

**HEPATIC DRUG METABOLISM IN ANIMALS WITH RENAL FAILURE****A. C. A. Yoosuf***(State Pharmaceuticals Corporation, Colombo)*

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The patient with renal failure responds to many drugs differently from the subject with normal renal function. There is evidence that the metabolism of some drugs may be altered in patients with renal failure.

To gain a better understanding of the mechanisms of the alterations in drug handling observed in patients with renal failure various animals have been used. These include the rat, guinea pig, cat, rabbit and the dog. The most extensively studied animal in this respect is the rat. The five-sixths nephrectomy described by McCance and Morrison (1956) has been used in this study to induce chronic renal failure in male Wistar rats. This study investigates those alterations that are due to metabolism alone in rats with chronic renal failure and isolated hepatic microsomal preparations were used to investigate changes in the hepatic oxidative, reductive and glucuronidating pathways.

A slowly progressive form of chronic renal failure with sustained elevation of plasma urea and creatinine concentrations were observed at various stages of renal failure. A significant reduction in the activity of ethylmorphine N-demethylase and p-nitrobenzoate reductase, but increased o-aminophenyl glucuronyl transferase and unchanged NADPH-cytochrome c reductase activity was observed in the chronic uraemic rats. Significant decreases in microsomal protein, cytochrome P-450 and cytochrome b<sub>5</sub> content were observed.

The data obtained from this study could contribute to the understanding of altered pharmacokinetic behaviour of drugs employed in uraemic patients.