

4th Symposium of Young Researchers on Pharmacognosy

# BOOK OF ABSTRACTS

(ed. Judit Hohmann)

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## 7 – SHORT LECTURE

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## Thymoquinone-protoflavone hybrids: Studies into anticancer potentials

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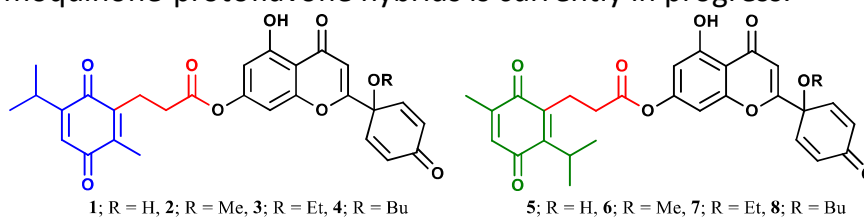
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Cancer represents the second leading cause of death worldwide [1]. Among its types; breast and cervical cancer are classified among the leading causes of death among women [2], another very common and aggressive tumour type is glioblastoma multiforme [3].

Protoapigenone; a rare flavonoid from *Thelypteris torresiana* Gaud., and its semisynthetic protoflavone derivatives demonstrated promising activity against multiple cancer cell lines. Thymoquinone; a monoterpene from the seeds of *Nigella sativa* L., is another molecule described as a promising lead for cancer therapy, acting through multiple mechanisms of action [4–7].

Our work aimed to combine these two compounds into potentially antitumour hybrid molecules. Eight ester-coupled hybrids were prepared and tested on a cancer cell line panel in comparison with their fragments alone and in combination. Among the new hybrids, compound **5** showed the most promising result against HeLa, MDA-MD-231, MCF-7, and U87 cell lines with IC<sub>50</sub> values of 1.06, 0.52, 1.2, and 1.16, respectively. Compound **5** was more potent than the combination of its thymoquinone and protoflavone fragments and the positive controls (17.05, 20.65, and 5.78 μM for cisplatin against MDA-MB-231, HeLa and MCF-7 cell lines, respectively, and 388.2 μM for temozolomide against U87 cell line). Kinetic studies on the ester-coupled hybrids showed their susceptibility to hydrolysis. To overcome this problem, the synthesis of more stable thymoquinone-protoflavone hybrids is currently in progress.



### References

- [1] WHO. Cancer. **2022**; Available from: [https://www.who.int/health-topics/cancer#tab=tab\\_1](https://www.who.int/health-topics/cancer#tab=tab_1); [2] Giaquinto, AN, et al. *CA Cancer J Clin* **2022**, 72(6):524–541. doi: 10.3322/caac.21754; [3] Taylor, OG, et al. *Front Oncol* **2019**, 9:963. doi: 10.3389/fonc.2019.00963; [4] Homayoonfal, M, et al. *Cell Mol Biol Lett* **2021**, 26:43. doi: 10.1186/s11658-021-00286-5; [5] Homayoonfal, M, et al. *Cell Mol Biol Lett* **2022**, 27:21. doi: 10.1186/s11658-022-00320-0; [6] Karim, S, et al. *Int J Mol Sci* **2022**, 23(4):2305. doi: 10.3390/ijms23042305; [7] Al-Rawashde, FA, et al. *Asian Pac J Cancer Prev* **2021**, 22(12):3959–3965. doi: 10.31557/APJCP.2021.22.12.3959

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