Design, Synthesis and Biological Evaluation of Novel Chalcone Analogs as Potential Therapeutic Agents for Prostate Cancer

Ola Hussein1, Feras Alali1, Ala-Eddin Al Mustafa2,3, Ashraf Khalil1

1College of Pharmacy, 2College of Medicine and 3Biomedical Research Center, QU Health, Qatar University, Doha, Qatar

Background

- Prostate cancer (PCa) is the second most frequently diagnosed malignancy and a leading cause of cancer-related mortality in men globally.
- Despite the initial improvement to hormone targeted therapy, most patients ultimately develop resistance.
- Castration resistant prostate cancer is associated with poor prognosis and available therapies cannot prolong survival for more than 5 months.
- Chalcones (C6-C3-C6) are highly attractive scaffolds that possess a wide variety of biological activities.

Objectives

1. Design, synthesize and elucidate the structure of novel tetralone-based chalcones.
2. Evaluate their in-vitro anticancer activity and in-ovo antiangiogenic effect.

Methods

Synthesis of novel Chalcones (Using Claisen-Schmidt condensation reaction)

Chemical purification (column chromatography or recrystallization)

Structure Elucidation (1H and 13C NMR and LC/MS)

Results - Biological Activity

A) PC3 cell viability (48h)

B) Effect of OH14 on Cell Morphology

Figure 3: Effect of the compounds on cell viability of PC3 (A) and cell morphology of PCa cell lines (D). Values are expressed as mean ± SEM (n=2x4).*P < 0.01, **P < 0.001 vs. control.

Figure 4: Effect of compounds OH19 and OH22 on apoptosis

Figure 5: Effect of OH14 and OH19 on apoptosis related proteins in PC3

Figure 6: Effect of compound OH19 on soft agar colony formation

Results - Chemistry

Conclusion

- Twenty novel tetralone-based chalcones were designed and synthesized.
- Compounds OH14, OH19 and OH22 showed potent antiproliferative activities at low micromolar levels with IC50 values ranging between 4.4 and 10 µM against PC3 and DU145 cell lines.
- Compound OH19 significantly inhibited colony formation, migration and angiogenesis and induced apoptosis.
- These results indicate that OH19 could serve a potential promising lead molecule for the treatment of PCa and thus, further in-vitro and in-vivo testing is warranted.

Legend

* * * * *