Heterocyclic chalcone derivatives: Synthesis and biological activity evaluation

C. Machado 1,4, P. Pinto 2, P. Silva 3,5, D. Almeida 3, J. Moreira 1,6, M. Pinto 1,2,3, H. Bousbaa 5,6, H. Cidade 1,6

1 Laboratório de Química Orgânica e Farmacêutica, Departamento de Ciências Químicas, Faculdade de Farmácia, Universidade do Porto, Portugal
2 Laboratório de Química Farmacêutica, Faculdade de Farmácia, Universidade de Coimbra, Portugal
3 Center for Biomedical Research, CBMR, University of Algarve, Faro 8005-139, Portugal
4 Departamento Ciências Biomédicas e Medicina, University of Algarve, Faro, Portugal
5 CESP, Instituto de Investigação e Formação Avançada em Ciências e Tecnologias da Saúde, IINFACS, 4585-116 Gandra PRD, Portugal
6 Centro Interdisciplinar de Investigação Marinha e Ambiental (CIMAR/CIMAR), Universidade do Porto, Portugal

E-mail address: ccmmariana3@hotmail.com
(C. Machado).


Introduction: Natural chalcones have been intensively studied for their wide range of biological activities, namely antitumor. 1 Possessing two electrophilic reactive centers at α,β-unsaturated ketone group, chalcone derivatives can participate in addition reactions leading to the synthesis of promising bioactive compounds with a more rigid structure, like isoxazoles and pyrazoles. 2

Methods: Chalcones were synthesized by base catalysed Claisen Schmidt condensation via microwave assisted organic synthesis (MAOS). The antiproliferative activity was assessed using sulforhodamine B assay. 3

Results: Seventeen chalcone derivatives were synthesized and identified as having in vitro growth inhibitory activity on three human tumor cell lines from breast, lung and melanoma (MCF-7, NCI-H460, and A375–C5).

Conclusion: Most of the synthesized chalcones revealed to be promising growth inhibitors of human tumor cell lines. The molecular mechanisms involved in their antiproliferative effect are being evaluated.

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References

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A posttranslational modification in histones as prognostic/predictive marker in Estrogen-Positive Breast Cancer

S. Lobo 1,2,∗, M. Fontes-Sousa 2,3, S. Salta 2, P. Lopes 2,4, J. Lobo 2,4, S. Sousa 3, R. Henrique 2,4,5, C. Jerónimo 1,6

1 Faculty of Science – University of Porto (FCUP-UP), Porto, Portugal
2 Cancer Biology and Epigenetics Group, IPO Porto Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO Porto), Porto, Portugal
3 Department of Medical Oncology: Portuguese Oncology Institute of Porto, Portugal
4 Department of Pathology, Portuguese Oncology Institute of Porto, Porto, Portugal
5 Department of Pathology and Molecular Immunology, Institute of Biomedical Sciences Abel Salazar – University of Porto (ICBAS-UP), Porto, Portugal
6 E-mail address: silvana_lobo_sousa@live.com.pt
(S. Lobo).

Aim: This work aims to evaluate H3K27me3 expression in luminal-like breast tumors, using immunohistochemistry assay, to assess the prognostic value of this epigenetic alterations in estrogen positive breast cancer (BrC).

Introduction: BrC is the second most incident cancer worldwide. In Portugal, in 2012, BrC was simultaneously the leading cancer in incidence and mortality in women. 1 Around 70% of all BrC are hormone-receptor positive, that is the major part of breast tumors is luminal-like. 2 H3K27m3 is a gene repression marker 3 and is associated with gene silencing, playing a crucial role in cell proliferation and differentiation. 1 H3K27me3 may have some clinical value in several types of cancer since it can be used as a biomarker. This histone modification has been associated with poor prognosis of some BrC subtypes. 2

Methods: It was used a cohort of BrC patients of the Portuguese Oncology Institution of Porto (IPO-Porto), diagnosed between 1994 and 2002. A total of 102 luminal-like tumor cases were assessed by immunohistochemistry, to H3K27me3 expression. To verify the prognostic value of H3K27me3 levels, Cox regression with a log rank test was performed for both disease-specific and disease-free survival.

Results: Through the result analysis, it was established that only tumor grade (p = 0.021) was significant associated with disease-specific survival. Nevertheless, both luminal subtype (p = 0.016) and H3K27me3 expression (p = 0.012) were significantly associated with disease-free survival. Indeed, H3K27me3 high expression is associated with higher recurrence risk, especially in Luminal A.

Conclusion: We could confirm the prognostic value of H3K27me3 expression in luminal A subtype BrC patients. Therefore, higher H3K27me3 expression in luminal A tumors is associated with a greater probability of recurrence.

However, studies in larger cohorts are mandatory to validate its clinical utility.

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