

### 10.3 – *CASTANEA SATIVA* MILL. FLOWERS AS POTENTIAL CHEMOPREVENTIVE AGENT AGAINST RAT PROSTATE CANCER MODEL

Elisabete Nascimento-Gonçalves<sup>1</sup>, Mónica Silva<sup>2</sup>, Fernanda Seixas<sup>3</sup>, Margarida Fardilha<sup>4</sup>, Rita Ferreira<sup>5</sup>, Maria João Neuparth<sup>6</sup>, Ana I. Faustino-Rocha<sup>1,7</sup>, Bruno Colaço<sup>1</sup>, Carlos Venâncio<sup>1</sup>, Eduardo Rosa<sup>1</sup>, Lilian Barros<sup>1</sup>, Isabel C.F.R. Ferreira<sup>8</sup>, Maria Manuel Oliveira<sup>2</sup>, Francisco Peixoto<sup>2</sup>, Paula Oliveira<sup>1</sup>

<sup>1</sup>CITAB, UTAD, Vila Real; <sup>2</sup>Chemistry Department, UTAD, Vila Real, Portugal; <sup>3</sup>CECAV, UTAD, Vila Real, Portugal; <sup>4</sup>Laboratory of Signal Transduction, Institute for Research in Biomedicine, Medical Sciences Department, University of Aveiro (UA), Aveiro, Portugal; <sup>5</sup>Organic Chemistry, Natural Products and Food Stuffs, UA, Aveiro, Portugal, <sup>6</sup>Advanced Polytechnic and University Cooperative, Institute of Research and Advanced Training in Health Sciences and Technologies, Gandra, Portugal, <sup>7</sup>Faculty of Veterinary Medicine, Lusophone University of Humanities and Technologies, Campo Grande, Lisbon, Portugal, <sup>8</sup>Centro de Investigação de Montanha, Campus Santa Apolónia, Bragança, Portugal.

**Introduction:** Prostate cancer is one of the most common cancer among men, having a huge impact in their health [1]. This work aimed to evaluate the influence of a decoction extract obtained from *C. sativa* flowers (CF) on chemically and hormonally induced rat prostate cancer animal model.

**Material & Methods:** All the animal experiments were approved by the Institutional Animals Ethics Committee and by Portuguese national authorities (DGAV nº 021326). Forty male Wistar Unilever rats were randomly divided into four groups: control group (n=10), induced group (n=15), CF control group (n=5) and CF induced group (n=10). Animals from induced groups received a multistep induction protocol, which consisted of sequential administration of flutamide, testosterone propionate, the carcinogenic agent MNU and crystalline testosterone. The CF extract, rich in ellagitannins especially trigalloy-HHDP-glucose, was administered in the drinking water (3 mg/animal/day) for 49 weeks. Animals were sacrificed at 61 weeks of age and organs were collected, weighed and processed for light microscopy. Data were analysed using SPSS and GraphPad Prism software.

**Results:** There were no significant differences in relative mean liver weight among groups exposed and not exposed to the CF extract and no animals developed severe hepatic changes. Animals from CF induced group developed less prostatic intraepithelial neoplasia than induced group. Also, animals exposed to the CF extract did not present areas of inflammation of the dorsolateral prostate lobe greater than 50% unlike the groups not exposed (p<0.05). The administration of CF in induced animals was able to decrease the activity of CAT and GST by 36% and 20%, respectively (p<0.05).

**Conclusions:** These results suggest that CF extract was well tolerate by the animals and did not cause severe hepatic and renal toxicity. *C. sativa* flowers extract may be used as chemopreventive agent against prostate cancer and seems to have an antioxidant role.

**References:** [1] Nascimento-Gonçalves E et al. *Life Sci.* 2017; 203: 201-224; [2] Carocho M et al. *Ind Crop Prod.* 2014; 62: 42-46.

**Acknowledgments:** This work was supported by European Investment Funds by FEDER/ COMPETE/POCI - Operational Competitiveness and Internationalization Programme, under Project POCI-01-0145-FEDER006958 and National Funds by FCT - Portuguese Foundation for Science and Technology, under the project UID/AGR/0433/2019, UID/QUI/00062/2019 (QOPNA), UID/AGR/00690/2019 (CIMO), PEst-OE/QUI/UI0616/2014 and the project PTDC/DTP-DES/6077/2014 and post-graduation grant SFRH/BD/136747/2018. L. Barros also thanks the national funding by FCT, P.I., through the institutional scientific employment program-contract for her contract. Funding: Interreg Program for the financial support of the Project IBERPHENOL, Project Number 0377\_IBERPHENOL\_6\_E, co-financed by European Regional Development Fund (ERDF) through POCTEP 2014-2020.

**Conflict of interests:** None to declare.