CHAPTER 4

Conclusion

4.1 Conclusion

Evidences from *in vitro* and *in vivo* assays have pointed out that phytochemicals interact with many drug transporters immensely, like substrates, inhibitors as well as inducers, and it is obvious that transporter modulations by the phytochemicals are sophisticated, relying on a type of herbal source, regimen, route, administration dose, and target organ. These interactions may occur, particularly, in the gastrointestinal tract, as herbs are most often taken by oral administration. Furthermore, the multiple phytochemicals in herbs may inhibit/induce intestinal drug transporters for example P-gp, and hence alter an absorption rate and extent of a co-administrated drug.

High throughput screening (HTS) experiments may stand for a helpful stratagem for a study of molecular interactions between herb and transporter. These experiments are proficient of dispensation the large number of phytochemicals (for example a single medicinal plant ordinarily stows dozens of compounds), and possess the capability to give *in vitro* inhibitory information like criteria for monitoring herb-drug interactions associating drug transporters of human (particularly P-gp).

In silico techniques stand for a helpful tool for an herb–P-gp interaction study as proved by our studies and studies by other researchers. Our established ligand-based model like QSAR model, and structure-based models like docking, pharmacophore, and dynamical models could readily distinguish the most flavonoid inhibitor of P-gp. Therefore, these models could be utilised as a HTS tools to analyse flavonoid constituents of herbal products that inhibit P-gp, afore proceeding *in vitro* tests. This will aid to evade co-administration of drugs that are extensively transported by P-gp with herbal products that showed inhibitory effects on this transporter.

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Herb–P-gp interactions may have significant clinical implications that some effective rigorous examinations for conceivable drug interactions with extensively utilised herbs are a necessity. It is probably time to regard herbs not like alternative medicines depended on traditions and experiences, but like phytotherapy, and an integrated part of conventional medical remedy. Medicinal plant regulations may be desirous, but this may be a subject of considerable disputation. Notwithstanding, safety (for example herb-drug interactions), quality and efficacy should be testified, depended on an objectivity and proper standard like for conventional medicines.

However, herb-drug interactions are tough to characterise and resolve, by reason of the destitution of extensive federal regulations respecting safety, efficacy, and manufacturing standards for herbal products. It has been proffered that herbal products are properly labelled to forewarn consumers to conceivable interactions with other co-used drugs and to instruct a deliberation with their general practitioners, pharmacists, and other medical careers. Adverse event monitoring when herbal products are co-administered with drugs should be systematically actuated and potential herb-drug interactions should be analysed. This would enable more exact product labelling and a body of helpful data on potential herb-drug interactions to medical professionals.

In conclusion, we present our discoveries upon construction and validation of comprehensive computational models of P-gp with the hope that it offers further insights into the factors that determine the mechanism of action and binding modes of herbal compounds as inhibitors to P-gp and therefore grant us to correctly predict the potential of new and phytochemicals as P-gp inhibitors. Screening of high-affinity ligands for P-gp from herbal formula utilising several computational models is expedient approaches to analyse potential herb-drug interactions. In future, the combining computational methods (e.g. QSAR, molecular docking, molecular dynamics, etc.), may offer vigorous tools to solve the puzzles within the complex field of P-gp.

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