Biotransformation of Formestane by *Rhizopus Oryzae*

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Introduction

Formestane is a steroidal aromatase inhibitor that is used in the treatment of breast and ovarian cancers in postmenopausal women. It suppresses the production of estrogen by inhibiting the aromatase enzyme that converts androgens into estrogens.[1] Despite these advances in the development of aromatase inhibitors there are still growing concerns of major side effects and possibly cellular resistance to these drugs over time. The search for better aromatase inhibitors with fewer side effects have led to the synthesis of other compounds.[2-4] In our ongoing search for new chemical agents for the treatment of breast cancer, analogs of formestane were prepared by microbial means.

Experimental

Formestane was incubated with the microbial cultures of *Rhizopus oryzae* ATCC 11145. The extract of fermentation was purified on a silica gel column. ^{1}H, ^{13}C, and 2D NMR spectra for the formestane analogs were recorded on a Bruker Avance 500 Console with 5 mm TXI probe and Bruker Avance II 600 MHz NMR spectrometer equipped with NHMF Lab's 1 mm triple-resonance high-temperature superconducting (HTS) cryogenic probe. Formestane and its analogs will be tested for cytotoxic and aromatase effects at the University of Hawaii at Hilo.

Results and Discussion

Incubation of the steroid formestane with the fungus *R. oryzae* has resulted in the formation of three metabolites. Structure elucidation utilizing 1 & 2D NMR and mass spectrometry data has confirmed the identities of two metabolites with one pending further analysis. The potential of formestane and its analogs as aromatase inhibitors and cytotoxic agents is presently in progress.

Conclusions

The biotransformation of formestane has produced new analogs with potential biological activities. In addition, the NHMFL 1 mm HTS probe is ideal for the analysis of sample-limited natural products.

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References

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