Screening for Potential Interactions of Six Herbal Products in Development with the Major Drug Metabolising Human Cytochrome P450 Isoforms

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Introduction and Aim: It is well known that patients often use prescribed drugs with traditional medicines, and this has led to a rise in the incidence of drug-herbal interactions. It is therefore appropriate for anyone contemplating developing traditional remedies to explore their potential interactions with the Western medicines. Currently, the Medical Research Council (MRC)’s Lead Programme of Indigenous Knowledge Systems has isolated and tested a number of promising compounds from traditional-herbal medicines which hold hope for human use for treatment of malaria and HIV. On the other hand, cytochrome P450 (CYP450) isoforms CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4 are responsible for metabolism of many drugs that may be used together with the herbal products. Therefore, interaction with any of these isoforms has implications on the drugs metabolized by the respective isoform. As part of the MRC led collaborative project on “The development of novel compounds with antiplasmodial and antiretroviral activity isolated from indigenous Southern African traditional medicinal plants”, the aim of this study was to screen herbal extracts/compounds in development for possible interaction with these cytochrome P450 isoforms.

Methods: Six herbal extracts, A-PHL, B-PHK-H2O, C-LEAF, D-HLNY-H2O, E-HLNY-DCM and F-LEFA, were dissolved in 60% ethanol to final a concentration of 10 mg/ml. Analytical methods for enzyme metabolic markers with their metabolites were developed and validated. The effect of the ‘herbal product’ on the activity of a specific P450-isoform was tested by observing for changes in the rate of metabolism after addition, to the reaction mixture, of increasing amount of the ‘herbal product’ to final concentrations of 10, 20 and 40 ug/ml. This was done separately for each of the Human P450-isoforms (Baculosomes) tested. Results were expressed as percentage activity of the control.

Results: Only product E-HLNY-DCM was demonstrated to inhibit activity of CYP2C19 whereby activity was 75%, 30% and 0% of control at 10, 20 and 40 ug/ml, respectively. The other herbal products had no effect on the activity of CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4. The higher activity than control observed in some of the test samples may be due to catalysts in the herbal extracts.

Conclusion: In conclusion, these screening tests indicated that there was no significant interaction of the herbal products with P450 isoforms CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4, which implies that these herbal products may be used safely with drugs that are metabolised by these isoforms, but the observations on product E (HLNY, DCM) and CYP2C19 need further evaluation.