

Chemopreventive effects of *Santolina chamaecyparissus* in a rat model of chemically-induced mammary cancer

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Breast cancer is the most frequently diagnosed cancer in women and a leading cause of death worldwide. *Santolina chamaecyparissus* L. is a plant with several medicinal properties, including anti-cancer effects. This study aimed to assess the chemopreventive effects of *S. chamaecyparissus* aqueous extract (SCE) in *N*-methyl-*N*-nitrosourea (MNU)-induced mammary cancer in female rats. UTAD's ORBEA approved this study (834-e-CITAB-2020). Twenty-eight four-week-old female Wistar rats were divided into four groups: control, MNU-induced (IND), SCE-supplemented (SCE), and SCE+IND. SCE was added to water (120 µg/mL). MNU (50mg/kg) was administered intraperitoneally at 50 days of age. Body mass, drink and food intake, humane endpoints and mammary tumours were monitored weekly. Twenty weeks after MNU administration, animals were humanely sacrificed. Blood samples were collected for biochemical analysis, liver and kidney

samples were used for oxidative stress analysis and tumour tissue for gene expression analysis.

SCE's chemical composition was analysed using LC-MS, and nineteen phenolic compounds were identified, being myricetin-*O*-glucuronide and 1,3-*O*-dicafeoylquinic acid the most abundant ones. SCE supplementation delayed the appearance of the first mammary tumour by six weeks. A slight decrease in tumour volume and mass was observed ($p > 0.05$). SCE had no impact in serum parameters or antioxidant enzymes activity. Gene expression analysis showed significantly reduced *VEGF* expression levels ($p = 0.0158$) and slightly reduced *PCNA* and *ER-α* ($p > 0.05$) expression in tumours from group SCE+IND.

As there were no negative effects on liver and kidney function or animal welfare, the findings suggested that SCE could be a promising therapeutic option for breast cancer treatment.

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