Macedonian pharmaceutical bulletin, 68 (Suppl 2) 147 - 147 (2022)
ISSN: 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2022.68.04.066
Short communication

From experience to evidence, a long and risky road of *Salvia miltiorrhiza* Depsides Salts

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Abstract

The road of drug discovery and development is tortuous and full of risk. Thanks for its long-history practice as folk medicine, TCM afford us a lot clue to develop a new drug more efficiently and less costly, compared with developing from scratch. *Salvia miltiorrhiza* Bunge, known as "Danshen", is a typical TCM for promoting blood circulation and removing blood stasis. Its preparations were widely applied clinically for the treatment of cardiovascular and cerebrovascular disease. However, most of them cannot keep consistent efficacy and safety because of its obscure constituents and uncontrollable quality.

Based on the investigation of hydrophilic constituents of *Salvia miltiorrhiza*, magnesium lithospermate B (MLB) and other depsides salts were identified as the most effective components for ameliorating ischemic myocardial injury. Fortunately, MLB is also abundant in the herb even though it is mixed with other salt forms and derivatives. This finding inspired us to use MLB as the key quality control marker for innovative drug of *Salvia miltiorrhiza*, differentiating from other traditional preparation. A quality standard including fingerprinting, as well as preparation process was elaborated to enrich MLB and afforded consistent and identified constituents and controllable quality. Mode of action investigation indicated depsides salts can protect cardiovascular system by selectively modulating L-type calcium current in ventricular myocytes, modulating intracellular calcium concentration in vascular smooth muscle cells, inhibiting migration and proliferation of VSMC, antioxidation, anti-platelet aggregation and anti-inflammation, respectively.

After 13 years R&D, Salvia Miltiorrhiza Depsides Salts (SMDS) has been confirmed to be safe and effective for the treatment of patients with coronary artery disease and chronic angina pectoris in multi-centre clinical trials. It was licensed by CFDA in 2005. After launching the market, another 13 years passed. Series of post-marketing investigation including Phase IV clinical trial, efficacy and safety in real world and several RCT study of SMDS were conducted to afford more evidence supporting its application in clinic effectively and safely. Till now, more than 20 million patients were benefited from SMDS. A blockbuster with billions of RMB in annual sales is rising.

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