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Poster Communication Abstract – 7.30

FLAX TISSUE CULTURES AS BIOFACTORY FOR LIGNAN PRODUCTION

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Lignans are the main secondary metabolites synthetized by *Linum* species as plant defense compounds. Because they are also valuable for human health, the demand for these secondary metabolites has increased in recent years due to their application in pharmaceutical and nutraceutical industries. Lignans, a large group of polyphenols, are divided into three main classes based on their chemical structure: aryltetralin-type (ATLs), arylnaphtalene-type(ANLs) and dibenzylbutyrolactone-type (DBBLs). The genus *Linum* includes more than 200 species taxonomically divided into five or six sections and each section produce a specific class of lignans. ANLs such as justicidin B and ATLs such as podophyllotoxin (PTOX) are the most interesting compounds due to their therapeutic properties. Despite the recent advance in chemical synthesis, this strategy is not always economically feasible as well as the direct extraction from plants due to the low production. Plant tissue cultures can overcome this bottleneck and metabolite production of these cultures can be induced through elicitor treatments. In this work, *Linum austriacum* in vitro cultures, cells (Cc), adventitious roots (ARc) and hairy roots (HRc), were developed for the production of justicidin B and adventitious root cultures of three Linum species (*L. flavum*, *L. mucronatum* and *L. dolomiticum*) were developed to produce podophyllotoxin and 6-methoxypodophyllotoxin. The results obtained showed that ARc and HRc from *L. austriacum* were the highest productive tissues and that methyl jasmonate (MeJA)and coronatine (COR) treatments induced the synthesis of justicidin B more than three times than control. Furthermore, for the first time, the intracellular localization of justicidin B in ARc was investigated through

microscopic analysis showing its cytosolic localization. HRc were also used to assess the feasibility of justicidin B production in a small scale bioreactor, which production was four times higher than that observed in flask.

Regarding the ATLs production, our results indicated the *L. dolomiticum* ARc as the best producer, among the three species investigated, for all the aryltetralins highlighted in this system: podophyllotoxin, 6-methoxypodophyllotoxin and 6-methoxypodophyllotoxin-7-O-β-glucoside. The most striking result was the production of MPTOX–Glc by *L. dolomiticum* ARc, 70.8 mg/gDW rising to 92.6 mg/mDW after 10 µM COR elicitation. This value is one of the highest reported for this molecule even when compared to hairy roots of other species. Due to the cytotoxic activity, MPTOX can be used as lead compounds for the development of new anticancer drug.

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