Study of the effects of plasmatic concentrations of sertraline, duloxetine and fluoxetine on THP-1 cells using the comet assay

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Antidepressants are widely prescribed for the long-term treatment of major depressive disorder (MDD) and other psychiatric conditions, being selective serotonine reuptake inhibitors and serotonine and noradrenaline reuptake inhibitors first-line drugs. According to the neuroinflammatory hyphotesis, increased inflammatory events in the brain and at the periphery of depressed patients may play a key role in the pathogenesis of MDD. Moreover, a long-term increase of proinflammatory markers is linked to the production of oxygen reactive species (ROS), a major inducer of oxidized bases in the DNA.

Because of the difficulty to recruit drug-free depressed patients, and with the final purpose of studying the effect of this disease on the level of oxidized bases, in this work we aim to study the effect of the three most prescribed antidepressant drugs, at plasmatic concentrations, on this biomarker. We evaluated the potential of duloxetine, sertraline and fluoxetine to induce DNA stand breaks (SBs) and oxidized bases on THP-1 cells after 6 and 24 hours of treatment. For this purpose, plasmatic concentrations of fluoxetine (1 and 10 μM), duloxetine (0.43 and 4.30 μM) and sertraline (0.18 and 1.8 μM) were used and the standard and formamidopyrimidine DNA glycosylase (Fpg)-modified comet assays were applied. Moreover, the vulnerability or resilience of antidepressant-treated cells to $KBrO_3$, an oxidant agent, was also studied.

Results indicate that none of the antidepressants produce SBs or oxidized bases. Moreover, none of the antidepressants alter the level of oxidized bases induced by $KBrO_3$.