

## Design, synthesis and biological evaluation of novel chalcone derivatives as potential microtubule targeting agents

Tomasz Stefański,<sup>a</sup> Rafał Kurczab,<sup>b</sup> Zbigniew Dutkiewicz,<sup>c</sup> Renata Mikstacka,<sup>d</sup>  
Artur Korzański,<sup>a</sup> Violetta Krajka-Kuźniak,<sup>e</sup> Katarzyna Papierska,<sup>e</sup> Mariusz Kaczmarek,<sup>f</sup>  
Anna Teubert,<sup>g</sup> Adam Hogendorf,<sup>b</sup> Maciej Kubicki<sup>a</sup>

<sup>a</sup>Department of Crystallography, Faculty of Chemistry, Adam Mickiewicz University,  
Umultowska 89B, 61-614 Poznań, Poland

<sup>b</sup>Department of Medicinal Chemistry, Institute of Pharmacology, Polish Academy of  
Sciences, Smętna 12, 31-343 Kraków, Poland

<sup>c</sup>Department of Chemical Technology of Drugs, Faculty of Pharmacy, Poznan University of  
Medical Sciences, Grunwaldzka 6, 60-780 Poznań, Poland

<sup>d</sup>Department of Inorganic and Analytical Chemistry, Collegium Medicum in Bydgoszcz,  
Nicolaus Copernicus University in Toruń, Jurasza 2, 85-089 Bydgoszcz, Poland

<sup>e</sup>Department of Pharmaceutical Biochemistry, Poznan University of Medical Sciences,  
Święcickiego 4, 60-781 Poznań, Poland

<sup>f</sup>Department of Immunology, Poznan University of Medical Sciences, Rokietnicka 5D,  
60-806 Poznań, Poland

<sup>g</sup>Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14,  
61-704 Poznań, Poland

*e-mail: tomasz.stefanski@amu.edu.pl*

The microtubular system with its dynamic nature characterized by the polymerization and depolymerization of  $\alpha,\beta$ -tubulin heterodimers, is essential in a variety of cellular processes, including maintenance of cell shape, regulation of motility and cell division [1]. Because of the latter function microtubules are one of the significant and more successful molecular target for designing of new active molecules possessing anticancer activity. Among this group of compounds chalcones (1,3-diphenylprop-2-en-1-on derivatives) represent a promising class of compounds with a simple structure, taking the possibility of extensive structural modifications that improve their natural anticancer properties.

Their mechanism of action including the inhibition of tubulin assembly by binding to the colchicine binding domain resulting from their structural similarity to other active ligands that have the same molecular target (e.g. combretastatin A-4, CA-4). Our successful investigation on novel potent inhibitors of tubulin polymerization from group of CA-4 thioderivatives [2] prompted us to extend our research on chalcone scaffold.

Herein we present synthesis, molecular modelling studies, X-ray structural characteristics and biological evaluation of novel chalcone thioderivatives. Their antiproliferative activity was determined using panel of human cancer and normal cell lines, tubulin inhibition, and cell cycle analyses.

[1] Mikstacka, R. et al. *Cell. Mol. Biol. Lett.* 2013, 18, 368-397

[2] Stefański, T. et al. *Eur. J. Med. Chem.* 2018, 144, 797-816

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