# Biocompatibility of *Salix viminalis*, *Salix atrocinerea* and *Salix fragilis*

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Current consumer trends point at an increase in the interest, and subsequent demand, of more natural products with less added chemicals. Considering this shift in mentality, natural extracts present themselves as an interesting alternative to traditional additives, particularly as they may contribute not only to the stabilization of the matrix they are incorporated into, but also its functionality. *Salix* extracts have been traditionally used as a part of herbal medicine and therefore present an interesting venue through which to improve the functionality of edible and cosmetic matrixes. However, the use of extracts may raise some safety concerns, particularly when considering that, even when the extracts are attained from edible source, the overall intake of bioactive ingredients may be significantly higher than that a normal diet would encompass. Considering this, the present work aimed at characterizing the biocompatibility of three different hydrophilic *Salix* extracts (*S. viminalis*, *S. atrocinerea* and *S. fragilis*) considering their impact upon the metabolic activity, proliferation and membrane integrity of CaCo-2, HaCat and L929.
Overall, metabolically wise, CaCo-2 cell line was the less susceptible to the extracts presence with only the highest concentration of *S. atrocinerea* (2.5 mg/mL) and the lowest concentration of *S. viminalis* (0.625 mg/mL) resulting in metabolic inhibitions above 20%. In fact, the lower concentrations of *S. atrocinerea* (1.25 and 0.625 mg/mL) and all concentrations of *S. fragilis* (2.5, 1.25 and 0.625 mg/mL) resulted in a stimulation of cell metabolism. All extracts exhibited some inhibitory effect upon L929 cell line with only the lower concentrations of *S. atrocinerea* and *S. fragilis* (1.25 and 0.625 mg/mL) exhibiting inhibitions below 20%. For HaCat the lower concentrations of *S. viminalis* (1.25 and 0.625 mg/mL) and the highest concentration of *S. atrocinerea* (2.5 mg/mL) were the only ones that exhibited inhibition percentages above 20% with the lower concentrations of *S. atrocinerea* and *S. fragilis* (1.25 and 0.625 mg/mL) exhibiting some metabolic stimulation. Moreover, it is interesting to note that, while in most cases, the loss in metabolic activity was not accompanied with an increase in lactate dehydrogenase release (an indicator of membrane damage) all extracts, regardless of the concentration tested, resulted in inhibitions of cell proliferation for HaCat and L929, ranging from 35 to 55%, respectively. The only exception was CaCo-2 whose proliferation appeared to be stimulated by all extracts.

***Keywords:*** *Salix* extracts, metabolic inhibition, membrane damage, cell proliferation