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PaperTitle **Biotransformation of Mangiferin, A Major Phenolic Compound in Honeybush Tea: Implications for its Bioactivity:**

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ABSTRACT

Clinical studies on phenolic compounds have indicated that very little of the unchanged compound can be found in plasma after ingestion, and that the concentration of conjugated metabolites of polyphenols, in particular the glucuronic acid conjugates, are high. Mangiferin, a xanthone glucoside, is the major phenolic compound in *Cyclopia* spp. (honeybush) and has several acclaimed health promoting properties demonstrated *in vitro*. The *in vivo* activity of mangiferin is however not known, since limited information is available on its metabolism. As minor alterations to the polyphenol structure are known to influence the biological properties, studies on biotransformation is essential.

This study was undertaken to investigate possible metabolites resulting from mangiferin glucuronidation. It will contribute to the groundwork for bioavailability studies of mangiferin from *Cyclopia* spp. and future biomarkers of exposure for studies on disease prevention by honeybush tea.

A rat liver microsomal fraction was used as a source of glucuronosyltransferase. HPLC analysis revealed the formation of one major and two minor peaks, concomitant with a significant decrease in the mangiferin concentration. Subsequent LCMS analysis indicated two "new" mass fractions, $m/z = 597$ and $m/z = 611$, which correspond to a mangiferin glucuronic acid conjugate and a methylated mangiferin glucuronic acid conjugate, respectively. Studies on biotransformation of mangiferin by other liver conjugating enzymes are currently in progress.

The change in the structure of mangiferin, as affected by biotransformation, have important implications for its bioactivity *in vivo* and needs to be assessed to clarify health claims associated with honeybush tea consumption.