

ABSTRACT

Strychnos nux-vomica L.f. (SNV) and *Strychnos potatorum* L. (SPs) are medicinally important plants traditionally used for their therapeutic properties, including antioxidant and antidiabetic activities. However, the extraction of the bioactive compounds from these plants and many others has been the most challenging and deterioration-prone step. The advent of green chemistry further endorses the use of eco-friendly and green solvents to replace toxic and volatile organic solvents. In this research, we have attempted to prepare deep eutectic solvents (DES) comprising ammonium acetate–propanoic acid (AA/PA) and glycerol–sodium acetate (Gly/NaOAc). The former was applied for the extraction of SNV seed bioactive coupled with ultrasound-assisted extraction (UAE) and heating shaker extraction (SHA), whereas the latter (Gly/NaOAc) was applied for the extraction of SPs bioactive. The Factors affecting extraction efficiencies, *i.e.* extraction time, temperature, and solvent-to-solid ratio, were studied at different levels. The extraction efficiencies were predicted and optimized following Response Surface Methodology (RSM) and Artificial Neural Networking (ANN) with extraction time, temperature, and solvent-to-solid ratio as independent variables. The dependent variables optimized include % yield, total phenolic and flavonoid content (TPC & TFC), DPPH-radical scavenging capacity, and antidiabetic activity (α -amylase inhibitory activity). At optimal conditions, SPs-UAE achieved a yield of $6.82 \pm 0.16\%$, while SHA yielded $4.76 \pm 0.35\%$. Similarly, SNV showed $6.31 \pm 0.04\%$ with UAE and $3.31 \pm 0.01\%$ with SHA; all values were comparatively higher than those offered by ethanol as a solvent. The highest TPC was recorded for SNV-UAE (64.72 ± 0.01 mg GAE/g DW), while SNV-SHA showed the highest TFC (128.36 ± 0.02 mg QE/g DW). In terms of free radical scavenging, SNV-UAE extracts

exhibited $89.87 \pm 0.02\%$ DPPH scavenging, whereas SNV-SHA offered $85.78 \pm 0.01\%$ neutralization of DPPH free radicals. The antidiabetic potential was also varied significantly ($p \leq 0.05$) with the change in extraction conditions, with SNV-UAE showing $68.53 \pm 0.07\%$ α -amylase inhibition and SPs-UAE $47.33 \pm 0.07\%$. ANN predictions consistently outperformed RSM across all parameters, with lower prediction errors (%AAD, RMSE, PPE, %RSD) and statistically significant improvements ($p < 0.05$) in most responses, confirming its robust predictive capability. SEM-EDX analysis confirmed enhanced cellular disruption due to DES-ultrasound synergy, facilitating greater compound release. LC-MS authenticated the presence of strychnine and other flavonoids in SNV extracts, while molecular docking (binding score -8.78 kcal/mol) validated its α -amylase inhibitory potential. A strong correlation was observed between TPC and TFC in both plants ($p < 0.005$). Overall, this study demonstrates that DESs combined with UAE or shaker-assisted extraction, particularly when modelled using ANN, offer a sustainable and highly efficient extraction technique for the recovery of valuable phytochemicals from SNV and SPs, supporting their application in nutraceutical and pharmaceutical industries.