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Research Article
The Anti-Arthritis Effect of Cinnamaldehyde on Adjuvant Arthritis Rats

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Abstract

Background and Objective: Cinnamaldehyde, the main component of volatile oil was isolated from the traditional Chinese herb medicinal *Cinnamomum cassia*. A variety of pharmacological and biological activities of cinnamaldehyde have been fully demonstrated, such as antiviral, antidiabetic, anti-inflammatory, anticancer and antithrombotic effects. The present study aimed to evaluate the anti-arthritic effects of a 70% aqueous ethanol extract of the *Cinnamomum cassia* in a chronic inflammatory model and reveal the underlying molecular mechanism. **Materials and Methods:** Induction of adjuvant arthritis in rats was by injection of Complete Freund's Adjuvant (CFA) into the plantar of the right hind paw of Sprague-Dawley rats. Paw swelling, body weight, arthritis index, thymus index and spleen index were and evaluated. Examine the level of TNF-α, IL-1, IL-6, IL-10 and PGE_2 in sera by using ELISA. Measure the histopathological conversions in joint tissues by using Hematoxylin and Eosin (H and E). **Results:** Cinnamaldehyde significantly relieved body weight loss, refrained arthritis index and paw swelling, decreased the thymus index and spleen index induced by CFA. Furthermore, cinnamaldehyde significantly suppressed the overproduction of and serum TNF-α, IL-1, IL-6 and PGE_2 and increased serum IL-10 production in and CFA-induced rats. Histopathological examination indicated that cinnamaldehyde attenuated synovial hyperplasia, bone and cartilage damage and inflammatory cell infiltration. **Conclusion:** These results suggest that cinnamaldehyde has the potential protective effect against CFA-induced arthritis in rats.

Key words: *Cinnamomum cassia*, cinnamaldehyde, adjuvant-induced arthritis, anti-inflammation, anti-arthritis, cartilage, cell infiltration

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic systemic autoimmune disease, often referred to as "immortal cancer", which is characterized by joint swelling, chronic proliferative synovitis and progressive cartilage damage[1]. Inflammatory cells infiltrate into the synovium of the joint, causing excessive production of inflammatory mediators and massive cell infiltration, causing destruction of cartilage and bone tissue, eventually develop irreversible systemic inflammation and bone and joint damage, seriously affecting the human quality of life and even leading to death. RA has a high economic burden and mental stress on patients and society due to its high incidence rate worldwide and its difficulty in treatment[2]. Hence, more and more clinical medical workers are solving this problem and it is a very urgent and long-term task to develop more effective, safer and more economical anti-RA drugs.

The traditional Chinese medicine *cassia* twig is the dry twig of cinnamon *Cinnamomum cassia*, which is contained in the "Shen Nong's Herbal Classic". It dispels cold and has the effect of warming and meridian[3]. Since the Han Dynasty Zhang Zhongjing's "Treatise on Febrile Diseases", *Cinnamomum cassia* has been widely used by doctors of various dynasties. Cinnamaldehyde is an alkenyl organic compound extracted from the cinnamon tree and is the main component of its volatile oil. A large number of pharmacological studies on cinnamaldehyde have shown that it has various pharmacological activities such as anti-inflammatory, antipyretic and analgesic, anti-tumour, antibacterial, hypoglycemic and anti-obesity[4].

Many *in vitro* studies have shown that cinnamaldehyde has a significant anti-inflammatory effect. It has been shown in the inflammatory model of RAW264.7 cells stimulated by Interleukin-1β (IL-1β) or Lipopolysaccharide (LPS), cinnamaldehyde was found significant inhibition of Nitric Oxide (NO), Tumour Necrosis and Factor-α (TNF-α) and Prostaglandin E2 (PGE_2) secretion, down-regulation of and membrane-associated prostaglandin synthase 1 (mPGES-1) and cyclooxygenase-2 (COX-2) mRNA expression, inducible Nitric Oxide Synthase (iNOS), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) protein expression, has obvious anti-inflammatory and antipyretic effects[5].

The anti-inflammatory activity of cinnamaldehyde is also manifested in the treatment of various diseases[6]. In the LPS/D-galactosamine-induced acute hepatitis model, Cinnamicaldehyde can significantly reduce the levels of Alanine Transaminase (ALT), Aspartate Transaminase (AST), Interleukin-6 (IL-6) and TNF-α in serum. Liver histopathology also showed that cinnamaldehyde reduced the incidence of liver injury caused by LPS/D-galactosamine. This indicates that cinnamaldehyde may play a role in liver protection through anti-inflammatory activity, but its mechanism needs further study. In the mouse model of viral myocarditis[7], cinnamaldehyde has no antiviral activity *in vitro*, but it has the effect of reducing viral titer and inhibiting TLR-4-NF-κB signalling *in vivo* and has a therapeutic effect on mice with viral myocarditis. Compared with the model group, the mortality of the Cinnamicaldehyde group was significantly decreased and the median survival time was prolonged. On the 10th day, the Coxsackie B Virus 3 (CVB3) mRNA content and serum NO content in the myocardium were analyzed. The expression of iNOS, TNF-α, activated NF-κB P65 and TLR4 protein in the myocardium decreased significantly ($p<0.05$) and the pathological scores decreased significantly on day 10 and 21. In the rat model of myocardial ischemia, cinnamaldehyde pretreatment significantly reduced Electrocardiogram (ECG) ST-segment elevation induced by acute myocardial ischemia and the level of Creatine Kinase (CK), Lactate Dehydrogenase (LDH), TNF-α and IL-6 expression in serum, indicating that cinnamaldehyde can play a cardioprotective function through anti-inflammatory activity[8]. In gastrointestinal related diseases, the anti-inflammatory effect of cinnamaldehyde was also very obvious. In experiments with AGS/MKN-45 cells and Helicobacter pylori co-culture, it was found that cinnamaldehyde can significantly inhibit the expression of IL-8 secreted by gastric epithelial cells infected with Helicobacter pylori and Helicobacter pylori-induced NF-κB activation and degradation of I-κB. In addition, cinnamaldehyde has a certain therapeutic effect on mucositis[9]. Oral administration of cinnamaldehyde (10 mg kg^{-1}) in the carrageenan-induced rat foot swelling model can significantly reduce swelling, the expression of related inflammatory factors in serum[10] and exert anti-inflammatory effects without damaging gastric mucosa[11]. Cinnamaldehyde can also inhibit neutrophil chemotaxis[12], reduce mast cell-mediated release and expression of pro-inflammatory mediators[13]. Cinnamaldehyde can produce strong anti-inflammatory effects on cells and serum. It has a certain structure-activity relationship as a compound, which may be related to the position and number of its chain substituents.

However, up to now, there is no clear evidence that cinnamaldehyde has an anti-arthritis effect *in vivo* and its potential mechanism in the treatment of RA. Therefore, as part of evaluating the anti-inflammatory effects of natural compounds, this study aimed to confirm the anti-arthritis effect *in vivo* and elucidate the underlying mechanism of cinnamaldehyde in adjuvant-induced arthritis in rats.

MATERIALS AND METHODS

Study area: The research was conducted in the School of Laboratory Pharmacy, Anhui University of Traditional Chinese Medicine, China from July-December, 2020.

Animals: Total 40 SD rats (180±20 g) were purchased from the Chinese experimental animal Anhui University of Chinese medicine. The laboratory experimental conditions are provided by the laboratory of the College of Pharmacy of the Anhui University of Chinese Medicine. The rats were kept in cages, with 8 rats per cage. Animals were adapted to domesticated 7 days before the experiment, room temperature 24±2°C, relative humidity 50-60%, good ventilation and light, good sanitary conditions, free feeding, drinking water, changing drinking water every day, changing padding once every 2 days. All animal experimental procedures were carried out following the guidelines of the Animal Experimental Ethics Committee of Anhui University of Chinese Medicine (Anhui, China).

Drugs and reagents: The main drugs and reagents used in this experiment included Complete Freund's Adjuvant (CFA), ELISA test kits, cassia twig extract, cinnamaldehyde monomer and Zheng qing Feng tong ning tablets. The CFA and the ELISA test kits were purchased from Anhui Xinle Biological Co., Ltd. (Hefei, Anhui, China). Crude slices of the herb *Cassia* twig were purchased from TCM markets (Bozhou, Anhui, China). Cinnamaldehyde monomer was purchased from Sigma Chemical Co (St. Louis, Mo). Zheng qing Feng tong ning tablets were purchased from Zhengqing Pharmacy Co., Ltd. (Hunan, China). *Cassia* twig was extracted in the laboratory. The extraction process was to take the appropriate amount of *cassia* twig, add 10 times the amount of 70% ethanol reflux for 2 times, each time for 1 hr[14], recover the ethanol under reduced pressure, concentrate and store in a refrigerator at 4°C. Zheng qing Feng tong ning Tablet is a commercially available drug for the treatment of RA and was used as a positive control in this experiment[15]. Cinnamaldehyde monomer and Zheng qing Feng tong ning tablet suspension: Calculate the daily dose of rats of different bodyweight according to the conversion factor of 6.25 kg^{-1} b.wt. of rats and adults, accurately weighed, made with 0.5% sodium carboxymethyl cellulose into a suspension[16].

Establishment of rat adjuvant arthritis and treatment regimen: The rats were immunized with 0.1 mL CFA by intradermal injection into the right hind paw[17]. The day of injection of the adjuvant was determined as the first day of modelling. On the 17th day of modelling, the rats were randomly divided into 4 groups according to the paw swelling of the rats, which were the positive control group (Zheng qing Feng tong ning), the *Cassia* twig extract group, the cinnamaldehyde monomer group and the physiological saline group, eight rats per group. There was also a group of normal rats (not modelled and not administered). The above groups were recorded as follows: (1) CFA+ZF group, (2) CFA+CE group, (3) CFA+CA group, (4) CFA+PS group and (5) normal group. For intragastric administration, the daily dose was calculated based on a dose conversion factor of 6.25 kg^{-1} b.wt. of rats and adults. The dose of CFA+ZF group was 5 mg per day/200 g rat. The dose of the CFA+CE group was 0.2 g per day/200 g rat. The dose of the CFA+CA group is 2.4 mg per day/200 g rat. The CFA+PS group was given the same dose of physiological saline. The normal group and the model group were orally administered with an equal amount of 0.5% sodium carboxymethylcellulose suspension. All the above groups were intragastrically administered at 10:00 am every day from the 17th day of modelling and continued for 7 days.

Evaluation of arthritis swelling: Observe the body hair colour, consciousness and activity status of the rats and changes in diet. Before the CFA immunization, the amount of swelling of the right hind paw of each rat was measured with the rat toe volume meter and then measured as the main swelling at intervals of 3 days until the 28th day.

As described previously, the visual arthritis index was used to assess the severity of arthritis[18]. In this scoring system, the appearance of arthritis in the peripheral joints, tails, ears and eye nebula of the rats was visually examined and the severity of arthritis was scored. The paws, ears, nose, eyes and tail are graded separately and the cumulative score depends on redness and swelling. Observation records were recorded by observers who ignored the study. Arthritis scores ranged from 0-3, with 0 indicating no change, 1 indicating mild inflammation, 2 indicating moderate inflammation and 3 indicating significant inflammation.

Determination of rat body weight: The body weight of each group of rats was weighed and recorded with an electronic balance on (0d) and 3, 6, 9, 12, 15, 18, 21, 24 and 27 d after inflammation.

Determination of serum TNF-α, IL-1, IL-6, IL-10 and PGE_2: On the 28th day, the rats were anaesthetized with pentobarbital. Blood was taken by rat abdominal aorta puncture and serum

was collected by centrifugation at 3000 rpm for 10 min. The concentrations of TNF-α, IL-1, IL-6, IL-10 and PGE_2 in the serum were measured by ELISA test kits using commercially available reagents according to the manufacturer's instructions. The absorbance values of each pore were measured at 450 nm and the appropriate standard curves were established. The levels of these cytokines were expressed in picoliter or picomolar per litre serum.

Spleen index and thymus index: After blood collection, the rat spleen and thymus were removed and weighed. The spleen index and thymus index is expressed as the ratio of spleen wet weight to rat body weight (mg g^{-1}).

Histopathological examination of joints: The knee joint of the rats was removed for histological analysis. The joint was fixed in 10% buffered formalin, decalcified in decalcification solution for 30 days, embedded in paraffin and then cut into sections of about 5 mm thick, using hematoxylin-eosin (H and E)) stained and observed by an optical microscope. As mentioned earlier, two independent examiners scored the parts of the experimental protocol that were not known[19].

Statistical analysis: All values were expressed as Means±SD. One-way analysis of ANOVA was used to assess differences between the treatment groups. The p-value of 0.05 was considered significant.

RESULTS

Effects of cinnamaldehyde on arthritis index and paw swelling in CFA-induced rats: As shown in Fig. 1a, after CFA immunization, the paw swelling of the right hind paw of the rat was significantly increased as compared with the normal group, indicating that arthritis was significantly induced and the paw swelling reached the maximum on the 17th day of induction. On the 17th day of induction, the rats were administered continuously for one week. In the saline group, the paw swelling of the rats was not significantly alleviated in Fig. 1b. Compared with the saline group, the positive control group (Zheng qing Feng tong ning) had a significant decrease in paw swelling and significant relief of arthritis in Fig. 1c-e, the paw swelling of the cinnamaldehyde group and *Cassia* twig extract group were also decreased. It indicates that Zheng qing Feng tong ning, *Cassia* twig extract and cinnamaldehyde monomer can alleviate the paw swelling of CFA-induced arthritis rats.

As shown in Fig. 2, the arthritis index of the rats immunized with CFA was significantly increased as compared with the normal group. On the 17th day of induction, the arthritis index reached its peak. Compared with the saline group, the positive control group (Zheng qing Feng tong ning) showed a significant decrease in the arthritis index after administration and the arthritis index in the cinnamaldehyde group and *Cassia* twig extract group also decrease.

Effects of cinnamaldehyde on body weight in CFA-induced rats: The connection between weight loss and the extent of joint inflammation were examined. As shown in Fig. 3, the rats lost weight after receiving CFA immunity compared to the normal group. From the 17th day, the Zheng qing Feng tong ning group significantly reduced the weight loss of the rats and the cinnamaldehyde group and *Cassia* twig extract group also relieved the weight loss of the rats. The saline group did not significantly improve the weight loss of the rats. However, rats were given a normal diet and water every day. Over time, the weight of each group of rats increased slightly, which is a normal physiological phenomenon.

Effects of cinnamaldehyde on spleen and thymus index in CFA-induced rats: It is well known that CFA-induced arthritis can cause swelling or hyperplasia of the immune organs (spleen and thymus) in rats. As shown in Fig. 4, the spleen index and the thymus index of the rats in the saline group after CFA immunization were significantly increased as compared with the normal group. However, the spleen index and thymus index of the rats in Zheng qing Feng tong ning group, cinnamaldehyde group and *Cassia* twig extract group decreased significantly, which was closer to the normal group.

Effects of cinnamaldehyde on serum TNF-α, IL-1, IL-6, IL-10 and PGE_2 in CFA-induced rats: Serum TNF-α, IL-1, IL-6, IL-10 and PGE_2 levels were measured by ELISA test kits. As shown in Fig. 5a-e, TNF-α, IL-1, IL-6 and PGE_2 levels were significantly increased and IL-10 level was significantly decreased after CFA immunization compared with the normal group. However, the positive drug group (Zheng qing Feng tong ning) significantly decreased TNF-α, IL-1, IL-6 and PGE_2 levels and increased IL-10 levels. As expected, the model drug group (Cinnamaldehyde and *Cassia* twig extract) also produced the same pharmacological effects as the positive drug group.

Effects of cinnamaldehyde on histopathological changes of the knee joint in CFA-induced rats: Histochemical staining of H and E was used to detect the effect of cinnamaldehyde on rat knee joints. As shown in Fig. 6a, the histopathological changes of the knee joint in the normal group were not

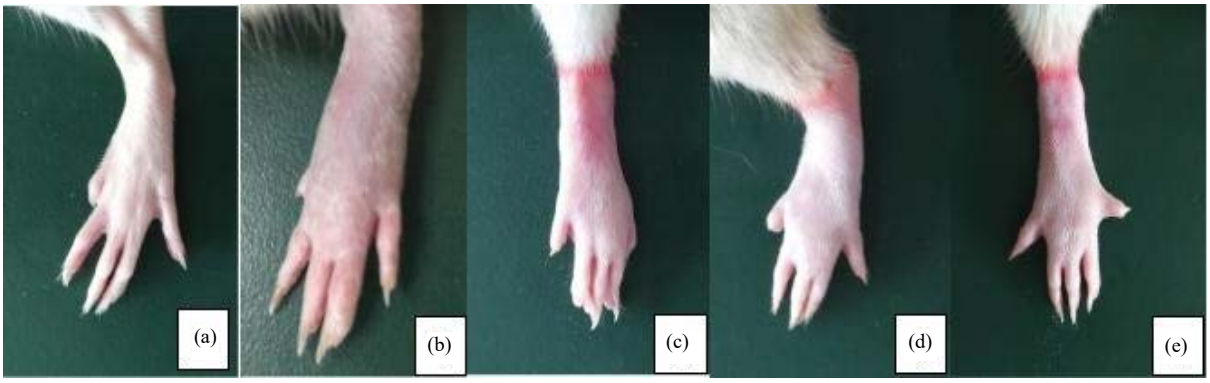

Fig. 1(a-e): Effect of cinnamaldehyde on paw swelling in CFA-induced rats, (a) Normal group, (b) CFA+PS group, (c) CFA+ZF group, (d) CFA+CE group and (e) CFA+CA group

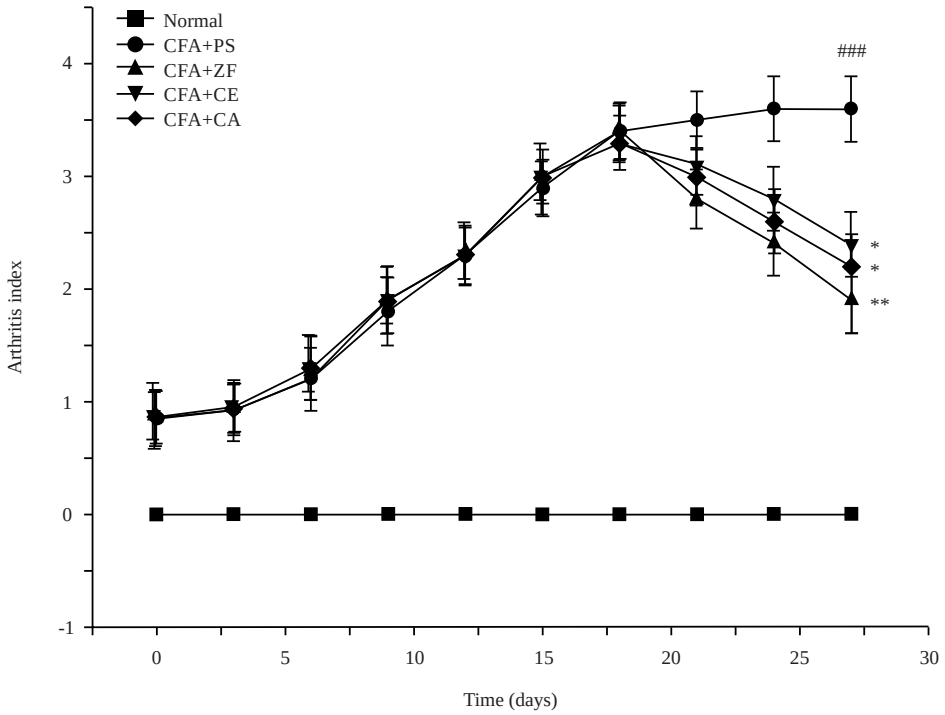

Fig. 2: Effect of cinnamaldehyde on arthritis index in CFA-induced rats

Rats were administered with physiological saline (CFA+PS), Zheng qing Feng tong ning tablet suspension (CFA+ZF), *Cassia* twig extract (CFA+CE) and cinnamaldehyde monomer suspension (CFA+CA), the arthritis index was evaluated at 3-day intervals, values are expressed as Mean±SD, compared to the CFA+PS group: *p<0.05, **p<0.01 and compared to the normal group: ###p<0.001

observed. In the saline group, the knee joints of rats showed severe histopathological changes in Fig. 6b. The main characteristics of the knee joint in rats were obvious joint space narrowing, synovial hyperplasia, massive inflammatory cells infiltrated into synovial tissue, partial bone and cartilage destruction. However, compared with the saline group, In Fig. 6c, the positive drug group (Zheng qing Feng tong ning) and model drug group (cinnamaldehyde and *Cassia* twig extract) greatly attenuated the inflammation of the knee joint induced by CFA and reduced the degree of partial bone and cartilage destruction in Fig. 6d-e.

As shown in Fig. 7, compared with the normal saline group, the positive drug group (Zheng qing feng tong ning) and the model drug group (cinnamaldehyde and *Cassia* twig extract) greatly reduced the pathological changes of rat joint histopathology.

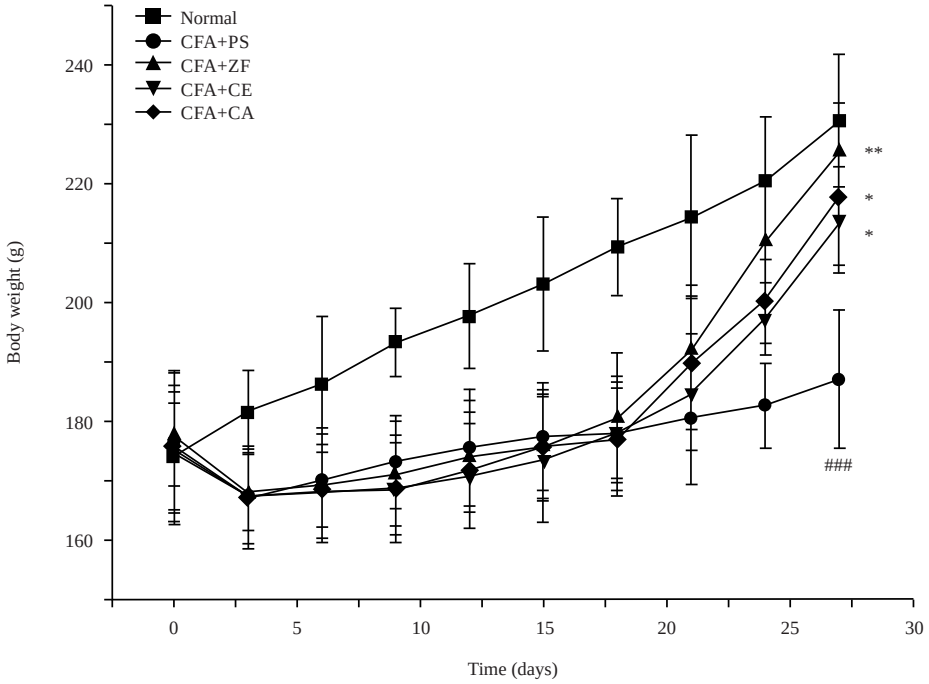

Fig. 3. Effect of cinnamaldehyde on body weight in CFA-induced rats

Rats were administered with physiological saline (CFA+PS), Zheng qing Feng tong ning tablet suspension (CFA+ZF), *Cassia* twig extract (CFA+CE) and cinnamaldehyde monomer suspension (CFA+CA), the body weight of rats was measured at 3-day intervals, values are expressed as Mean±SD, compared to the CFA+PS group: *p<0.05, **p<0.01 and compared to the normal group: ###p<0.001

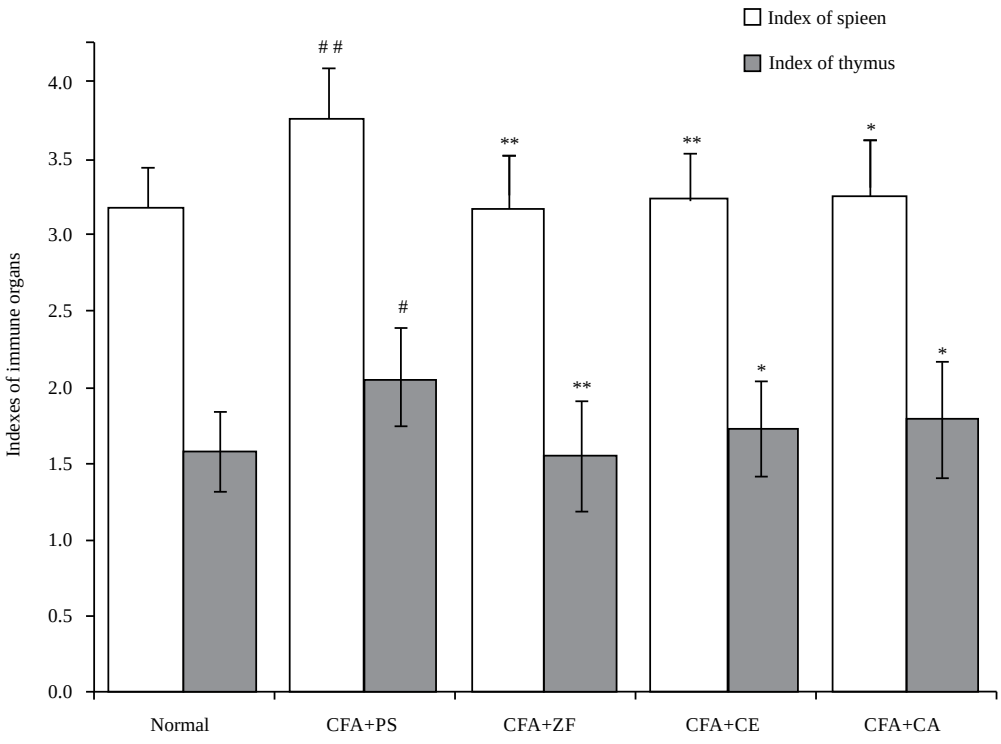

Fig. 4: Effects of cinnamaldehyde on spleen index and thymus index in CFA-induced rats

Rats were administered with physiological saline (CFA+PS), Zheng qing Feng tong ning tablet suspension (CFA+ZF), *Cassia* twig extract (CFA+CE) and cinnamaldehyde monomer suspension (CFA+CA), the thymus and spleen were removed and weighed on day 28 after CFA immunization and the spleen index and thymus index were calculated, values are expressed as Mean±SD, compared to the CFA+PS group: *p<0.05, **p<0.01 and compared to the normal group: ##p<0.01

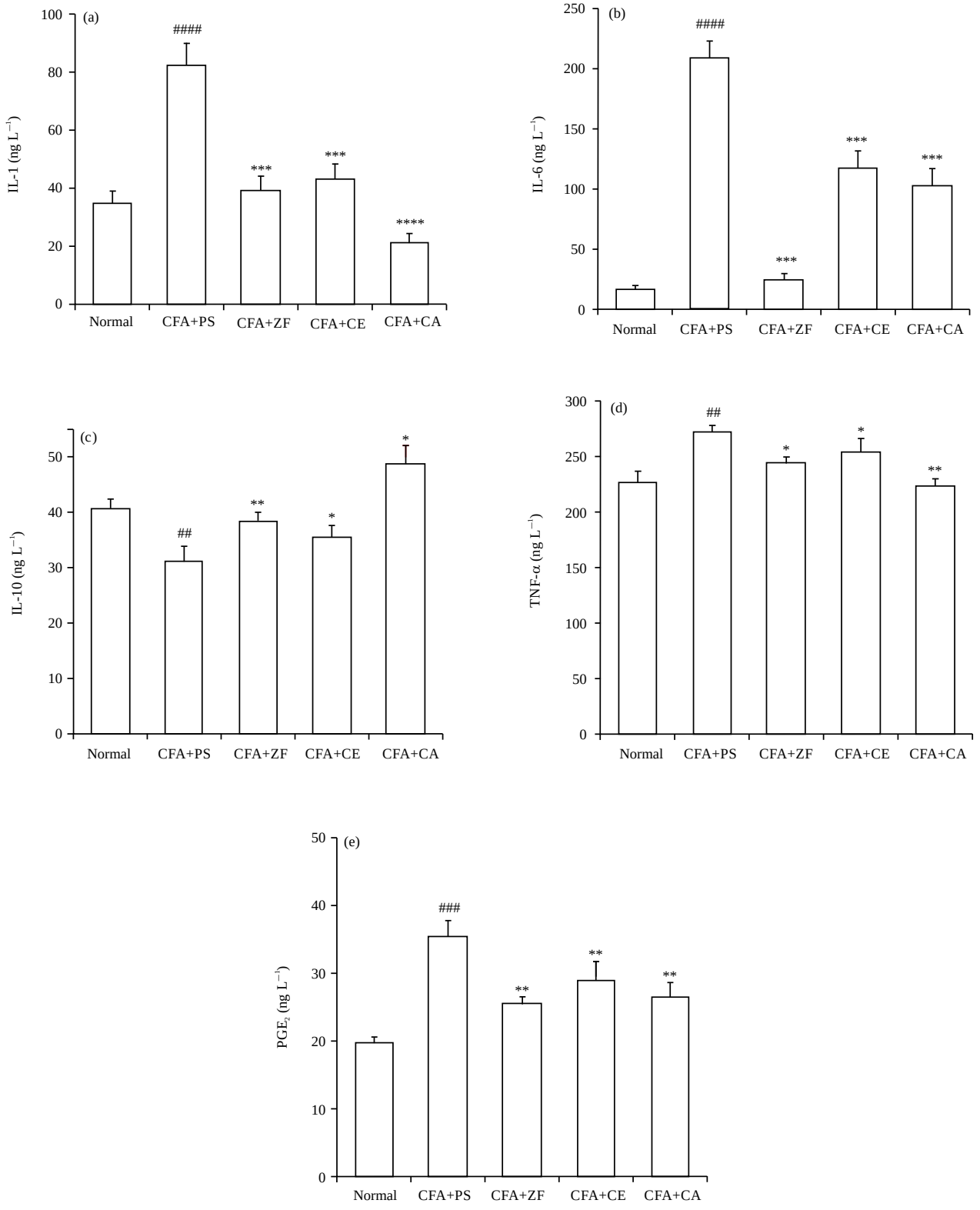

Fig. 5(a-e): Effects of cinnamaldehyde on serum TNF-a, IL-1, IL-6, IL-10 and PGE_2 levels in CFA-induced rats

Rats were administered with physiological saline(CFA+PS), Zheng qing Feng tong ning tablet suspension (CFA+ZF), *Cassia* twig extract (CFA+CE) and cinnamaldehyde monomer suspension (CFA+CA), blood was collected on day 28 after CFA immunization to analyze TNF-a, IL-1, IL-6, IL-10 and PGE_2 levels by ELISA test kits, values are expressed as Mean±SD, compared to the CFA+PS group: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 and compared to the normal group: $^{\#}$p<0.05, $^{\#\#}$p<0.01, $^{\#\#\#}$p<0.001, $^{\#\#\#\#}$p<0.0001

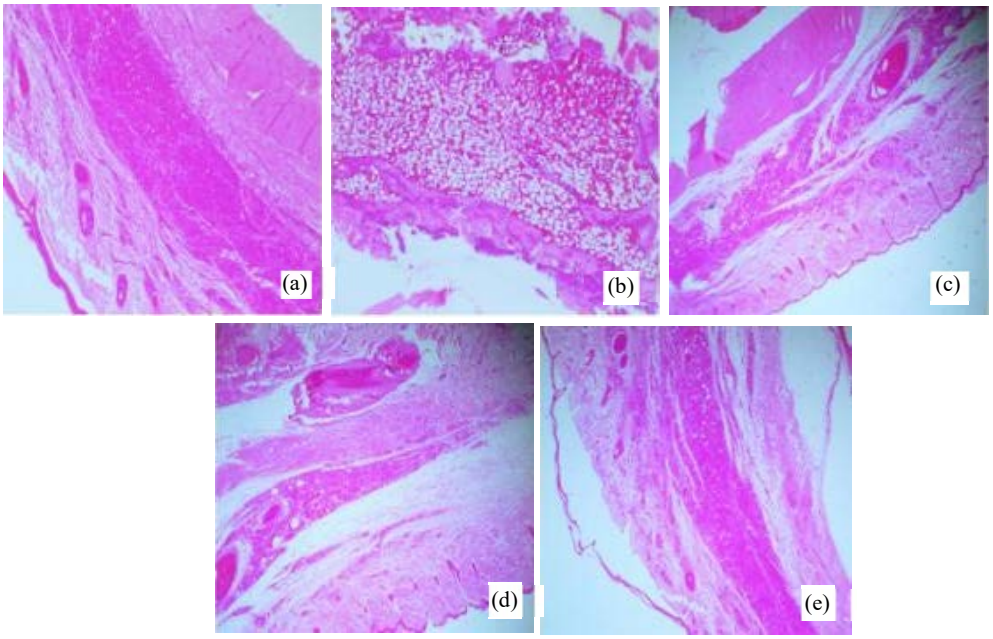

Fig. 6(a-e): Effect of Cinnamaldehyde on histopathological changes of joints in CFA-induced rats, (a) normal group, (b) CFA+PS group, (c) CFA+ZF group, (d) CFA+CE group and (e) CFA+CA group

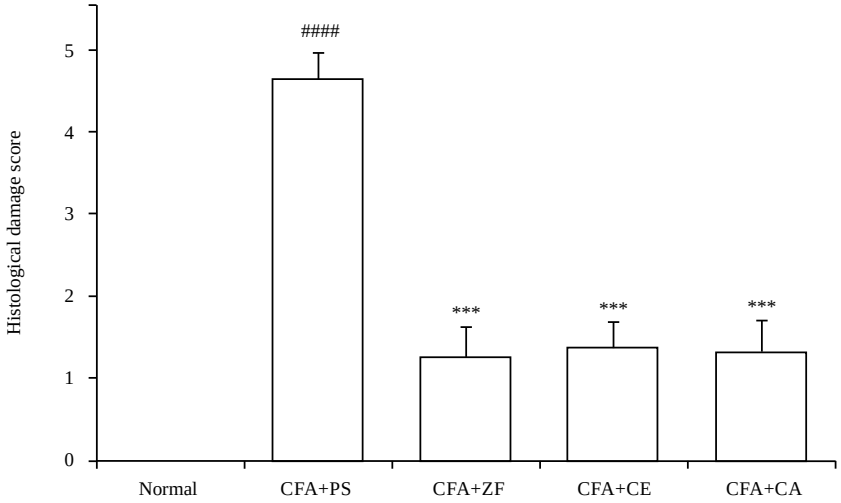

Fig. 7: Histological analysis of Cinnamaldehyde on the knee joint induced by CFA

Rats were administered with physiological saline (CFA+PS), Zhengqing Fengtongning Tablet Suspension(CFA+ZF), Cassia twig extract(CFA+CE) and Cinnamaldehyde monomer Suspension(CFA+CA). Values are expressed as Mean±SD. Compared to the CFA+PS group: ***P<0.001; Compared to the normal group: ###p<0.001

DISCUSSION

The results showed that cinnamaldehyde and *Cassia* twig extract significantly inhibited the destruction of bone and cartilage, reduced synovial hyperplasia and alleviated inflammatory cell infiltration in the joint and Peri-synovial inflammation.

RA is an autoimmune disease, there is no exact pathogenesis, there is still no cure for RA drugs worldwide. Most non-steroidal anti-inflammatory drugs and biological agents are mainly to alleviate the symptoms of RA and have more serious side effects and adverse reactions[20]. For thousands of years, Chinese herbal medicine has been widely used in the treatment of RA because of its mild side effects

and adverse reactions. In recent years, Chinese herbal medicine as a Complementary and Alternative Medicine (CAM) component of RA treatment has been widely used in clinical or preclinical research[21,22]. Therefore, Chinese herbal medicine has become a new therapeutic strategy against RA. The treatment of RA with Chinese herbal medicine has attracted more and more scholars' strong interest all over the world. At the same time, the clinical application of Chinese herbal medicine in the treatment of RA needs to be further improved[23,24].

Rat adjuvant arthritis is an experimental model commonly used in preclinical studies to evaluate therapeutic drugs. It has the advantage of being similar to human RA and having a short operating time and simple measurement[25]. Therefore, in this study, an adjuvant-induced arthritis model was established by intradermal injection of CFA into the metatarsal footpad of rats. We first explored the effect of cinnamaldehyde and *Cassia* twig extract on CFA-induced arthritis in rats. Experimental data show that cinnamaldehyde and *Cassia* twig extract has a potential protective effect on adjuvant arthritis in rats.

Measurement of paw swelling is an important indicator of the anti-arthritis activity of therapeutic drugs and the arthritis index is used to assess the severity of arthritis[26]. The method of measuring paw swelling and arthritis index is sensitive and rapid and can directly reflect the severity of arthritis in rats and the therapeutic effect of drugs on arthritis[27]. In this study, cinnamaldehyde and *Cassia* twig extract significantly reduced the paw swelling and arthritis index in arthritis rats compared with the saline group. The histopathological examination further confirmed the protective effect of cinnamaldehyde and *Cassia* twig extract on CFA induced arthritis.

Studies have shown that the degree of arthritis inflammation is closely related to weight changes and animal weight changes are used as indicators of the effectiveness of drug treatment[28]. In this study, the results showed that the degree of joint inflammation was positively correlated with weight loss in rats. Compared with the normal group, the rats injected with CFA showed significant weight loss. However, compared with the saline group, cinnamaldehyde and *Cassia* twig extract treatment group significantly inhibited CFA induced weight loss. The CFA induced RA model has a strong immune function, resulting in lymphatic hyperplasia and splenomegaly in rats[29]. The results showed that the thymus index and spleen index of RA rats in the cinnamaldehyde and *Cassia* twig extract treatment group were significantly lower than those in the saline group. The results showed that cinnamaldehyde and *Cassia* twig extract could counteract the hyperfunction of immune organs and restore normal immune function.

RA is a clinically common chronic systemic autoimmune disease. The pathogenesis is an immune disorder leading to synovitis and invasive neovascularization, which often leads to the destruction of cartilage and bone, leading to severe joint deformities and even disability[30,31]. However, RA still has not been completely cured, because its exact cause and its pathogenesis have not yet been fully elucidated. Recent studies have shown that a variety of pro-inflammatory cytokines are also involved in the bone loss and joint damage process of RA[32]. Studies have shown that IL-1, IL-6 and TNF-α can promote the formation of osteoclasts, while IL-10 can inhibit its formation. TNF-α also contributes to inflammation by stimulating the expression of PGE_2 by type 2 cyclooxygenase (COX-2)[33,34]. Therefore, inhibition of these pro-inflammatory cytokines and media has a great effect on the treatment of RA. The results of this study showed that compared with the saline group, the cinnamaldehyde and *Cassia* twig extract group significantly promoted the production of IL-10 and inhibited the production of IL-1, IL-6, TNF-α and PGE_2 induced by CFA. This indicates that the therapeutic effect of cinnamaldehyde and *Cassia* twig extract on arthritis in rats may be related to the inhibition of the production of pro-inflammatory cytokines and mediators.

CONCLUSION

This study demonstrates that cinnamaldehyde extracted from Chinese herbal medicine *Cassia* twig has anti-arthritic effects on CFA-induced rat arthritis. The anti-arthritic effect of cinnamaldehyde may inhibit the swelling and arthritis index, reduce weight loss, synovial hyperplasia and inflammatory cell infiltration, decrease spleen index and thymus index, increase serum IL-10 level and inhibit serum TNF-α, IL-1, IL-6 and PGE_2 levels are related. This study suggests that cinnamaldehyde may prove to be an effective treatment for RA.

SIGNIFICANCE STATEMENT

This study found that cinnamaldehyde has a potential protective effect on CFA-induced arthritis in rats. It shows that cinnamaldehyde may prove to be an effective method for the treatment of RA. This research can help clinical medical staff explore the development of more effective, safer and more economical anti-RA drugs.

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