

Accepted Manuscript

A new class of flavonol-based anti-prostate cancer agents: design, synthesis, and evaluation in cell models

Xiang Li, Guanglin Chen, Xiaojie Zhang, Qiang Zhang, Shilong Zheng, Guangdi Wang, Qiao-Hong Chen

PII: S0960-894X(16)30776-4
DOI: <http://dx.doi.org/10.1016/j.bmcl.2016.07.050>
Reference: BMCL 24094

To appear in: *Bioorganic & Medicinal Chemistry Letters*

Received Date: 1 June 2016
Revised Date: 20 July 2016
Accepted Date: 21 July 2016

Please cite this article as: Li, X., Chen, G., Zhang, X., Zhang, Q., Zheng, S., Wang, G., Chen, Q-H., A new class of flavonol-based anti-prostate cancer agents: design, synthesis, and evaluation in cell models, *Bioorganic & Medicinal Chemistry Letters* (2016), doi: <http://dx.doi.org/10.1016/j.bmcl.2016.07.050>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



A new class of flavonol-based anti-prostate cancer agents: design, synthesis, and evaluation in cell models

Xiang Li^a, Guanglin Chen^a, Xiaojie Zhang^a, Qiang Zhang^b, Shilong Zheng^b,

Guangdi Wang^{b,c}, Qiao-Hong Chen^{a,*}

^a Department of Chemistry, California State University, Fresno, 2555 E. San Ramon Avenue, M/S SB70, Fresno, CA 93740, USA.

^bRCMI Cancer Research Center, Xavier University of Louisiana, 1 Drexel Drive, New Orleans, LA 70125, USA

^cDepartment of Chemistry, Xavier University of Louisiana, 1 Drexel Drive, New Orleans, LA 70125, USA

Abstract — Flavonoids are a large class of polyphenolic compounds ubiquitously distributed in dietary plants with an array of biological activities. Flavonols are a major sub-class of flavonoids featuring a hydroxyl group at C-3. Certain natural flavonols, such as quercetin and fisetin, have been shown by *in vitro* cell-based and *in vivo* animal experiments to be potential anti-prostate cancer agents. However, the Achilles' heel of flavonols as drug candidates is their moderate potency and poor pharmacokinetic profiles. This study aims to explore the substitution effect of 3-OH in flavonols on the *in vitro* anti-proliferative potency against both androgen-sensitive and androgen-insensitive human prostate cancer cell lines. Our first lead flavonol (3',4'-dimethoxyflavonol), eight 3-O-alkyl-3',4'-dimethoxyflavonols, and six 3-O-aminoalkyl-3',4'-dimethoxyflavonols have been synthesized through aldol condensation and the Algar-Flynn-Oyamada (AFO) reaction. The WST-1 cell proliferation assay indicates i) that all synthesized 3-O-alkyl-3',4'-dimethoxyflavonols and 3-O-aminoalkyl-3',4'-dimethoxyflavonols are more potent than the parent 3',4'-dimethoxyflavonol and the natural flavonol quercetin in suppressing prostate cancer cell proliferation; and ii) that incorporation of a dibutylamino group to the 3-OH group through a three- to five-carbon linker leads to the optimal derivatives with up to 292-fold enhanced potency as compared with the parent flavonol. Flow cytometry analysis showed

Download English Version:

<https://daneshyari.com/en/article/10592195>

Download Persian Version:

<https://daneshyari.com/article/10592195>

[Daneshyari.com](https://daneshyari.com)