

Effects of *Convolvulus arvensis* (Binweed) on the Activity of Drug Metabolizing Enzymes in Liver of Rats

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Abstract: The effects of feeding *convulvulus arvensis* (binweed) at 0.5 and 1g/rat were investigated. Binweed produced no clinical effects or gross lesions in rats. The plant caused decreased concentration of protein in liver homogenate and inhibited the activity of phase-1 but not phase-2 drug metabolizing enzymes. In view of binweed modulating effects on drug metabolizing enzymes, consumption of binweed by human and animal should be prohibited.

Key words: *Convolvulus arvensis*, liver, drug metabolizing enzymes, rats

INTRODUCTION

Convolvulus arvensis (Binweed) is a creeping weed widely distributed in the the Middle East^[1]. It became the dominant plant growing under the date palm trees in Eastern region of Saudi Arabia and due to overgrazing with periodic drought, animals may be forced to consume varying amounts of this plant. Native people in this area add the plant leaves to their daily salad dish or use it in herbal medication. All parts of the plant contain tropane alkaloids with atropine-like action^[2]. Binweed has rarely been associated with poisoning in animals^[2]. However in a few studies in mice fed the plant exclusively died and had severe hepatic necrosis^[3]. The liver is the most important site for the biotransformation of a wide array of xenobiotics to which animals are exposed^[4,5]. Therefore, this study was carried out to investigate the activities of drug metabolizing enzymes in liver of rats fed binweed at low doses.

MATERIALS AND METHODS

Plant collection: Fresh leaves of binweed locally known as "Fidagh" was collected from date palm farms in Al-Ahsa region, Saudi Arabia during the rainy season from December to February. The plant was grown wildely as a

creeping weed under the trees. Botanical identification of the plant was made by Dr. Mohammed Al-Fredan, Department of Biology, College of Science, King Faisal University, Saudi Arabia.

Animals and treatments: Male and female adult Wistar rats (n = 50) weighing between 120-130 g were used in the study. The rats were kept at room temperature (23-25°C) with a 12 h light/dark cycle. Tap water and feed (standard granules for mouse and rats, ARASCO, Saudia Arabia) were available *ad libitum*. Animals were divided into 5 groups of 10 rats each. Group 1 animals were given the standard diet and kept as controls. Group 2 animals were fed each with 0.5 g fresh binweed mixed in their diet for 10 days. Animals were fed 1.5g of fresh plant without showing any toxic signs. Group 3 animals were fed the plant at a dose of 1g each for two consecutive days alternating with standard diet for two days, the duration of this experiment was for one month.

Collection of tissues and estimation of enzyme and proteins: At the end of the experiment rats were killed and livers were immediately removed, weighed and homogenized in ice-cold isotonic KCl. The crude homogenates were then centrifuged at 10,000g for 15 min. A microsomal and cytosolic fractions were prepared as described by Maze^[6]. Protein concentrations in these

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Table 1: Mean \pm SD concentration of protein and values of activity of drug metabolizing enzymes in microsomal protein homogenate of liver of rats

Protein (mg g ⁻¹)	Group 1 untreated (control) (n = 10)	Group 2 binweed treated (0.5g/rats) (n = 10)	Group 3 binweed treated (1g/rats) (n = 10)
Whole homogenate	190.31 \pm 20.45	108 \pm 2.5*	96 \pm 2.46*
Cytosolic fraction	114.31 \pm 10.30	86 \pm 3.2*	80 \pm 2.91*
Microsomal fraction	30.91 \pm 2.11	22 \pm 1.61*	20 \pm 1.31*
Enzyme activity of microsomal protein (nmol g ⁻¹)			
Cytochrome P-450	0.222 \pm 0.012	0.131 \pm 0.012	0.121 \pm 0.03
Aminopyrine-N-demethylase	11.70 \pm 1.31	8.31 \pm 0.061	7.11 \pm 0.063
Aniline-4-hydroxylase	0.281 \pm 0.02	0.081 \pm 0.011	0.061 \pm 0.012
UDP-glucuronyltransferase	1.103 \pm 0.051	1.133 \pm 0.050	1.061 \pm 0.41
Glutathione-S-transferase	172 \pm 12	168 \pm 13	173 \pm 12

* significantly (p<0.05)

fractions were determined by the method of Lowry^[7]. The activities of aminopyrine-N-demethylase and aniline-4-hydroxylase were determined using the method of Mazel^[6] by estimating the concentrations of formaldehyde and p-aminophenol, respectively. The method of Dutton and Storey^[3] was used to determine UDP-glucuronyltransferase activity by estimating o-aminophenyl-glucuronide concentration using o-aminophenol as a substrate. The activity of glutathione-S-transferase was determined in the cytosolic fraction by estimation of 2,4-dinitrophenylglutathione concentration according to the method described by Habig *et al.*^[9]. The concentration of cytochrome p-450 was determined in the microsomal fraction according to the method of Omura and Sato^[10]. The enzyme activities were linear with time, protein and substrate concentration^[11, 12].

Statistical tests: Data are presented as mean \pm SEM. Student's *t-test*^[13] was used to analysis the data. The probability value p<0.05 was considered significant.

RESULTS

Rats fed binweed ate the plant readily. None of rats in group 1, 2 and 3 developed any signs of abnormality. On postmortum examination; no gross lesion was observed. Protein concentrations and the activity of drug metabolizing enzymes are presented in Table 1. Binweed significantly (p<0.05) decreased protein concentration in whole homogenate, cytosolic and microsomal fractions in animals of group 2 and 3 compared to animals of group 1 (controls). The activity of cytochrome P-450, aminopyrine-N-demethylase, aniline-4-hydroxylase, was significantly (p<0.05) decreased by binweed in group 2 and 3. No effect was seen on the activity of UDP-glucuronyltransferase and glutathione-S-transferase.

DISCUSSION

Feeding of low doses of binweed to rats produced no clinical effects or gross lesions. Similarly feeding of smaller amounts of binweed had no effects in mice^[3].

Binweed from pasture was found to contain the tropane alkaloids tropine, pseudotropine and tropinone and the pyrrolidine alkaloids cusecohygrine and hygrine^[14, 2]. Their effects included a competitive reversible antagonism of acetylcholine at muscarinic and nicotinic receptors^[15].

Within 24 h 77 to 94% of alkaloids or their metabolites are excreted in the urine^[15] which may explain lack of susceptibility to poisoning by low doses of binweed.

Feeding of binweed to rats decreased protein concentration of liver homogenate and activity of phase-1 metabolizing enzymes such as cytochrome P-450, aminopyrine-N-demethylase and aniline-4-hydroxylase. Similar effects have been produced by Latex of *Calotropis procera* in goats^[11] and Signal grass in sheep^[16].

Binweed failed to produce any effect on phase-2 drug metabolizing enzymes represented by UDP-glucuronyltransferase and glutathione-S-transferase. Activity of phase-2 drug metabolizing enzymes were found to be resistant to hepatotoxin induced liver injury^[17, 11]. This is probably due to deep location of these enzymes within endoplasmic reticulum close to inner surface of the membrane^[17, 18].

Consumption of binweed which is capable of modulating activity of drug metabolizing enzymes may result in unpredictable pharmacodynamic and toxicologic effects of drugs and xenobiotics and therefore human and animals should not be allowed to consume the plant.

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