Combination Effect of Selected Medicinal Herb Extracts Against in-Vitro Anti-Diabetic Properties

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Abstract
Herbal plants are considered to be the best natural remedies, as they are rich in phytochemicals. Drug combinations are widely used to achieve synergistic effects in therapeutic use. In treating diabetes and its' associated complications, *Gymnema sylvestre* R. Br, *Salacia reticulata* Wight, *Syzygium cumini* (L.) Skeel and *Camellia sinensis* (L.) Kuntze has been claimed to have strong anti-diabetic properties. Though, these plants have proven records on anti-diabetic potency as individual plants, no systematic investigation of their combined behavior. Therefore, first the inhibitory effect of crude ethanolic extracts of *Gymnema sylvestre* leaves (GS), *Salacia reticulata* bark (SR), *Syzygium cumini* bark (SC) and *Camellia sinensis* tender shoots (CS) against the α-amylase and α-glucosidase enzymes, glycation and glucose diffusion were tested using in-vitro trials. Highest inhibitory activity for α-amylase, α-glucosidase, anti-glycation and glucose diffusion were reported from *S.cumini* (IC_{50} = 18.50µg/mL), *S.reticulata* (IC_{50} = 7.85µg/mL), *S.cumini* (IC_{50} =15.20 µg/mL) and *G.sylvesre* (GDRI = 68.60% at 200 µg/mL concentration), respectively. All these values reported to have dose-dependent inhibition ($p<0.05$). Secondly, it was designed to investigate the combined effect of two-factor combination series. Some combinations exhibited strong antagonistic and synergistic effects (Fa>60%) against the anti-amylase and anti-glucosidase enzyme activity assays. For the anti-glycation assay, combinations having *Camellia sinensis* and *Salacia reticulata* as principle components exhibited strong antagonism, while all the other combinations were reported to have a synergistic effect against the glycation activity. All the combinations reported a strong synergistic effect against the glucose diffusion activity. The combination of *Camellia sinensis* and *Gymnema sylvestre* exhibited the highest glucose diffusion inhibition at 200µg/mL concentration (GDRI = 69.37%). It was clear that the combinations show comparatively higher antagonistic effects in enzyme-dependent pathways due to the molecular masking activity, competitive inhibitions, chemical bond depletions and any other possible mechanism. This study recommended investigating the chemical reactions at the preliminary stage of the drug combinations to increase drug effectiveness.

Keywords: Anti-diabetic properties*, Camellia sinensis*, In-vitro assays, *Gymnema sylvestre, Salacia reticulata, Syzygium cumini*
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