

The effect of novel pyrrolidinedione-thiazolidinone hybrid on autophagy in breast cancer cells

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INTRODUCTION

Breast cancer (BC) is the major cause of morbidity and mortality among other malignant tumors in the world. This oncological disease is one of the serious public health challenges worldwide and kills more European women than any other type of cancer. The rapid development of drug resistance is the main problem of modern targeted drugs, which leads to the rapid progression of cancer. Moreover, triple negative breast cancer does not respond to traditional treatments, and most targeted drugs are useless. Therefore, chemotherapy remains one of the main systematic methods of breast cancer treatment, but its effectiveness in many cases is low. It was proved that a series of pyrrolidinedione-thiazolidinone hybrid molecules exert promising anticancer activity.

The aim of the study was to check the effect of novel pyrrolidinedione-thiazolidinone hybrid (**Les-6287**) on autophagy in breast cancer cells.

RESULTS

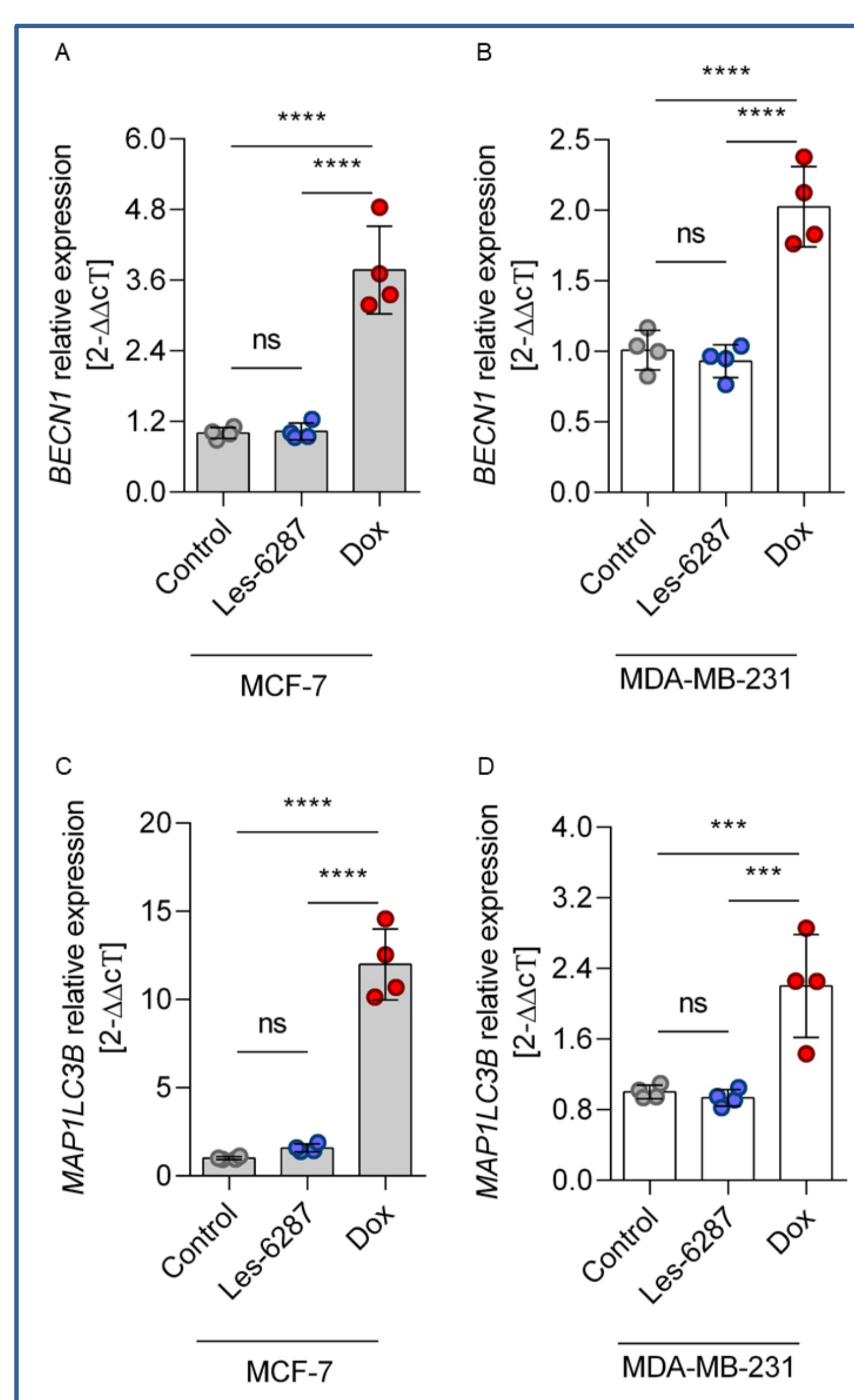


Figure 1. The expression of *BECN1* and *MAP1LC3B* genes in MCF-7 and MDA-MB-231 breast cancer cells after 24 h incubation with Les-6287 and doxorubicin at 1 μ M concentration: *BECN1* expression in MCF-7 (A) and MDA-MB-231 (B) cells; *MAP1LC3B* expression in MCF-7 (C) and MDA-MB-231 (D) cells. Data presented as M \pm SD from three independent experiments performed in duplicate is presented. *P < 0.5; **P < 0.01; ***P < 0.001; ****P < 0.0001; ns – non-significant changes.

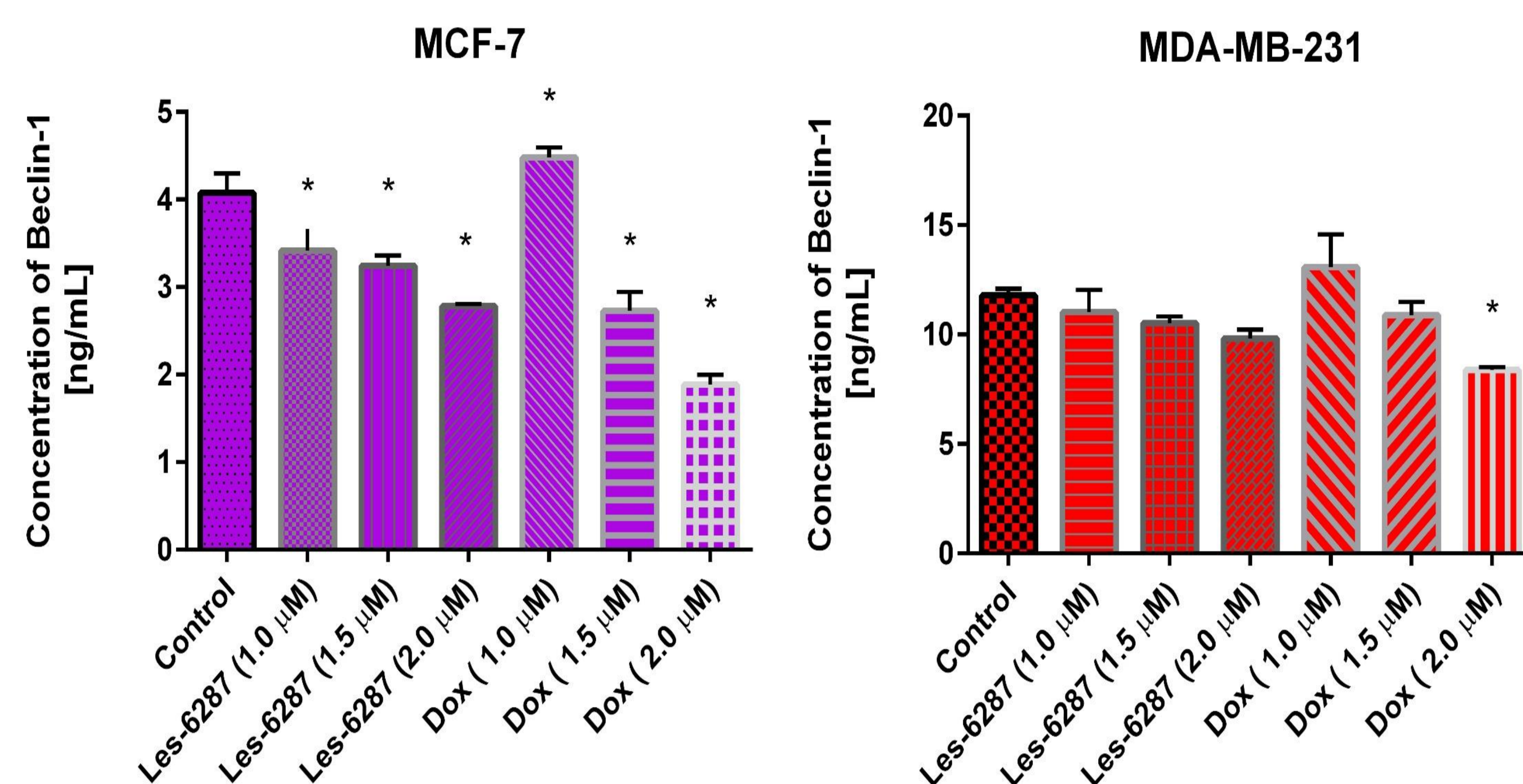


Figure 2. The concentration of Beclin-1 in MCF-7 and MDA-MB-231 cells after 24 h incubation with Les-6287 and doxorubicin at 1 μ M, 1.5 μ M, and 2 μ M concentration. Data presented as M \pm SD from three independent experiments performed in duplicate is presented. *P < 0.05 compared to control (non-treated) cells.

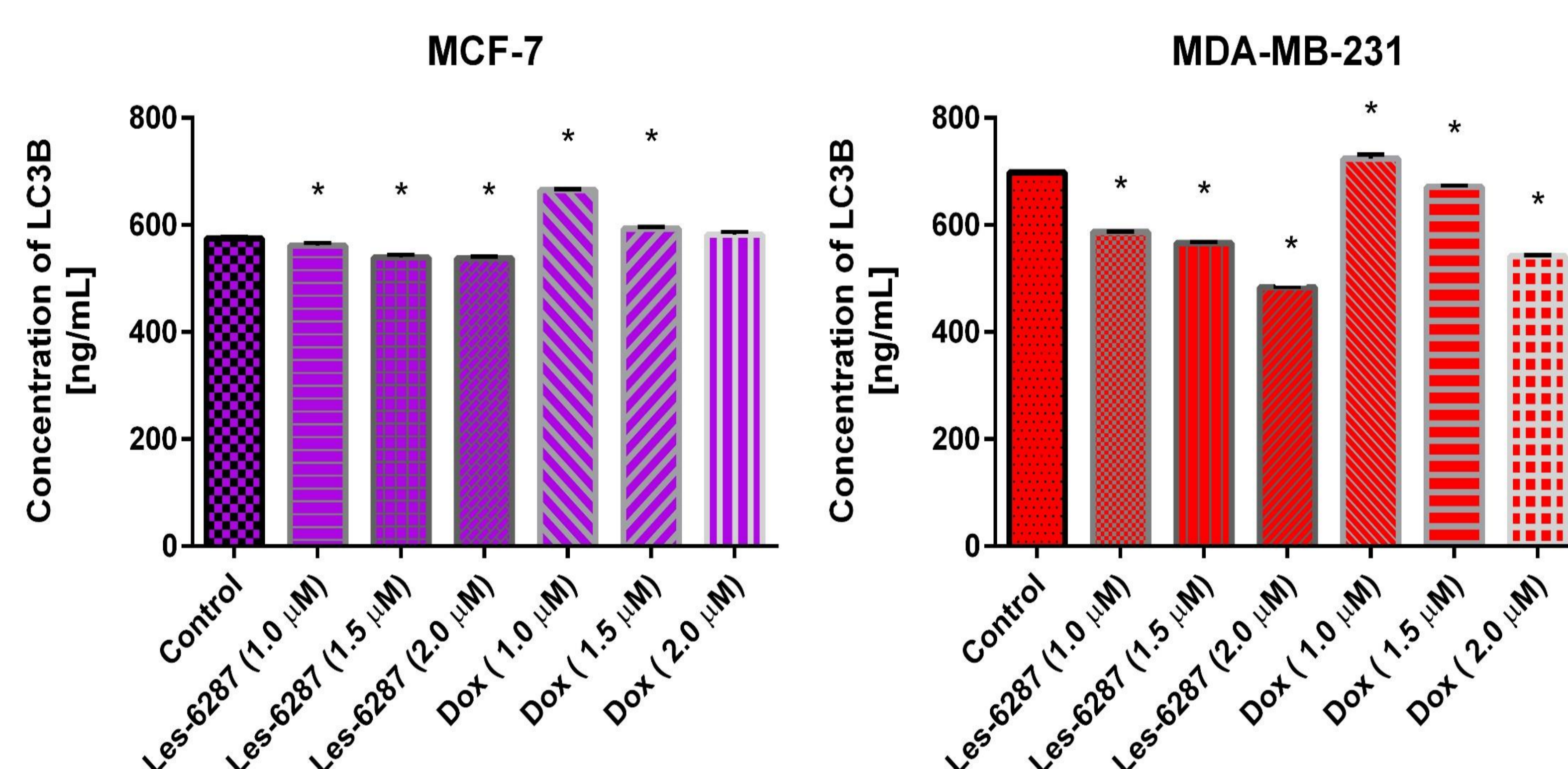


Figure 3. The concentration of LC3B in MCF-7 and MDA-MB-231 cells after 24 h incubation with Les-6287 and reference drug (doxorubicin) at 1 μ M, 1.5 μ M, and 2 μ M concentration. Data pre-sented as M \pm SD from three independent experiments performed in duplicate is presented. *P < 0.05 compared to control (non-treated) cells.

CONCLUSIONS

We found that MCF-7 and MDA-MB-231 cells treated for 24 hours with doxorubicin significantly increased the expression of both *MAP1LC3B* and *BECN1* genes compared to control cells. In contrast, incubation of MCF-7 and MDA-MB-231 with Les-6287 did not change *MAP1LC3B* and *BECN1* expression. The most significant increase in Beclin-1 and LC3B concentrations was observed after treatment with doxorubicin in breast cancer cells. Additionally, 24h incubation with Les-6287 resulted in the reduction of autophagy markers concentration in both analyzed breast cancer cells.

We demonstrated that novel compound (**Les-6287**) did not induce cell death through the autophagy mechanism.



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