



ABSTRACT

The effect of oxidative stress on indole alkaloids accumulation by cell suspensions and root cultures of *Uncaria tomentosa* in bioreactors was investigated. Hydrogen peroxide (H_2O_2 , 200 μM) added to *U. tomentosa* cell suspension cultures in shaken flasks induced the production of monoterpenoid oxindole alkaloids (MOA) up to 40.0 $\mu\text{g/L}$. In a stirred tank bioreactor, MOA were enhanced by exogenous H_2O_2 (200 μM) from no detection up to 59.3 $\mu\text{g/L}$. Root cultures grew linearly in shaken flasks with a $\mu=0.045 \text{ days}^{-1}$ and maximum biomass of $12.08 \pm 1.24 \text{ g DW/L}$ (at day 30). Roots accumulated 3 α -dihydrocadambine (DHC) $2354.3 \pm 244.8 \mu\text{g/g DW}$ (at day 40) and MOA $348.2 \pm 32.1 \mu\text{g/g DW}$ (at day 18). Exogenous addition of H_2O_2 had a differential effect on DHC and MOA production in shaken flasks. At 200 μM H_2O_2 , MOA were enhanced by 56% and DHC by 30%; while addition of 800 and 1000 μM H_2O_2 , reduced by 30–40% DHC accumulation without change in MOA. Root cultures in the airlift reactor produced extracellular H_2O_2 with a characteristic biphasic profile after changing aeration. Maximum MOA was 9.06 mg/L at day 60 while at this time roots reached ca. 1 mg/L of DHC. Intracellular H_2O_2 in root cultures growing in the bioreactor was 0.87 $\mu\text{mol/g DW}$ compared to 0.26 $\mu\text{mol/g DW}$ of shaken flasks cultures. These results were in agreement with a higher activity of the antioxidant enzymes superoxide dismutase and peroxidase by 6- and 2-times, respectively. *U. tomentosa* roots growing in the airlift bioreactor were exposed to an oxidative stress and their antioxidant system was active allowing them to produce oxindole alkaloids.

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