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# Toxic Effects of Alternaria Fungi Metabolites on the Antioxidant Defense System of Rats

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## INTRODUCTION & AIM

Recent studies indicate substantial contamination of food products with Alternaria toxins (ATs), which are toxic metabolites produced by mold fungi of the genus Alternaria. Their ability to exert cyto- and genotoxic effects may pose a significant risk for human health. The most widespread AT is tenuazonic acid (TeA), which is currently not regulated in food products. In this regard, the aim of the present study was to investigate the effects of ATs, particularly TeA, on the antioxidant defense system of the organism.

## TOXIN ISOLATION

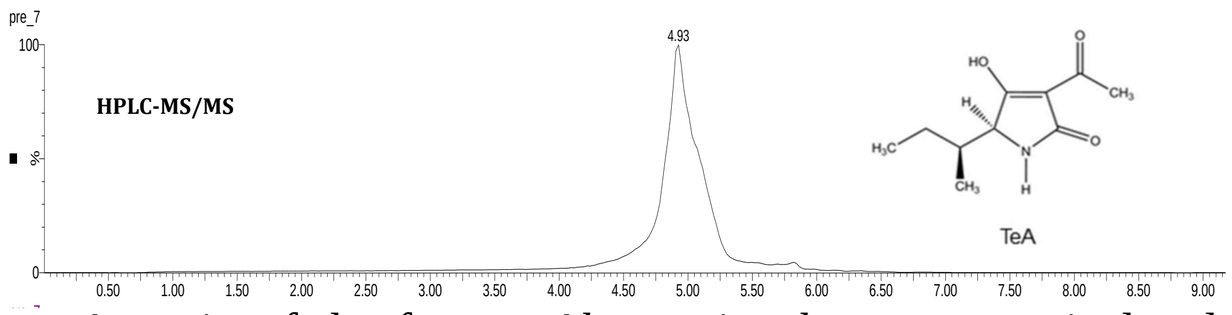
**Cultivation**
*A. alternata* 10.12/167, tomato paste, 24°C for two weeks

**Extraction**
ethyl acetate/HCOOH; 100/1 (200 см$^3$)

Ultrasound (60 min)

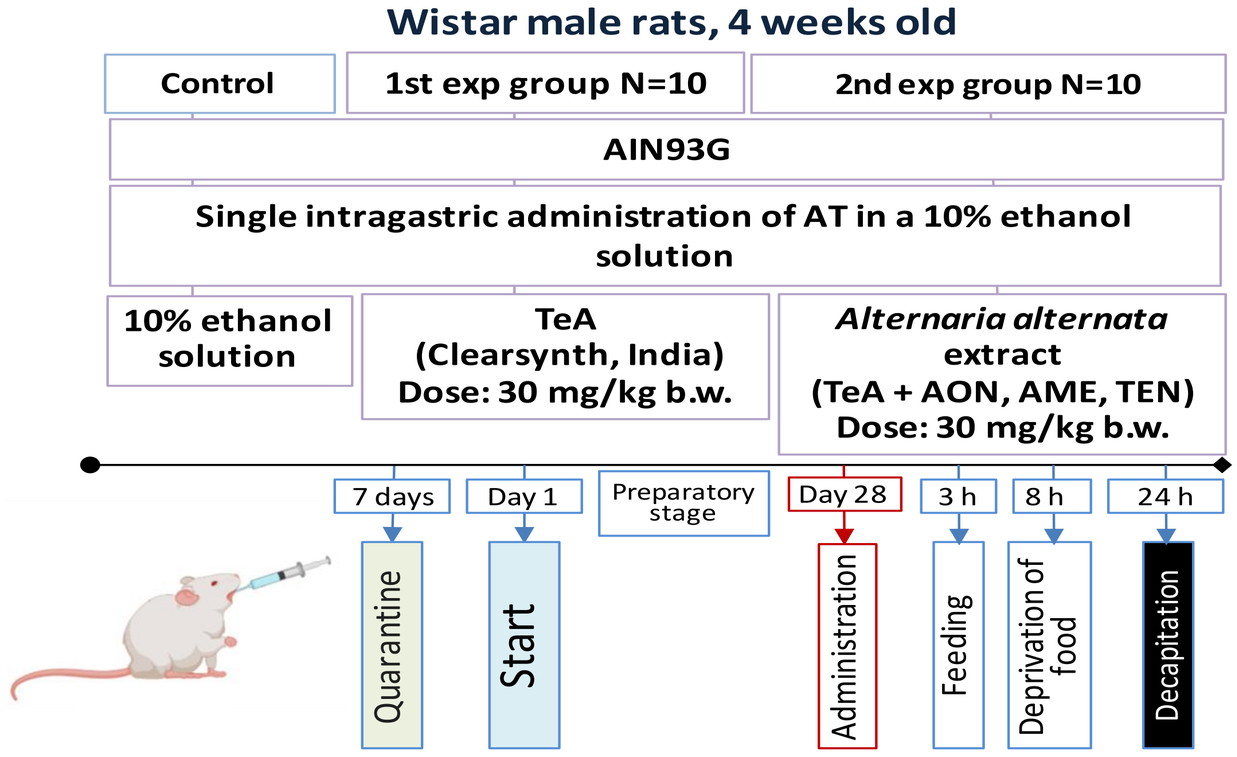
Stirring (60 min)

**Evaporation**
T = 50$^0$C




A strain of the fungus *Alternaria alternata* was isolated from barley grain and cultivated on tomato paste. The mixture of ATs was extracted from the resulting substrate using a solvent system (ethyl acetate, formic acid). After evaporation, the extract was dissolved in methanol.

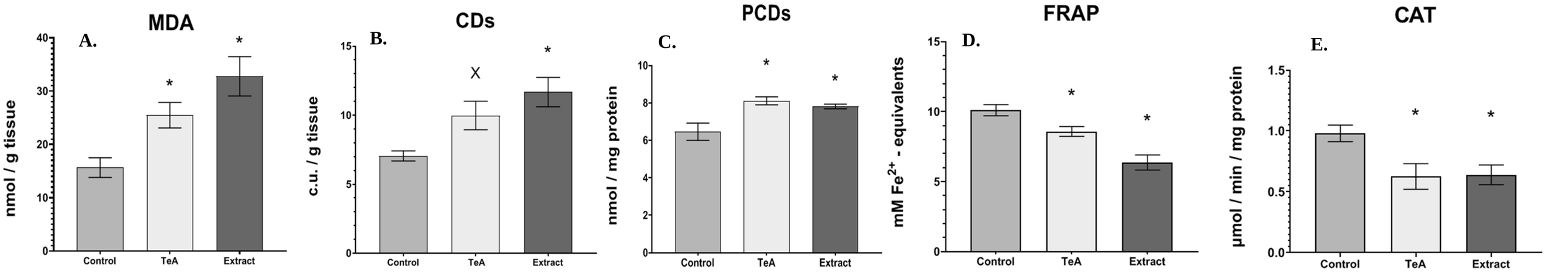
## EXPERIMENTAL DESIGN



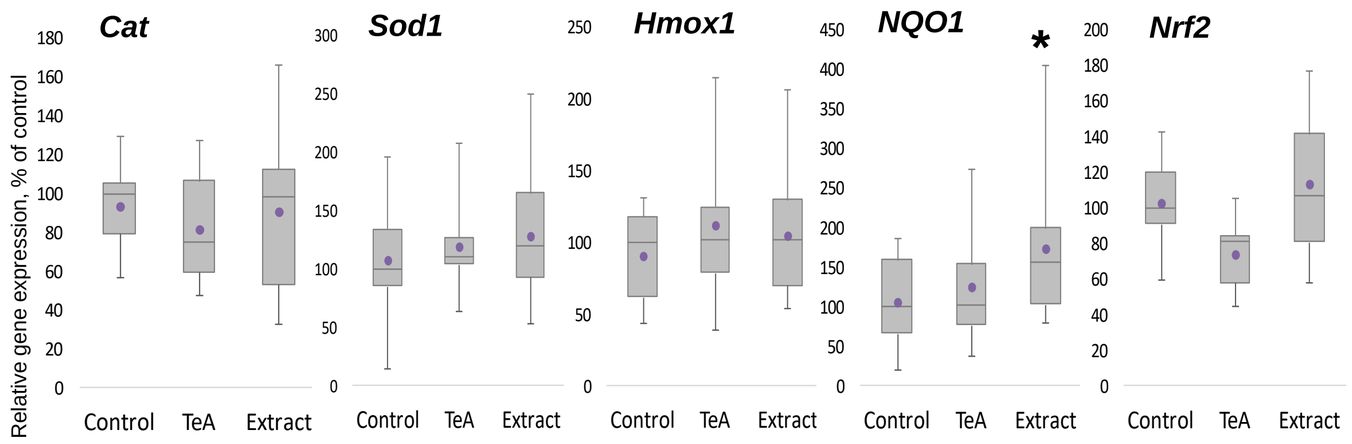

A single oral administration of pure TeA (30 mg/kg b.w.) or an extract containing a mixture of AT: TeA (30 mg/kg b.w.), alternariol (0.276 mg/kg b.w.), alternariol monomethyl ether (0.902 mg/kg b.w.), and tentoxin (0.018 mg/kg b.w.) was used to evaluate their effects on antioxidant parameters in male Wistar rats.

To assess the effects on the antioxidant defense system in rats, the following parameters were analyzed: malondialdehyde (TBARS, HPLC-FLD); conjugated dienes (spectrophotometric assay following Folch extraction); protein carbonyl derivatives (spectrophotometric detection after DNPH derivatization and gel filtration); antioxidant defense enzymes (FRAP assay and catalase activity); and expression of antioxidant defense–related genes (RT-PCR).

## RESULTS




*Levels of oxidative stress markers and antioxidant defense indicators: A) Malondialdehyde; B) Conjugated dienes; C) Protein carbonyl derivatives; D) Ferric Reducing Antioxidant Power; E) Catalase.*




*Effects of ATs on antioxidant defense–related genes: transcription factor NFE2-like bZIP transcription factor 2 (Nrf2), catalase (Cat), superoxide dismutase (Sod1), heme oxygenase 1 (Hmox1), NAD(P)H quinonedehydrogenase 1 (Nqo1)*

*Designations: $p < 0.05$ vs. * Control*

## CONCLUSION

It was found that both the AT mixture and TeA reduced total antioxidant activity and induced oxidative stress, as evidenced by increased levels of its markers: carbonyl derivatives; malondialdehyde, conjugated dienes, and protein decreased activity of antioxidant defense enzymes; and altered expression of the corresponding genes. Notably, the AT mixture demonstrated more pronounced effects.

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