# Abstract

Cardiovascular disease is one of the leading causes of death worldwide, and atherosclerosis is the common pathology of most cardiovascular diseases. The root of *Panax notoginseng* (Burk.) F.H. Chen (*P. notoginseng*), called *Sanqi* in Chinese, is a highly valued and commonly used Chinese medicinal herb, and has been widely prescribed for the treatment of cardiovascular diseases. However, its pharmacological basis is poorly understood. On the other hand, the main bioactive constituents of *P. notoginseng* were considered as drammarane triterpenoid saponins. It was reported that the type and content of saponins varied in different parts of *P. notoginseng,* thus possess distinct therapeutic effects. With more and more extensive clinical application of the root and other parts of *P. notoginseng*, for ensuring the efficacy and safety of their medication, it is urgent to understand their chemical ingredients, and develop the efficient method for quality control of different parts of *P. notoginseng* and their related preparations. In the present study, therefore, atheroprotective effect of *P. notoginseng* and its underlying mechanisms were investigated *in vivo* and *in vitro*. Furthermore, analytical methods for quality control of the root and other parts of *P. notoginseng* were also developed systemically.

The knowledge and techniques of phytochemistry, pharmaceutical analysis and pharmacology were comprehensively adopted and applied. Firstly, the antiatherogenic effect of total saponins of *P. notoginseng*, and its underlying mechanisms were elucidated by *in vivo* and *in vitro* studies. The results also found that the anti-vascular inflammatory effect of 20(S)-protopanaxdtriol saponins (PDS) was more potent than that of PNS and 20(S)-protopanaxatriol saponins (PTS). Thus, secondly, an efficient method for the preparative separation of PDS and PTS from PNS or root of *P. notoginseng* was established. Furthermore, several chemical standards were prepared from *P. notoginseng* by phytochemical approaches for the further quality control studies. Finally, several analytical methods were established systematically using HPLC-ELSD, HPLC-MS/MS and fingerprinting technology for quality control of the root and other parts from *P. notoginseng*. The main innovations and academic contributions in the present study were listed as follows:

(1) The antiatherosclerotic effect of *P. notoginseng* and its underlying mechanisms was investigated using apoE knockout mice and en face method for the first time.

(2) It was found, for the first time, that PDS showed the more potent effect on anti-vascular inflammation than PNS and PTS, suggesting that PDS might be developed as anti-antiatherogenic drug.

(3) A simple, efficient and environment-friendly method for separation of PDS and PDS from *P. notoginseng* with macroporous resins was developed for the first time. The method is suitable for large-scale industrial production of PTS and PDS and ensue the source of PDS and PTS for further pharmacological study.

(4) A rapid and simple method for simultaneous preparation of notoginsenoside R1, ginsenoside Rg1, Re, Rd and Rb1 was firstly developed using pre-HPLC and ethanol -water elution system, which will provide ample chemical standards of these 5 saponins for the quality control and pharmacological studies of *P. notoginseng* (Sanqi), *P. ginseng* (Asian Ginseng), *P. quinquefolium* (American ginseng) and their related medical preparations

(5) A novel compound, designated as dedihydro-ginsenoside Rb1, was isolated from *P. notoginseng.*

(6) An efficient and sensitive method was developed using HPLC-ELSD for simultaneous determination of 11 saponins for quality control of *P. notoginseng.*

(7) The chromatographic fingerprint of *P. notoginseng* was constructed using HPLC-UV coupled with PLE.

(8) The chemical profiles of different parts of *P. notoginseng* (e.g. rhizome, root, fibra root, stem, leaf, flower and seed) were compared using HPLC-ELSD. The results demonstrated that the developed method was suitable for the quality control of different parts of *P. notoginseng.*

(9) An HPLC-ESI-MS/MS method was developed, for the first time, to systematically compare the chemical profiles of different parts of *P. notoginseng.*

(10) The pharmacological studies showed that PDS exhibited potent anti-antiatherogenic effects, thus, the leaf and flower of *P. notoginseng*, which contained large amounts of PDS, have the potential to be developed as anti-antiatherogenic products.

In summary, the atheroprotective effect of *P. notoginseng* and its underlying mechanisms were elucidated, and the developed analytical methods could be used for the quality control of different parts of *P. notoginseng*. The strategy of studying the chemical and pharmacological properties of *P. notoginseng* together in a systematic way will

contribute to the better understanding of this highly-valued Chinese Medicine.

**Keywords:** *Panax notoginseng*, protopanaxadiol saponins, protopanaxatriol saponins, quality control, chromatographic fingerprint, HPLC-ELSD, anti-atherosclerosis, anti-vascular inflammation.