Ascorbate Enhances the Antiproliferative Effect and the Senescent Phenotype Induced by Phenylaminonaphthoquinones Against T24 Cells

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INTRODUCTION: The antitumor activity of quinones relies on a quinone redox cycling capacity that triggers oxidative stress in cancer cells. Such a quinone redox cycling is strong enhanced by the reducing activity of ascorbate moreover cancer cells are highly sensitive to oxidative stress, we investigated the antiproliferative effect and the senescent phenotype on T24 cells induced by two phenylaminonaphthoquinones (Q7 and Q9) in the absence or in the presence of ascorbate. MATERIAL AND METHODS: Cell proliferation, cell cycle arrest and senescence phenotype were monitored by the colony forming assay, flow cytometry and SA-β-galactosidase activity, respectively. Results were expressed by means and standard deviations and were analyzed using one-way ANOVA and Tukey-Kramer test. A p-value<0.05 was considered statistically significant. RESULTS AND DISCUSSION: Q7 and Q9 alone or associated with ascorbate caused reduction in colonies number (C= 191.3 ± 10.5; ASC= 168.7 ± 4.9; Q7= 184.7 ± 6.8; Q7+ASC= 121.0 ± 22.6; Q9= 134.5 ± 9.2; Q9 + ASC= 21.5 ± 2.1) when compared to control (C) and inhibited the cancer cell growth. The association of Q9 + ASC impaired cell cycle causing a decrease in the number of cells in the G2/M phase (C= 16.75 ± 0.35; ASC= 17.75 ± 1.05; Q9= 21.0 ± 3.3; Q9 + ASC= 10.7 ± 3.1%). Furthermore, phenylaminonaphthoquinones with ascorbate association increased significantly the SA-β-galactosidase activity (C= 0.96 ± 0.44; ASC= 2.09 ± 1.24; Q7= 15.45 ± 1.3; Q7+ASC= 56.63 ± 1.6; Q9= 23.1 ± 4.0; Q9 + ASC= 75.76 ± 2.4%). CONCLUSION: These results led us to conclude that phenylaminonaphthoquinones in the presence of ascorbate inhibit the proliferation of cancer cells also demonstrate a senescent cancer phenotype.

Palavra chave: antiproliferative effect, ascorbate, phenylaminonaphthoquinones, senescence
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