Synthesis and Investigation into the estrogen receptor antagonist activity of isoflavans and their synthetic derivatives

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Abstract

Background

Breast cancer (BC) is the most invasive and prevalent cancer in women in South Africa, with numbers as high as 1 in 8 women in urban areas and with a large percentage being ER-positive (ER+). ER+ BC cells are reliant on the binding of the natural ligand 17β-estradiol (E2) to ERα and ERβ isoforms which drives tumor growth[1]. ER antagonists and inhibitors of estrogen synthesis are therefore widely used therapeutic agents in the treatment of BC. Isoflavans are natural products found in many dietary plants. They are phytoestrogens, able to act as natural anti-breast cancer agents, acting as ER antagonists [3].

Method

The aim of the study is to investigate the ER antagonist activity of natural isoflavans and their synthetic derivatives. We are synthesizing a small library of non-natural isoflavans which have different substituents at the 4'-position of the isoflavan ring. The synthesis makes use of a [4+2] cycloaddition reaction between an o-quinone methide and the aryl-substituted enol ether based on a method by Gharpure et al[2]. The synthesized compounds will be tested using a luciferase reporter assay to establish if they have antagonist activity in CV1 cells expressing the ER.

Results

Results pending

Conclusion

In this project, we aim to develop new chemistry for isoflavans and to establish isoflavan structure-activity relationships. The results of the study may aid in the future design of more potent ER receptor antagonists for breast cancer therapy.

References

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