinese medicine (TCM). It is an important link in the transformation of normal gastric tissue into gastric cancer. In recent years, the incidence rate has increased and the incidence rate is younger. It is an internationally recognized precancerous lesion of the stomach. In 2022, the global incidence and mortality of gastric cancer ranked fifth among all cancers in the world, and the incidence and mortality of gastric cancer in China ranked fifth and third among all cancers in China respectively; the incidence and mortality of gastric cancer in China accounted for 37.02% and 39.44% of the global gastric cancer respectively, which is higher than the proportion of the Chinese population in the global population, and needs to be paid close attention. Studies have shown that CAG leads to a 4.12-fold increase in the incidence of gastric cancer and a more than 2-fold increase in the incidence of esophageal cancer and esophageal squamous cell carcinoma <sup>[1,2]</sup>. Therefore, timely control of inflammatory progression and reversal of gastric mucosal atrophy and intestinal metaplasia are key stages in preventing the occurrence of gastric cancer, which belongs to the category of “preventive treatment” in TCM. Currently, modern medicine has no specific treatment for CAG, but TCM has obvious advantages in preventing and treating CAG.

ShenLian Granules is an empirical formula developed by Professor Zhou Sufang, Chief Physician of the Department of Gastroenterology at the First Affiliated Hospital of Guizhou University of TCM, for the treatment of CAG. It consists of 12 herbs: *Pseudostellariae radix*, *Scutellariae scutellariae*, stir-fried *Atractylodes macrocephalae*, Poria, Coix Seed, *Hedyotis diffusa* Herba, *Curcuma atractylodes*, *Fritillariae thunbergii*, calcined *Corundum fructus*, stir-fried Malt, *Gallus gallus domesticus*, and roasted Licorice Root. Over many years of clinical practice, this formula has demonstrated robust clinical efficacy, but its underlying mechanism remains unclear. This study aimed to investigate the efficacy of ShenLian Granules in improving CAG through the lens of antioxidant activity and liver and kidney protection.

## 2. Materials and methods

### 2.1. Materials

#### 2.1.1. Experimental animals

94 SPF-grade Sprague-Dawley rats, half male and half female, weighing 180–220 g each, were purchased from the Laboratory Animal Research Institute of Guizhou University of TCM. Laboratory Animal Production License Number: SCXK (Qian) 2021-0003; Laboratory Animal Use License Number: SYXK(Qian) 2021-0005. They were housed in individual cages at the Animal Experimental Center of Guizhou University of TCM at a room temperature of  $(23 \pm 1) ^\circ\text{C}$ , an air humidity of 55–65%, and a 12-h light-dark cycle. All rats in this study were anesthetized and sacrificed by cervical dislocation. Experimental procedures adhered to the principles of animal experimentation ethics and were approved by the Laboratory Animal Ethics Committee of Guizhou University of TCM (Ethics Approval Number: 20240307001).

#### 2.1.2. Medication

*Pseudostellariae pseudoginseng*, stir-fried *Atractylodes macrocephala*, Poria cocos, Coix seed, *Hedyotis diffusa*, *Scutellaria barbata*, vinegared *Curcuma zedoaria*, *Fritillaria thunbergii*, calcined *Cortex roxburghii*, stir-fried Malt, stir-fried *Gallus gallus domesticus*, and roasted Licorice root (granules, purchased from the First Affiliated Hospital of Guizhou University of TCM); Morodan honey pills (9 g × 9 bags/box, Handan Pharmaceutical Co., Ltd., approval number: National Medicine Standard Z13021324); sodium deoxycholate (Shanghai Aladdin Biochemical Technology Co., Ltd., product number S104198), 1% ammonia solution (Solarbio, product number G1822), N-methyl-N-nitro-N-nitrosoguanidine (MNNG) (Shanghai Aladdin Biochemical Technology Co., Ltd. product number M105583), 10% chloral hydrate solution (Legen Biotechnology, product number R00635), and 4% paraformaldehyde (Biosharp, product number BL539A).

#### 2.1.3. Reagents and instruments

Alanine aminotransferase assay kit, aspartate aminotransferase assay kit, urea assay kit, and creatinine assay kit were all purchased from Shenzhen Raydu Life Science Co., Ltd. with catalog numbers S03030, S03040,

S03036, and S03076. Malondialdehyde (MDA) assay kit, total superoxide dismutase (T-SOD) assay kit, and reduced glutathione (GSH) assay kit were all purchased from Nanjing Jiancheng Bioengineering Institute with catalog numbers A003-1-2, A001-3-1, and A006-2-1, respectively. H1-16KR tabletop high-speed refrigerated centrifuge (Hunan Kecheng Instrument Equipment Co., Ltd.), SPX70B III (Fisher Instruments (Hebei) Co., Ltd.), ICV-450 electric constant temperature incubator (ASONE, Japan), EnVision microplate reader (PerkinElmer); Rayto fully automatic biochemical analyzer (Chemray240), Tissuelyser-24L multi-sample tissue grinder (Shanghai Jingxin Industrial Development Co., Ltd.), DK-20000-III electric constant temperature water bath (Fisher Instruments (Hebei) Co., Ltd.), Clever-S15 superpure water meter (Zhiang Instruments (Shanghai) Co., Ltd.), FA1204 FA series multifunctional analytical electronic balance (Changzhou Lucky Electronic Equipment Co., Ltd.), ND-100 ultra-micro UV-visible spectrophotometer (Hangzhou Miou Instrument Co., Ltd.).

## 2.2. Methods

### 2.2.1. Drug preparation

#### (1) Shenlian granules (no decoction)

*Pseudostellariae radix* 15 g, stir-fried *Atractylodes macrocephalae* 15 g, Poria 15g, Coix Seed 20 g, *Hedyotis diffusa* Grass 15 g, *Scutellariae scutellariae* 15 g, Curcuma 10 g, *Fritillariae thunbergii* 10 g, calcined *Corrugated fructus* 15 g, stir-fried Malt 18 g, Chicken Gizzard Stone 10 g, roasted Licorice Root 6 g. Dissolve in warm water.

#### (2) Morodan honey pills

Lily bulb, Poria cocos, *Scrophularia ningpoensis*, *Lindera striata*, *Alisma orientalis*, *Ophiopogon japonicus*, *Angelica sinensis*, *Atractylodes macrocephala*, *Artemisia capillaris*, White peony root, *Dendrobium candidum*, *Acorus calamus*, Chuanxiong rhizome, *Panax notoginseng*, *Sanguisorba officinalis*, *Corydalis yanhusuo*, Pollen pollen, Chicken gizzard lining. Dissolve in warm water.

### 2.2.2. Model establishment

#### (1) Modeling method

The experimental animals were divided into three groups using the random function method in the preliminary experiment, with 6 animals in each group. Three males and three females were housed in separate cages at the Animal Experimental Center of Guizhou University of TCM. The room temperature was  $(23 \pm 1)^\circ\text{C}$ , the air humidity was 55–65%, and the light intensity was 12 h day and night. The animals were fed freely for one week before modeling.

Group A: First, the rats were allowed to drink 0.1% ammonia solution and 20 mmol/L sodium deoxycholate solution alternately; second, the rats were fed with food on one day of satiety and the next day of starvation to create an abnormal state of hunger and satiety; third, the rats were clamped by the tail with a plastic clamp once every 30 minutes on the satiety day.

Group B: First, MNNG was prepared into a 1 g/L aqueous solution (stored at  $4^\circ\text{C}$  in the dark), diluted to 100  $\mu\text{g/mL}$  immediately before use, and the rats were allowed to drink freely in brown bottles (protected from light). The drinking amount was recorded every time the solution was changed (changed every 24 hours). Second, the rats were fed with food on a one-day full diet and one-day starvation schedule to create a state of abnormal hunger and satiety.

Group C: First, MNNG was prepared into a 1 g/L aqueous solution (stored at  $4^\circ\text{C}$  in the dark), diluted to 200  $\mu\text{g/mL}$  before use, and the rats were allowed to drink freely in brown bottles (protected from light). The drinking amount was recorded every time the solution was changed (changed every 24 hours). Second, the rats were fed with a one-day full meal and one-day starvation diet to create an abnormal state of hunger and satiety.

On the first day of the 7th week, the first day of the 8th week, the first day of the 9th week, and the first day of the 10th week of modeling, gastric mucosa of one rat or one male and one female rat in each group were taken for tissue sections to observe the pathological changes of gastric mucosa in rats.

#### (2) Result determination

The success of the model was determined by thinning of the gastric mucosa, reduction or shrinkage of the intrinsic glands of the mucosa, and inflammatory cell

infiltration. At the same time, changes in the appearance and behavior of the rats were observed as a reference. Based on the comparison of the results of the three groups of preliminary experiments, the modeling method of Group A, “chemical method + physical stimulation method + hunger and satiety disorder method”, was determined as the modeling method for the formal experiment, and the continuous modeling time was 10 weeks.

### 2.2.3. Animal experiments

#### (1) Modeling method and animal grouping

Replica modeling method was as follows. 76 SD rats were housed separately, male and female. After one week of adaptive feeding, five rats of each sex were randomly selected as blank groups. The remaining 66 rats were then recreated using the pre-experimental CAG rat modeling method. Firstly, 0.1% ammonia solution and 20 mmol/L sodium deoxycholate solution were alternately given free access to food. Then, a diet was administered on a one-day satiety cycle followed by a one-day starvation cycle to create a state of hunger and satiety imbalance. After that, the tails of rats were clamped with a plastic clip once every 30 minutes on the satiety day. This “chemical method + physical stimulation method + hunger and satiety imbalance” modeling method was used to replicate the modeling for 10 weeks. On the fifth day of the sixth, eighth, and tenth weeks of modeling, one rat of each sex was observed for changes in the intrinsic glands of the gastric mucosa. Drug administration was initiated after successful replication of the modeling method. One female rat died in the ninth week of modeling, and one male rat died in the tenth week of modeling, leaving 58 rats in the modeling group. For animal grouping, 10 rats in the blank group, 58 model rats were randomly divided into 10 model group, 12 rats in the Morodan group, and 12 rats in the low-concentration group, medium-concentration group, and high-concentration group of Shenlian Granules.

#### (2) Administration method

Treatment group: The low-concentration

group, medium-concentration group, and high-concentration group were given Shenlian granules at a concentration of 1.65 g/kg, 3.3 g/kg, and 6.6 g/kg, respectively, dissolved in 2 mL of pure water according to the body surface area of humans and rats, and administered orally once a day; Model group : administered orally with 2 mL of pure water, once a day; Blank group: administered orally with 2 mL of pure water, once a day; Positive control group: administered orally with Morodan, dissolved in 2 mL of pure water at a concentration of 2.43 g/kg (based on the body surface area of humans and animals), once a day; The treatment time for each group was 70 days. During the treatment period, the rats in each group were fed with normal feed and drinking water.

#### (3) General observation

Observe the changes in the appearance and behavior of the rats, and weigh the rats in each group once every 10 days.

#### (4) Specimen collection

After the animals were anesthetized by intraperitoneal injection of 10% chloral hydrate solution, the abdomen was disinfected with 75% alcohol, and the abdomen was cut open along the linea alba. Blood was first collected from the abdominal aorta. After standing at room temperature for 2 hours, the blood was centrifuged at 3500 rpm for 10 minutes, and the supernatant was collected for testing.

#### (5) Automatic biochemical analyzer to detect ALT, AST, BUN, Cre

Whole blood specimens should be placed at room temperature for 2 hours or at 4°C overnight, then centrifuged at 3000 rpm for 15 minutes at 2–8°C. The supernatant can be immediately tested. Alternatively, the specimens can be aliquoted and stored at -20°C or -80°C, avoiding repeated freezing and thawing. Thawed specimens should be centrifuged again before testing.

#### (6) ELISA method to detect MDA, SOD, and GSH content

SD rat serum was collected and centrifuged

at 3000 rpm for 10 min. The supernatant was collected and tested according to the operating procedures of the three ELISA kit instructions.

### 2.3. Statistical analysis

The experimental results were analyzed using SPSS26.0 statistical software. For data that were in line with the normal distribution, the *t*-test was used between the two groups, and the univariate or multivariate analysis of variance was used for comparison between multiple groups. The data were expressed as  $\bar{x} \pm s$ ,  $p < 0.05$  indicated that the difference was statistically significant, and  $p < 0.01$  indicated that the difference was statistically significant.

## 3. Experimental results

### 3.1. Effects on the general condition of animals

During the modeling period, the fur color of SD rats gradually changed from smooth and white to rough and withered. Their overall behavior was quiet (sleepy) the day after a full meal and restless such as scratching and biting the day after a hunger. The blank group rats showed a trend of gaining weight, while the modeling group showed a thin state, which may be related to spleen and stomach weakness and insufficient “Qi” and blood production [3]. However, during the treatment period, the fur color and texture of SD rats in the treatment group and the control group gradually became smooth and white. It was particularly obvious that the SD rats in the model group showed a state of restlessness, resistance to scratching, and even running, which was similar to the manifestation of “liver depression and fire transformation” in TCM.

At the same time, the weight of rats in the blank group and the treatment group showed a gradual increase trend. The weight of rats in the model group did not change significantly before and after treatment; the weight of rats in the control group and the low-concentration group showed a gradual increase trend, but there was no statistical difference. Starting from the 21st day, the *p*-value of the medium-concentration group and the high-concentration group of Shenlian Granules was less than 0.01 compared with the model group, which was statistically significant. Starting from day 41,

the low-concentration Shenlian Granule group and the control group showed statistically significant differences compared to the model group ( $p$ -values  $< 0.01$ ). The high-concentration group showed statistically significant differences compared to days 1 and 11 ( $p$ -values  $< 0.05$ ) on day 71 (Table 1).

This indicates that the body weight of SD rats is positively correlated with drug concentration and treatment duration after treatment. However, on day 71, all groups except the high-concentration group showed a downward trend, indicating that the dependence on treatment duration is relative.

### 3.2. Effects on rat serum ALT, AST, BUN, and Cre

This experiment used an automated biochemical analyzer to measure serum ALT, AST, BUN, and Cre levels in CAG rats. The results showed that the differences between the model group and the blank group were statistically significant ( $p < 0.01$ ), further confirming the successful modeling. Furthermore, compared with the model group, ALT, AST, BUN, and Cre levels decreased in all Shenlian Granule groups.

The differences in ALT, AST, and BUN between the medium and high Shenlian Granule concentration groups were statistically significant ( $p < 0.05$ ). Cre levels decreased in the high Shenlian Granule concentration group ( $p < 0.05$ ), indicating that Shenlian Granule can reduce serum ALT, AST, BUN, and Cre levels in CAG rats, with a positive correlation with increasing concentration.

This suggests that Shenlian granule can restore liver and kidney function in rats with chronic atrophic gastritis caused by chemical drugs, physical stimulation (emotional disorders), and other factors (refer Table 2).

### 3.3. Effects on rat serum MDA, T- SOD, and GSH -Px

In this experiment, the ELISA method was used to detect the levels of MDA, T- SOD, and GSH -Px in the serum of CAG rats.

The results showed that: compared with the blank group, the model group had a  $p < 0.01$  difference, which was statistically significant, further indicating that the modeling method of this experiment was feasible;

**Table 1.** Changes in rat body weight during treatment ( $\bar{x} \pm s$ )

|                                           | Day 1                           | Day 11                          | Day 21                          | Day 31                          | Day 41                          | Day 51                          | Day 61                          | Day 71 <sup>*</sup>                |
|-------------------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|------------------------------------|
| Blank group<br>(n = 9)                    | 430.33 ±<br>40.202              | 417.22 ±<br>39.358              | 457.78 ±<br>40.882              | 459.67 ±<br>39.061              | 474.33 ±<br>48.422              | 479.33 ±<br>48.845              | 503.11 ±<br>50.434              | 462.222<br>±<br>42.728             |
| Model group<br>(n = 10)                   | 291.74 ±<br>11.973              | 284.93 ±<br>11.812              | 319.69 ±<br>12.413              | 289.77 ±<br>15.405              | 319.12 ±<br>13.544              | 306.36 ±<br>13.875              | 316.00 ±<br>15.546              | 309.20<br>±<br>16.239              |
| Control group<br>(n = 10)                 | 303.75 ±<br>17.748              | 301.42 ±<br>17.260              | 331.75 ±<br>18.188              | 340.00 ±<br>17.330              | 367.73 ±<br>23.002 <sup>▲</sup> | 373.91 ±<br>25.038 <sup>▲</sup> | 384.55 ±<br>26.268 <sup>▲</sup> | 368.00<br>±<br>25.159 <sup>▲</sup> |
| Low concentration<br>group<br>(n = 10)    | 308.69 ±<br>14.160              | 304.69 ±<br>15.307              | 337.31 ±<br>22.506              | 344.31 ±<br>18.101              | 370.31 ±<br>22.506 <sup>▲</sup> | 376.62 ±<br>24.065 <sup>▲</sup> | 380.42 ±<br>26.856 <sup>▲</sup> | 359.00<br>±<br>24.733 <sup>▲</sup> |
| Medium<br>concentration group<br>(n = 10) | 312.38 ±<br>17.086              | 316.08 ±<br>17.191              | 364.92 ±<br>20.264 <sup>▲</sup> | 370.85 ±<br>19.690 <sup>▲</sup> | 383.46 ±<br>21.751 <sup>▲</sup> | 391.16 ±<br>25.622 <sup>▲</sup> | 399.00 ±<br>26.358 <sup>▲</sup> | 380.92<br>±<br>25.449 <sup>▲</sup> |
| High concentration<br>group<br>(n = 10)   | 322.54 ±<br>18.500 <sup>△</sup> | 324.92 ±<br>19.913 <sup>△</sup> | 372.31 ±<br>25.811 <sup>▲</sup> | 378.00 ±<br>30.090 <sup>▲</sup> | 383.18 ±<br>35.211 <sup>▲</sup> | 387.45 ±<br>35.735 <sup>▲</sup> | 385.57 ±<br>29.371 <sup>▲</sup> | 424.86<br>±<br>41.531 <sup>▲</sup> |

\*Specimen collection day. <sup>△</sup>Comparison between day 71 (note: specimens were collected on this day, and the animals were fasting) and days 1 and 11,  $p$ -value < 0.05, statistically significant. <sup>▲</sup>Comparison with the model group,  $p$ -value < 0.01, statistically significant.

**Table 2.** Effects of Shenlian granules on ALT, AST, BUN, and Cre in the serum of CAG rats ( $\bar{x} \pm s$ )

| Group                                        | ALT                         | AST                           | BUN                         | Cre                         |
|----------------------------------------------|-----------------------------|-------------------------------|-----------------------------|-----------------------------|
| Blank group                                  | 39.127 ± 4.024              | 87.148 ± 10.089               | 15.739 ± 1.287              | 31.568 ± 4.074              |
| Model Group                                  | 96.907 ± 7.614*             | 235.383 ± 12.319*             | 36.343 ± 2.670*             | 70.533 ± 7.914*             |
| Shenlian granule low concentration group     | 89.616 ± 6.123              | 217.666 ± 14.110              | 33.089 ± 2.023              | 66.047 ± 6.521              |
| Shenlian granules Medium concentration group | 72.995 ± 5.837 <sup>▲</sup> | 183.053 ± 9.957 <sup>▲</sup>  | 29.214 ± 1.902 <sup>▲</sup> | 60.996 ± 5.698              |
| Shenlian granule high concentration group    | 60.713 ± 6.103 <sup>▲</sup> | 156.841 ± 11.193 <sup>▲</sup> | 23.696 ± 1.901 <sup>▲</sup> | 54.256 ± 5.739 <sup>▲</sup> |
| Positive control group                       | 46.098 ± 3.147 <sup>▲</sup> | 139.362 ± 11.659 <sup>▲</sup> | 22.030 ± 1.932 <sup>▲</sup> | 45.983 ± 6.366 <sup>▲</sup> |

\*Compared with the blank group,  $p$  < 0.01, the difference is statistically significant; <sup>▲</sup>Compared with the model group,  $p$  < 0.01, the difference is statistically significant.

**Table 3.** Effects of Shenlian granules on MDA, SOD, and GSH-Px in the serum of CAG rats ( $\bar{x} \pm s$ )

| Group                                        | MDA                                | T-SOD                               | GSH-Px                              |
|----------------------------------------------|------------------------------------|-------------------------------------|-------------------------------------|
| Blank group                                  | 2.737 $\pm$ 0.429                  | 62.100 $\pm$ 3.390                  | 76.089 $\pm$ 3.862                  |
| Model group                                  | 9.005 $\pm$ 0.501 *                | 31.683 $\pm$ 2.655 *                | 29.227 $\pm$ 3.708 *                |
| Shenlian granule low concentration group     | 7.727 $\pm$ 0.428 $\blacktriangle$ | 37.669 $\pm$ 2.376 $\blacktriangle$ | 36.499 $\pm$ 4.182 $\blacktriangle$ |
| Shenlian granules medium concentration group | 6.027 $\pm$ 0.463 $\blacktriangle$ | 43.395 $\pm$ 2.804 $\blacktriangle$ | 47.466 $\pm$ 6.299 $\blacktriangle$ |
| Shenlian granule high concentration group    | 4.531 $\pm$ 0.470 $\blacktriangle$ | 49.476 $\pm$ 2.672 $\blacktriangle$ | 65.511 $\pm$ 7.479 $\blacktriangle$ |
| Positive control group                       | 4.228 $\pm$ 0.361 $\blacktriangle$ | 56.823 $\pm$ 3.159 $\blacktriangle$ | 67.131 $\pm$ 2.366 $\blacktriangle$ |

\*Compared with the blank group,  $p < 0.01$ , the difference is statistically significant;  $\blacktriangle$  Compared with the model group,  $p < 0.01$ , the difference is statistically significant.

compared with the model group, the low, medium, and high concentration groups of Shenlian Granules had a  $p < 0.01$  difference, which was statistically significant.

This indicates that Shenlian granules could significantly reduce the MDA content in the serum of CAG rats and increase the levels of T- SOD and GSH -Px, and were positively correlated with the increasing concentration, suggesting that Shenlian granules can treat chronic atrophic gastritis through antioxidant effects (refer **Table 3**).

## 4. Discussion

chronic progressive gastric disease characterized by atrophy of gastric mucosal glands, intestinal metaplasia or dysplasia, and is a very important link in the transformation of chronic gastritis to gastric cancer. Studies have shown that the occurrence of this disease may be related to *Helicobacter pylori* (Hp) infection, bile reflux and intestinal flora imbalance, poor eating habits, anxiety, depression and other emotional factors <sup>[4-7]</sup>. This experiment used a “chemical method + hunger and satiety disorder + physical stimulation” composite model, in which 0.1% ammonia solution simulated Hp infection, 20 mmol/L sodium deoxycholate solution simulated bile reflux, “one day of fullness and one day of hunger” simulated irregular diet, and physical tail clamping stimulation simulated “emotional disorder” <sup>[8,9]</sup>. In our preliminary experiment, we set up different concentrations of “N-methyl-N’-nitro-N-nitrosoguanidine (MNNG) + hunger and satiety disorders + physical stimulation” groups for control.

The animals also showed different degrees of intrinsic gland reduction, but the stability was not as good as the modeling method finally selected in this experiment, which is consistent with the views in the literature <sup>[10,11]</sup>.

Professor Zhou Sufang’s “Shenlian Granules” are designed to nourish the stomach and spleen, dissipate blood stasis, and detoxify. The formula, comprised of *Pseudostellaria baicalensis*, *Poria cocos*, stir-fried *Atractylodes macrocephala*, and roasted Licorice root, is a “Four Gentlemen Decoction” that nourishes the stomach and spleen. Roasted malt and chicken’s gizzard lining invigorate the spleen and stimulate appetite, while coix seed invigorates the spleen and dissipates dampness. *Scutellaria barbata* and *Hedyotis diffusa* clear away heat and detoxify. *Curcuma zedoaria* activates blood circulation and dissipates blood stasis. *Fritillaria thunbergii* and calcined Corrugated Barley seed resolve phlegm, reduce acidity, and relieve pain. Modern pharmacological studies have shown that *Houttuynia cordata* combined with *Scutellaria barbata* can exert its anti-gastric cancer effects by inhibiting inflammatory cytokines, inducing cell apoptosis, inhibiting cell proliferation, and improving the immune microenvironment <sup>[12,13]</sup>. *Atractylodes macrocephala* combined with *Poria cocos* is the most commonly used drug pair for the treatment of CAG <sup>[14]</sup>. Coix seed combined with chicken gizzard lining can strengthen the spleen, remove dampness, and eliminate tumors <sup>[15]</sup>. *Curcuma zedoaria* is pungent in taste, can move around, guide the meridians and dredge the collaterals, and specializes in “blood stasis in the “Qi” ”, and can also

inhibit the activation of the NF- $\kappa$ B signaling pathway and improve the atrophic state of the gastric mucosa<sup>[16,17]</sup>.

MDA is a product of peroxidation damage, reflecting the degree of lipid peroxidation damage in the body; SOD can scavenge oxygen free radicals and reduce cell apoptosis; GSH-Px is widely present in the cell fluid and mitochondrial matrix, and can catalyze the reaction of reduced glutathione (GSH) with hydrogen peroxide ( $H_2O_2$ ), which helps protect cells from oxidative stress<sup>[18]</sup>. Overexpression of oxygen free radicals plays an important role in gastric mucosal damage in CAG patients. MDA can aggravate mucosal damage, while SOD can enhance the body's ability to scavenge oxygen free radicals<sup>[19]</sup>. Modern studies have confirmed that Chinese herbal formulas, Du channel fire dragon moxibustion, and Chinese herbal formulas combined with acupuncture can promote the recovery of chronic atrophic gastritis by improving serum BUN, Cr, MDA, SOD, GSH-Px and other indicators in SD rats<sup>[20–24]</sup>.

Emotions have a significant impact on the

development and progression of CAG. Clinically, many CAG patients experience symptoms such as anxiety and irritability. This study used tail clamping to create a “liver dysfunction” model. During treatment, rats in the untreated model group exhibited significant irritability, frantic behavior, aggression (running), and screaming. However, CAG rats treated with Shenlian Granules were significantly more docile (easily grasped during medication administration). This suggests that clinical attention should be paid to the psychological factors of CAG patients, including strengthening psychological counseling and disease awareness education to improve clinical treatment efficacy and compliance.

In conclusion, Shenlian Granules can better regulate multiple substances in the serum of CAG rats to resist oxidation and repair liver and kidney function, and significantly improve the behavioral state and body weight of CAG rats, thereby achieving the purpose of treating CAG.

## Funding

The Gifth Batch of National Excellent Clinical Talent Training Project of Traditional Chinese Medicine funded by the State Administration of Traditional Chinese Medicine (Project No.: Guozhongyiyaorenjiaohan [2022] No.1); Wu Wenyao National Famous Traditional Chinese Medicine Expert Inheritance Studio of the State Administration of Traditional Chinese Medicine (Project No.: Guozhongyiyaorenjiaofa [2013] No.47); Graduate Research Fund of Guizhou University of Traditional Chinese Medicine (Project No.: YCXKYB2024011); Inheritance and Innovation Talent Team of Traditional Chinese Medicine for Prevention and Treatment of Liver Diseases, Spleen and Stomach Diseases, The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine (Project No.: GZYYFY2025003)

## Disclosure statement

The authors declare no conflict of interest.

## References

- [1] Hu Z, Zhu X, Ge W, et al., 2025, Analysis of Global and Chinese Gastric Cancer Incidence and Mortality in 2022. *Journal of Naval Medical University*, 46(6):767–774.
- [2] Li J, Pan J, Xiao D, et al., 2024, Chronic Atrophic Gastritis and Risk of Incident Upper Gastrointestinal Cancers: A Systematic Review and Meta-Analysis. *Journal of Translational Medicine*, 22(1):429.
- [3] Zhang D, Li F, Jiang D, 2024, Exploring the Application of Differentiation and Treatment Ideas of Chronic Atrophic Gastritis from the Perspective of “Qi Deficiency Should Be Treated with Restraint and Guidance”. *Jilin Traditional Chinese Medicine*, 44(2):165–169.

- [4] Li Y, Long X, Mao X, et al., 2024, Microbiological Characteristics of *Helicobacter pylori* and Its Correlation with Chronic Atrophic Gastritis. *Laboratory Medicine*, 39(5):497–503.
- [5] Eastmond A, Shetty C, Rizvi S, et al., 2022, A Systematic Review of the Gastrointestinal Microbiome: A Game Changer in Colorectal Cancer. *Cureus*, 14(8): e28545.
- [6] Tian F, Liu W, Li Y, et al., 2025, Correlation Between Risk Factors, TCM Syndrome Distribution and Endoscopic Pathology of Chronic Atrophic Gastritis in Chongqing Area. *Chinese Journal of Integrated Traditional and Western Medicine in Digestion*, 33(1):30–34.
- [7] Li Y, Shang H, 2024, Treatment of Chronic Atrophic Gastritis Based on “The Earth Gets the Wood and Reaches the Sky”. *Chinese Journal of Ethnic Medicine*, 30(3):7–9.
- [8] Hong Y, Tu W, Zhu J, et al., 2024, Metabolomics-Based Study on the Central Regulatory Effect of Chaishao Liujun Decoction on Rats with Chronic Atrophic Gastritis of Liver Depression and Spleen Deficiency Type. *Chinese Journal of Experimental Traditional Chinese Medicine*, 30(2):148–155.
- [9] Zhu J, Huang W, Hong Y, et al., 2023, Mechanism of Chaishao Liujun Decoction in Treating Rats with Chronic Atrophic Gastritis and Liver Depression and Spleen Deficiency Based on EGFR/JAK1/STAT1 Signaling Pathway. *Chinese Journal of Traditional Chinese Medicine*, 38(7):3334–3338
- [10] Liu Y, Wang L, Long K, et al., 2024, Evaluation of the Composite Modeling Method for Chronic Atrophic Gastritis and Precancerous Lesions. *Journal of Shanxi Medical University*, 55(2):170–174.
- [11] Yao Y, Lin X, Lei X, et al., 2013, Establishment and Stability Evaluation of Chronic Atrophic Gastritis Rat Model. *Chinese Journal of Pharmacology and Clinic*, 29(4):162–166.
- [12] Yuan Q, Li M, Zhang L, 2024, Study on the Anti-Inflammatory Effect of Water Extract and Alcohol Extract of Fresh *Hedyotis Diffusa*. *Anti-Infective Pharmacy*, 21(6):559–563.
- [13] Zhang X, Wang N, Dai M, et al., 2024, Research Progress on the Material Basis and Mechanism of Action of *Hedyotis Diffusa*–*Scutellaria Barbata* Drug Pair in the Treatment of Gastric Cancer. *Chinese Journal of Clinical Pharmacology and Therapeutics*, 29(7):831–840.
- [14] Wu D, Su Z, Meng H, et al., 2022, Study on the Medication Rules of Traditional Chinese Medicine Compound in the Treatment of Chronic Atrophic Gastritis Based on Patent Data. *World Traditional Chinese Medicine*, 17(11):1621–1626.
- [15] Yang F, Cao J, 2024, Examples of Commonly Used Drug Pairs in Clinical Practice by Shan Zhaowei. *Journal of Traditional Chinese Medicine*, 39(10):2154–2158.
- [16] Wang L, Feng J, Chen J, et al., 2023, Study on the Treatment of Chronic Atrophic Gastritis with *Curcuma Zedoaria* Based on the Theory of Collateral Disease. *Shandong Journal of Traditional Chinese Medicine*, 42(3):225–228.
- [17] Fang Y, Li Y, Yu Y, 2024, Exploring the Mechanism of Action of *Curcuma Zedoaria* Extract in the Treatment of Chronic Atrophic Gastritis Based on HDAC6/NF- $\kappa$ B Signaling Pathway. *Chinese Journal of Hospital Drug Evaluation and Analysis*, 24(10):1217–1220.
- [18] Aujo N, Tali N, Ngatcha G, et al., 2023, *Helicobacter pylori* Infection—A Risk Factor for Lipid Peroxidation and Superoxide Dismutase Over-Activity: A Cross-Sectional Study Among Patients with Dyspepsia in Cameroon. *JGH Open*, 7(9):618–628.
- [19] Chen X, Luo Y, Zhang D, 2020, Effects of Shenqi Jianwei Granules on Gastrointestinal Hormones and Oxidative Stress in Patients with Chronic Atrophic Gastritis with Spleen and Stomach Deficiency and Cold Syndrome. *Chinese Journal of Drugs and Clinics*, 20(1):1–5.
- [20] Guo H, Wang X, Li Z, et al., 2025, Study on the Mechanism of Fuzheng Xiaowei Decoction in Treating Chronic Atrophic Gastritis in Rats. *Shaanxi Journal of Traditional Chinese Medicine*, 46(6):729–733 + 740.
- [21] Li X, Zeng Q, Xie J, 2025, Observation on the Efficacy of Bamboo Ring Salt Moxibustion Combined with Modified

- Liujunzi Decoction in the Treatment of Chronic Atrophic Gastritis of Spleen and Stomach Deficiency Type and Its Effect on Oxidative Stress Indicators. *Journal of Rare Diseases*, 32(6):138–140.
- [22] Zhao Y, Yang H, 2025, Effects of Huazhuo Tongqing Decoction Combined with Acupuncture and Enteric-Coated Pancreatic Enzyme Tablets on Gastric Mucosal Repair, Inflammatory Factors and Oxidative Stress in Patients with Chronic Atrophic Gastritis. *Hebei Traditional Chinese Medicine*, 47(7):1158–1162 + 1167.
- [23] Hu Z, Wang X, 2025, Effects of Du Meridian Fire Dragon Moxibustion on Gastrointestinal Hormones and Oxidative Stress Levels in Chronic Atrophic Gastritis with Spleen and Stomach Deficiency and Cold Syndrome. *Journal of Clinical Acupuncture and Moxibustion*, 41(2):53–57.
- [24] Wang X, 2025, Analysis of the Effect and Mechanism of Jianpi Hewei Decoction Combined with Acupuncture in the Treatment of Chronic Atrophic Gastritis Based on Gastric Motility and Antioxidant Effects. *Medical Theory and Practice*, 38(15):2579–2582.

**Publisher's note**

*ART AND DESIGN PRESS INC. remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.*