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Exploring the anxiolytic potential of *Breynia androgyna* (L.) a phytopharmacological, *in vivo* and *in silico* investigation

Disha Bhuvan Dangui[1], Liesl Maria Fernandes e Mendonça[1]* & Arati Anil Dhatkar[1]

[1]Department of Pharmacology, Goa College of Pharmacy, Panaji 403001, Goa India

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Anxiety is a state of distress, affecting people worldwide. It is usually mitigated by conventional anxiolytic medications that produce dependency and adverse effects, thus highlighting the need for safer alternatives derived from natural sources. *Breynia androgyna*, a perennial shrub of the family Phyllanthaceae, has profound medicinal benefits, but its anxiolytic potential remains inadequately explored. The current study, hence, envisaged exploring the anxiolytic potential of the ethanolic leaf extract of *Breynia androgyna* (EEBA) and its acetone fraction (AEBA) through experimental and computational approaches. Phytochemical screening and quantification of total phenolic and flavonoid content were carried out using established procedures. EEBA and AEBA (200 and 400 mg/Kg) were administered per orally to Wistar albino rats for a period of 14 days, and the possible anxiolytic activity was assessed using the Elevated Plus Maze, Light and Dark Model, Mirror Chamber Test, and Opto-Varimex Open Field Test. One-way ANOVA was used to analyse the data, followed by Dunnett's test. Molecular docking was conducted *in silico* to examine interactions between the phytoconstituents and the $GABA_A$-Cl^- ion channel receptor. Flavonoids, tannins, phenolics, and triterpenoids were detected in the extract and biofraction, with AEBA displaying higher phenolic (54.35 mg GAE/g) and flavonoid (67.81 mg QUE/g) content than EEBA. AEBA displayed superior *in vitro* antioxidant activity and produced significant anxiolytic effects at 400 mg/Kg ($P < 0.05$) across all behavioural models. Molecular docking studies revealed strong interactions between major phytochemicals and the $GABA_A$ receptor. In conclusion, the acetone fraction of *Breynia androgyna* demonstrated notable anxiolytic potential, probably attributed to its enriched flavonoid content, supporting its relevance as a promising natural anxiolytic therapeutic.

Keywords: Elevated Plus Maze, Light and Dark Model, Mirror Chamber, Opto-Varimex, $GABA_A$