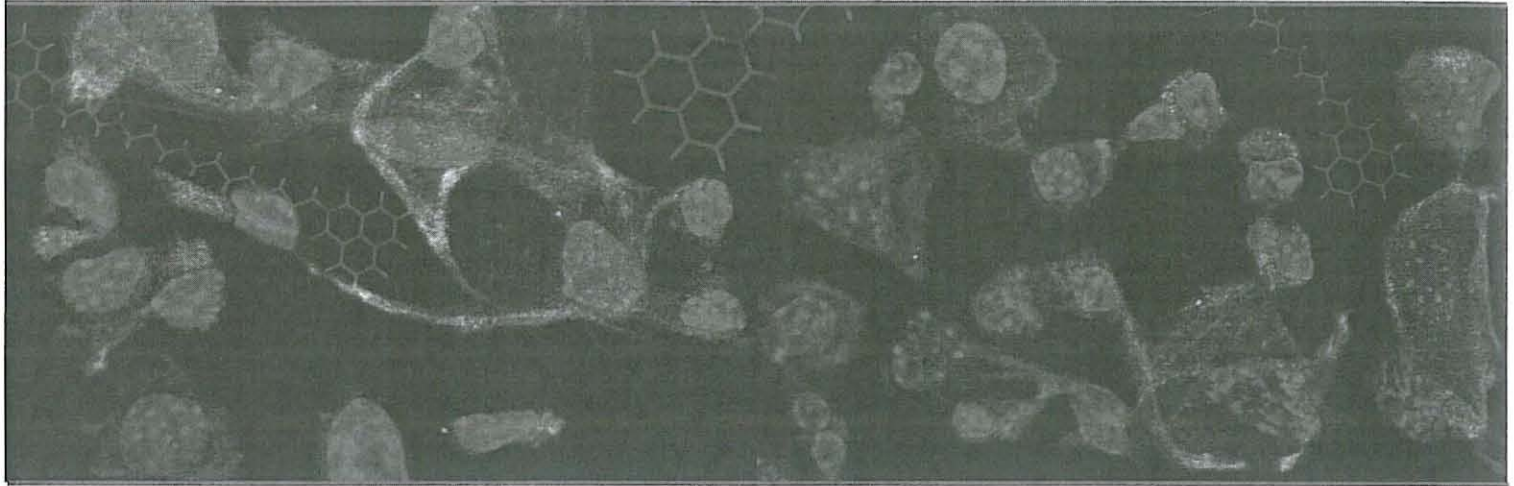


workshop

Antiparasitic and Antitumour drugs



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P2. Bioactivity and chemical characterization of *Fistulina hepatica* extracts

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Fistulina hepatica, the beefsteak fungus, belongs to the order Agaricales and is commonly found all over Europe, North America, Australia and North Africa. Being a good edible species, it has also been investigated for its medicinal and pharmaceutical capacities. The anti-tumor activity of *F. hepatica* polysaccharides extracts from the mycelial culture was reported after intraperitoneally administration into white mice [1].

Nevertheless, nothing has been reported with phenolic and polysaccharidic extracts from the fruiting body. The aim of this work was to evaluate the antioxidant activity and tumour cell growth inhibitory potential of those extracts, and to further characterize their chemical composition. Phenolic (methanolic and ethanolic) and polysaccharidic (boiling water) extracts were prepared and their antioxidant properties were evaluated through its reducing power (RP), radical scavenging activity (RSA) and lipid peroxidation inhibition capacity by the β -carotene-linoleate system (CLS). The tumour cell growth inhibitory potential was studied with the sulforodamine B (SRB) assay in the MCF-7 (breast) and in the HCT-15 (colon) cell lines.

Chemical characterization was possible by chromatographic analyses: HPLC-DAD for phenolic compounds and HPLC-RI for sugars. Results showed that the polysaccharidic extract was the most effective as antioxidant with the following EC50 values: RP (2.60 ± 0.06 mg/ml), RSA (2.71 ± 0.23 mg/ml) and CLS (0.84 ± 0.01 mg/ml). The main sugars present were arabinose (7.76 ± 0.63 g/100 g dw), trehalose (2.95 ± 0.22 g/100 g) and mannitol (2.12 ± 0.22 g/100 g). Among the phenolic extracts, the methanolic one was more active with EC50 values ≤ 5.32 mg/ml. The main phenolic acids present in the extract were: protocatechuic (6.76 ± 0.17 mg/100 g dw), p-hydroxybenzoic (4.19 ± 0.90 mg/100 g) and cinnamic (0.22 ± 0.01 mg/100 g) acids. Results from the tumour cell growth inhibitory activity revealed that these extracts are not strong inhibitors of tumour cell growth since the GI50 concentration was not achieved with the maximum concentration tested (400 μ g/ml).

Despite the good antioxidant properties found in the extracts from the fruiting body, they did not show growth inhibitory activity in the tested cell lines. Therefore, it would be important to test the activity in other cell lines and to produce mycelium in order to evaluate its bioactivity.

References: [1] Ohtsuka et al. UK Patent 1331513, 1973.

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P3. Paromomycin nanoformulations with improved antileishmanial properties

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The lack of effective drugs for treatment of leishmaniasis constitutes a major threat for millions of people worldwide. As there are no novel compounds expected to be approved in a short term, efforts should be made to improve the efficacy of currently available drugs. One of these strategies may be the use of drug delivery systems, such as liposomes. These lipid systems are able to optimize the therapeutic performance of existing antileishmanial compounds, through a preferential intracellular accumulation of drugs in macrophage-rich organs such as liver and spleen where parasites proliferate. This strategy can result in shorter treatments, lower administered doses, reduction on side-effects and emergence of drug resistance.

Paromomycin (PRM) is an aminoglycoside with proved antileishmanial activity since 1960s. This antibiotic is poorly absorbed into systemic circulation after oral administration and it is absorbed rapidly from intramuscular sites of injection. In a clinical trial conducted in India this antibiotic has shown to be efficacious against visceral leishmaniasis. However, its efficacy is far from ideal as last clinical trials were controversial and irregular: a 94% of cure was registered in some trials whereas a failure was observed in others.

Our strategy was the encapsulation of PRM in liposomes in order to improve its therapeutic performance. Systematic studies concerning selection of best liposomal formulations able to maximize the loading