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AI-Driven Virtual Screening of *Lemna minor* Phenolic Compounds in the Search for Novel Glycemic Control Agents

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The protein tyrosine phosphatase 1B (PTP1B; EC 3.1.3.48), encoded by the PTPN1 gene, dephosphorylates the activated insulin receptor and IRS-1, acting as a negative regulator of insulin and leptin. PTP1B knockout mice, which are more insulin sensitive and resistant to diet-induced obesity, genetically validate PTP1B as a dual target for type 2 diabetes and obesity. However, no inhibitor has made it to clinical trials. We applied an integrated and phased flow, with prior validation, to the 53 phenolic compounds of *Lemna minor*, found in literature and hosted in the LMW Database against PTP1B (PDB 2QBS): (1) validation by redocking of the co-crystallized inhibitor; (2) molecular docking (AutoDock Vina) [4]; (3) consensus by second scoring function (Vinardo) and by machine learning (RF-Score); (4) AI co-folding with confidence metric (Boltz-2); and (5) internal control with cross-validation in the literature. *Lemna minor* was rich in PTP1B ligands (about two-thirds of the phenolics showed a strong predicted interaction). Flavone luteolin stood out as a lead in all criteria (docking -9.14 kcal/mol; best flavonoid by affinity; ipTM 0.90), corroborated by literature: luteolin derivatives inhibit PTP1B (luteolin-7-diglucuronide, $IC_{50} = 2.10$ μ M); quercetin is a reference inhibitor of aldose reductase ($IC_{50} = 6.6$ μ M); and apigenin inhibits α -glucosidase ($IC_{50} = 10.5$ μ M). *Lemna minor* extracts emerge as multi-component, multitarget antidiabetic candidates, with a solid basis for subsequent in vitro experimental confirmation.

Corresponding author email

felipemacedo.alves20@gmail.com

Scientific Session

Applications

Keywords

Extract;PTP1B;luteolin;flavonoids;diabetes;docking

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Primary author(s) : Mrs. ALVES, Felipe (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal/2Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecología e Alimentación (IAA)—CITEXVI, Universidade de Vigo, 36310 Vigo, Spain); Mrs. SEITE, Carlos (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal); Mrs. ABREU, Rui (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal); Dr. FELICIANO, Manuel (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal); Dr. CAROCHO, Márcio (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal); Dr. LAGE, Miguel (2Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecología e Alimentación (IAA)—CITEXVI, Universidade de Vigo, 36310 Vigo, Spain)

Presenter(s) : Mrs. ALVES, Felipe (1CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal/2Nutrition and Bromatology Group, Department of Analytical Chemistry and Food Science, Instituto de Agroecología e Alimentación (IAA)—CITEXVI, Universidade de Vigo, 36310 Vigo, Spain)

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