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## **Review of the pharmacological effects of astragaloside IV and its autophagic mechanism in association with inflammation**

Yang Y *et al.* Astragaloside IV and its autophagy mechanism

Ying Yang, Meng Hong, Wen-Wen Lian, Zhi Chen

### **Abstract**

Astragalus membranaceus Bunge, known as "Huangqi", is used to treat various diseases for a long time. Astragaloside IV (AS-IV) is one of the primary active ingredients of the aqueous "Huangqi" extract. At present, many studies in experimental models have shown that AS-IV exerts broad beneficial effects on cardiovascular disease, nervous system diseases, lung disease, diabetes, organ injury, kidney disease, and gynaecopathy. This review demonstrates and summarizes the structure, solubility, pharmacokinetics, toxicity, pharmacological effects, and autophagy mechanism of AS-IV. The autophagy effects are associated with multiple signalling pathways in experimental models, including the PI3K I/Akt/mTOR, PI3K III/Beclin-1/Bcl-2, PI3K/Akt, AMPK/mTOR, PI3K/Akt/mTOR, SIRT1-NF- $\kappa$ B, PI3K/AKT/AS160, and TGF- $\beta$ /Smad signalling pathways. Based on this evidence, AS-IV could be used as a replacement therapy for treating the multiple diseases referenced above.

**Key Words:** Astragaloside IV; Pharmacological effect; Autophagy; Inflammation

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**Core Tip:** Astragaloside IV (AS-IV) is one of the main active ingredients of the aqueous extracted "Huangqi". At present, lots of studies in experimental models have shown that AS-IV has broad beneficial effects on various diseases. This review demonstrates and summarizes pharmacological effects, and autophagy mechanism of AS-IV. The autophagy effects are associated with inflammation or not and multiple signaling pathways in experimental models. Based on this evidence, AS-IV will be used as replacement therapy for treating the above various diseases.

## INTRODUCTION

Traditional Chinese medicine (TCM) has been used to treat various diseases with great effects for a long time (1). Radix Astragali (Huangqi) is a prevalent TCM. Compared to Western medicine treatments, TCM treatments have significantly fewer side effects (2). In addition to polysaccharides, flavones, and amino acids, the primary components are astragalosides (3). Astragaloside IV (AS-IV) is the primary active astragaloside, whose pharmacological effects have been reported in various diseases *in vitro* and *in vivo*. A search strategy was performed of published studies from 2001 to present using keyword searches "(astragaloside IV) AND (inflamm\*)" in PubMed. Then we included the studies related to autophagy and excluded the studies not related to autophagy. In this review, we summarize the protective effects and autophagic mechanism of AS-IV.

## CONCLUSION

AS-IV, the primary active astragaloside from Radix Astragali, has been reported to have pharmacological effects on various diseases. The pharmacokinetics characterization revealed that 12 tissues, including the liver and kidney, detected AS-IV. AS-IV not only promotes but also inhibits autophagic activity through a variety of signalling pathways to improve various diseases. These pathways include the PI3K I/Akt/mTOR, PI3K III/Beclin-1/Bcl-2, PI3K/Akt, AMPK/mTOR, PI3K/Akt/mTOR, SIRT1-NF- $\kappa$ B, PI3K/AKT/AS160, and TGF- $\beta$ /Smad signalling pathways. The suggested pathway in this literature review is that the autophagy proteins Atg7/ Atg12 are mediated by DCP1A

and TMSB4X. When the level of Atg7/Atg12 were reduced, the level of DCP1A and TMSB4X were also decreased. The autophagy-related proteins include Beclin-1, LC3-II, p62, ATG16L1, ATG9B, and ATG4D. In a word, AS-IV distributed widely in various tissues and the autophagy mechanism of AS-IV is a basic biological mechanism. Hence, AS-IV is an effective therapeutic drug for treating various diseases. According to existing research, AS-IV potentially possesses broad beneficial effects in many diseases, and the autophagy mechanism deserves further investigation.

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