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Semi-bionic extraction of compound turmeric protects against dextran sulfate sodium-induced acute enteritis in rats

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ABSTRACT

Ethnopharmacological relevance: Compound turmeric has been widely used as a remedy for infectious diseases in China. It is a classic multi-herb prescription in traditional Chinese medicine, commonly used in the treatment of enteritis, pneumonia, and abdominal pain for hundreds of years. However, throughout this history, the powder of multi-herbs was directly swallowed, which is currently difficult to administer to patients. The extract of Chinese herbal medicine is made by semi-bionic extraction technology, which is great progress in the modernization of powders of traditional Chinese medicine. The aim of this work is to investigate the protective effects of semi-bionic extraction of compound turmeric (SET) on acute enteritis (AE) induced by dextran sulfate sodium (DSS) in rats.

Materials and methods: SET was extracted in artificial gastric juice or artificial intestinal juice and mixed. After vacuum drying, the SET powder was dissolved in distilled water. Adult male Sprague–Dawley rats were randomly divided into six groups. Rats were given salazosulfapyridine (SASP, 175.0 mg/kg) or SET (0.42 or 0.21 g/kg) before intragastric administration of 5% DSS solutions (0.75 g/kg). The treatments lasted 7 days. The food intake in 24 h, disease activity index (DAI), and wet/dry (W/D) weight ratios and histological changes in colon tissue were measured. The tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-1β, IL-8, and IL-10 in serum were determined at 1, 4, or 7 d after DSS challenge. Myeloperoxidase (MPO), malonaldehyde (MDA), diamine oxidase (DAO), and glutathione peroxidase (GSH-Px) activities in colon tissue were determined at 7 d. In addition, the nuclear factor-kappa (NF-κ B) and intercellular cell adhesion molecule-1 (ICAM-1) activations in colon tissue were analyzed by reverse transcription-polymerase chain reaction (RT-PCR) and Western blot.

Results: In rats with AE, SET significantly reduced DAI at 7 d after DSS treatment, increased the body weight of rats and the food intake in 24 h at 3 or 6 d after DSS challenge, and reduced the colon W/D ratio. SET also reduced the TNF-α, IL-6, IL-1β, and IL-8 in serum and increased IL-10 in serum at 4 and 7 d. In addition, SET decreased MPO, MDA, DAO, and GSH-Px activities in colon and attenuated histological changes in the colon at 7 d after DSS treatment. Further studies demonstrated that SET significantly inhibited NF-κB and ICAM-1 activations in colon tissue.

Conclusions: The current study demonstrated that SET has potent protective effects on DSS-induced AE in rats through its anti-inflammatory and anti-oxidant activities.

1. Introduction

Compound turmeric is a traditional medicine in China and has long been used for the treatment of acute or chronic enteritis, diarrhea, infectious fever, pneumonia, hepatitis, and common inflammation since the Ming Dynasty (CA. 1400s) (Liao and Li, 1990; Chinese Veterinary Drug Standard Committee, 2005; Yang and Pi, 2004). Compound turmeric and the adjusted prescription were used for the treatment of acute and chronic enteritis and diarrhea of cattle (Fu, 2015), horses (Ma et al., 1997), cows, and dogs (Lu et al., 2015). The clinical effect was improved, with a cure rate of more than 90%. The adjusted prescription of compound turmeric is used in the treatment of acute gastroenteritis to significantly reduce antibiotic use, which can effectively alleviate bacterial drug resistance (Ji et al., 2013).

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Phytochemical studies found that compound turmeric contains several alkaloids, anthraquinones, flavonoids, essential oils, and some polysaccharides (Qin and Li, 1994, 1995). The chemical composition of each herb in compound turmeric was studied and achieved gratifying results, such as curcumin, demethoxycurcumin, bisdemethoxycurcumin, turmerone, and curcumene were found in *Curcuma wenyujin Y, H.* Chen et *C.* Ling (Weng et al., 2015; Tang and Li, 1998); chebulinic acid, chebulagic acid, ellagic acid, gallic acid, and neochebulinic acid were found in *Terminalia chebula* Retz; berberine, palmatine, jatrorrhizine, and baicalin were found in *Coptis chinensis* Franch (Zhao et al., 2015); emodin, rhein, chrysophanol, and physcion were found in *Rheum palmatum* L. (Lian et al., 2013; Fu et al., 2011); and albiflorin, oxypaeoniflorin, paeoniflorin, and benzoic acid were found in *Paeonia lactiflora* Pall (Huang et al., 2014a, b; Wang et al., 2014, 2015a). Unfortunately, the chemical components and active ingredients of compound turmeric have rarely been reported.

According to pharmacological studies, compound turmeric exhibits various biological effects, such as anti-inflammation, antipyretic, antibiosis, antivirus, analgesic, and anti-tumor (Fu et al., 2011; Wang et al., 2014, 2015; Huang et al., 2014a, b). Alkaloids, anthraquinones, flavonoids, and essential oils are considered to be the main components for anti-inflammatory and analgesic (and similar) effects; this mutually reinforcing phenomenon has been confirmed (Wu et al., 2014; Zhang et al., 2015a, b; Yi et al., 2012; G. Y. Zhang et al., 2012; Zhang, 2012, W. Zhang et al. 2012). Compound turmeric has significant anti-inflammatory (Cui et al., 2015), antibiosis (Lv, 2014), and antivirus effects.

Semi-bionic extraction (SBE) is different from routine phytochemistry methods; it is a special extraction technology following the guideline of use of traditional Chinese medicine and characteristics of the human gastrointestinal environment. SBE combines the overall drug research and molecular medicine research, according to the reality that efficacious substances efficacy substances are complex and difficult to predict in traditional Chinese medicine. As a multi-herb prescription, its active components are extracted as much as possible to maintain the efficacy of a classic prescription, which is very important. SBE is the better choice because of the following advantages. First, the complex chemical components in a multi-herb prescription are treated by biological processing, which is a perfect incorporation between the inheritance and innovation on basic principles of traditional Chinese medicine. Second, organic solvents are not used in SBE; thus, there is no residue of organic solvent in the extraction. Finally, the extraction temperature is relatively lower, such that components sensitive to heat can avoid damage. SBE can as early as possible remove some ingredients that cannot be dissolved or absorbed in the gastrointestinal tract, which helps to solve a problem—the dosage of traditional Chinese medicine is too large to use conveniently. SBE is an innovative extraction adapted from the perspective of bio-pharmaceutics and simulated oral administration processes, which embody the characteristics of Chinese traditional medicine (Zhang and Sun, 1995). SBE is in line with Chinese medicine theory, paying attention to pharmacodynamic responses in the extraction process design. Since 1995, more than 20 traditional Chinese medicines have been studied and fully successful (G.Y. Zhang et al., 2012, Zhang, 2012,W. Zhang et al., 2012; Chen et al., 2012). However, there are some disadvantages to SBE, such as the high cost due to artificial gastrointestinal fluid and wasted time due to the speed of emptying and promoting the gastrointestinal tract. For compound turmeric, it is a multi-herb prescription including 240 g herbs in each day, which is too large to use inconveniently in dosages; the daily dosage decreased by 20% after SBE. Turmeric volatile oil, jasminoidin, paeoniflorin, and other compounds were stable at 37 °C, and the extraction solvent is bionic artificial gastric and intestinal fluid, so the resulting extraction is readily accepted by the body. Based on the above reasons, SBE was used in the study.

Acute enteritis (AE) is a severe inflammatory disease characterized by excessive activation of macrophages, colon edema, and mucosal injury (Tetsuya et al., 2009; Shao et al., 2014). AE is associated with the development of colon dysfunction, which plays a pivotal role in the death of patients with shock, and multiple transfusions (Yasuyuki et al., 2007; Håkansson, 2015). AE is also characterized by the production of pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, IL-8 (Yoshinori et al., 2002; Zachrisson et al., 2001), and IL-10 (Yamamoto et al., 2001).

Although compound turmeric is used to treat diseases related to inflammation in China and has exhibited a therapeutic effect on inflammation, pain, and diarrhea, research has mainly led to partial findings. Whether semi-bionic extraction of compound turmeric (SET) has protective effects on AE and what the underlying mechanisms of SET action are have not been reported. In the present study, compound turmeric, a classical multi-herb prescription in traditional Chinese medicine, was modernized to obtain a unique extraction with innovative SBE technology. We studied the effects of SBE of compound turmeric on an experimental model of AE induced by DSS to clarify the mechanisms involved. Our results may provide a pharmacological basis for its folkloric use in the treatment of AE.

2. Materials and methods

2.1. Material and chemicals

2.1.1. Preparation of SET

Curcuma wenyujin Y, H. Chen et *C.* Ling, *Terminalia chebula* Retz., *Scutellaria baicalensis* Georgi, *Rheum palmatum* L., *Coptis chinensis* Franch., *Phellodendron amurense* Rupr., *Gardenia jasminoides* J. Ellis, and *Paeonia lactiflora* Pall. were obtained from affiliated Hospital of Gansu University of Chinese Medicine (Gansu, China) and identified by Dr. Feng lin Liu, Gansu University of Chinese Medicine. Voucher specimens (reference number: 150,310-03～10) have been deposited in the herbarium stock room of the Key Laboratory of Pharmacology and Toxicology of Traditional Chinese Medicine of Gansu Province, Lanzhou, China. The extraction and purification of SET were performed according to previous reports (Li et al., 2014; G.Y. Zhang et al., 2012, Zhang, 2012, W. Zhang et al. 2012; Chen et al., 2013). Briefly, *Curcuma wenyujin Y, H.* Chen et *C.* Ling, *Terminalia chebula* Retz., *Scutellaria baicalensis* Georgi, *Rheum palmatum* L., *Coptis chinensis* Franch., *Phellodendron amurense* Rupr., *Gardenia jasminoides* J. Ellis, and *Paeonia lactiflora* Pall. (800 g, the proportion of 2:1:2:4:2:2:2:1) were powdered and extracted three times with stirring and heating (extraction temperature 60 ± 0.5 °C), the extraction procedure of the first was 10 times the amount of water, pH 2.0, and extraction times were 120 min. The second was 6 times the amount of water, pH 7.0, and extraction times were 90 min. The third was 6 times the amount of water, pH 9.0, and extraction times were 90 min. The solution was filtered, mixed and concentrated, and 166.2 g of a brown powder was obtained.

2.1.2. Quality control of SET

2.1.2.1. Measurements of the content of main constituents by Ultraviolet spectrophotometer. SET (1.0 g) was precisely weighed and dissolved in 8% HCl in $CHCl_3$ (60 ml), then boiled under reflux for 1.0 h, cooled, then transferred to a separator funnel and was extracted three times with 30 ml $CHCl_3$, the $CHCl_3$ liquid was combined, and the $CHCl_3$ was removed. The residual powder was dissolved in 0.5% Mg $(Ac)_2$ in methanol (10 ml) and allowed to sit