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BOOK OF ABSTRACTS

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INVESTIGATING THE ULTRASOUND EFFECTS OF DIFFERENT CHEMICAL COMPOUNDS TO HIGHLIGHT THE IN VITRO SONODYNAMIC PROCESS

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Introduction
Ultrasound (US) can be used to trigger the cytotoxicity of chemical compounds, known as sonosensitisers, to yield cancer cell death in an approach that has been defined sonodynamic therapy (SDT). Although SDT mechanisms are still a matter of debate between a cavitation-induced i) photo-activation via sonoluminescence or ii) homolytic splitting of water, it is generally accepted that reactive oxygen species (ROS) are the main effector of sonosensitised cell damage (1). Therefore, this work aims to investigate the US-responsiveness of different chemical compounds in an attempt to clarify the mechanisms underpinning the sonodynamic process

Methods
US were used to trigger the cytotoxicity of different chemical compounds at noncytotoxic concentrations *per se,* such as metalloporphyrin, *i.e.* Pd(II) porphyrin, and chemotherapeutic drugs, *i.e.* doxorubicin and paclitaxel. US-mediated ROS generation were analysed *ex cellulo* by EPR spectroscopy and *in vitro* by DCF-DA flow cytometric assay. The US-mediated anticancer activity of Pd(II) porphyrin, doxorubicin and paclitaxel was then evaluated on the human colon cancer, HT-29, the ovarian cancer, A2780, and the breast cancer, MCF-7, cell lines, respectively. Mitochondrial membrane potential, DNA damage, lipid peroxidation, cell cycle and cell death were analysed by flow cytometric assays and gene expression by real-time-RT-PCR

Results
Our results showed, through EPR analysis, that Pd(II) porphyrin and doxorubicin were more efficient in generating ROS under US exposure than paclitaxel with different patterns of ROS production under US exposure for each compound. These findings were also confirmed when noncytotoxic concentrations of Pd(II) porphyrin and doxorubicin, activated by US in HT-29 and A2780 cells, showed a significant intracellular ROS production and a remarkable reduction in cancer cell growth, along with significant mitochondrial membrane potential impairment and an increase in apoptotic and necrotic cells, respect to paclitaxel in MCF-7 cells. These results suggest that the US-responsiveness of the compounds can be related to their photosensitising properties

Discussion
Since Pd(II) porphyrin and doxorubicin, well known photosensitisers, were able to elicit a significant ROS generation yielding cancer cell death when triggered by US compared to paclitaxel, it might be reasonable to assume that the US-mediated sonosensitiser activation can be due to a sort of photo-activation via cavitation-induced sonoluminescence rather than a radical path process via homolytic splitting of water

Conclusion
The results reported herein support the intracellular ROS generation as the main effector in the sonodynamic process and new insight in the underlying mechanism.

Continued

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Conflicts of Interest
The authors declare no conflict of interest

References

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