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 anticancer 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 PROTOLICHSTERIC ACID**

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**Introduction** Protolichsteric 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
on growth factor signalling are secondary. PA inhibits DNA replication and earlier studies indicated direct effects of PA on HIV reverse transcriptase (RT) and DNA polymerase. RT inhibitors are known to affect mitochondria.

**Material and methods** Molecular modelling software (Glide, Schrödinger, LLC) was used to test for the ability of PA to bind onto DNA polymerases α, β, γ and θ. The crystal structures of polymerases were acquired from Protein Data Bank (PDB ID: 4QCL, 5TB8, 4ZTZ and 5A9F, respectively) and PA was docked into each structure. The effects of PA on mitochondria were assessed morphologically by electron microscopy and metabolically by measuring extracellular glucose and lactate concentrations in cell medium after 6 and 24 hour (ABL90 FLEX blood gas analyzer) in the pancreatic cancer cell line Aspc-1, the breast cancer cell line T47D, normal skin fibroblast and MCF-10 non-tumorigenic breast epithelial cell line.

**Results and discussions** PA docked to all four types of DNA polymerases, creating multiple hydrogen bonds directly with the enzymes/polymerases and with the metal ion (Mg$^{2+}$) cofactor. Hydrogen bonds to the metal ions bridging the interaction to the enzyme appeared important and might be necessary/important for the activity of protolichesterinic acid and explain its mechanism of action. Morphological changes in mitochondria were observed following exposure to PA in both cancer cell lines, but these were difficult to interpret. Aspc-1 pancreatic cancer showed a significant increase in lactate production after 24 hour exposure to PA. This was not observed in the breast cell lines, T47D and MCF-10. Aspc-1 is less sensitive to the anti-proliferative effects of PA than the breast cell lines. Further metabolomics studies are in progress.

**Conclusion** Docking study of crystal structures of DNA polymerases indicates that PA could affect activity of several types of DNA polymerase, but this remains to be tested experimentally. PA may affect mitochondrial structure but increased lactate production is associated with relative resistance to its anti-proliferative effects.

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**PO-422 DISAGREGATION IN BIOLOGICAL MEDIUM OF PROMISING THERANOSTIC AGENTS FOR CANCER**

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**Introduction** We recently developed a new type of photochemically stable platinum (II) chlorins, which are remarkable photosensitizers that can be used in photodynamic therapy (PDT), due to its therapeutic capacity. Simultaneously, due to its highly luminescence properties, in the biological relevant 630–850 nm red and near infrared spectral region, they may be used for biological imaging. In addition, photophysical studies indicate that they may be used as ratiometric oxygen sensors.

**Material and methods** Compounds with different degrees of hydrophilicity were synthesised and characterised. Photocytotoxicity studies were carried out against two human tumour cell lines, the OE19 line of oesophageal carcinoma and the A375 line of melanocytic melanoma. The formulation of the sensitizers consisted in a 1 mg/mL solution in DMSO and the desired concentrations being achieved by successive dilutions. The sensitizers were administered in several concentrations (from 50 nM to 10 μM) and, 24 hour after incubation, cells were washed with PBS and new drug-free medium was added. Plates were irradiated (<580 nm) with a fluence rate of 7.5 mW/cm², to reach 10 J. Controls were performed on every test. Evaluation by MTT assay was performed 24 hour after the photodynamic treatment. The IC$_{50}$ values were calculated.

**Results and discussions** Preliminary cytotoxicity studies indicate that, in both cell lines, platinum (II) chlorins with more hydrophilic features require lower doses of photosensitizer to induce a significant photocytotoxic effect on tumour cells. Our best results were IC$_{50}$ value of 165.9 nM (confidence interval at 95%: [77.9; 356.6]) for A375 line and 498.6 nM (confidence interval at 95%: [283.5; 876.5]) for OE19 line. However, and given that the confidence intervals were too large, it was hypothesised that this type of compounds would be aggregating in the biological medium. This hypothesis was corroborated by additional photophysical studies. As such, disaggregation was performed with the use of a non-ionic surfactant since surface active agents (surfactants) has been widely used for enhancing solubilisation of poorly soluble drugs.

**Conclusion** Although photocytotoxicity studies reveal that the platinum (II) chlorins tested would be very promising for PDT, further cytotoxicity studies will be carried out using a novel formulation.