

Accepted Manuscript

Arylureas derived from colchicine: Enhancement of colchicine oncogene downregulation activity

Víctor Blasco, Ana C. Cuñat, Juan F. Sanz-Cervera, J. Alberto Marco, Eva Falomir, Juan Murga, Miguel Carda



PII: S0223-5234(18)30282-4

DOI: [10.1016/j.ejmech.2018.03.039](https://doi.org/10.1016/j.ejmech.2018.03.039)

Reference: EJMECH 10304

To appear in: *European Journal of Medicinal Chemistry*

Received Date: 17 January 2018

Revised Date: 1 March 2018

Accepted Date: 13 March 2018

Please cite this article as: Ví. Blasco, A.C. Cuñat, J.F. Sanz-Cervera, J.A. Marco, E. Falomir, J. Murga, M. Carda, Arylureas derived from colchicine: Enhancement of colchicine oncogene downregulation activity, *European Journal of Medicinal Chemistry* (2018), doi: 10.1016/j.ejmech.2018.03.039.

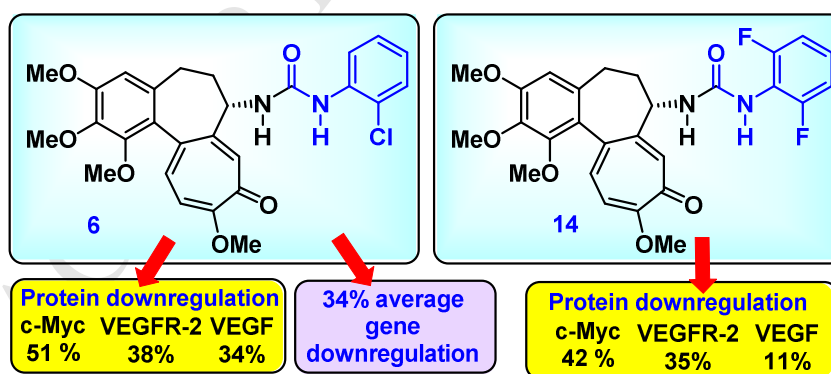
This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please 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.

Arylureas derived from colchicine: Enhancement of colchicine oncogene downregulation activity

Víctor Blasco, Ana C. Cuñat, Juan F. Sanz-Cervera, J. Alberto Marco, Eva Falomir, Juan Murga and Miguel Carda

Graphical Abstract

Twenty-seven *N,N'*-disubstituted ureas containing a colchicine moiety and an aryl fragment have been synthesized and biologically evaluated. The cytotoxicity of the compounds, their ability to inhibit the expression of oncogenes related to telomerase activation and to the VEGF/VEGFR-2 autocrine process, such as *c-MYC*, *hTERT* and *VEGF* and their capability to downregulate *c-MYC* and VEGFR-2 proteins and the secretion of VEGF have been measured. In these biological evaluations, we have found that the change of the acetyl group in colchicines for an *N*-arylurea unit causes a great improvement in anticancer properties. The most promising derivatives were compounds **6** (*o*-Cl) and **14** (*o,o*-di-F) as they were able to downregulate all the tested targets at a concentration below their IC₅₀ values. Thus, the arylurea unit enhances the potential of colchicine as an anticancer agent.



Download English Version:

<https://daneshyari.com/en/article/7796639>

Download Persian Version:

<https://daneshyari.com/article/7796639>

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