Preparation of Curcumin Derivatives and Cytotoxic Activity in Human Bladder Cancer Cells

Bruna S. Pacheco[1] (PG), Marina Ritter[1] (TC), Mariana Sonego[2] (PG), Rosiane M. Martins[2] (PG), Chayane Porto[1] (PG), Caroline C. da Silva[1] (IC), Tiago Collares[2] (PQ), Claudio M. P. Pereira[1] (PQ).

[1]*Universidade Federal de Pelotas, Centro de Ciências Químicas, Farmacêuticas e de Alimentos – CCQFA.*
[2]*Universidade Federal de Pelotas, Centro de Desenvolvimento Tecnológico – CDTec.* *** pacheco.sbruna@gmail.com**

Key-words: *curcumin derivatives, bladder cancer.*

Abstract

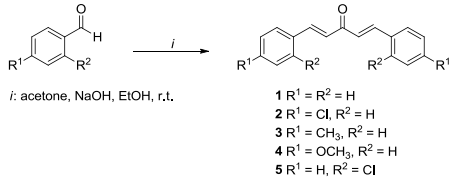
Five curcumin derivatives were synthesized and evaluated by cytotoxic activity in bladder cancer and non-tumor cells.

Introduction

Curcumin is the major constituent extracted from dried rhizomes of *Curcuma longa*, a commonly spice used in traditional Indian medicine (Ayurveda) with various purposes.[1]However, the potential of curcumin as a biomolecule with pharmacological activities is limited by its chemical and metabolic instability and low solubility in water. Because of this, many strategies to improve solubility and availability of curcumin are being established in order to enable the use of this compound, among them, the production of curcumin nanoparticles[2] and synthesis of curcumin derivatives[3] have been proposed to solve these problems. Continuing the work of our group with bioactivity molecules[4], the aims of this study were to synthesize curcumin derivatives and evaluate whether they have cytotoxic effect in human bladder cancer cells.

Results and discussions

Five curcumin derivatives **1-5** were synthesized by the synthetic route shown in Scheme 1.The structure and purity of synthesized curcumin derivatives were analyzed by Gas Chromatography coupled to Mass Spectrometry (GC-MS) and yields ranging from 50% to 90%. Cells were treated with different concentrations (6.25 – 100 μM) of curcumin derivatives for 24 hours. The viability was assessed by measuring the reduction of soluble MTT.



Scheme 1. Synthesis of curcumin derivatives

The less effective compound against 5637 cells was methyl substituted **1**, because this group has a lower electronegativity when compared to other substituents. Compounds **2, 3** and **4** showed similar cytotoxicity, although curcumin derivative with methoxy group showed slight decrease of cytotoxicity. Derivative **5** with substituent chloro in *ortho* position was the most effective in inhibition of 5637 cells (**Figure 1**).

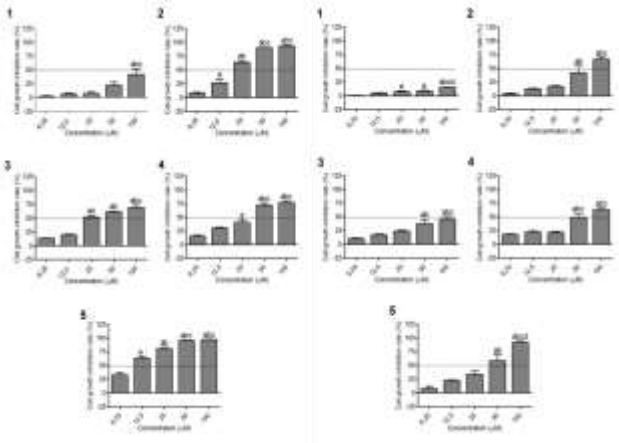


Figure 1. Concentration effect of compounds **1-5** against human bladder cancer cell 5637 (left) and non-tumor CHO (right) in 24 hours.

Conclusions

Data presented indicated that curcumin derivatives are able to induce growth inhibition human bladder cancer cells (5637) and demonstrating the influence of different substituents on aryl rings, although the potential mechanisms of action deserve further research.

Acknowledgments

The authors are grateful to CNPq and CAPES for financial support.

[1]Elias, G.; Jacob, P. J.; Hareeshbabu, E.; Mathew, V. B.; Krishnan, B. and Krishnakumar, K . *International Journal of Pharmaceutical Sciences and Research*. **2015**, *6*, 2671.
[2]Basniwal, R. K.; Buttar, H. S.; Jain, V. e Jain, N. *J. Agr Food Chem*. **2011**, *59*, 2056.
[3]Chittigori, J.; Kumar, A.; Li, L.; Thota, S.; Kokil, A.; Samuelson, L. A.; Sandman, D. J.e Kumar, J. *Tetrahedron.* **2014**, *70*, 991.
[4]Oliveira, S.; Pizzuti, L.; Quina, F.; Flores, A.; Lund, R.; Lencina, C.; Pacheco, B.; Pereira, C.; Piva, E. *Molecules*, **2014**, *19*, 5806.