

Optimization of ultrasound-assisted extraction of *Pistacia lentiscus* L. leaves in a green way to obtain the highest content of polyphenols using a response surface methodology

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Abstract: *Pistacia lentiscus* L. leaves are used in several applications, thanks to their polyphenolic abundance. Different methods are used for the extraction of these compounds. We aimed to optimize the ultrasound-assisted extraction (UAE) of *P. lentiscus* to obtain higher amounts of polyphenols in a greener way. A Box-Behnken design using temperature (30-50 °C), solvent volume (15-30 mL) and ethanol fraction (30-50 %) was conducted. Galloyl and myricetin derivatives were the most abundant compounds detected (HPLC-DAD-MS analysis). The regression analyses of total polyphenol (TPC), total tannins (TTC), total flavonoids (TFC) and myricitrin contents (MYC) showed good fit of the models. The maximum yields of TPC ($51.3 \pm 1.8 \text{ mg g}^{-1} \text{ DW}$) and TTC ($40.2 \pm 1.4 \text{ mg g}^{-1} \text{ DW}$) are obtained using 18 mL of 40 % ethanol at 50 °C. For flavonoids, an extraction with 20 mL of 50 % ethanol at 50 °C predicts the highest content ($10.2 \pm 0.8 \text{ mg g}^{-1} \text{ DW}$), while 15 mL of 30 % ethanol at 30 °C results in the maximum of MYC ($2.6 \pm 0.19 \text{ mg g}^{-1} \text{ DW}$). This greener process decreased in 25 % the percentage of ethanol and in half the time of the usual ethanolic extraction. Therefore, these UAE conditions can be applied to obtain polyphenolic enriched extracts from *P. lentiscus* leaves, which can be further employed for several industrial purposes.

Keywords: Anacardiaceae; design of experiments (DOE); flavonoids; green extraction; HPLC-DAD; LC-MS; tannins; ultrasound assisted-extraction (UAE)