The absorptive property of Paeoniflorin-6-O'-benzenesulfonate (CP-25) in peripheral blood mononuclear cells

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Objective Paeoniflorin-6'O-benzene sulfonate (CP-25) is a newly derivative of Paeoniflorin (Pae). We have previously reported CP-25 shows better anti-inflammatory activity and higher bioavailability than that of Pae. This study was mainly performed to investigate absorptive behavior and mechanism of CP-25 in PBMCs both in vivo and vitro.

Methods Peripheral blood mononuclear cells (PBMCs) were collected from normal rats and stimulated by TNF-a for imitating the inflammatory response in vitro. A specific and sensitive ultra-performance liquid chromatography - tandem mass spectrometry (UPLC-MS/MS) assay for rapid determination of CP-25 and Pae in the rats' PBMCs was developed and validated for the first time.

Results CP-25 had a maximum intracellular level in the rats' PBMCs at 120 min after incubation in vitro. Likewise, CP-25 showed an maximum intracellular level in PBMCs at 3h after the oral signal administration. Interestingly, the intracellular levels of CP-25 were higher than Pae both in vivo and vitro. Moreover, TNF-a pre-stimulated PBMCs showed an increase in the level of P-gp expression, and an reduced absorption of CP-25, which partially inhibited by P-gp inhibitors, including GF120918, LY335979 and verapamil. In vivo studies, the P-gp levels in PBMCs of rats with adjuvant arthritis (AA) were significantly higher than that of normal rats, and we noticed the level of CP-25 in PBMCs of AA rats were significantl higher than that of norma rats.

Conclusion Absorption of CP-25 in PBMCs is better than Pae both in vitro and vivo. Inflammatro response induced increase in the P-gp expression limited the permeable absorption of CP-25 at intracelluar levels.

Key words: CP-25; Paeoniflorin; Peripheral blood mononuclear cells; P-glycoprotein

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The presentation of first author:

Chun Wang received his degrees of M.S. and Ph.D. from Institute of Clinical Pharmacology of Anhui Medical University. The main research direction of Chun Wang is the roles of ABC transporters & organic anion transporters in the cellular pharmacokinetics of anti-inflammatory drugs at auto-immune diseases and new immunomodulatory drugs development.