ABSTRACT

The current thesis reports the development of an antidiabetic polyherbal phytoceutical with evidence based approaches for better applicability of the same in the light of translational health research. A polyherbal phytocomposite (PHC) prepared from the leaf powders of *Ficus benghalensis* (Banyan), *Syzigium cumini* (Jamun), and *Ocimum sanctum* (Tulsi) inhibited the enzymes found to play a role in the pathogenesis of Type 2 diabetes. The significantly lower IC50 values of the PHC (3.38 ± 0.07, 3.37 ± 0.11, 21.42 ± 0.51, 43.05 ± 1.11, 0.36 ± 0.02) in inhibiting alpha amylase, alpha glucosidase, aldose reductase, angiotensin converting enzyme and DPP4 substantiates its antidiabetic potentialities. It also inhibited pancreatic lipase (hypolipidemic) and exhibited antioxidant potentials in relevant in vitro enzyme inhibitory assays (DPPH, ABTS and FRAP assays). Chemoprofiling of PHC identified pharmacologically active compounds viz. lupeol, eugenol, ursolic acid, rutin etc. by chromatographic and spectroscopic techniques. In vitro findings were validated by in silico molecular GRIP docking studies where Rutin showed maximum binding affinity with DPP4 and eugenol with alpha amylase. In acute toxicity studies with PHC no death was observed upto a dose of 7.5 g/kg b.w. Hypoglycemic-hypolipidemic action of 100 mg/kg PHC when compared with its constituent plant species (Banyan, Jamun and Tulsi) and metformin was found to be significantly better ($p<0.001$) thus suggesting phytosynergism amongst the phytomolecules present within PHC. Natural polymers viz. gum kondagogu, gum karaya, Aegle marmelos gum were used as release retardant. Optimized batch of conventional and SR tablets showed 99.8 % and 99.9% release respectively with zero order release kinetics. Pharmacokinetic parameter (Cmax, Tmax, AUC, maximum retention time) values show that plasma concentrations of PHC are maintained and confirms to the criteria for conventional and SR formulations. In vitro- in vivo correlation (IVIVC) of three different formulations were in the order of sustained release ($r2= 0.99$) > microcapsules ($r2= 0.97$) > conventional ($r2= 0.90$) and thus Level A correlation have been established suggesting dissolution a surrogate for biowaiver studies. Extrapolation of animal dose to predict human dose and pharmacokinetic parameters by Allometric scaling (‘single species rat method’) was found to be convenient, simple and cost effective.