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•Exploring Terrestrial and Marine Fungi for New Anticancer Agents from Saudi Arabia's Ecosystem

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INTRODUCTION & AIM

Cancer remains a leading cause of death worldwide, and despite major advances in therapy, drug resistance and toxicity remain major challenges. The search for safer and more effective treatments has renewed global interest in natural products as sources of new anticancer agents.

Fungi are particularly promising due to their ability to produce diverse bioactive secondary metabolites with cytotoxic, antioxidant, and apoptosis-inducing properties. Many fungal metabolites also show potential for enhancing the effects of existing therapies and reducing side effects.

Saudi Arabia's unique terrestrial and marine ecosystems — from deserts and caves to coastal marine environments — offer a rich and largely unexplored source of fungi. Exploring these environments may lead to the discovery of novel fungal species and metabolites with potent anticancer properties.

Aim

To explore terrestrial and marine fungi from Saudi Arabia's ecosystems as potential sources of new anticancer agents.

Specific objectives:
Isolate fungi from soil, plants, and marine samples collected across diverse Saudi regions.
Screen fungal extracts for antifungal and anticancer activities using Candida albicans, breast (MDA-MB-231), and colon (HCT116) cancer cell lines.
Identify and characterize bioactive compounds responsible for cytotoxic effects.
Use in-silico analysis to predict mechanisms of action, drug-likeness, and safety profiles.

METHOD

Sample Collection
•Terrestrial sources: Soil and plant samples were collected from Wadi Hanifa, Heat and Burma caves, and Al-Thumama desert (Riyadh region).
•Marine sources: Seagrass, sponges, and algae were collected from the Red Sea (Jeddah) and the Arabian Gulf (Eastern Province).
•Samples were stored in sterile containers and transported in ice boxes (4–10 °C) for further processing.

Fungal Isolation and Identification
•Fungi were isolated using dilution and soil-plate methods on Potato Dextrose Agar (PDA) and Sabouraud Dextrose Agar.
•Plates were incubated at 28 °C for 7 days, and distinct colonies were purified by sub-culturing.
•Colony morphology (color, shape, hyphae) was used for preliminary identification.

DNA Extraction and Molecular Analysis
•Genomic DNA was extracted using the InstaGene method.
•PCR amplification and sequencing were used for fungal identification.

Extraction of Bioactive Compounds
•Identified fungi were cultivated on a large scale to produce metabolites.
•Metabolites were extracted using solvent extraction and analyzed using chromatography and mass spectrometry.

Bioactivity Screening
•Antifungal assay: Tested against Candida albicans using inhibition zone measurement.
•Anticancer assay: Cytotoxicity evaluated against MDA-MB-231 (breast) and HCT116 (colon) cancer cell lines using the MTT assay.
•Isolates with $IC_{50} \leq 200$ µg/mL were considered active.

Mechanistic and In-Silico Studies
•Active metabolites were assessed for apoptosis induction using flow cytometry.
•Molecular docking and ADME-Tox analyses were conducted to predict interactions, pharmacokinetics, and safety profiles.

Data Analysis
•Data were analyzed using GraphPad Prism 10.
•Results expressed as mean ± SD from triplicates; statistical significance set at $p < 0.05$.

RESULTS & DISCUSSION

Antifungal Activity Against Candida albicans

Nine of the 17 fungal isolates exhibited measurable inhibition zones against Candida albicans, ranging from 1.18 mm to 1.51 mm. The remaining eight isolates showed no detectable antifungal activity under the test conditions.

Anticancer Activity

- MDA-MB-231 (Breast Cancer): All 17 isolates demonstrated cytotoxic activity as demonstrated in table 2. This uniform activity highlights the potential of these fungi in developing anti-breast cancer agents.

Efficacy of extracted samples on breast cancer cells MDA-MB-231

Extract	IC_{50} (ug/ml)	Extract	IC_{50} (ug/ml)
S4	28.55	S601	163.8
L3	33.46	S11P	172.5
F4	40	S11G	176.9
S12	71.89	F5	245.5
S6	83.35	F2	247.1
S2	102.5	F10	320.8
S101	105.8	S13	330.8
S7	111.2	S9	571.3

(Table 1 summarises the cytotoxicity of the samples against MDA-MB231 cell lines)

- HCT116 (Colon Cancer): Approximately 8 out of 17 isolates showed cytotoxic effects as shown in table 3. These were considered active based on defined IC50 thresholds.

Efficacy of extracted samples on colon cancer cells HCT116

Extract	IC_{50} (ug/ml)	Extract	IC_{50} (ug/ml)
S12	22.25	F4	No activity
F2	55.33	S6	No activity
S14	71.63	S101	No activity
S2	250.6	S601	No activity
S11P	383.1	F5	No activity
S11G	1678	F10	No activity
S7	No activity	S13	No activity
S4	No activity	S9	No activity
L3	No activity		

(Table 2 summarises the cytotoxicity of the samples against HCT116 cell lines)

- Overlap and Selectivity: Several isolates displayed dual cytotoxicity, while others showed selectivity for breast or colon cancer lines. The remaining isolates were inactive against HCT116 but still active against breast cancer cells.

Discussion

This study successfully demonstrated the anticancer and antifungal potential of fungal isolates from Saudi Arabia's terrestrial and marine ecosystems. All isolates showed activity against breast cancer cells, and about half were active against colon cancer cells. Several also inhibited Candida albicans. These results confirm that Saudi fungi represent an untapped source of bioactive metabolites with strong potential for developing new anticancer agents. Further purification and molecular characterization of active compounds are essential to advance them toward future drug discovery.

CONCLUSION

Fungal isolates from Saudi Arabia's terrestrial and marine environments exhibited significant anticancer and antifungal activity, with all showing cytotoxicity against breast cancer cells and about half active against colon cancer cells.
These findings highlight the rich potential of Saudi ecosystems as sources of novel bioactive metabolites. Continued characterization of these fungal compounds could lead to the development of new, effective anticancer drugs derived from natural sources.

FUTURE WORK / REFERENCES

•Purification and structure elucidation of the most active fungal metabolites using advanced spectroscopic and chromatographic techniques.
•Mechanistic studies to determine molecular targets and pathways involved in the observed anticancer activity.
•In vivo evaluation of selected compounds to assess efficacy, toxicity, and pharmacokinetic profiles.
•Genome mining and metabolomics to identify biosynthetic gene clusters responsible for metabolite production.