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).

Results The inflammatory score, cardiac interstitial fibrosis score, cardiac apoptotic index, protein expression levels of caspase-3, caspase-8 and caspase-9, HW/BW, level of NO and activity of iNOS, expression levels of iNOS mRNA, and caspase-3, caspase-8 and caspase-9 protein were all significantly higher in the model control group and experimental group than in the normal control group ($p < 0.01$), and the levels in the model control group were higher than in the experimental group. HW/BW was only slightly elevated in the model control group compared with the experimental group.
Conclusions The development of EAM is related to the NO catalyzed by iNOS. L-NAME protected cardiac myocytes through suppressing the activity of iNOS and further decreased production of NO in EAM. The mechanism may be related to inhibiting the apoptosis of cardiac myocytes mediated by the caspase family and protecting mitochondrial function.
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52 EFFECT OF EXTERNAL APPLICATION OF SPIKENARD WATER DECOCTION ON THE MOUSE PAIN MODEL

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Objectives To investigate the effects of external application of a spikenard water decoction on pain model mice.
Methods We investigated the effects of spikenard water decoction on the pain threshold in mice using the hot plate method. After injection of formaldehyde, the effects of spikenard water decoction on the formalin-induced pain incubation period and biting times were observed.
Results Each dose of spikenard water decoction obviously or significantly improved the pain threshold of pain model mice ($p < 0.01$, $p < 0.05$), significantly prolonged the pain licking incubation period ($p<0.01$) and obviously or significantly reduced the number of instep licks in 5 min and 10 min ($p < 0.01$, $p < 0.05$).
Conclusions External application of spikenard water decoction has a good analgesic effect in the mouse pain model.

53 SYNTHESIS OF A NOVEL PROTEIN-FRIENDLY AMPHIPHILIC MATERIAL AND ITS APPLICATION IN PROTEIN DRUG DELIVERY

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Objectives We synthesized an environmentally friendly amphiphilic material PK3-PEI with good mechanical properties, pH sensitivity and biocompatibility, aiming at improving the acidic microenvironment produced by the degradation of polyester compounds and poor mechanical properties of PK3. PK3-PEI spontaneously forms micelles in pH 7.4 PBS and rapidly degrades into non-toxic small molecules in acidic conditions. Surface PEI with large positive charges effectively promotes cell targeting and accelerates the release of drug after entering the cells.
Methods PK3 and PEI were linked using a connection molecule. Activation of –OH groups on PK3 (0.46 g) was accomplished using HMDI (50-fold) in chloroform at 80°C for 4 hours. The intermediate was precipitated with diethyl ether and incubated with PEI (Mw 2000 kDa, linear, 0.46 g) in chloroform at 80°C for 4 hours. PK3-PEI was collected through repeated precipitation in diethyl ether. For the preparation of PK3-PEI micelles, 100 μL of BSA solution (40 mg/mL) and 40 mg of PK3-PEI were dispersed in chloroform in dialysis bags. The PK3-PEI micelles were obtained by dialysis against pH 7.4 PBS.
Results The connection ratio of PK3 and PEI was 1:1. The particle size and ζ potential of micelles were 50.3 nm and 25.7 mV, respectively. The *in vitro* release profile showed PK3-PEI had a shorter hydrolysis cycle and higher pH sensitivity than PK3. The MTT assay showed blank PK3-PEI micelles had lower cytotoxicity (4.6%) than free PEI (18.7%). Cellular uptake indicated PK3-PEI micelles had higher uptake efficiency than PK3 ($p < 0.01$).
Conclusions PK3-PEI micelles have a better degradation curve and targeting effect for the delivery of antitumor drugs and can be used as a promising carrier in cancer treatment.

54 ANTI-GLIOMA ACTIVITY OF *RANA TEMPORARIA CHENSINENSIS* EGG PROTEIN HYDROLYSATE

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Objectives *Rana temporaria chensinensis* only live in the Changbai mountain area in the northeast of China. The eggs of *R.temporaria chensinensis* contain many special ingredients that modulate incretion. This study aimed to investigate the effects of *R.temporaria chensinensis* egg protein hydrolysate on human glioma C_6 cell proliferation and apoptosis.
Methods We extracted *R.temporaria chensinensis* egg protein (500 mg/mL) and investigated its effects on human glioma C_6 cell cultures, and subjected it to an MTT assay, colony forming assay, Western blot assay and flow cytometry analysis of apoptosis. We further investigated the effects of *R. temporaria chensinensis* egg protein hydrolysate (1.5 g/kg) on glioma development and progression *in vivo* using a mouse model of glioma.
Results *R.temporaria chensinensis* egg protein hydrolysate inhibited the proliferation of glioma cells; these effects were mediated by the phosphoinositide 3-kinase (PI3K)/AKT signalling pathway.
Conclusions This study suggested that *R.temporaria chensinensis* egg protein hydrolysate promotes apoptosis of glioma cells both in vitro and in vivo.
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Healthcare Informatics

55 RESEARCH ON LAST MILE DISTRIBUTION OF EMERGENCY MEDICAL SUPPLIES IN EARTHQUAKE DISASTERS

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Objectives A model based on time and cost is proposed in order to quantitatively study last mile distribution of emergency medical supplies. Because cost is not particularly important in the