

COMPARISON OF ANTI-INFLAMMATORY AND ANTI-NOCICEPTIVE ACTIVITIES OF *CURCUMA WENYUJIN* Y.H. CHEN ET C. LING AND *SCUTELLARIA BAICALENSIS* GEORGIJue Zhou¹, Fan Qu^{2*}, Hang-Jun Zhang³, Xiao-Hong Zhuge⁴ and Liang-Zhong Cheng⁵

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*Email: qufan43@yahoo.com.cn**Abstract**

The study aimed to compare the anti-inflammatory and anti-nociceptive activities of *Curcuma wenyujin* Y.H. Chen et C. Ling (*Curcuma wenyujin*) and *Scutellaria baicalensis* Georgi (*Scutellaria baicalensis*). This study used three parts to compare the two herbs. Firstly, animals were randomly divided into a *Scutellaria baicalensis* group, a *Curcuma wenyujin* group, an indomethacin group, and a model-control group to perform an ear edema test, a carrageenin-induced paw edema test, a cotton pellet-induced granuloma formation test, and an acetic acid-induced writhing test. Secondly, model rats with pelvic inflammation were established, and the serum levels of TNF- α and IL-6 in each group was detected with the Enzyme-Linked Immunosorbent Assay (ELISA). Thirdly, pharmacokinetics analysis of *Scutellaria baicalensis* and *Curcuma wenyujin* was conducted on the model rats. The ear edema test, carrageenin-induced paw edema test, cotton pellet-induced granuloma formation test, and acetic acid-induced writhing test all showed that *Curcuma wenyujin* had stronger anti-inflammatory and anti-nociceptive effects than *Scutellaria baicalensis*. There is significant difference between the effects of *Curcuma wenyujin* and *Scutellaria baicalensis* on the levels of TNF- α and IL-6 for the model rats. *Curcuma wenyujin* decreased the levels of TNF- α and IL-6 more than *Scutellaria baicalensis*. The pharmacokinetics analysis showed that curcumol's T_{max} , C_{max} , and the area under the curve (AUC) were all higher than baicalin's. This study indicated that for pelvic inflammation, *Curcuma wenyujin* had better anti-inflammatory and anti-nociceptive effects than *Scutellaria baicalensis*.

Key words: *Curcuma wenyujin*; *Scutellaria baicalensis*; Anti-inflammatory; Anti-nociceptive; Pharmacokinetics analysis.

Introduction

Curcuma wenyujin Y.H. Chen et C. Ling (*Curcuma wenyujin*) have been used as common traditional Chinese medicinal herbs to remove blood stasis and to alleviate pain for more than a thousand years in some Asian countries. Some Chinese families have prepared it as a health food supplement (Deng et al., 2006). Previous researches have suggested that herbal remedies had potential advantages as analgesic and anti-inflammatory agents (Linde et al., 2003).

The essential oils of *Curcuma wenyujin* have been considered to possess anti-inflammatory, anti-nociceptive, antitumor and antiviral activities (Nie et al., 2003; Xia et al., 2004). The major components of the essential oils in *Curcuma wenyujin* are curcumol, curdione, and germacrone, which are commonly used as the quality control markers (Zheng et al., 1997; Wang and Wang., 2001; Manzan et al., 2003). In the study, *Curcuma wenyujin* from Zhejiang China, is considered the best source among different members of *Curcuma wenyujin* (Zheng., 2000).

Scutellaria baicalensis has been used for a long time in some Asian countries as a widely-recognized herb with strong anti-inflammatory and anti-nociceptive effects (Kubo et al., 1984; Huang et al., 1986). Baicalin, a flavonoid compound purified from *Scutellaria baicalensis*, was often used as an anti-inflammatory agent in the treatment of a variety of inflammatory diseases such as bronchitis, nephritis, hepatitis, and asthma (Chen et al., 2001). Baicalin has been found to treat inflammation through its antioxidant properties and its ability to regulate immune responses (Hwang et al., 2005).

In previous clinical practices, the authors found that when treating female patients with pelvic inflammation, *Curcuma wenyujin* often led to stronger anti-inflammatory and anti-nociceptive effects than *Scutellaria baicalensis*. To test the hypothesis, the present research established pelvic inflammation model with rats, and the serum levels of TNF- α and IL-6 were detected with the Enzyme-Linked Immunosorbent Assay (ELISA). The results of the research can guide doctors who usually administer *Scutellaria baicalensis* and *Curcuma wenyujin* to treat patients. Therefore, this study compared the anti-inflammatory and anti-nociceptive effects of *Scutellaria baicalensis* and *Curcuma wenyujin*. Pharmacokinetic analysis of the two herbs was also conducted on the model rats with pelvic inflammation.

Materials and Methods

Animals

Female Sprague-Dawley (SD) rats were used in the tests which include: carrageenan-induced rat paw edema test, effect of *Scutellaria baicalensis* and *Curcuma wenyujin* in female model rats with pelvic inflammation, and pharmacokinetics analysis. Female Imprinting-Control-Region (ICR) mice weighing 40–60 g were used in the tests involving: the ear edema test, cotton pellet-induced granuloma formation test, and the acetic acid-induced writhing test. All the animals were provided by the Laboratory Animal Center of Zhejiang University (Hangzhou, China). All the animals were kept in a room under environmentally controlled temperature of $24\pm 1^{\circ}\text{C}$ and a 12h light–12h dark cycle. They were acclimatized at least once a week before starting the experiments. The animal experimentation was carried out in an ethically proper way by following guidelines as set by the World Health Organization.

Plant materials and extract preparation

Scutellaria baicalensis and *Curcuma wenyujin* were purchased from Huqing Yutang Pharmaceutical Co., Ltd (Hangzhou, China) and identified by the College of Pharmaceutical Sciences, Zhejiang University (Hangzhou, China). Standard curcumin and baicalin were purchased from the National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China). Twenty grams of powdered *Curcuma wenyujin* and *Scutellaria baicalensis* were extracted by refluxing them with 200 ml of distilled water for 60 min, followed by filtration. The same procedure was repeated once, and the extracts combined and condensed to a concentration of 1 g/ml.

Anti-inflammatory and anti-nociceptive activity

Ear edema test in mice

The methods of Brattsand et al. (1982) and Young et al. (1983) were used in the test. Twenty four female mice (weighing 40–60 g) were randomly divided into four groups with six in each group: The *Curcuma wenyujin* group received extracts of *Curcuma wenyujin* (0.05g/kg; po). The *Scutellaria baicalensis* group received extracts of *Scutellaria baicalensis* (0.05g/kg; po). The indomethacin group received indomethacin (1.44mg/kg; po). The model control group received saline (8ml/kg, po)

Ear edema was induced by topical application of arachidonic acid (AA) dissolved in acetone to the inner and outer surfaces of both ears with an automatic microliter pipette. Test drugs were applied topically in volumes of 20 μl just before

the irritant was applied. The model control group received vehicle treatment only. Before and at 0.25h, 0.5h, 1hr and 2hr after the edema induction, the thickness of each ear was measured by vernier calipers. Percent inhibition was calculated thus: inhibition (%) = $(V_c - V_t) / V_c \times 100\%$, where V_c and V_t respectively represented the average ear edema volume of the model control rat and the rat under drug treatment.

Carrageenan-induced rat paw edema test in rats

The method of Winter et al. (1962) was used in the test. Twenty four female rats (weighing 100-120g) were randomly divided into four groups with six in each group: The *Curcuma wenyujin* group received extracts of *Curcuma wenyujin* (0.36g/kg; po). The *Scutellaria baicalensis* group received extracts of *Scutellaria baicalensis* (0.36g/kg; po). The indomethacin group received indomethacin (9.97 mg/kg; po). The model control group received saline (8ml/kg. po)

Test drugs were orally administered 1hr prior to carrageenin injection. 0.1ml of 1% freshly prepared suspension of carrageenin was administered into the sub-planter region of the right hind paws to lead to the formation of edema in situ due to localized inflammation. Percent inhibition was calculated thus: inhibition (%) = $(V_c - V_t) / V_c \times 100\%$, where V_c and V_t respectively represented the average paw volume of the model control rat and the rat under drug treatment.

Cotton pellet-induced granuloma formation tests in mice

The method of Swingle and Shideman (1972) was used in the test. Twenty four female mice (weighing 40-60 g) were randomly divided into four groups with six in each group: The *Curcuma wenyujin* group received extracts of *Curcuma wenyujin* (0.05g/kg; po). The *Scutellaria baicalensis* group received extracts of *Scutellaria baicalensis* (0.05g/kg; po). The indomethacin group received indomethacin (1.44mg/kg; po). The model control group received saline (8ml/kg. po)

The back skin was shaved and disinfected with 75% ethanol. An incision was made in the lumbar region. Subcutaneous tunnels were formed with a blunted forceps. Then, a sterilized cotton pellet weighing 50 ± 1.0 mg was introduced in the groin region of the mouse under light ether anesthesia. Test drugs were administered once daily throughout 7 day experimental period. Twenty four hours after the treatment ended, the animals were sacrificed and the cotton pellets were excised, which were then dried until the weight remained constant. The increase of the pellet weight was considered as granuloma tissue deposit.

Acetic acid-induced writhing test in mice

The methods of Collier et al. (1968) and Nakamura et al. (1986) were used in the test. Twenty four female mice (weighing 40-60 g) were randomly divided into four groups with six in each group: The *Curcuma wenyujin* group received extracts of *Curcuma wenyujin* (0.05g/kg; po). The *Scutellaria baicalensis* group received extracts of *Scutellaria baicalensis* (0.05g/kg; po). The indomethacin group received indomethacin (1.44mg/kg; po). The model control group received saline (8ml/kg. po).

A writhing response was produced by injection of an aqueous solution of 0.6% acetic acid in a volume of 0.1 ml/10g body weight into the peritoneal cavity. The animals were then placed in a transparent plastic box. Test drugs and vehicle control were administered 30 min before the acetic acid injection. The number of writhes, a response consisting of a contraction of an abdominal wall and pelvic rotation followed by hind limb extension, was counted during continuous observation for 15 min, beginning 5 min after the acetic acid injection.

The effects of *Scutellaria baicalensis* and *Curcuma wenyujin* in treating female model rats with pelvic inflammation

Fifty female SD rats (weighing 180-200 g) were used in the test. Ten rats were randomly taken as the normal

control and the other forty rats were established as the model rats with pelvic inflammation. The pelvic inflammation of the model rats was established by injecting 0.08ml of 20% phenol mucilage into the right uterus of the rats to induce a pathological condition similar to pelvic inflammation (Xiang et al., 2007). The rats were anesthetized with sodium pentobarbital (40 mg/kg, i.p.). 20% phenol mucilage was obtained by combining 8ml of phenol with 32ml of 1% carboxymethylcellulose sodium mucilage. 15 days after the model rats were established, they were randomly divided into five groups with 10 rats in each group.

The *Curcuma wenyujin* group received extracts of *Curcuma wenyujin* (0.36g/kg; po) for 28 consecutive days; The *S. baicalensis* group received extracts of *Scutellaria baicalensis* (0.36g/kg; po) for 28 consecutive days; The indomethacin group received indomethacin (9.97 mg/kg; po) for 14 consecutive days; The model control group received saline (8ml/kg. po) for 28 consecutive days; The normal control group received saline (8ml/kg. po) for 28 consecutive days.

When the treatment ended, each of the rats was anesthetized with sodium pentobarbital (40 mg/kg, i.p.). The serum sample taken from caudal vein was used to detect the levels of tumor necrosis factor-alpha (TNF- α) and IL-6 with the Enzyme-Linked ImmunoSorbent Assay (ELISA). The ELISA assay kits were provided by Boster Biotechnology Ltd., Wuhan, China.

Pharmacokinetic analysis of *Scutellaria baicalensis* and *Curcuma wenyujin* in treating pelvic inflammation

Pharmacokinetic analysis

Ten female model rats with pelvic inflammation were used in the pharmacokinetic analysis: five rats for each group. The blood samples for the analysis of curcumol content were taken from the oculi chorioideae vein at 0.083, 0.167, 0.5, 1, 1.5, 2, 3, 4.5, 7, 9, 12 and 24 h following the oral administration. The blood samples for the analysis of baicalin content were taken from the oculi chorioideae vein at 0.25, 0.5, 1, 2, 3, 4, 6, 8, 10, 12 and 24hr following oral administration of the extracts. The blood samples were immediately transferred into heparinized Eppendorf tubes and centrifuged at 3000 rpm for 10 min at 4°C, and then the plasma was obtained. All the plasma samples were stored at -20°C until analysis. The pharmacokinetic parameters, elimination rate constant (K_e), absorption half-life ($T_{1/2\alpha}$), and elimination half-life ($T_{1/2\beta}$) were calculated using one or two compartmental methods with 3P87 software (Chinese Society of Mathematical Pharmacology). The area under the curve (AUC) was calculated using the trapezoidal method. The half-life ($T_{1/2\alpha}$ and $T_{1/2\beta}$) values were calculated using the equation: $T_{1/2}=0.693/K$. The data and the pharmacokinetic parameters were given as mean \pm SD.

High Performance Liquid Chromatography (HPLC) conditions

The HPLC (Waters model 600E system, Waters, Milford, MA, USA) was equipped with a photodiode array detector (Waters 2996) and an inline-degasser AF (Waters, Milford, MA, USA). A diamonsil C18 column (250mm \times 4.6mm, 5 μ m) from Dikma Technologies (Beijing, China) was equipped with a pre-column (4mm \times 5mm) C18. Acetonitrile (as solvent A) and water/Acetic acid (0.8% v/v, pH=6.0; used as solvent B) were used as mobile phase with a linear gradient elution at a flow rate of 1.0 mL/min.

The linear gradient elution for *Curcuma wenyujin* was as follows: 0–10 min, linear gradient 30–45% A; 10–30 min, isocratic 45–50% A; 31–60 min, linear gradient 80–80% A. The linear gradient elution for *Scutellaria baicalensis* was as follows: 0–60 min, 5–50% A.

The column temperature was 40°C, and the injection volume of each sample was 20 μ L. The solvents were filtered through a 0.45 μ m Millipore filter and degassed prior to use.

Preparation of stock and working standard solutions

The standard stock solution of curcumol was prepared by dissolving 0.93g of curcumol in 10 mL of methanol to

obtain a concentration of 9.30 mg/mL. The stock solution was kept at 4°C. The standard working solutions of curcumin were respectively prepared at various concentrations of 0.09, 0.93, 9.30, 93.00, and 930.00 µg/mL by diluting the stock solution with methanol. The standard stock solution of baicalin was prepared by dissolving 0.30 g of baicalin in 10 mL of methanol to obtain a concentration of 30.0mg/mL. The stock solution was kept at 4°C. The standard working solutions of baicalin were respectively prepared at various concentrations of 0.03, 0.30, 3.00, 30.00 and 300.00µg/mL by diluting the stock solution with methanol.

Preparation of the samples

Perchloric acid solution (0.2 mL) was added into 1L of plasma. The mixture was then vortex-mixed for 2 min. After centrifugation at 3,000 rpm for 10 min, the supernatant was filtered through a 0.45 µm membrane filter unit. 20 µL of each sample solution was analyzed by HPLC.

Preparation of calibration standards

The samples used to construct the standard calibration curve of curcumin were prepared by spiking 100 µl of the blank rat plasma with 100 µL of the appropriate working solutions to yield curcumin concentrations of 0.05, 0.46, 4.65, 46.5 and 465.00µg/mL. The samples used to construct the standard calibration curve of baicalin were prepared by spiking 100µl of the blank rat plasma with 100µL of the appropriate working solutions to yield baicalin concentrations of 0.02, 0.15, 1.50, 15.00 and 150.00 µg/mL. The calibration curve was plotted with the concentrations as X-axis and the peak areas as Y-axis using un-weighted linear regression.

Statistical analysis

Results were analyzed by an independent statistician using computer software, namely, Statistical Package for Social Sciences (SPSS 13.0 for Windows). Analysis of variance (ANOVA) was employed in comparing the anti-inflammatory and anti-nociceptive activities including: edema value of ear edema test in mice, carrageenan-induced rat paw edema test in rats, granuloma weight of cotton pellet-induced granuloma formation tests in mice, number of writhes induced by acetic acid in mice; and in comparing the changes of TNF-α and IL-6 of various groups.

A significance level of 5% ($P<0.05$) and two-tailed tests were used for all hypothesis tests. The pharmacokinetics parameters were calculated using one or two compartmental methods with 3P87 software (Chinese Society of Mathematical Pharmacology).

Results

Anti-inflammatory and anti-nociceptive activity

Ear edema in mice

The results of the ear edema test in mice are presented in Table 1. All the test drugs showed significant inhibition of ear edema. Indomethacin had a stronger anti-inflammatory effect from 0.25 hr to 1hr than the two herbs. However, at 2 hr there was no significant difference between *Curcuma wenyujin* and indomethacin. *Curcuma wenyujin* had a stronger inhibitory effect than *Scutellaria baicalensis* at 2 hr. They had a similar inhibitory effect from 0.25 h to 1 hr.

Table 1: Comparison of ear edema test results

Group	Edema thickness (um)				Edema inhibition(%)			
	0.25h	0.5h	1h	2h	0.25h	0.5h	1h	2h
Model control	260±14	315±14	377±17	396±12	-	-	-	-
<i>Scutellaria baicalensis</i>	78±13* [#]	96±13* [#]	120±12* [#]	131±19* [#]	70	70	68	67
<i>Curcuma wenyujin</i>	80±20* [#]	105±15* [#]	119±16* [#]	113±22* [@]	69	67	68	71
Indomethacin	46±10*	56±12*	79±15*	111±10*	82	83	80	72

Note: *P<0.05, compared with model control group; [#] P<0.05, compared with indomethacin group; [@] P<0.05, compared with *Scutellaria baicalensis* group.

Carrageenan-induced rat paw edema test in rats

All the test drugs showed significant reduction of the carrageenan-induced paw edema volume (Table 2).. *Curcuma wenyujin* and *Scutellaria baicalensis* had lower inhibitory effects than indomethacin from 1 hr to 2 hr. While from 3 hr to 5 hr, there was no significant difference between *Curcuma wenyujin* and indomethacin's inhibitory effects. *Curcuma wenyujin* had a higher inhibitory effect than *Scutellaria baicalensis* from 3 hr to 5 hr.

Table 2: Comparison of carrageenin-induced paw edema test results

Group	Edema volume (ml)				Edema inhibition (%)			
	1h	2h	3h	5h	1h	2h	3h	5h
Model control	0.91±0.10	1.11±0.07	1.45±0.06	1.66±0.08	-	-	-	-
<i>Scutellaria baicalensis</i>	0.78±0.04* [#]	0.96±0.06* [#]	1.20±0.05* [#]	1.33±0.05* [#]	14	14	17	20
<i>Curcuma wenyujin</i>	0.80±0.06* [#]	0.99±0.08* [#]	1.10±0.08* [@]	1.16±0.04* [@]	12	11	24	30
Indomethacin	0.66±0.11*	0.80±0.08*	1.10±0.07*	1.25±0.10*	25	28	24	21

Note: *P<0.05, compared with model control group; [#] P<0.05, compared with indomethacin group; [@] P<0.05, compared with *Scutellaria baicalensis* group.

Cotton pellet-induced granuloma formation tests in rats

The results of chronic-inflammatory test with cotton pellets are presented in Table 3. All the test drugs demonstrated significant inhibitory activities on the weight of granuloma. The extracts of *Curcuma wenyujin* exerted better inhibition than *Scutellaria baicalensis* and indomethacin, on the granuloma formation.

Acetic acid-induced writhing test in mice

As shown in Table 4, all the test drugs had significant inhibitory activities on the writhing response. *Curcuma wenyujin* had significantly higher inhibition than the others.

Comparison of the serum levels of TNF- α and IL-6

As shown in Table 5, the serum levels of TNF- α and IL-6 in all the test drug groups were significantly lower than

those of the model control group. The serum levels of TNF- α in the *Scutellaria baicalensis* group and *Curcuma wenyujin* group were significantly lower than in the indomethacin group. The serum levels of TNF- α and IL-6 of the *Curcuma wenyujin* group were both significantly lower than those of the *Scutellaria baicalensis* group.

Table 3: Comparison of cotton pellet-induced granuloma formation test results

Group	Dry granuloma weight (mg/mg cotton)	Granuloma inhibition (%)
Model control	5.52 \pm 0.12	-
<i>Scutellaria baicalensis</i>	3.07 \pm 0.11* [#]	43
<i>Curcuma wenyujin</i>	2.96 \pm 0.21* [#] [@]	46
Indomethacin	3.78 \pm 0.09*	35

Note:*P<0.05, compared with model control group; [#] P<0.05, compared with indomethacin group; [@] P<0.05, compared with *Scutellaria baicalensis* group.

Table 4: Comparison of the results of acetic acid-induced writhing tests

Group	Number of writhes	Inhibition of writhing response (%)
Model control	56.0 \pm 6.3	-
<i>Scutellaria baicalensis</i>	18.8 \pm 3.9*	62
<i>Curcuma wenyujin</i>	10.0 \pm 3.0* [#] [@]	82
Indomethacin	19.5 \pm 5.4*	65

Note:*P<0.05, compared with model control group; [#] P<0.05, compared with indomethacin group; [@] P<0.05, compared with *Scutellaria baicalensis* group.

Pharmacokinetic analysis of *Curcuma wenyujin* and *Scutellaria baicalensis* in treating pelvic inflammation

The plasma concentration–time course of curcumol ($n=5$) and baicalin ($n=5$) is presented in Figure 1. The parameters were calculated using 3P87 software for pharmacokinetic analysis. The pharmacokinetic models (one-vs.two-compartment) were compared according to Akaike's information criterion (AIC) and the Schwarz criterion (SC). Minimum AIC and SC values were regarded as the best representation of the plasma concentration time course data. The pharmacokinetic parameters are presented in Table 6.

The time courses of curcumol and baicalin both fitted the one compartment models. The T_{max} and C_{max} values of curcumol were 4.00 \pm 0.18h and 838 \pm 92.51 μ g/ml respectively. The T_{max} and C_{max} values of baicalin were 2.84 \pm 0.22 h and 0.09 \pm 0.03 μ g/ml respectively. The concentration of curcumol in the plasma reached the maximum at approximately 4 h, while the concentration of baicalin in the plasma reached the maximum at approximately 3h. The AUC of curcumol and baicalin were, respectively, 6778.73 μ g·h /ml and 89.69 μ g·h /ml.

Discussion

In the present research, the ear edema test, carrageenin-induced paw edema test, cotton pellet-induced granuloma formation test, and acetic acid-induced writhing tests all showed that *Curcuma wenyujin* had stronger anti-inflammatory and anti-nociceptive effects than *Scutellaria baicalensis*. *Curcuma wenyujin* decreased the levels of TNF- α and IL-6 more significantly than *Scutellaria baicalensis* in model rats. In the pharmacokinetic analysis, the time courses of curcumol and baicalin both fitted the one compartment models. The T_{max} and C_{max} values of curcumol were 4.00 \pm 0.18h and 838 \pm 92.51 μ g/ml respectively. The T_{max} and C_{max} values of baicalin were 2.84 \pm 0.22h and 0.09 \pm 0.03 μ g/ml respectively.

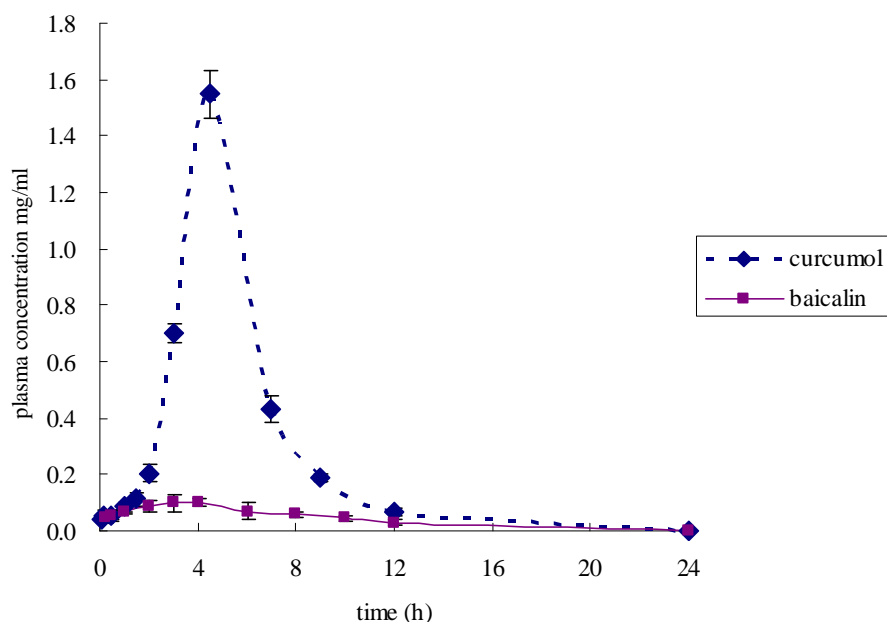
Table 5: Comparison of TNF- α and IL-6 serum levels

Group	TNF- α	IL-6
Normal control	0.073 \pm 0.004*	0.131 \pm 0.009*
<i>Scutellaria baicalensis</i>	0.104 \pm 0.011* [#]	1.079 \pm 0.013*
<i>Curcuma wenyujin</i>	0.089 \pm 0.015* ^{#@}	0.099 \pm 0.010* ^{#@}
Indomethacin	0.126 \pm 0.005*	1.102 \pm 0.010*
Model control	0.162 \pm 0.009	1.241 \pm 0.015

Note:*P<0.05, compared with model control group; [#] P<0.05, compared with indomethacin group[@] P<0.05, compared with *Scutellaria baicalensis* group.

Table 6: Main pharmacokinetic parameters of baicalin and curcumol after oral administration *Scutellaria baicalensis* and *Curcuma wenyujin* extracts (mean \pm S.D.)

Parameters	Unit	Values	
		<i>Scutellaria baicalensis</i>	<i>Curcuma wenyujin</i>
K_e	1/h	0.15 \pm 0.02	0.25 \pm 0.06
K_a	1/h	0.68 \pm 0.06	0.48 \pm 0.10
$t_{1/2(ka)}$	H	1.02 \pm 0.11	1.44 \pm 0.22
$t_{1/2(ke)}$	H	4.58 \pm 0.21	2.75 \pm 0.39
T_{max}	H	2.84 \pm 0.22	4.00 \pm 0.18
C_{max}	μ g/ml	0.09 \pm 0.03	838 \pm 92.51
AUC	μ g·h /ml	89.69 \pm 5.35	6778.73 \pm 103.33

**Figure 1:** The plasma concentration time profiles of curcumol and baicalin after oral administration of *Curcuma wenyujin* and *Scutellaria baicalensis* extracts.

The concentrations of curcumol in the plasma reached its maximum at approximately 4hr, while the concentration of baicalin in the plasma reached its maximum at approximately 3hr. The AUC of curcumol and baicalin was respectively 6778.73 $\mu\text{g}\cdot\text{h}/\text{ml}$ and 89.69 $\mu\text{g}\cdot\text{h}/\text{ml}$.

In the present research, model rats with pelvic inflammation were established by injecting 0.08ml of 20% phenol mucilage into the right uterus of the rats to induce a pathological condition similar to pelvic inflammation. Phenol mucilage was widely used in China to induce chemical salpingitis in sterilization operations in 1970 (Chen et al., 1979), and it has been applied to establish animal models with pelvic inflammation since 1980 (Chen et al., 1986). The method has been adopted in most animal experiments on pelvic inflammation in China (Gao, 1999; You, 2007). The aim of injecting 0.08ml of 20% phenol mucilage into the right uterus was to compare the effect of phenol mucilage in inducing pelvic inflammation to the untouched left uterus (You, 2007). This method of establishing model rats with pelvic inflammation not only simulated the pathological condition of pelvic inflammation from the viewpoints of pathology but also simulated the pathological condition of blood stasis from the viewpoint of traditional Chinese medicine on pelvic inflammation (Gao and Wu, 1997; You, 2007). Preliminary research demonstrated that 48 hrs after injecting 0.08 ml of 20% phenol mucilage into the right uterus, rats would show typical pelvic inflammatory conditions based on an endometrial biopsy and hemorheology detection. The method is thought to be simple to manipulate, to be effective at inducing pelvic inflammation, and to create an effect similar to human pathology (Gao and Wu, 1997 ; Gao, 1999; You, 2007).

As a complex defense mechanism, inflammation is characterized by leukocyte migration from the vasculature into the damaged tissues to destroy injurious agents. During the process of acute inflammation, the leukocyte is initially mostly neutrophilic, but after 24 hrs, monocytic cells began to predominate (Richter et al., 1999; Hurst et al., 2001; Fenton et al., 2002). The mechanisms of the transition from neutrophil to monocyte recruitment during inflammation have not been well known. It has been proposed that IL-6 with its soluble receptor plays an important role in this transition (Buckley et al., 2001). IL-6 plays a rather protective role in decreasing neutrophil and favoring monocyte recruitment, leading to the resolution of inflammation and the initiation of an immune response (Xing et al., 1998; Atreya et al., 2000). As an important inflammatory cytokine, IL-6 has been regarded as a useful adjunct to the diagnosis of pelvic inflammatory disease clinically (Richter et al., 1999). The presence of IL-6 in many inflammatory diseases suggests that IL-6 has an important role in either the inflammatory disease process or the host's response to the disease (Fenton et al., 2002). TNF- α , primarily produced by immune cells such as monocytes and macrophages, has been found to play a primary role during the inflammatory process (Toth et al., 1992; Pereda et al., 2006; Villa and Ghezzi, 2004). Over-production of TNF- α has been found to be pivotal in the induction of inflammatory genes and in the recruitment and activation of immune cells (Warren et al., 1988; Shen and Pervaiz, 2006). It has been regarded as one of the major mediators of systemic progression and tissue damage in inflammatory disease, and it can help to propagate the extension of a local or systemic inflammatory process (Utsunomiya et al., 1998; Frode et al., 2001). As IL-6 and TNF- α are both important cytokines during the process of pelvic inflammation (Toth et al., 1992; Richter et al., 1999;), they were used to compare the curative effects of the various treatments on the female model rats with pelvic inflammation in the present research.

The present research showed that *Curcuma wenyujin* had better anti-inflammatory and anti-nociceptive activities than *Scutellaria baicalensis*. The results were further confirmed by the experiments conducted on the model rats with pelvic inflammation. The pharmacokinetics analysis conducted on the model rats with pelvic inflammation showed that the AUC of curcumol were higher than those of baicalin, which may be a basis to explain why *Curcuma wenyujin* led to more satisfactory curative effects than *Scutellaria baicalensis* when treating pelvic inflammation. Further study with more samples should be conducted on the mechanism and to determine why and how *Curcuma wenyujin* works to create this stronger effect.

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