Pharmaceutical Analysis

49 THE AMELIORATING EFFECT OF DANGGUI SHAOYAO POWDER ON EXPERIMENTAL DIABETIC NEPHROPATHY

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Objectives Danggui Shaoyao powder (DSS), a Chinese herbal compound, has been used in China with established therapeutic efficacy in patients with diabetic nephropathy (DN). The purpose of this study was to investigate the possible mechanism of DSS improving DN.

Methods Wistar rats with streptozotocin (STZ)-induced diabetes were used for evaluation of the effect of treatment with DSS on DN. Rats were randomly divided into three groups: control, diabetic and diabetic+DSS. Blood glucose, serum creatinine (Cr), blood urea nitrogen (BUN), superoxide dismutase (SOD) activity, malondialdehyde (MDA) and hydroxyproline (Hyp) were measured in kidney tissue. Glomerular morphology was observed by light microscopy. Immunohistochemistry and Western blot were employed to determine the proteins levels of TGF-β_1 and type IV collagen.

Results Compared with the control group, Cr, BUN, MDA and Hyp levels in DN rats were significantly increased but were significantly decreased by treatment with DSS.

While SOD activity in renal tissue was decreased, DSS can increase SOD activity. The renal pathological changes in the DSS treatment group were ameliorated. Furthermore, the DSS decreased the expression of TGF-β_1 and collagen IV protein.

Conclusions These results demonstrate that DSS can ameliorate STZ-induced experimental DN. The mechanism may be related to modulating the expression of collagen IV and TGF-β_1 protein.

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50 SYNTHESIS, CHARACTERIZATION AND STABILITY OF FIVE TAVABOROLE-BASED PHARMACEUTICAL COCRYSTALS

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Objectives Pharmaceutical cocrystals have received attention in the pharmaceutical industry due to their potential for readily changing the physicochemical and biological properties of free active pharmaceutical ingredients (API). Tavaborole is an antifungal agent with strong moisture absorption leading to poor stability. The objective of this investigation was to prepare five pharmaceutical tavaborole cocrystals and to optimize their stability.

Methods The five novel pharmaceutical cocrystals with tavaborole as the API were synthesised using the grinding method, with p-aminobenzoic acid (cocrystal 1), m-aminobenzoic acid (cocrystal 2), 2,3'-dihydroxybenzoic acid (cocrystal 3), salicylic acid (cocrystal 4) and 2,6'-pyridinedicarboxylic acid (cocrystal 5). Characterization with XRD and TGA further identified a new phase. The thermal stability, chemical stability and moisture absorption rate of API and cocrystals were also measured and discussed.

Results The thermal stability of the five cocrystals was significantly improved compared to the API alone. Chemical degradation and a hydration reaction of cocrystals did not occur in 43%, 58%, 75% and 92% relative humidity at 25°C. The moisture absorption rate of API and cocrystals decreased in the order: API>cocrystal 2>cocrystal 1>cocrystal 4>cocrystal 3>cocrystal 5.

Conclusions In this study, we used the grinding method to synthesize pharmaceutical cocrystals of tavaborole. The thermal stability, chemical stability and hygroscopic stability of cocrystals were significantly better than those of API alone.

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51 L-ARGININE AMELIORATES THE PROGRESSION OF AUTOIMMUNE MYOCARDITIS

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Objectives Nitric oxide (NO) plays a dual role: it can inhibit the inflammatory process under physiological conditions, but on the other hand, a large amount of NO can be involved in inflammation in autoimmune myocarditis. We investigated the effects of N-nitro-L-arginine methyl ester (L-NAME), an inducible nitric oxide synthase (iNOS) inhibitor, in the treatment of BALB/c mice with experimental autoimmune myocarditis (EAM) and discuss the therapeutic mitochondrial mechanism induced by apoptosis.

Methods Sixty male BALB/c mice aged 4–5 weeks were randomly divided into a normal control group, a model control group and an experimental group. EAM was induced in the model control group and experimental group by injection of porcine cardiac myosin subcutaneously into the groin and axilla and intraperitoneal injection of pertussis toxin on days 0 and 7, respectively. The model control group was intraperitoneally administered 5 mg/kg/day of physiological saline after injection of myosin and pertussis toxin. The experimental group was intraperitoneally given 5 mg/kg/day of L-NAME on days 1–21. At the end of the intervention, mice were euthanatized and hearts were harvested on day 21. The inflammatory score, fibrosis score, protein expression levels of caspase-3, caspase-8 and caspase-9, serum NO level, iNOS, iNOS mRNA, caspase-3, caspase-8 and caspase-9 mRNA, cardiac reactive oxygen species (ROS) production rate and mitochondrial membrane potential were measured. Mouse heart weight/body weight was calculated (HW/BW).