

Simultaneously determination of five ginsenosides in rabbit plasma using solid-phase extraction and HPLC/MS technique after intravenous administration of ‘SHENMAI’ injection

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Abstract

In this study, a sensitive and reliable analytical method for the simultaneous determination of five ginsenosides (R_{g1} , R_f , R_e , R_d and R_{b1}) in rabbit plasma was developed by high performance liquid chromatography-electrospray ionization mass spectrometry (HPLC-ESI-MS). Chromatographic separation was carried out on a Zorbax SB-C₁₈ Column (150 mm × 2.1 mm i.d., 5.0 μm particle size) with a simple linear gradient elution. The detection was conducted on a single quadrupole mass spectrometer by selected ion monitoring mode via electrospray ionization source. Good linearity over the investigated concentration ranges was observed with the values of R^2 higher than 0.991 for all the analytes. Limits of detection of the analytes varied from 0.25 ng/ml to 1.45 ng/ml, and the average recoveries, examined at three concentration levels, ranged from 90.6% to 106.9%. The validated method was successfully applied to the determination of the ginsenosides in the rabbit plasma after intravenous administration of ‘SHENMAI’ injection.

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Keywords: ‘SHENMAI’ injection; Ginsenosides; HPLC-ESI-MS; Rabbit plasma; Solid-phase extraction; Quantitative analysis

1. Introduction

Traditional Chinese medicine (TCM), considered as the alternative medicine in the West, has a long history for the medicinal practice in China and some Oriental countries [1,2]. An increasing effort over recent decades to prepare TCM as botanical drugs improves the therapeutic effect and ease of use of these traditional medicines. Due to the fact that the TCM-derived botanical drugs are commonly prepared from multiple medicinal plants, a huge quantity of work has been performed in order to develop various analytical methods for the identification, quantification and quality control of the active components in raw plant materials, extracts and the final products. However, the studies on the absorption, distribution, metabolism and excretion of these botanical drugs are seldom reported. One of the main reasons lies on the lack of the sensitive, specific and reliable analytical

methods for the pharmacokinetic studies of the TCM-derived botanical drugs [3–5].

Ginsenosides are the major active components contained in the important Oriental herb “ginseng” derived from the roots and rhizomes of different *Panax* species, which is mainly used to increase resistance to physical, chemical and biological stress [6]. Immune system modulation, antistress activities and antihyperglycemic activities are among the most attractive features of ginseng in laboratory and clinical trials [7]. Moreover, some studies also indicate that some ginsenosides have antitumor properties and other bioactivities related to cancer. Owing to their potent pharmacological activities, ginseng is widely used to prepare the TCM-derived botanical drugs. For example, ‘SHENMAI’ injection, which is derived from a TCM formula named “SHEN MAI SAN” and mainly composed of red ginseng and ophiopogon, is now commonly used in China [8,9]. Therefore, the pharmacokinetic studies of ginsenosides are of great importance for the further development and the rational use of the related botanical drugs. Up to now, a number of analytical methods have been developed for the determination of some major

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ginsenosides in the raw materials or the final ginseng products based on thin layer chromatography [10], gas chromatography [11], micellar electrokinetic chromatography [12], HPLC [13,14] and some other techniques [15]. Among these analytical techniques, HPLC has become the routine choice. Although ultraviolet (UV) detector was widely employed for HPLC analysis, it is not sufficient for the sensitive analysis of ginsenosides within the biological matrices. The main problem is attributed to the high level of baseline noise and the poor sensitivity caused by the weak UV absorption of ginsenosides. In recent years, HPLC/MS technique has been successfully applied to the sensitive analysis of ginsenosides [16–18], and some advantages of mass spectrometry such as the higher specificity, selectivity, sensitivity, and the lower limit of detection enhance its application to the development of the analytical methods for the pharmacokinetic studies of ginsenosides [19–21]. However, most of these methods were concentrating on one or two constituents in ginseng, thus the effort to develop the method for the simultaneous quantifying the multiple active components of the raw materials or final products of ginseng in the biological matrices is still necessary for the pharmacokinetic studies.

‘SHENMAI’ injection is used for the treatment of coronary atherosclerotic cardiopathy and viral myocarditis, and it is also capable of raising tumor patient’s immunity. Ginseno-

side such as R_{g1} , R_f , R_e , R_d and R_{b1} (their chemical structures have been shown in Fig. 1) are the main effective components contained in this botanical drug. Development of a sensitive method for the simultaneous determination of these components in plasma or other biological matrices is very helpful for the pharmacokinetic study of ‘SHENMAI’ injection. In our early studies [22,23], HPLC/MS technique was not only used to characterize the constituents of ‘SHENMAI’ injection, but also to develop a HPLC/MS fingerprinting for its quality evaluation. In this work, a sensitive HPLC-ESI-MS method coupled with solid-phase extraction was developed for the simultaneous determination of ginsenosides R_{g1} , R_f , R_e , R_d and R_{b1} in rabbit plasma. This method was applied to the development of the concentration–time profiles of the five components in rabbit plasma after intravenous administration of ‘SHENMAI’ injection.

2. Experimental

2.1. Chemicals and reagents

Standard compounds ginsenosides R_{g1} , R_f , R_e , R_d and R_{b1} were all purchased from National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China).

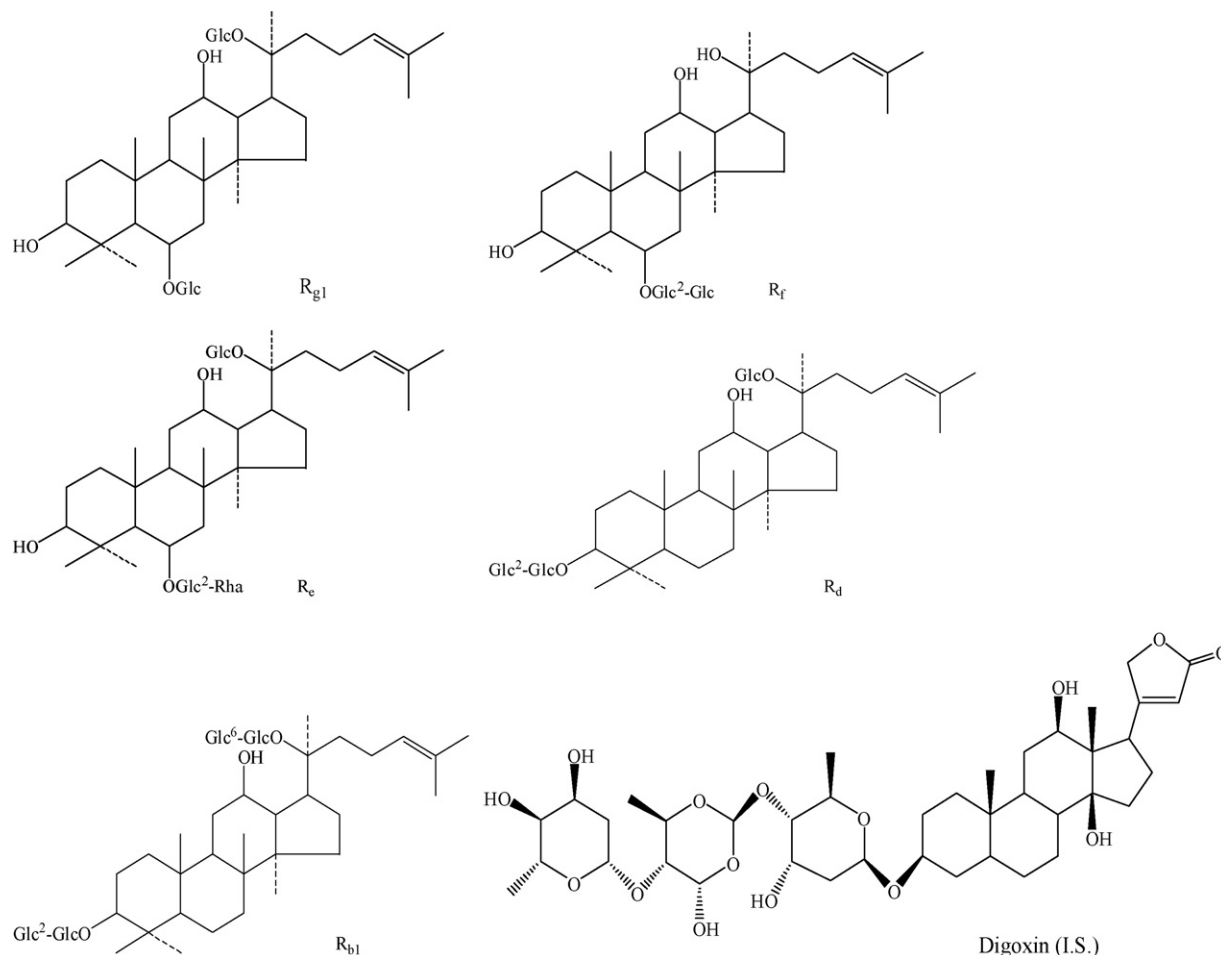


Fig. 1. Chemical structures of five ginsenosides and the I.S. compound.

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