Antitumor effect of LQB-223 hydrochoride in chronic myeloid leukemia and diffuse large B cell lymphomas cells

Mariana Alberti Gonçalves[1], Rebeca Sousa Brum[1], Joseane A. Mendes[2], Camila D. Buarque[2], Raquel Ciuvalschi Maia[1], Roberta Soares Faccion[1]
1- Laboratório de Laboratório de Hemato-Oncologia Celular e Molecular, INCA, RJ, Brasil.
2- Departamento de Química, Pontifícia Universidade Católica do Rio de Janeiro, PUC-Rio, RJ, Brasil.
e-mail: marianalberti@hotmail.com

ABSTRACT

Diffuse large B-cell lymphomas (DLBCL) are the most frequent type of non-Hodgkin lymphomas (NHL) with aggressive clinical behavior and are also those with poorer response to conventional treatment. In half of the cases treatment fails and the disease is lethal. Acute myeloid leukemia (AML) is a condition in which myeloblasts expand, accumulate and suppress normal hematopoietic activity. Despite the progress in others fields of oncology, treatment of AML is still challenging. Remission rates after induction therapy reach 80%, but the cure is only achieved for 20% of the patients. Thus, in both types of hematological malignancies it is necessary to carry out studies that can lead to the discovery of potential new treatments. The compound known as LQB-223 (11a-N-Tosyl-5-deoxiazapterocarpano) is a promising agent in the treatment of several hematological malignancies. Therefore, the present study aims to evaluate the potential effect of new compounds derived from LQB-223 in DLBCL and LMA cells. The cells lines derived from AML (K562-Lucena) and DLBCL (SULDH4), were cultured in RPMI culture media supplemented with 10% fetal bovine serum and maintained in culture at 37 °C 5% CO2. It is worth noting that the cell line K562-Lucena is derived from K562 cells that were cultured in progressively higher concentrations of vincristine. Thus, Lucena cells are resistant to 60 nM of this chemotherapeutic agent. The compound LQB-223 hydrochoride was tested at concentrations of 1 uM, 2.5 uM, 5 uM, 7.5 uM, 10 uM, 15 uM, 20 uM, and its cytotoxicity was assessed by the MTT cell viability assay. This technique is a colorimetric assay, which measures the activity of mitochondrial dehydrogenases and may be used to evaluate cell viability and proliferation. To evaluate the percentage cell viability upon treatment, absorbance of treated cells divided by untreated control cells was calculated. The first compound derived from the LQB-223 tested was the LQB-223 hydrochoride. The cytotoxicity assay showed that in both cell lines tested so far (Lucena and SULDH4) no significant reduction in cell viability is observed in any of the concentrations tested. However, after 48h a small decline in cell viability is noted from the concentration of 15 uM in a dose independent manner. According to recent data from our group, the LQB-223 compound significantly decreases cell viability of Lucena cells. However this new compound derived from LQB-223 did not yield the same effect. In conclusion, the LQB-223 hydrochoride was not effective in cells evaluated. The perspectives of the present study are to evaluate the antitumor potential of other compounds derived from LQB-223. We will also carry out tests in other AML cell lines such as the parental K562 and DLBCL Toledo.

MATERIAL AND METHODS

The human cells lines derived from CML (K562-Lucena) and DLBCL (SULDH4 and Toledo) were used in the study. The cell line SUDHL4 is characterized as GCB subtype and has a sensitivity profile of treatment response. The cell line Toledo is characterized as ABC subtype and has a profile of resistance to treatment. Were cultured in RPMI culture media supplemented with 10% fetal bovine serum and maintained in culture at 37 °C 5% CO2. It is worth noting that the cell line K562-Lucena is derived from K562 cells that were cultured in progressively higher concentrations of vincristine. Thus, Lucena cells are resistant to 60 nM of this chemotherapeutic agent. The compound LQB-223 hydrochoride was tested at concentrations of 1 uM, 2.5 uM, 5 uM, 7.5 uM, 10 uM, 15 uM, 20 uM, and its cytotoxicity was assessed by the MTT cell viability assay. The assay was done according to the protocol illustrated in Figure 1.

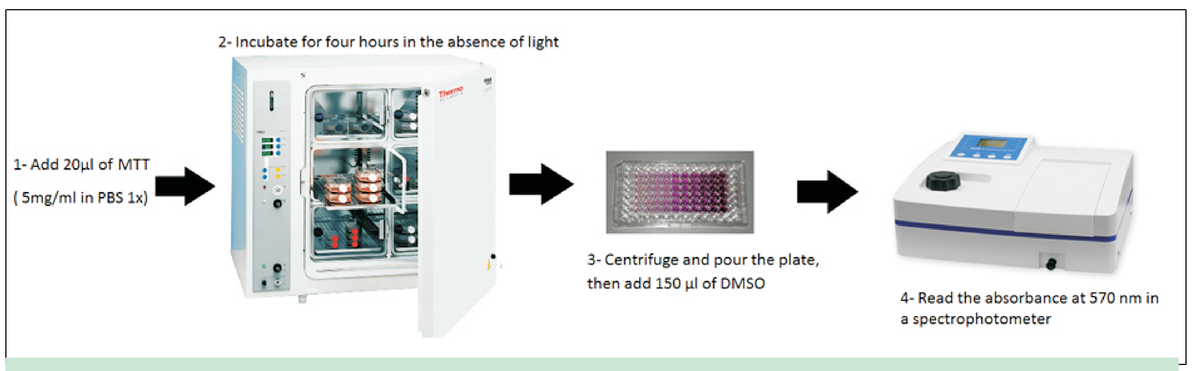

Figure 1: MTT colorimetric assay. Used to evaluate cell viability and proliferation. To evaluate the percentage cell viability upon treatment, absorbance of treated cells divided by untreated control cells was calculated.

RESULTS

The first compound derived from the LQB-223 tested was the LQB-223 hydrochoride. The cytotoxicity assay showed that in all cell lines tested so far (Lucena, Toledo and SUDHL4) no significant reduction in cell viability is observed in any of the concentrations tested. However, after 48h a small decline in cell viability is noted from the concentration of 15 uM in a dose independent manner in Lucena and SULDH4. According to recent data from our group, the LQB-223 compound significantly decreases cell viability of Lucena cells. However this new compound derived from LQB-223 did not yield the same effect.

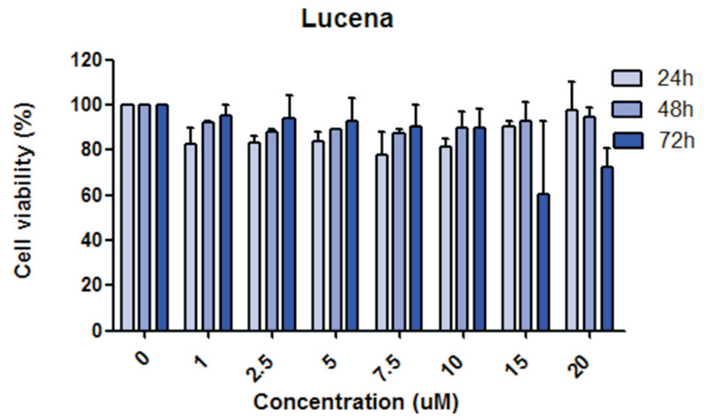

Figure 2: Cell viability of chronic myeloid leukemia Lucena cells after incubation with the synthetic compound LQB-223 hydrochoride, evaluated by MTT assay. Percentage of viable cells after incubation with different concentrations LQB-223 hydrosoluble for 24, 48 and 72 hours. Bars display the mean of two independent experiments. Erro bars represent the standart error.

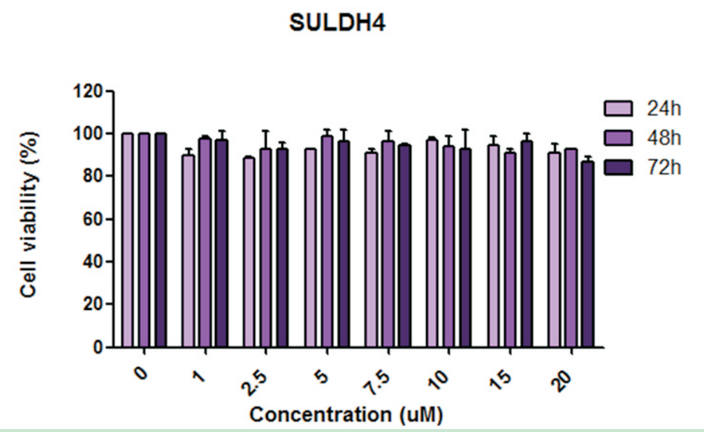

Figure 3: Cell viability of diffuse large B cell lymphoma SULDH4 cells after incubation with the synthetic compound LQB-223 hydrochoride, evaluated by MTT assay. Percentage of viable cells after incubation with different concentrations LQB-223 hydrosoluble for 24, 48 and 72 hours. Bars display the mean of two independent experiments. Erro bars represent the standart error.

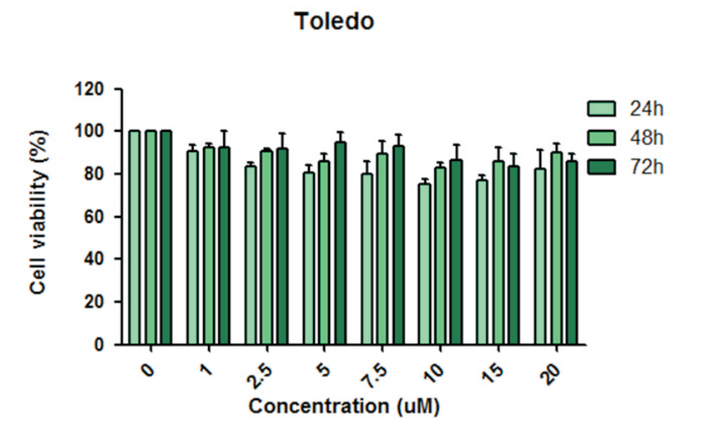

Figure 4: Cell viability of diffuse large B cell lymphoma Toledo cells after incubation with the synthetic compound LQB-223 hydrochoride, evaluated by MTT assay. Percentage of viable cells after incubation with different concentrations LQB-223 hydrosoluble for 24, 48 and 72 hours. Bars display the mean of one experiment. Erro bars represent the standart deviation.

CONCLUSION

In conclusion, the LQB-223 hydrochoride was not effective on the evaluated cells. The perspective of the present study is to evaluate the antitumor potential of other compounds derived from LQB-223. We will also carry out tests in other cell lines such as the parental K562 and the DLBCL-derived Toledo cells.

Keywords: New antitumoral agents; diffuse large B-cell lymphoma; chonic myeloid leukemia.
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