Fomes fomentarius (L.) Fr. 1849: natural antioxidant and novel inhibitor of aldo-keto reductase activity

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INTRODUCTION

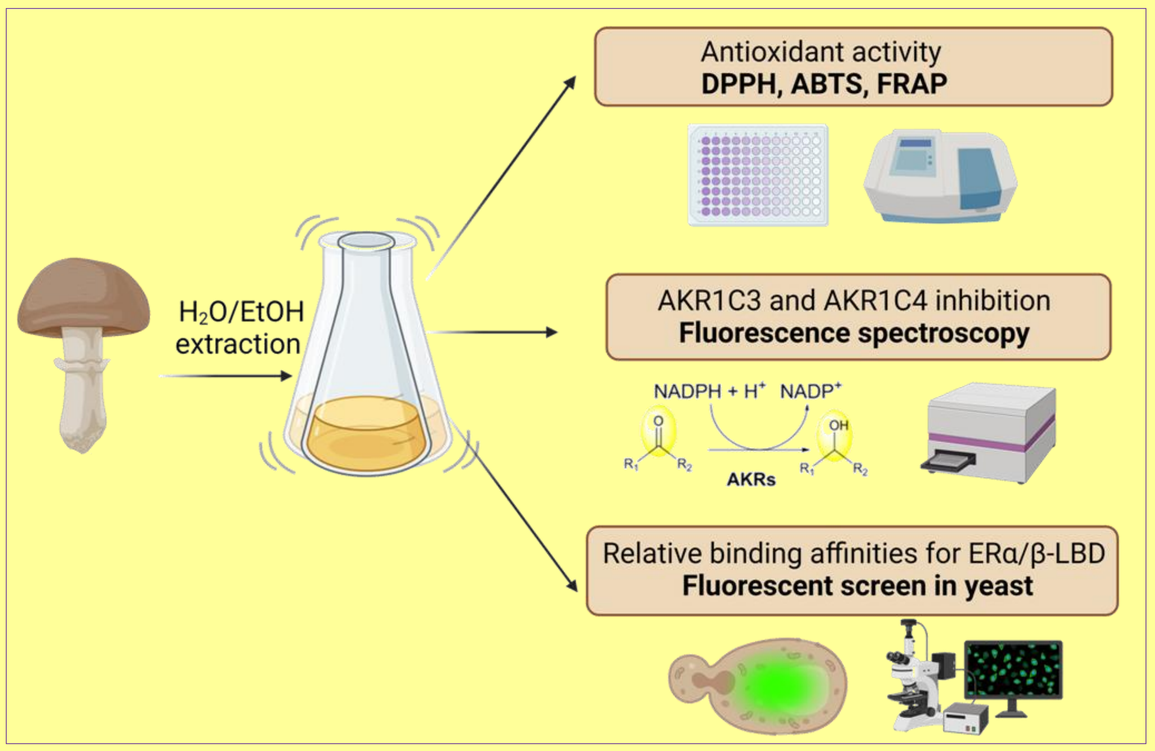
Fungi have received much attention as a source of bioactive compounds with variety of therapeutic properties such as antioxidant, antibacterial, antiviral, antiparasitic and anticancer activities. With great biomedical potential, these pharmacologically-active natural products tend to replace the currently used synthetic drugs.

Figure 1. *Fomes fomentarius*. Photo credit by Yusufjon Gafforov.

AIM

The objective of this study was to evaluate the antioxidant potential, aldo-keto reductase (AKR) inhibition, and estrogen receptor binding affinity of two different extract types (70% ethanolic and hot water) derived from one indigenous fungal species, *Fomes fomentarius* sampled from Uzbekistan (**Figure 1**). Evaluation of antioxidant activity in the tested fungal extracts was conducted using established *in vitro* assays, including ABTS, DPPH, and FRAP. Fungal extracts were tested *in vitro* for binding affinity to ligand-binding domains of estrogen receptor α and estrogen receptor β using fluorescent screen in yeast and their potential to inhibit aldo-keto reductases, valuable targets for the treatment of hormone-dependent diseases.

MATERIALS AND METHODS



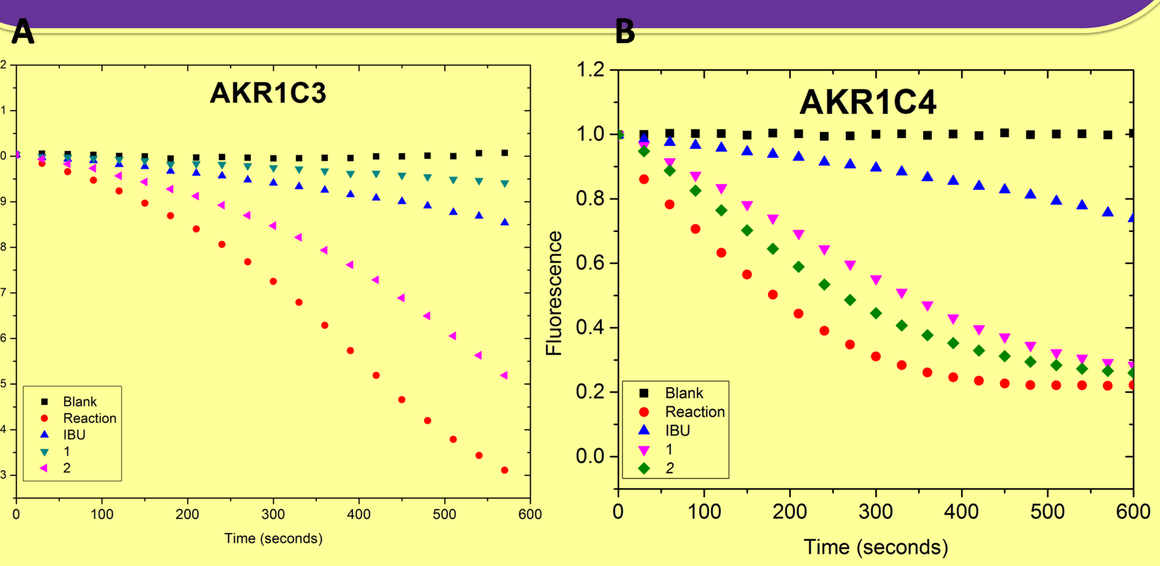


Figure 3. Evaluation of inhibitory activity of fungal extracts 1 (*F. fomentarius* 70% EtOH extract) and 2 (*F. fomentarius* H_2O extract) against AKR1C3 (**A**) and AKR1C4 (**B**) by fluorimetric NADPH consumption assay. AKR1C reduction of 9,10-phenanthrenequinone *in vitro* in the absence of inhibitor (Reaction) and inhibition by ibuprofen (IBU) and tested fungal extracts. Blank represents control-change in NADPH fluorescence intensity during time in the absence of enzyme.

Table 1. Antioxidant activity of tested *F. fomentarius* extracts.

Assay	*F. fomentarius* 70% EtOH 1	*F. fomentarius* H_2O 2
ABTS (mmol TEAC/g d.w.)	124.24 ± 1.43	71 .36± 1.27
DPPH (mmol TEAC/g d.w.)	12.11 ± 0.38	3.11 ± 0.01
FRAP (mmol TEAC/g d.w.)	350.52 ± 2.93	42.44 ± 2.12

RESULTS AND DISCUSSION

The results revealed that the highest scavenging activity and reducing power potential was observed for the analyzed 70% EtOH extract (DPPH: 12.11 mmol TEAC/g d.w., ABTS: 124.24 mmol TEAC/g d.w. and FRAP: 350.52 mmol TEAC/g d.w.). Similarly, the 70% EtOH extract of *F. fomentarius* exhibited higher inhibition potential against AKR1C3 (91.9%) than the hot water extract (35.7%) (**Figure 3**). These fungal extracts showed weak inhibition against AKR1C4 isoform and no estrogenicity (**Figure 3** and **4**), making them promising candidates for the design of anticancer therapeutics against estrogen-dependent breast cancer.

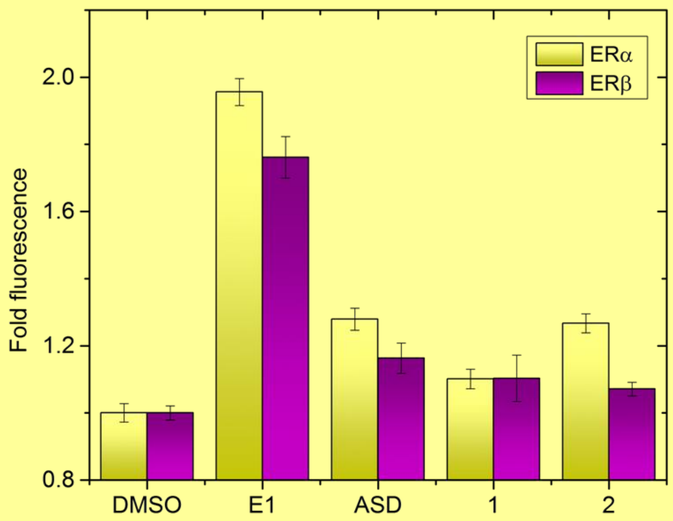


Figure 4. Relative binding affinities of fungal extracts 1 (*F. fomentarius* 70% EtOH extract), and 2 (*F. fomentarius* H_2O extract) for ERα-LBD and ERβ-LBD. DMSO-control in the absence of ligand; E1-estrone, positive control ligand; ASD- androstenedione, negative control ligand.

CONCLUSION

In summary, our research underscores the encouraging prospects of *F. fomentarius* extracts as a foundation for further investigation in the quest for new, naturally-derived anticancer drugs.

ACKNOWLEDGEMENT

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