from 0.8 to 50 μM) for 72 h. Leukemic cells were exposed to the presence of vehicle or different concentrations of compounds (ranged from 0.8 to 50 μM) for 24, 48 and 72 h. Next, 10 μl methylthiazoletetrazolium (MTT, Sigma-Aldrich) solution (5 mg.mL^{-1}) was added and incubated at 37°C, 5% CO2 for 4 h. The reaction was stopped using 100 μL 0.1 N HCl in anhydrous isopropanol. Cell viability was evaluated by measuring the absorbance at 570 nm. IC50 values were calculated using non-linear regression analysis in GraphPad Prism 5 (GraphPad Software, Inc., San Diego, CA, USA). SwissADME and pkCSM software were used to predict the properties of the compounds. **Results:** Of the compounds synthesized, A1, A2, A3 and A4 showed antileukemic activity. Compounds A1 and A4 were the least cytotoxic for both cell lines. A2 showed strong activity against Jurkat cells. The best compound in the study, A3, showed strong activity against both Jurkat and NB4 cells. In the investigation of apoptosis by flow cytometry, the baseline cell viability was greater than 85%, which indicates a good quality cell culture and reliability in the data obtained. A2 showed greater efficacy, but still limited in Jurkat cells compared to NB4 cells. Compound A4 was the most effective in both models tested. For Log P (consensus), all the molecules are within the molecular filters, with A3 having the highest value, 3.79. The final analysis of all those described in this study indicates that all the quinazolinones synthesized meet the parameters for oral bioavailability. **Conclusion:** In this study, we prepared a series of quinazolinones that exhibited antiproliferative activities in T-ALL and APL. The most promising result of the study was A3 for both T-ALL and APL cells, respectively. In the analysis of apoptosis by flow cytometry, the highlight was also A3, which was the most effective against both cell lines.

Keywords: Antileukemic, Jurkat, NB4, Quinazolinone.

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NEW FUNCTIONALIZED QUINAZOLINES AS POTENTIAL AGENTS AGAINST HEAD AND NECK AND LUNG CANCER

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A B S T R A C T

Introduction/Justification: Lung cancer (LC) and head and neck cancer (HNC) are high incidence tumors around the world. Patients with the tumors have been treated for years with cisplatin alone or in combination with other agents. More recently, hyperexpression of the epidermal growth factor receptor (EGFR) has been identified in most LC and HNC, and anti-EGFR agents have been incorporated into the treatment of tumor carriers. However, a substantial number of patients with tumors still die, which justifies the search for new antineoplastic agents. **Objectives:** Evaluate the antiproliferative activity of new functionalized quinazolines against FaDu, HaCat, SCC-25 and NCI-H460 cell lines. **Materials and Methods:** The quinazolines (Q1-Q6) were synthesized in the Laboratory of Synthesis of Natural Products and Drugs (Institute of Chemistry, Unicamp). Non-small cell lung cancer (NCI-H460), squamous cell pharyngeal cancer (FaDu), squamous cell carcinoma of the tongue (SCC-25), and epidermal keratinocytes (HaCaT) were selected for this study, and all cell lines comply with the International Organization for Standardization (ISO 10993-5 and ISO 10993-1). The cytotoxicity of each compound in the cell lines was determined by the MTT (3-(4,5-dimethylthiazol-2-yl)-2-5 diphenyl tetrazolium bromide) assay. Cisplatin and gefitinib were used as positive controls. MTT is captured by cells and reduced intra-cellularly in a mitochondrion-dependent reaction to yield a formazan product. The ability of cells to reduce MTT provides an indication of their intactness and mitochondrial activity that serves as a measure of viability. After a 48 h incubation with compounds (seven concentrations on a logarithmic scale from 1 to 1000 μg.mL-1), the plates were centrifuged to pellet the cells, the supernatant was removed, and 10 μL of MTT (Sigma, M5665) dissolved in 100 μL of phosphate-buffered saline (Sigma P4417) was added followed by incubation for 4 h at 37°C in a humid, 5% CO_2 atmosphere. After this period, the plates were centrifuged again, the supernatant was removed, and the insoluble formazan crystals were dissolved in 150 μL of Isopropyl alcohol. The absorbance was read in a Synergy ELISA plate reader (Bio Tek Instruments, Highland Park, Winooski, USA) at 570 nm. The results were expressed as percentage inhibition relative to control cells (considered as 100%). **Results:** Compounds Q1 and Q6 showed no cytotoxic activity. The synthetic intermediate, Q2 and the target compound Q3 showed an unexpected but interesting cytotoxic activity for the HaCat cells. Compound Q4 showed strong and selective cytotoxic activity against the FaDu cells. Analyzing the NCI-H460 cells, compound Q5 showed strong and selective cytotoxic activity. **Conclusion:** Compounds Q2 and Q3 deserve attention as potential agents for the treatment of actinic keratosis patients. The Q4 and Q5 compounds emerge as new potential agents for the treatment of patients with HNC and LC, respectively. Studies focusing on response and toxicity to agents in animal models are necessary to verify the efficacy and safety of agents before starting studies in humans.

Keywords: Antiproliferative, Lung cancer, Quinazoline.

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GOLD(I)-BASED COMPLEX AUDMAP: A PROMISING ANTIPROLIFERATIVE AGENT FOR MELANOMA TREATMENT

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