



Drug likeness, physicochemical properties, and *in silico* ADMET study of 4-hydroxy isoleucine

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INTRODUCTION

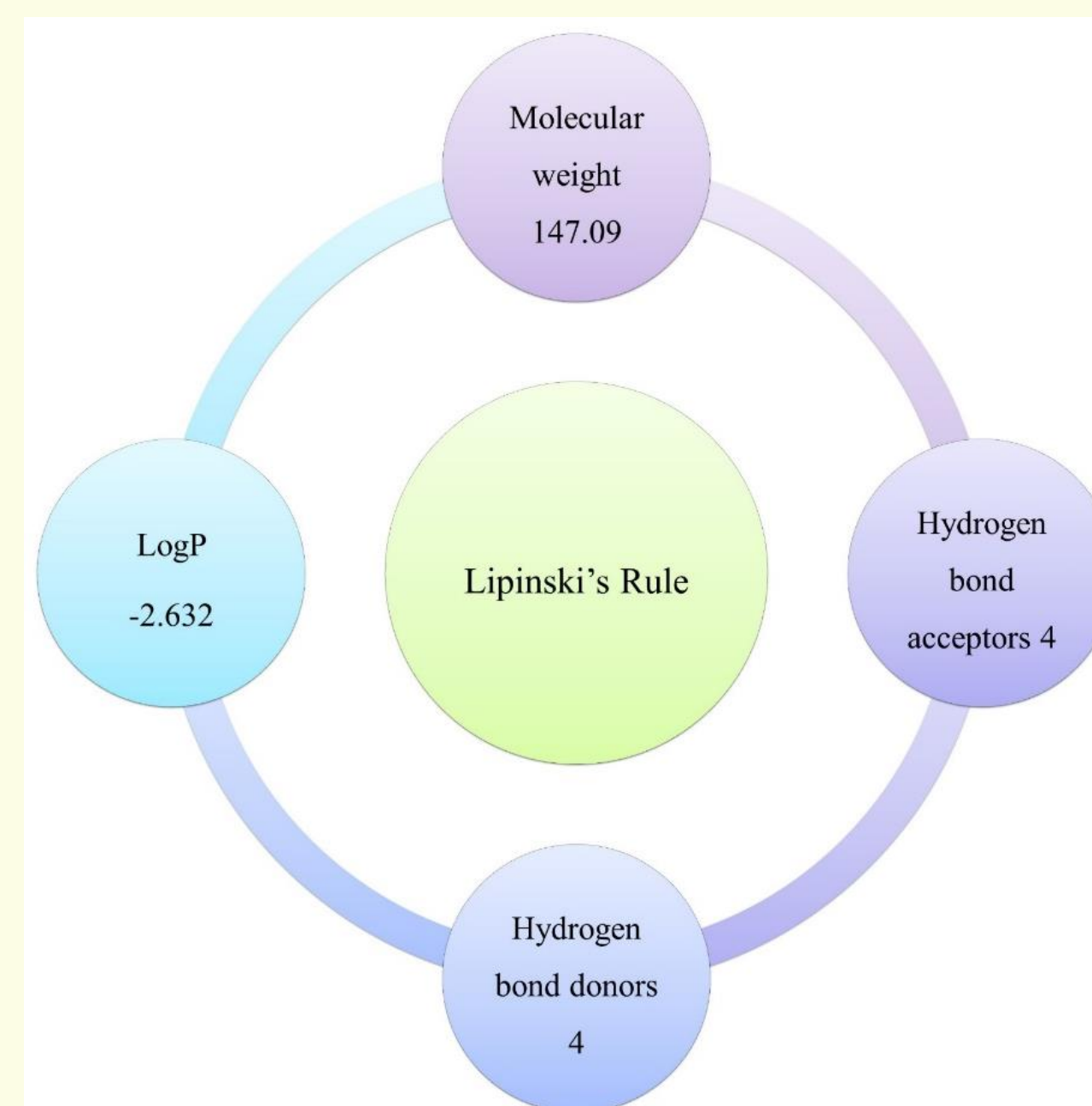
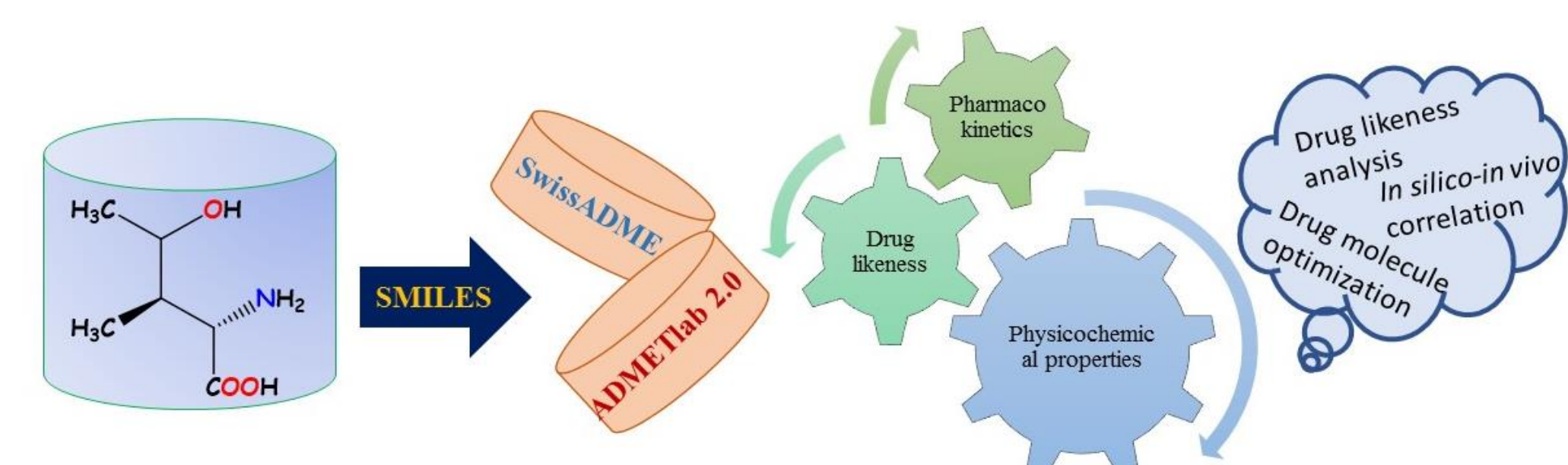
- ✓ 4-Hydroxy isoleucine (4HiL), an amino acid from *Trigonella foenum-graecum* increases glucose dependent insulin secretion via a direct effect without associated harm to other islet cells.
- ✓ It counters insulin resistance in muscles and liver by activation of insulin receptor substrate-associated phosphoinositide-3 kinase activity.
- ✓ Therefore, an attractive molecule for the treatment of metabolic syndrome, type 2 diabetes, obesity, and dyslipidemia.
- ✓ However, its pharmacokinetic and safety profiles are not reported completely.

METHODOLOGY

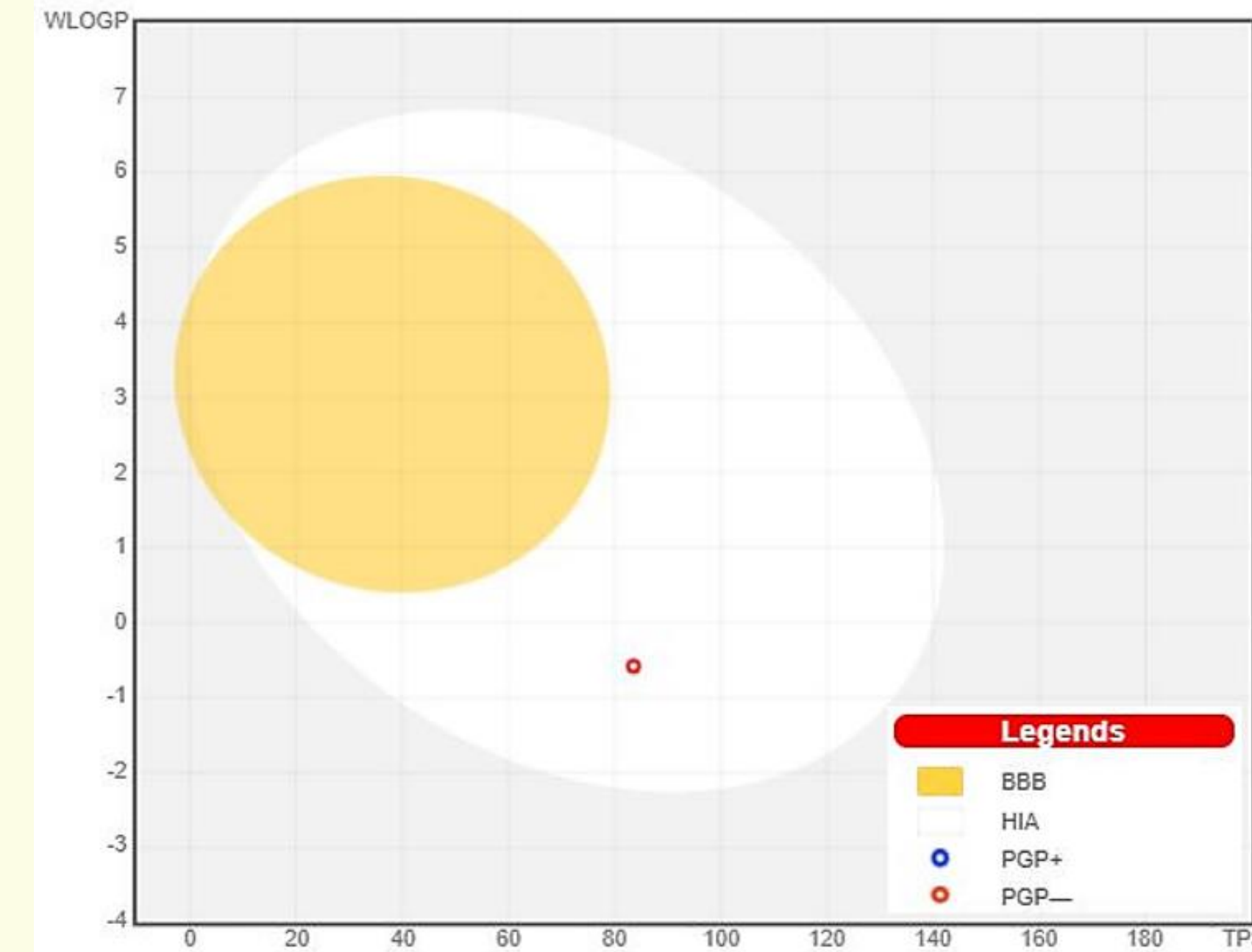
This work was focuses on detailed understanding of drug discovery interplay among physicochemical and pharmacokinetic properties of including toxicity endpoints.

Following are the techniques applied:

- ✓ Drug likeness
- ✓ Physicochemical properties
- ✓ Medicinal chemistry
- ✓ BOILEDDEGG graph
- ✓ Oral bioavailability radar chart
- ✓ hERG toxicity
- ✓ Toxicity parameters



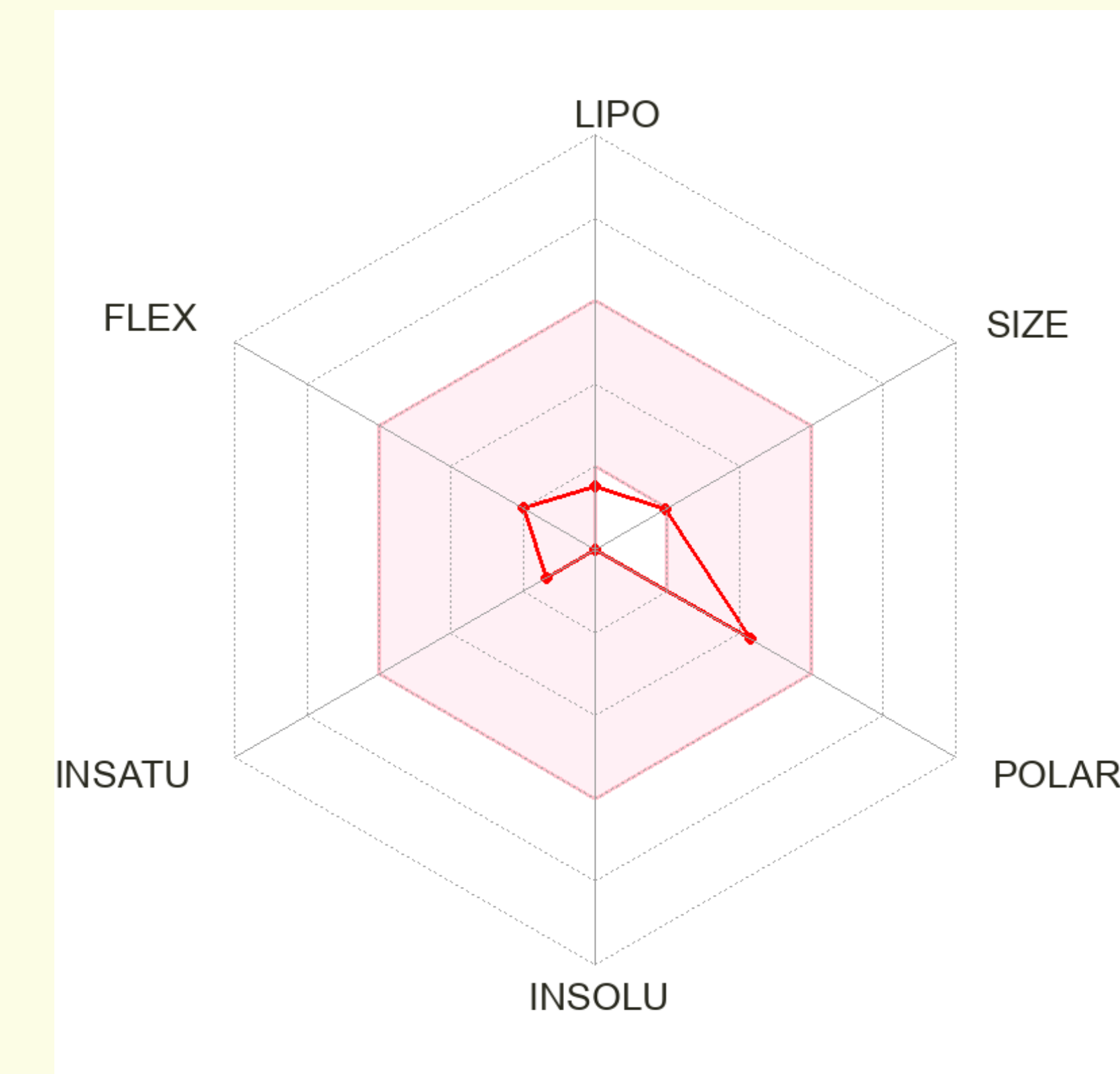
Lipinski rule of five evaluation of 4-Hydroxy isoleucine.



Boiled-egg plot from SwissADME database reveal HIA and not Pgp substrate.

RESULTS and DISCUSSION

Pharmacokinetics	Probability based prediction
MDCK Permeability	Moderate to high
Pgp-inhibitor	No
Pgp-substrate	No
F _{30%}	No
Plasma protein binding	6.735 %
VD	0.465 L/kg
BBB Penetration	0.835
Unbound fraction	85.29 %
Metabolism (CYP ₄₅₀)	No
CL	7.268 ml/min/kg
t _{1/2}	0.68



Oral bioavailability graph; the pink zone is the physicochemical space for oral bioavailability, and the red line defines oral bioavailability properties.

Sr. No.	Toxicity parameter	Probability based Prediction	Sr. No.	Toxicity parameter	Probability based Prediction
1	herg blocker	No	6	Skin Sensitization	No
2	HHT	No	7	Carcinogenicity	No
3	DILI	No	8	Eye corrosion	No
4	AMES Toxicity	No	9	Eye irritation	No
5	Rat oral Acute Toxicity	No	10	Respiratory toxicity	No



hERG blockage: Probability map of hERG blockage (Pred-hERG web tool), the red dotted lines reflect non-hERG Blocker. Contour lines with intense green colour if present indicate a higher positive contribution of an atom to hERG Blockade.

CONCLUSION

- ✓ 4-Hydroxy isoleucine has satisfactory physicochemical properties and medicinal chemistry.
- ✓ The pharmacokinetic profile is in the favour of oral bioavailability, efficient distribution to all tissues including the brain, and non-interruptive drug metabolism, with moderate clearance and half-life.
- ✓ Even it is undesirable for this molecule to disturb some of the most important receptors/targets such as gonadal receptors, p53, heat shock factor, mitochondrial membrane potential, or PPAR- γ .
- ✓ No more wait for clinical trials development.

Keywords: 4-Hydroxy isoleucine; Pharmacokinetics;

Computational chemistry; Drug likeness