Supplementary Material

Effects of standardized medicinal plant extracts on drug metabolism mediated by CYP3A4 and CYP2D6 enzymes

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1. RESULTS

1.1 Characterization of drug substrates and their metabolites

Table S1: Parameters obtained for the validation of the analytical methods.

	Concentration (μM)	Precision (RSD %)*	Accuracy (%)*
OH-midazolam	1	11.5	84.1-117.1
	2.5	12.4	82.5-116.6
	5	9.0	88.8 -116.3
OH-metoprolol	6.25	9.5	91.7-110.3
	50	1.2	99.0-101.4
	80	12.4	85.7-107.5
O-demethylmetoprolol	6.25	11.2	88.5-110.8
	50	10.8	89.2-110.7
	80	13.2	88.5-114.5

*The data correspond to three independent analyses.
RSD: Relative Standard Deviation

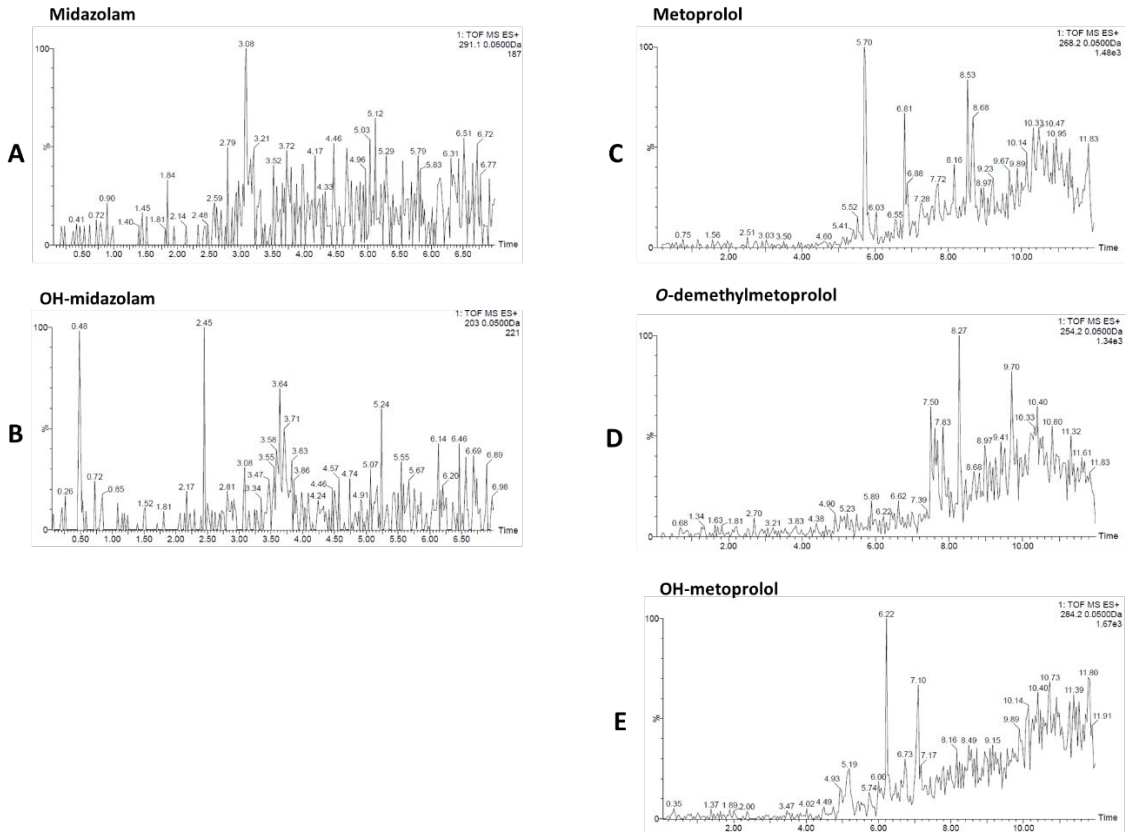

Figure S1: Specificity of the chromatographic method - Blank of the reaction mix. **A.** midazolam, **B.** OH-midazolam, **C.** metoprolol, **D.** *O*-demethylmetoprolol, **E.** OH-metoprolol.

1.2 Identification of the major phytoconstituents of *Cecropia glaziovii* and *Ilex paraguariensis* by UPLC-MS/MS

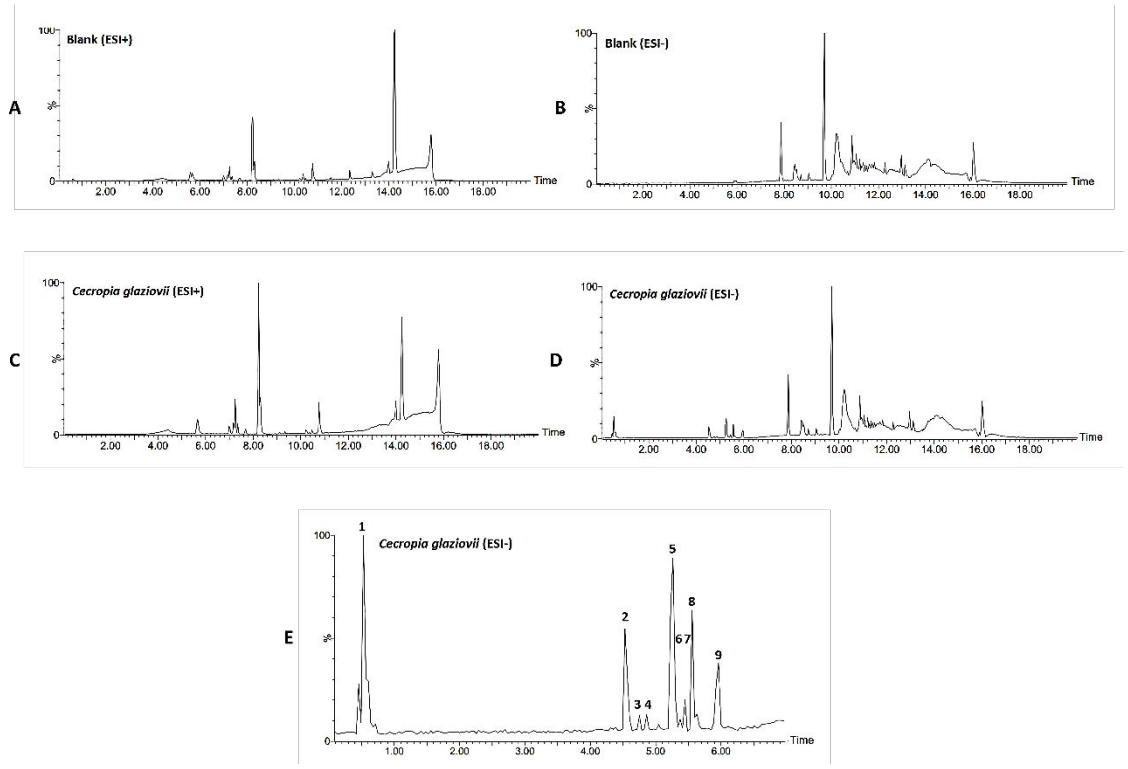

Figure S2: A. ESI+ and **B.** ESI-: solvent chromatograms; **C**. ESI+ and **D**. ESI-: complete chromatograms of *Cecropia glaziovii*; **E**. ESI-: chromatogram with numerical indications of peaks corresponding to the major compounds identified in *C. glaziovii* extract; all obtained by UHPLC-MS/MS. The identification of each numbered peak can be seen in Table 3 of the manuscript.

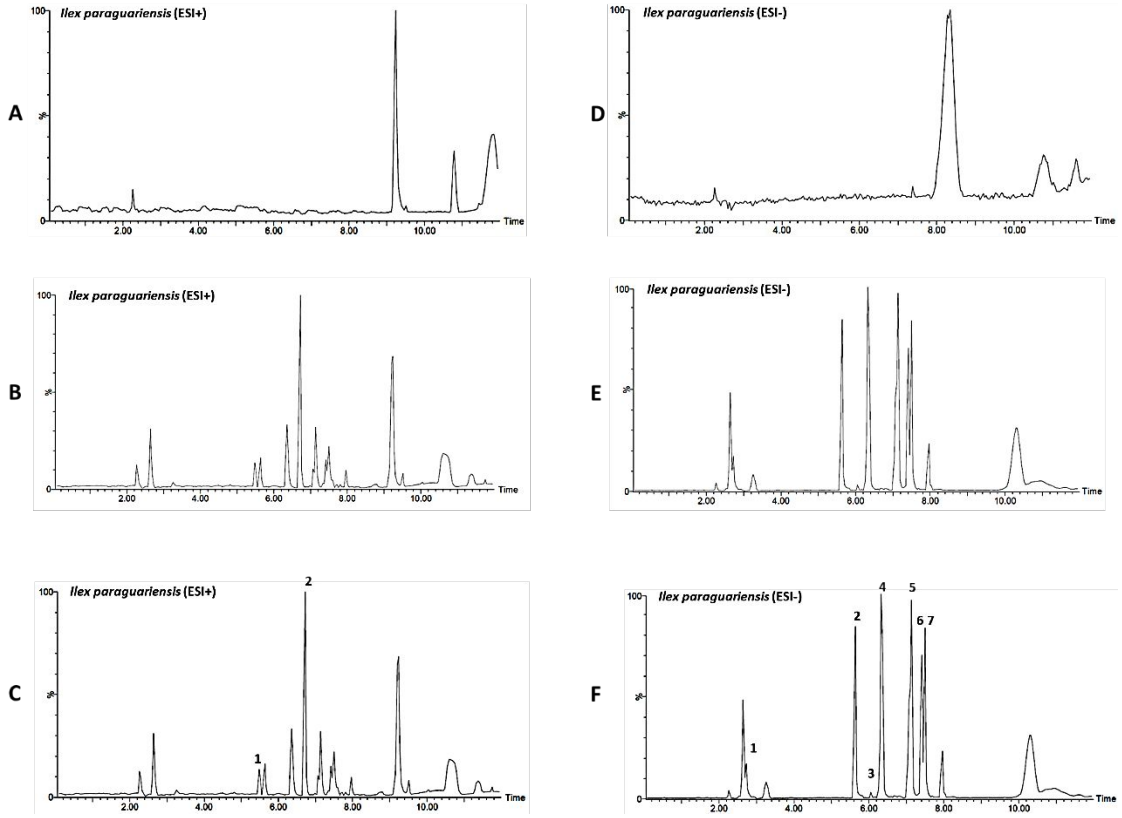

Figure S3: A. ESI+ and **D.** ESI -: solvent chromatograms; **B**. ESI+ and **E**. ESI-: complete chromatograms of *Ilex paraguariensis*; **C**. ESI+ and **F**. ESI-: chromatograms with numerical indications of peaks corresponding to the major compounds identified in the *I. paraguariensis* extract; all obtained by UHPLC-MS/MS. The identification of each numbered peak can be seen in Table 4 of the manuscript.