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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A B S T R A C T

Introduction/Justification: Melanoma is the most aggressive type of skin cancer, with increasing global incidence. Platinum-based chemotherapy, particularly cisplatin, remains a standard treatment, but its effectiveness is often limited by drug resistance and severe side effects. Gold-based complexes have gained attention as potential alternatives due to their greater chemical stability, selective cytotoxicity against platinum-resistant cells, lower systemic toxicity, and immunomodulatory effects. Previous studies from our group demonstrated the antiproliferative activity of AuDMAP, a gold(I)-based complex, in the UACC-62 melanoma cell line. Building on these findings, this study investigates the antiproliferative effects, cytotoxicity, and selectivity of AuDMAP in SK-MEL-28 and A-375 melanoma cells, as well as its impact on cell migration and potential anti-metastatic properties in comparison to cisplatin. **Objectives:** To evaluate the antiproliferative activity and cell death mechanisms induced by the AuDMAP complex in SK-MEL-28 and A-375 melanoma cell lines, as well as determining its toxicity against non-tumoral HaCaT cells. **Materials and Methods:** Melanoma and non-tumor cells were cultured in DMEM + 10% FBS + 1% penicillin-streptomycin and treated with AuDMAP (0.78–100 μM) for 48h, with cisplatin as a control. Sulforhodamine B (SRB) and Thiazolyl Blue Tetrazolium Bromide (MTT) assays were performed to determine cell viability, antiproliferative activity, and IC50 values. The wound healing assay assessed migration, and flow cytometry will be conducted to explore cell death mechanisms and cell cycle effects. **Results:** AuDMAP exhibited strong antiproliferative activity, inhibiting ~80% of cell proliferation at 6.25 μM in melanoma cells - 15x more effective than cisplatin for SK-MEL-28 and 3.3x for A-375. IC50 values were 2.61 μM (SK-MEL-28), 2.50 μM (A-375), and 1.81 μM (HaCaT), yielding a low Selectivity Index (0.69–0.72). Migration assays revealed that AuDMAP significantly reduced wound closure, suggesting anti-metastatic potential. In A-375, wound closure was -8.5% with AuDMAP vs. 62.8% with cisplatin (6.25 μM), while in SK-MEL-28, closure was 4.6% vs. -13.5%, respectively. Given these promising results, further studies will focus on cell cycle analysis and death mechanisms to better understand the biological effects of AuDMAP. **Conclusion:** AuDMAP is a gold(I)-based complex that demonstrates potent antiproliferative and antimigratory effects in melanoma cells, with efficacy significantly superior to cisplatin in the tested models. The inhibition of cell proliferation and migration suggests its potential as a promising anticancer agent, possibly disrupting tumor progression and metastasis. However, the low selectivity index observed indicates that its cytotoxic effects extend to non-tumor cells, raising concerns about the safety profile in intravenous administration. To further explore its therapeutic viability, future studies will investigate its mechanisms of action at the molecular level, focusing on cell cycle modulation and programmed cell death pathways. These findings contribute to the growing interest in gold(I) compounds as novel candidates for melanoma treatment, particularly for topical administration. **Acknowledgements:** This study was supported by grants from the Brazilian Agencies FAPESP (2021/10265-8 Cancer Theranostics Innovation Center - CEPID), and Program (PPPD) at the University of Campinas (UNICAMP, ID Number 325141).

Keywords: AuDMAP, Cell proliferation, Melanoma, Skin cancer.

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EVALUATION OF ANTIPROLIFERATIVE OF A POTENTIAL THERAPEUTIC ASSOCIATION OF SILVER COMPLEXES WITH LIMONENE IN SQUAMOUS CELL CARCINOMA AND MELANOMA CELL LINES

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A B S T R A C T

Introduction/Justification: Skin cancer, strongly associated with UV exposure, is the most common malignancy worldwide, including squamous cell carcinoma (SCC), and cutaneous melanoma (CM). Although cisplatin and 5-FU are standard treatments for SCC and CM, the development of new therapeutic alternatives is crucial. Silver complexes have shown promising anticancer potential, while the monoterpene limonene has demonstrated efficacy in enhancing skin permeation, supporting its application in topical drug delivery. **Objectives:** Our study aimed to evaluate the in vitro antiproliferative effects of silver complexes and limonene, isolated and in association. **Materials and Methods:** The silver complexes identified as I and II were synthesized at the Institute of Chemistry of University of Campinas. The pure substances R-(+)-limonene and S-(-)-limonene were acquired from Merck. Pharyngeal SCC (FaDU) and melanoma (A-375, SK-MEL-28) cells (4×10^3 cells/mL) were treated with complexes I e II (0.4–400 μM) or their combination with R-(+) and S-(-) limonene (4 μM). Cisplatin and 5-FU (100 μL/well, 0.4 to 400 μg/mL, in triplicate) were used as positive controls. Before (T0) and after (T1) sample addition, cells were fixed with 50% trichloroacetic acid (TCA, 50 μL/well), and were then resuspended in Tris base for subsequent absorbance at 540 nm with a microplate reader spectrophotometer (VersaMax, Molecular Devices). The difference between T0 and T1 absorbance values represented 100% cell growth. Effective concentration representing the sample concentration required to