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EFFECT OF *ASPARAGUS FALCATUS* EXTRACT ON HEPATIC REDUCED GLUTATHIONE LEVEL IN MICE. PROTECTION AGAINST PARACETAMOL TOXICITY.

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Paracetamol (Acetaminophen) is a commonly used analgesic and antipyretic drug sold over the counter. It is remarkably safe at therapeutic doses. However, large overdoses of paracetamol can produce fulminant hepatic and renal tubular necrosis which can be lethal both in humans and animals, Hepatotoxicity of paracetamol has been considered to be entirely the consequence of its metabolism in hepatocytes.

Asparagus falcatus ("Hathawariya") of the family Liliaceae is a plant used in traditional medicine to treat jaundice and liver congestion. In this study the effect of *Asparagus* tuber extract on paracetamol induced liver injury were investigated in vivo.

Healthy ICR mice of 30-35g of body weight were used and they had access to pelleted food and water *ad libitum*. Overnight fasted animals were randomly divided into six groups of 20 animals in each. Normal control and drug control groups received respective doses of distilled water and *Asparagus* extract (0.9 g/kg) orally by gavage. N-Acetyl cysteine (500mg/kg) was given as the positive control. Animals in both pre and post-treated groups were sacrificed 4 hours after the administration of a sub lethal dose of paracetamol (300mg/kg). Blood samples were collected for the biochemical analysis of serum ALT, AST, ALP and liver slices were collected for the determination of liver reduced glutathione (GSH) and histopathological assessment of liver damage. Results were analysed using Students t-test.

A marked increase in the serum enzyme levels and a decrease in the liver GSH were observed in the paracetamol control group compared to the normal control group. A statistically significant decrease ($p < 0.001$), in serum enzymes and a significant increase in the liver GSH level were observed in both pre and post-treated groups compared to the paracetamol control group, Pre- treatment resulted in a faster recovery of the liver in comparison with the post treatment. Microscopic changes of the liver slices also provided supportive evidence for the biochemical analysis.

Glutathione plays a key role in protecting liver against paracetamol toxicity. Bio-transformation of paracetamol to an active metabolite, NAPQI (N-acetyl parabenzo quinone imine) leads to a depletion of liver GSH which allows lipid peroxidation, hepatocellular damage and confluent necrosis. Increase in hepatic GSH level in *Asparagus* treated mice may result from the enhancement of either *de novo* GSH synthesis, GSH regeneration or a reduction in the synthesis of NAPQI.

These results suggest that the feeding regimen with *Asparagus falcatus* extract inhibited the progression of hepatic injury induced by paracetamol.