**AI-Driven Ayurniformatic Platforms for 3Rs-Based Drug Discovery: A Collaborative Model Between Industry and Academia Utilizing Indian Traditional Knowledge**

**Ashutosh Kumar Pandey1\***, Suvarna G Kini1, R Govindarajan 2, Angel Treasa Alex3, Navas Shereef E M3

 1Department of Pharmaceutical Chemistry, Manipal College of Pharmaceutical Sciences, Manipal 576104, Karnataka, INDIA
2Adret Retail Ltd (Kapiva), Bengaluru- 560103, Karnataka, INDIA

3Department of Pharmaceutical Biotechnology, Manipal College of Pharmaceutical Sciences, Manipal 576104, Karnataka, INDIA

**Background and aims.** Insomnia is a sleep disturbance linked to anxiety and depression. Therapeutic approaches include insomnia therapy, lifestyle modifications, and pharmacological interventions. To show therapeutic actions in the hippocampus of the brain, the drug needs to cross the BBB. So, pharmaceutical industry is developing lipophilic herbal medication concepts to improve drug delivery systems and reduce dependence on synthetic drugs as some of them are addictive as well.

**Methods.** A systematic 3Rs framework utilizing Ayur-informatics guided selection of traditional herbs, followed by molecular dynamics simulation and in-silico pharmacokinetic (ADME) and oral toxicity assessments using Schrodinger and ProTox software. Jatamansi extract was subjected to LC/MS for identification of major components, and simultaneously cytotoxicity of Valeranone and Nardosinone was evaluated in HEK 293 cells.

**Results.** The best compound's Glide docking score and oral toxicity for Valeranone docking score was -8.118 Kcal/mole and LD50 being 500mg/Kg, which was predicated as class IV toxicity with 100% Prediction accuracy. Similarly for Nardosinone docking score was -7.600 Kcal/mole and Toxicity LD50 5000mg/Kg, which was predicated as class V toxicity with 68.08% prediction accuracy respectively. This represents respective dose of toxicity was safe, by cytotoxicity on HEK293 cell and it was found that *Nardostachys jatamansi*  exhibited a higher IC₅₀ value of 102.33 ± 7.9 µg/ml.

**Conclusion/Discussion.** This study demonstrates that lipophilic herbal compounds, particularly Valeranone and Nardosinone from *Nardostachys jatamansi*, show promising pharmacokinetic profiles and low toxicity for insomnia therapy. Molecular docking and toxicity predictions indicate these compounds can safely interact with orexin B receptors, supporting their potential as alternatives to synthetic drugs. Such herbal-based approaches may enhance drug delivery across the blood-brain barrier, reduce adverse effects, and offer effective, safer insomnia management without being addictive.

**Acknowledgement:** Grateful toKapiva for industry & academia collaboration, and Department of Pharmaceutical Chemistry and Biotechnology, Manipal, for providing Lab facilities.

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