

## Molecular mechanism of reduction in aflatoxin B1 biosynthesis by *Heracleum persicum* and *Peganum harmala* extracts as indicated by traditional medical knowledge of Iran

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### Abstract:

**Background and Purpose:** Aflatoxin B1 (AFB1), produced by several species of *Aspergillus* on a wide range of food products, is a serious agricultural and medical threat. It is classified as a class one carcinogen, due to carcinogenic, mutagenic, teratogenic, hepatotoxic and immunosuppressive effects. Use of natural compounds that are able to prevent aflatoxin production, can be an alternative strategy to limit food and feed contamination in line with sustainable agriculture.

**Materials and Methods:** Based on Persian traditional medicine resources, this study evaluated the inhibitory effect of *Heracleum persicum* and *Peganum harmala* extracts on fungal growth and aflatoxin B1 production. In addition, we used LC-MS analysis and analyzed some key genes that are involved in the AFB1-producing gene cluster (*aflM*, *aflP* and *aflR*), to investigate the inhibition mechanisms of fungal growth and AFB1 by the herbal extracts, at the molecular and transcriptional level.

**Results:** In this study we showed that the extracts of *H. persicum* and *P. harmala* at concentrations of 4 and 6 mg/mL exhibited a 100% inhibitory effect on aflatoxin B1 production despite incomplete inhibition of fungal growth. The results of this study showed that addition of 4 mg/mL of *Heracleum persicum* extract in the YES culture medium of *A. flavus* leads to almost complete inhibition of *aflM*, *aflP* gene expression.

**Conclusion:** To summarize, the decrease in aflatoxin biosynthesis by *H. persicum* and *P. harmala* extracts can be due to decreased expression level of the associated gene cluster. Among the investigated genes, we found that the *aflP* gene is likely more involved in aflatoxin inhibition and probably plays a more critical role. Overall, this study reveals the anti-aflatoxigenic mechanisms of the selected plant extracts at the gene expression level and provides evidence for their use in food, feed and medicinal plants that are prone to this contamination.

**Keywords:** Aflatoxin B1, *Aspergillus*, Gene Expression, *Heracleum persicum*, *Peganum harmala*

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