

Biological evaluation of cytotoxic activity of novel thiopyrano[2,3-d]thiazoles in the MDA-MB-231 breast cancer cells

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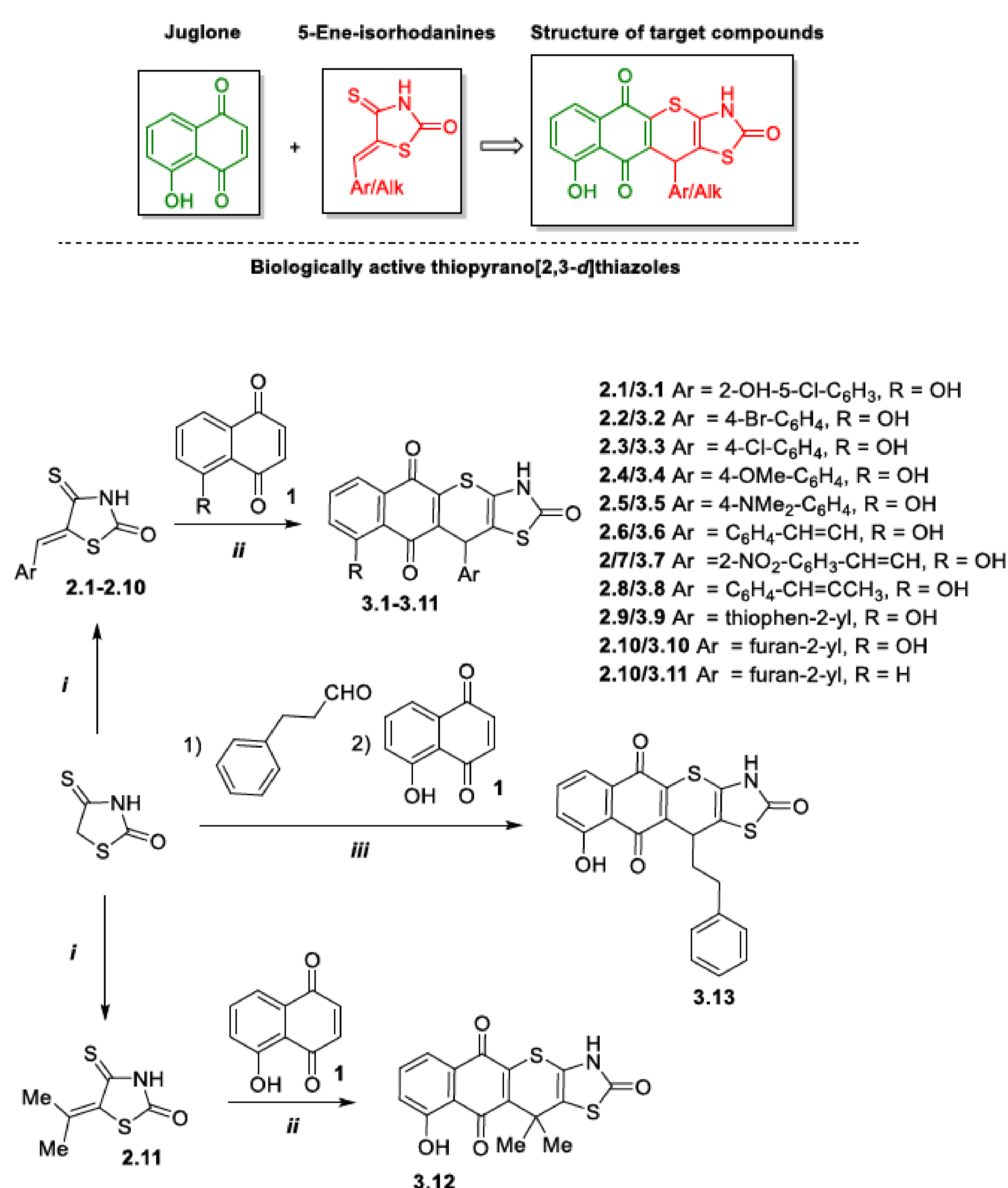
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INTRODUCTION

The goal of our study was the synthesis of condensed hybrid 4-thiazolidinone derivatives, namely thiopyrano[2,3-d]thiazoles with the juglone fragment in structure via the hetero-Diels-Alder reaction. Based on our previous studies of thiopyranothiazoles with a naphthoquinone moiety, we synthesized new derivatives via a hetero-Diels-Alder reaction of the juglone (5-hydroxy-1,4-naphthoquinone) as dienophile and 5-ene-4-thioxo-2-thiazolidinones **2**, as heterodienes (Figure 1). Analytical and spectral data (1H and 13C-NMR, LCMS) confirmed the structure of the synthesized compounds [1].

RESULTS



Scheme 1. Synthesis of target thiopyranothiazoles with a naphthoquinone moiety. Reagents and conditions: i) 4-thioxo-2-thiazolidinone (isorhodanine) (10 mmol), aldehyde or ketone (11 mmol), EDDA (5 μmol), EtOH (10 ml), reflux, 10 min, 70–90%; ii) 5-ene-4-thioxo-2-thiazolidinone (10 mmol), 1,4-naphthoquinone or 5-hydroxy-1,4-naphthoquinone (20 mmol), hydroquinone (5 μmol), AcOH (10 ml), reflux, 1 h, 62–79%; iii) isorhodanine (5.0 mmol), phenylpropionaldehyde (5.5 mmol), 5-hydroxy-1,4-naphthoquinone (10 mmol), EDDA (5.0 μmol), MeCN (10 ml), reflux, 2 h, 65%.

[1] Iryna Ivasechko et al. Molecular design, synthesis and anticancer activity of new thiopyrano [2,3-d]thiazoles based on 5-hydroxy-1,4-naphthoquinone (juglone). Eur. J. Med. Chem. 252 (2023) 115304 <https://doi.org/10.1016/j.ejmech.2023.115304>

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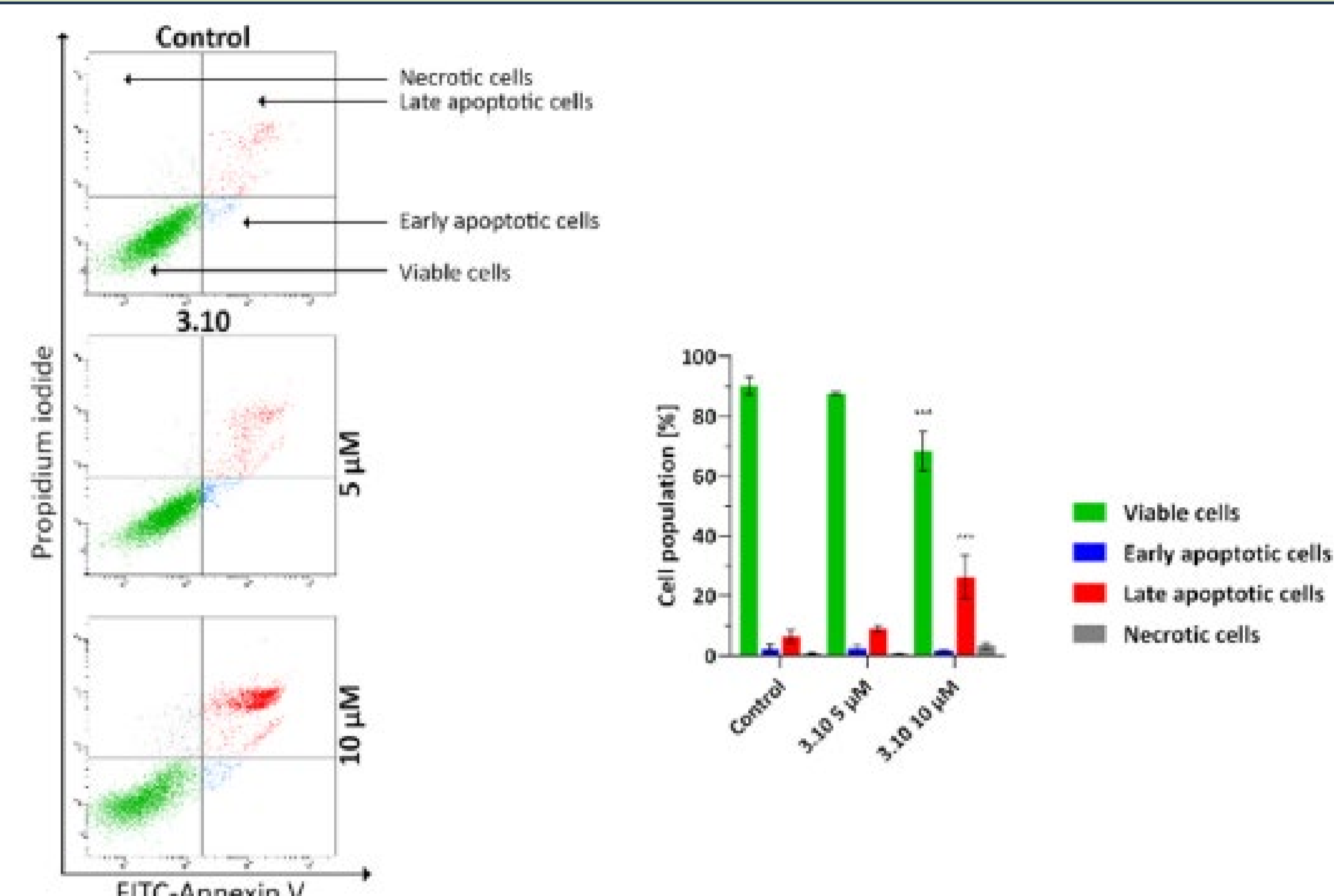


Fig. 1. Results of flow cytometry analysis of MDA-MB-231 breast cancer cells after 24 h incubation with **3.10** (concentration 5 μM and 10 μM) and subsequent staining of cells with Annexin V and propidium iodide. The obtained results are presented as mean values ± SD obtained from three independent experiments (n = 3) done in duplicate. *p < 0.05 vs. control group, ***p < 0.001 vs. control group.

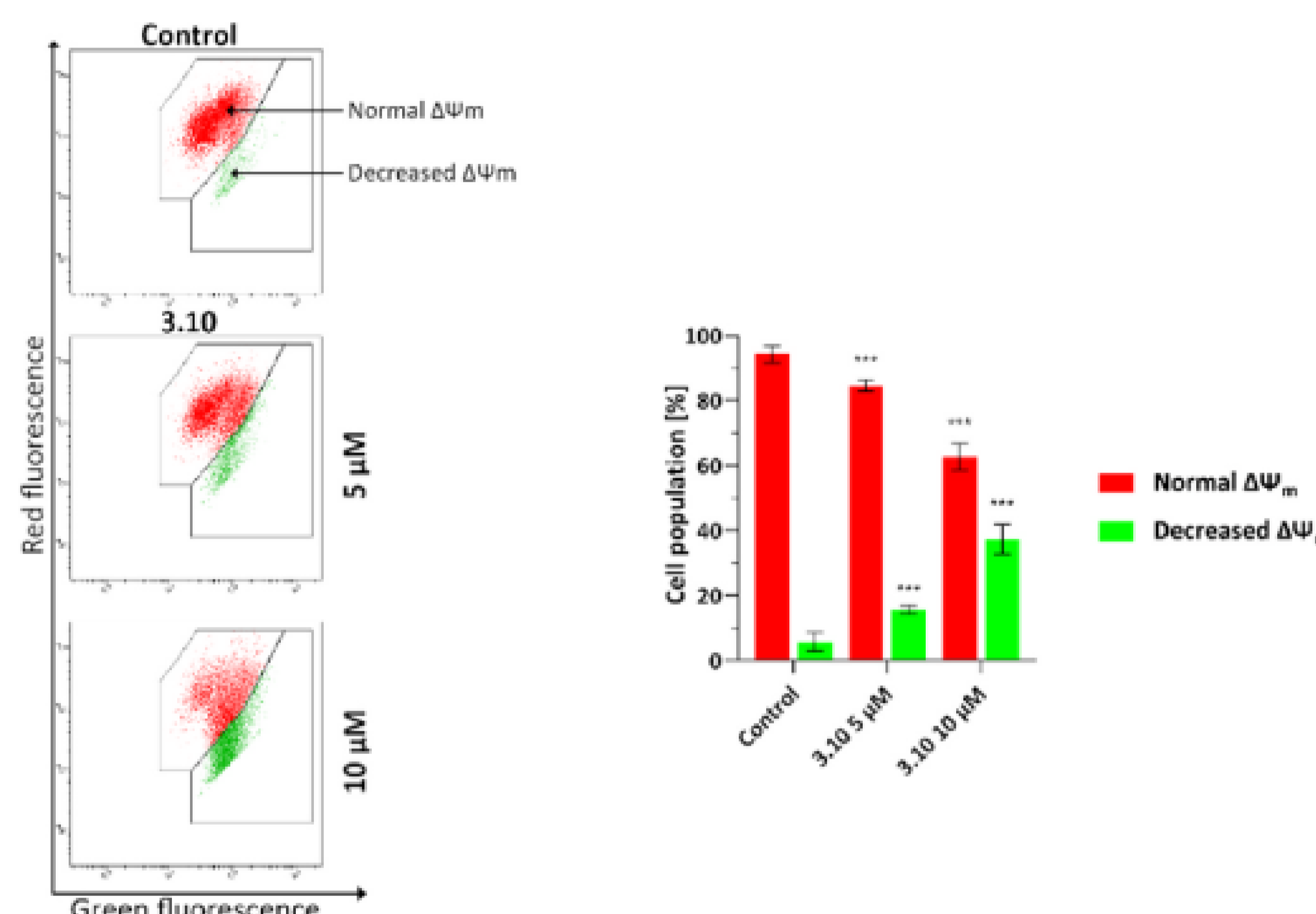


Fig. 2. Results of flow cytometry measurement of changes in the mitochondrial membrane potential ($\Delta\Psi_m$) in MDA-MB-231 breast cancer cells after 24 h treatment with **3.10** (concentration 5 μM and 10 μM). The obtained results are presented as mean values ± SD obtained from three independent experiments (n = 3) done in duplicate. ***p < 0.001 vs. control group.

CONCLUSIONS

1. According to the results of pre-screening, new thiopyrano[2,3-d]thiazoles possessed prominent antitumor activity and showed not only cytostatic effect but also cytotoxic properties.
2. We also investigated the effect of the more active compound **3.10** on the mitochondrial membrane potential ($\Delta\Psi_m$) in MDA-MB-231 cells. The tested compound **3.10** caused an increase in the percentage of cells with decreased $\Delta\Psi_m$ in the MDA-MB-231 breast cancer cell lines. It was also shown that this compound induced apoptosis in MDA-MB-231 cells, both through the extrinsic and intrinsic pathways.