Proceedings

In Vitro Study of Curcumin Derivatives with Potential Antitumor Activity †

Miruna S. Stan [1,*], Ionela Cristina Nica [2], Cristina Doina Nițu [3,4], Monica Raduly [5], Anca Dinischiotu [1], Avram Speranta [3], Dan Mihailescu [3] and Maria Mernea [3]

[1] Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Bucharest, 91-95 Splaiul Independentei, 050095 Bucharest, Romania; cristina.nica@drd.unibuc.ro (I.C.N.), anca.dinischiotu@bio.unibuc.ro (A.D.)
[2] Research Institute of the University of Bucharest–ICUB, University of Bucharest, 91–95 Splaiul Independentei, 050095 Bucharest, Romania
[3] Department of Anatomy, Animal Physiology and Biophysics, Faculty of Biology, University of Bucharest, Romania; cri_nitu@yahoo.com (C.D.N.), speranta.avram@bio.unibuc.ro (S.A.), dan.mihailescu@bio.unibuc.ro (D.M.), maria.mernea@bio.unibuc.ro (M.M.)
[4] Institute of Oncology "Prof. dr. Al. Trestioreanu", 252 Sos. Fundeni, 022328 Bucharest, Romania
[5] Research and Development National Institute for Chemistry and Petrochemistry – ICECHIM, 060021, Bucharest, Romania; radulymonica@yahoo.com
* Correspondence: miruna.stan@bio.unibuc.ro
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Abstract: Curcumin (diferuloylmethane) represents a polyphenol extracted from the plant *Curcuma longa* which has attracted the attention of scientists for medicinal purposes. In this context, we obtained 5 different derivates of curcumin (D1-D5) in order to test their anti-tumoral effect on human cervix cancer. Their biocompatibility was investigated on human fibroblast lung cells (MRC-5 cell line) and the anti-tumoral effect was tested on human cervix cancer cells (HeLa cell line) after 24 and 72 hours of incubation with concentrations up to 500 μg/mL of derivates. D1 and D2 derivatives decreased the number of viable tumor cells in a dose-dependent manner, and concentrations up to 200 μg/mL of these samples did not alter the viability of normal lung fibroblasts until 72 h of incubation. In addition, increased nitric oxide levels released in the cell culture media were noticed only for doses higher than 50 μg/mL. In the case of D5 sample, no changes were observed for both types of cell lines regardless the time of incubation or doses used. D3 and D4 samples killed almost all HeLa cells after the incubation with doses equal or higher than 50 μg/mL. In conclusion, the outcomes of our study performed in vitro revealed that curcumin derivates posed minimal toxicity towards normal lung cells and anti-proliferative efficiency on cancer cells.

Keywords: curcumin; anti-tumor effects; cervix cancer cells

1. Introduction

Curcumin (diferuloylmethane) represents a polyphenol extracted from the plant *Curcuma longa* which has attracted the attention of scientists for medicinal purposes. It was reported that different derivatives present the advantage of increasing curcumin efficacy, exhibiting potent activities against prostate, breast and colon cancer [1,2].

2. Materials and Methods

We developed 5 different derivates in order to test their anti-tumoral effect on human cervix cancer. In this context, we obtained five curcumin derivatives, two have the structure similar with two of the natural compounds, diferuloylmethane (D4) and p,p-dihydroxy di-cinnamoyl methane (D3), and the other three have modified structures with amide or amino groups (D1, D2 and D5). The compounds were synthesized in the microwave field and characterized by 1H-NMR and 13C-NMR spectroscopy, UV-Vis and infrared spectroscopy, fluorescence and thermal analysis. Their biocompatibility was investigated on human fibroblast lung cells (MRC-5 cell line) and the anti-tumoral effect was tested on human cervix cancer cells (HeLa cell line) after 24 and 72 hours of incubation with concentrations up to 500 μg/mL of derivates.

3. Results

D1 and D2 derivatives decreased the number of viable tumor cells in a dose-dependent manner (Figure 1), and concentrations up to 200 μg/mL of these samples did not alter the viability of normal lung fibroblasts until 72 h of incubation (Figure 2). In addition, increased nitric oxide levels released in the cell culture media were noticed only for doses higher than 50 μg/mL. In the case of D5 which has the auxochrome 4-N,N-diethyl group, no changes were observed for both types of cell lines regardless the time of incubation or doses used. D3 and D4 samples killed almost all HeLa cells after the incubation with doses equal or higher than 50 μg/mL. This antitumor effect was very well correlated with an increased level of nitric oxide. However, the high doses of curcumin derivatives induced death of non-tumoral cells and must be avoided in future experiments.

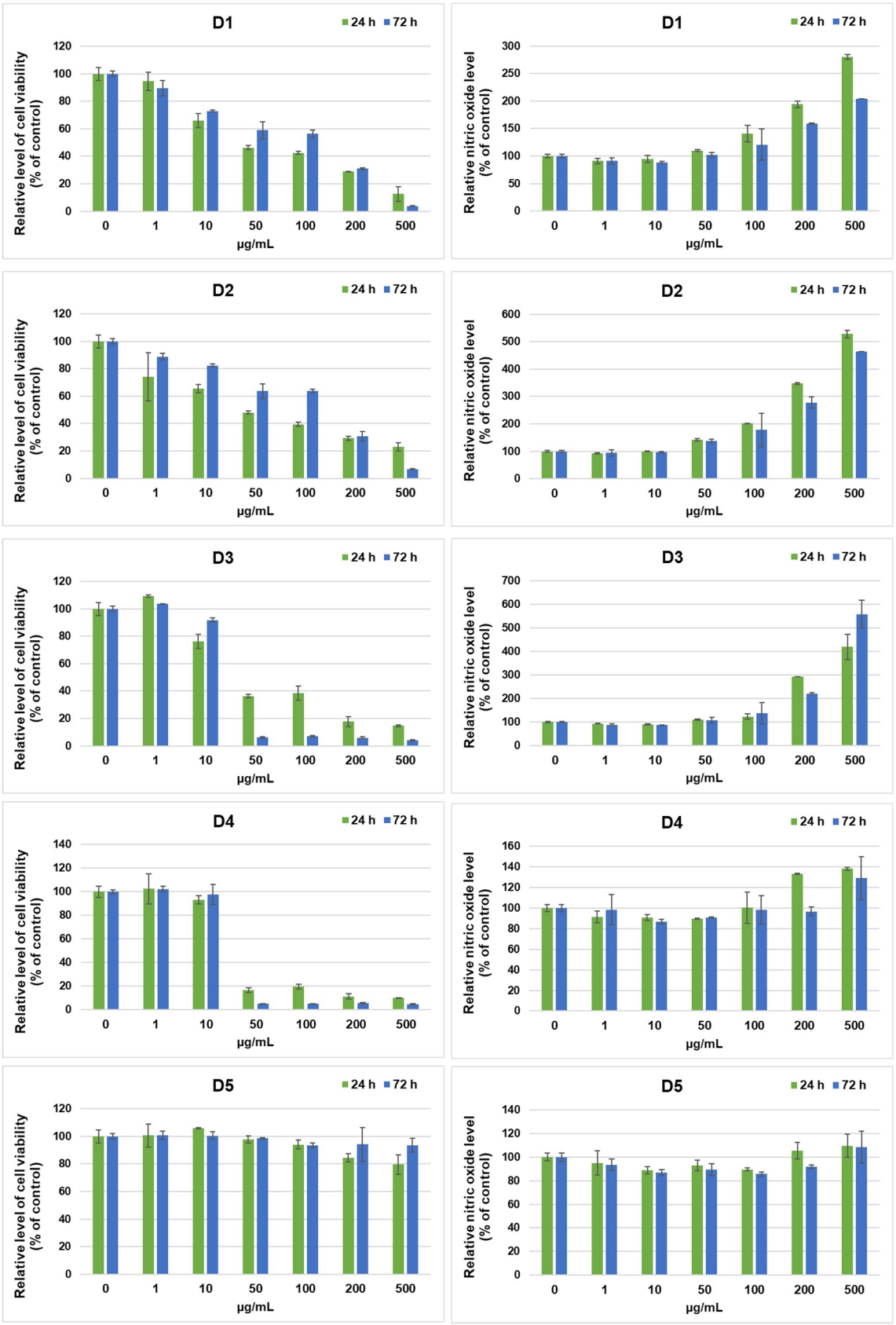

Figure 1. The viability (left column of graphs) of HeLa cells (cervix cancer) and the level of nitric oxide (right column of graphs) after the incubation of 24 and 72 hours with the different 5 derivatives of curcumin (D1, D2, D3, D4 and D5). Data are calculated as means ± standard deviation of 3 replicates and expressed relative to control.

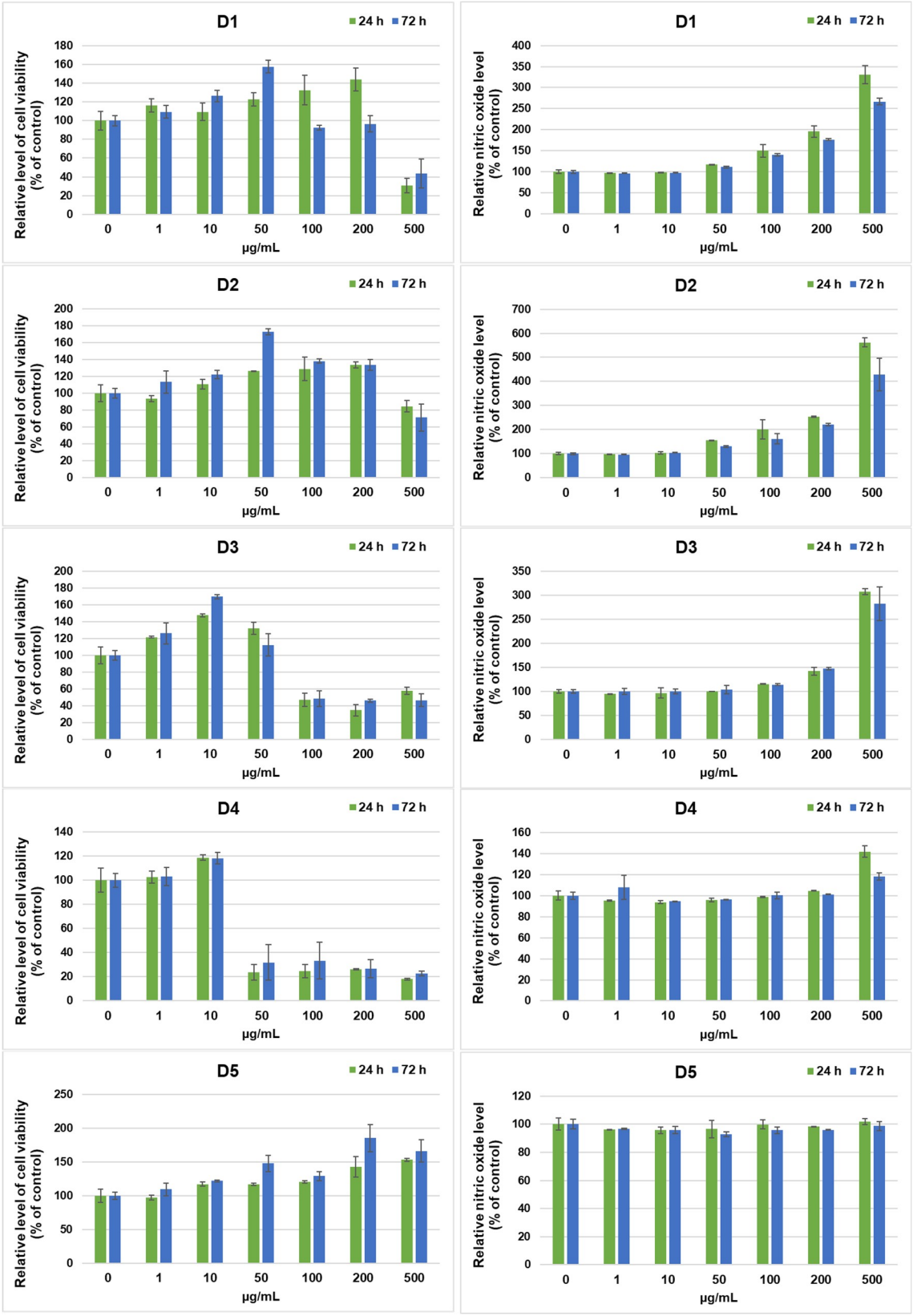

Figure 2. The viability (left column of graphs) of MRC-5 cells (non-tumoral lung fibroblasts) and the level of nitric oxide (right column of graphs) after the incubation of 24 and 72 hours with the different 5 derivatives of curcumin (D1, D2, D3, D4 and D5). Data are calculated as means ± standard deviation of 3 replicates and expressed relative to control.

4. Conclusions

The outcomes of our study performed in vitro revealed that curcumin derivates posed minimal toxicity towards normal lung cells and the anti-proliferative efficiency results experimentally shown on cancer cells seem very promising to be further translated on in vivo studies and human clinical trials which are limited for this moment.

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Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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