

Evaluation of synergistic anti-diabetic effects of different combinations of four selected plants (*Terminalia arjuna*, *Syzygium cumini*, *Ficus benghalensis* and *Salacia reticulata*) using yeast cell uptake and toxicity assay in Brine Shrimp (*Artemia salina*)

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Diabetes mellitus is rising globally and causing significant mortality that highlights the urgent need for therapeutic approaches. Herbal antidiabetic medications offer promising alternatives to synthetic treatments. Traditional Sri Lankan herbal plants, such as *Terminalia arjuna*, *Syzygium cumini*, *Ficus benghalensis*, and *Salacia reticulata*, have demonstrated significant antidiabetic properties. This study aims to investigate the synergistic antidiabetic effects and toxicity of different combinations of these plants to enhance therapeutic efficacy against diabetic mellitus using Yeast cell uptake and brine shrimp toxicity assay. Fifteen different combinations of *T. arjuna*, *S. cumini*, *F. benghalensis*, and *S. reticulata*, were prepared using factorial design (number of combinations+1= $2^n = 2^4$). Combined plant decoctions screened for toxicity using Brine Shrimp assay. Yeast cell uptake assessment was done for anti-diabetic activity. All procedures were conducted in accordance with protocols outlined in OECD guidelines. Among the 15 different combinations, the combination containing *F. benghalensis* and *S. reticulata* exhibited lowest glucose uptake of 36.98% and low Brine Shrimp LC50 value of 50 µg/ml. The combination with lowest glucose uptake and less toxicity shows synergistic antidiabetic effect of different combinations of these selected four plants, that can be used as an alternative herbal medication over synthetic antidiabetic medications. The result of the combination of *F. benghalensis* and *S. reticulata* shows promise for synergistic antidiabetic activity, underscoring the potential of natural plant decoctions in diabetes therapies.

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