



PAPER

# Aristolochic acid I induces impairment in spermatogonial stem cell in rodents

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## Abstract

Aristolochic acid I (AAI) is a natural bioactive substance found in plants from the *Aristolochiaceae* family and impairs spermatogenesis. However, whether AAI-induced spermatogenesis impairment starts at the early stages of spermatogenesis has not yet been determined. Spermatogonial stem cells (SSCs) are undifferentiated spermatogonia that balance self-renewing and differentiating divisions to maintain spermatogenesis throughout adult life and are the only adult stem cells capable of passing genes onto the next generation. The objective of this study was to investigate whether AAI impairs SSCs during the early stages of spermatogenesis. After AAI treatment, we observed looser, smaller and fewer colonies, decreased cell viability, a decreased relative cell proliferation index, and increased apoptosis in SSCs in a concentration- and/or time-dependent manner. Additionally, AAI promoted apoptosis in SSCs, which was accompanied by upregulation of caspase 3, P53 and BAX expression and downregulation of Bcl-2 expression, and suppressed autophagy, which was accompanied by upregulation of P62 expression and downregulation of ATG5 and LC3B expression, in a concentration-dependent manner. Then we found that AAI impaired spermatogenesis in rats, as identified by degeneration of the seminiferous epithelium, and increased apoptosis of testicular cells. Taken together, our findings demonstrate that AAI causes damage to SSCs and implicate apoptosis and autophagy in this process. The impairment of SSCs may contribute to AAI-induced testicular impairment. Our findings provide crucial information for the human application of botanical products containing trace amounts of AAI.

**Key words:** aristolochic acid I, spermatogenesis, spermatogonial stem cells, apoptosis, P53, BAX

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