In-silico Investigation of *Phyllanthus niruri* phytochemicals as Hepatic Fibrosis Modulators

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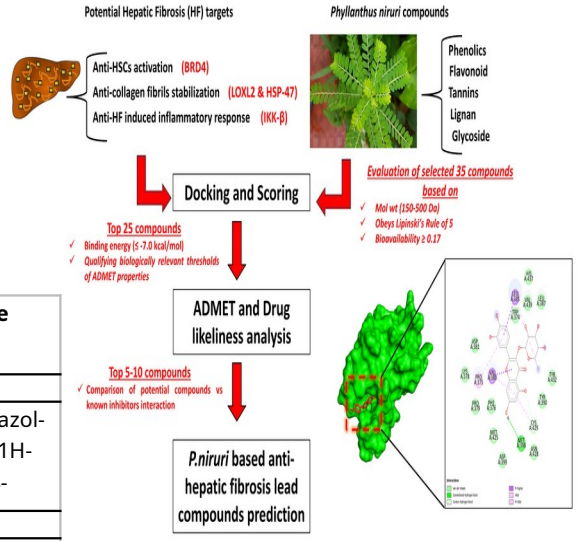
Introduction

- Liver is a pivotal internal organ that orchestrates major metabolic, detoxification and endocrine roles.
- Chronic liver injury is majorly attributed by the non-alcoholic fatty liver (**NAFLD**) spectra.
- **Liver fibrosis (LF)** is a challenging quest in hepatology for safer and higher specificity therapeutics.

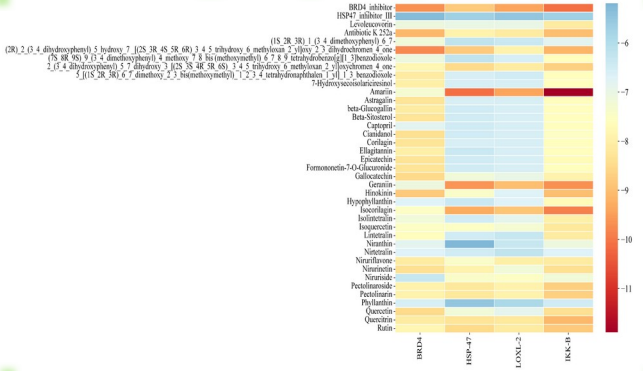
Target protein	PDB Id	Inhibitor compound opted for the molecular docking study
HSP-47	3ZHA	HSP47 inhibitor III
BRD4	6C7Q	BRD4 inhibitor {7-(3,5-dimethyl-1,2-oxazol-4-yl)-6-methoxy-2-methyl-N-(1-methyl-1H-indazol-3-yl)-9H-pyrimido[4,5-b]indol-4-amine}
IKK-B	3RZF	Antibiotic K 252a
LOXL-2	5ZE3	Levoleucovorin

Methodology

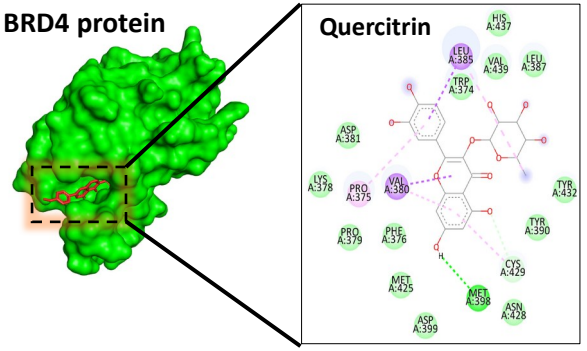


Results

Molecular docking Heat map results of P.niruri compounds



Schematic diagram of molecular docking interaction

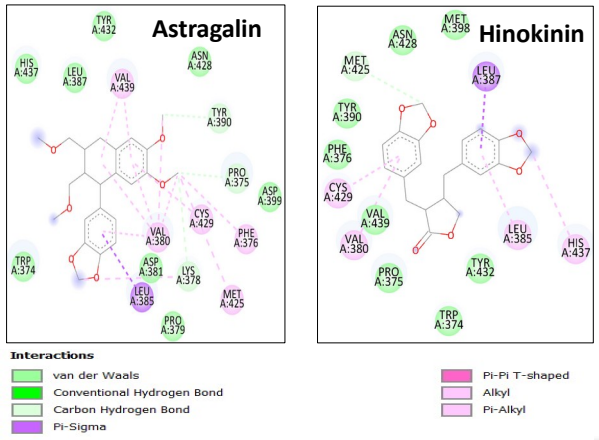


In-silico Toxicity Prediction

TABLE2: In-silico toxicity prediction of *P.niruri* compounds

Compounds	Predicted LD50 (mg/kg)	Predicted Toxicity Class	Hepato-toxicity	Carcino-genicity	Immuno-genicity	Tox21-Nuclear receptor signalling pathways: PPAR-γ	MMP	p53
BRD4 inhibitor	3000	5						
HSP47_inhibitor_III	1600	4						
Levoleucovorin	135	3						
Antibiotic K 252a	11	2						
(2R)_2_(3_4_dihydroxyphenyl)_5_hydroxy_7_[(2S_3R_4S_5R_6R)_3_4_5_trihydroxy_6_methyloxan_2_yl]oxy_2_3_dihydrochromen_4_one	12000	6						
2_(3_4_dihydroxyphenyl)_5_7_dihydroxy_3_[(2S_3S_4R_5R_6S)_3_4_5_trihydroxy_6_methyloxan_2_yl]oxychromen_4_one	5000	5						
5_[(1S_2R_3R)_6_7_dimethoxy_2_3_bis(methoxymethyl)_1_2_3_4_tetrahydronaphthalen_1_yl]_1_3_benzodioxole	214	3						
Amarin	620	4						
Astragalin	5000	5						
beta-Glucogallin	2240	5						
Beta-Sitosterol	890	4						
Cianidanol	10000	6						
Corilagin	2240	5						
Epicatechin	10000	6						
Formononetin-7-O-Glucuronide	5000	5						
Gallocatechin	10000	6						
Geraniin	300	3						
Hinokinin	1500	4						
Isocorilagin	5000	5						
Isoquercetin	5000	5						
Linetralin	214	3						
Niruriflavone	2919	5						
Niruristin	2000	4						
Niruriside	5000	5						
Pectolinaroside	5000	5						
Pectolinarin	5000	5						
Quercetin	159	3						
Quercitrin	5000	5						
Rutin	5000	5						

Colour pallet: ACTIVE / INACTIVE



Conclusive Summary

- Various compounds like hinokinin, astragalin, isocorilagin and niruriflavone have been identified to deter liver fibrosis (LF) via modulation of key downstream targets compared to known inhibitors and also within the permissible thresholds of ADMET parameters.
- Our in-silico results suggests that *Phyllanthus niruri* compounds have the potential to be developed as effective drug candidate towards the management of Hepatic fibrosis.

Future Work

- To study post-docking ligand-protein interactions via molecular dynamics simulations.
- To validate potency of *P.niruri* phytochemicals like hinokinin, niruriflavone and astragalin etc., via in-vitro study cell-based assays for identification of molecular mechanism.

References

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