Abstracts

(trifluoromethyl)benzyl)-1H-indazol-3-yl)furan-2-carboxamide), a patented anti-fascin molecule and compared its effect with migmastatin, a typical fascin inhibitor.

Material and methods We have used molecular modelling to predict the fascin aminoacids involved in G2 binding. A qPCR assay was carried to find out which from eight different colorectal cancer cell lines expressed the highest amount of fascin. After cell viability assay, scratch and IBIDI assays were performed to evaluate the anti-migratory effect of the compounds. Immunofluorescence for fascin was used for assessing lamellipodia formation. Anti-invasive effect was evaluated using cell invasion assay Transwell with matrigel and a myoma organotypic invasion model.

Results and discussions Molecular modelling using blind docking calculations identified a region in fascin possibly involved in G2 binding. HCT116 cells expressed the highest fascin levels and its migration capacity was clearly reduced by migmastatin and G2, the latter even at lower concentrations. Still, G2 inhibited the migration of all the cell lines demonstrating that G2 affected fascin functional capacity.

Invasion and confocal studies were performed with HCT116 cells and both inhibitors strongly abolished the protrusion of lamellipodium (p<0.003). The Transwell Matrigel invasion assay also evidenced the anti-invasive effects of migmastatin and G2. Myoma discs showed that both compounds were similarly able to significantly decrease both the invasion depth and invasion area of HCT116 cells at 50% (p<0.001).

Conclusion This study demonstrates an interesting anti-migratory and anti-invasive effect of G2 in a similar extent to migmastatin and provides significant evidence that G2 is an interesting candidate for further investigation/chemical modifications to develop new fascin-specific therapies for colorectal cancer.

Introduction Cancer cell lines and LS1034 and WiDr colorectal cancer cell lines were cultured in appropriate culture medium. The effect of the compounds on cell metabolic activity was evaluated by colorimetric MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) test. For this study, the cells were seeded in 48-well plates and after 24 hour were incubated with increasing concentrations of the complexes (0.5 to 200 µM). After 48 hour, cell proliferation was evaluated through MTT assay. Dose response curves were plotted and IC50 (half maximal inhibitory concentration) values for each ruthenium complex were determined.

Results and discussions All compounds induced a decrease in cell proliferation in a dose-dependent way. For breast cancer MCF-7 and HCC1806 cell lines the tetrachlorinated Ru(III) complex presents greater cytotoxicity (IC50 <4 µM) than the other compounds which have IC50 values between 10 and 20 µM. Similar results were observed for the colorectal cancer cell lines in the presence of the same complex (IC50 <4 µM) and, for the remaining compounds, IC50 values were between 15 and 30 µM. The tetrachlorinated Ru(III) complex is, consequently, the most promising, showing similar cytotoxic activity in all cell lines.

Conclusion All compounds revealed dose-dependent anti-proliferative effects. The tetrachlorinated Ru(III) complex was found to be the most promising, exhibiting high anticancer activity in all cell lines, namely in the HCC1806 and LS1034 chemoresistant cell lines.

PO-416 CYTOTOXICITY OF RU (II) AND RU (III) SALEN COMPLEXES AGAINST BREAST AND COLORECTAL CANCER CELL LINES

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Introduction Breast and colorectal cancer are the most common cancers, and are therefore responsible for a high mortality rate worldwide. The search for new anticancer drugs has increased in the last decades since chemotherapeutic drugs used nowadays show many adverse effects and cancer resistance. Previous studies have shown that metallic salen complexes exhibit antitumor activity. Additionally, Ru complexes have revealed cytotoxic activity, proving greater selectivity for tumour cells. They are less toxic relatively to Pt complexes, being for this reason pointed out in the literature as a credible alternative to current drugs used in chemotherapy. The aim of this study is to synthesise four novel Ru(III) and Ru(II) chlorinated salen complexes and test their cytotoxicity on breast and colorectal cancer cell lines.

Material and methods Ru salen complexes were synthesised from camphoric acid derivatives. MCF-7 and HCC1806 breast cancer cell lines and LS1034 and WiDr colorectal cancer cell lines were cultured in appropriate culture medium. The effect of the compounds on cell metabolic activity was evaluated by colorimetric MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) test. For this study, the cells were seeded in 48-well plates and after 24 hour were incubated with increasing concentrations of the complexes (0.5 to 200 µM). After 48 hour, cell proliferation was evaluated through MTT assay. Dose response curves were plotted and IC50 (half maximal inhibitory concentration) values for each ruthenium complex were determined.

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Conclusion All compounds revealed dose-dependent anti-proliferative effects. The tetrachlorinated Ru(III) complex was found to be the most promising, exhibiting high anticancer activity in all cell lines, namely in the HCC1806 and LS1034 chemoresistant cell lines.

PO-417 SYNTHESIS OF CU(II) COMPLEXES DERIVED FROM IMIDAZOLE AND CYTOTOXIC ACTIVITY EVALUATION AGAINST BREAST AND COLORECTAL CANCERS

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Introduction Despite the existence of new therapeutic options, breast (BC) and colorectal (CC) cancers remain the leading causes of cancer death and the most commonly diagnosed in worldwide. Studies have reported that imidazole derivatives show anticancer, antimicrobial, antibacterial, antifungal and antioxidant activities. Furthermore, recently it has been found that the association between imidazole ligands and copper increases their DNA binding affinity giving potential anticancer activity. Therefore, we synthesised three novel Cu(II) complexes using heterocyclic nitroimidazole derivatives as ligands. The aim of this study is to evaluate the cytotoxic activity of these complexes in two BC and two CC cell lines.

Material and methods Nitroimidazole derived ligands containing cyclohexylamine, morpholine and piperidine and the respective Cu(II) complexes were synthesised. MCF-7, HCC1806, LS1034 and WiDr cell lines were cultured and grown in proper conditions. To evaluate the cytotoxic activity of these Cu(II) complexes on four cell lines, MTT colorimetric assay was used. Cells were seeded in 48 well-plates and then were treated with increasing concentrations of the complexes, from 0.5 to 200 µM. After 48 hour of incubation, medium was removed and MTT was added. Two hours later, isopropanol was added in order to dissolve formazan crystals. The
absorbance was read at 570 and 620 nm and IC_{50} (half maximal inhibitory concentration) values determined.

**Results and discussions** Some Cu(II) complexes exhibit anti-cancer activity in cell lines. Studies show that for the MCF-7 and LS1034 cell lines, the nitroimidazole derived complex containing cyclohexylamine presents IC_{50} values of 22.2 and 23.9 μM, respectively. For WiDr cell line, the same complex has an IC_{50} of 50.5 μM. The best IC_{50} value (2.9 μM) for this complex occurs in the HCC1806 cell line, a chemoresistant BC cell line.

Curiously, the complex containing piperidine presents an IC_{50} of 3.8 μM in HCC1806 cell line, while in the other BC cell line (MCF-7) there is no anticancer activity.

The nitroimidazole derived complex containing cyclohexylamine is, consequently, the most promising compound in four cell lines.

**Conclusion** Cu(II) complexes derived from nitroimidazole presented anticancer activity against all cell lines. The complex containing cyclohexylamine revealed to be the most promising, especially in HCC1806, basaloid triple-negative breast cancer, known as therapy-resistant.

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**PO-419 USE OF ORIGANUM MAJORANA OIL IN LUNG CANCER THERAPY**

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**Introduction** Lung cancer is the most common form of cancer with the highest mortality rate in the world accounting for 1.69 million deaths in 2015 (WHO data). Despite the advances in targeted therapies, cure of lung cancer remains elusive and patients die due the development of distant metastasis, resistance to the treatment, and to the cytotoxicity of the drugs used.

A large number of the chemotherapeutic drugs used in cancer treatment are either from plant origin or chemically-altered plant products and phytochemicals. It has been shown that extract of Origanum majorana reduced the side effects induced by cyclophosphamide and cisplatin, two established anticancer drug, without altering their cytotoxicity.

**Material and methods** The question whether the pharmaceutically available Origanum Majorana ‘100% pure’ essential Oil will be a successful option in lung cancer therapy is a major challenge that we tried to address in this study using two major human lung cancer cells namely A549 and LNM35.

**Results and discussions** We demonstrate that Origanum majorana causes a concentration- and time-dependent decrease in the viability of the lung cancer cells (A549 and LNM35) and their related colonies growth in vitro. Similarly, treatment with Origanum majorana significantly decreased the growth of LNM35 and A549 xenografts in chick embryo and in nude mice models in vivo without significant side effects.

**Conclusion** This study increases our understanding of the potential benefit of using the Origanum Majorana Oil in lung cancer therapy. Based on these results, our next step is the identification and characterisation of Origanum Majorana Oil major constituents that mediate its anti-cancer effects.

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**PO-420 MECHANISMS OF ACTION OF ANTI-PROLIFERATIVE LICHEN COMPOUND PROTOLICHESTERINIC ACID**

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**Introduction** Protolichesterinic acid (PA), an aliphatic α-methyl-γ-lactone isolated from the lichen Iceland moss (*Cetraria islandica*) has an anti-proliferative effect against a variety human cancer cells. In multiple myeloma cells PA induces apoptosis. The anti-proliferative effect of PA is not mediated by the known inhibitory action of PA on 5- and 12-lipoxygenases and effects...