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Protective Effects of *Cichoricum intybus* Linn (Kasni) Against Dietary Aflatoxicosis in White Albino Rats

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Abstract: In the present study fifty four white albino rats were taken and randomly distributed in three groups C, T_1 and T_2. Further each group divided into 3 subgroup of having six rats in each. C, T_1 and T_2 served as control and two treatment groups supplemented with free diet + 0.00 ppm aflatoxin B_1, Free diet + 7.00 ppm aflatoxin B_1 and free diet + 7.00 ppm aflatoxin B_1 + Kasni (100 g/kg feed) by replacing maize in ration respectively. Each group was provided weighed quantity of respective diet daily up to end of 28 days experiment. Body weight and feed intake were recorded at regular interval. Blood samples were analysed to study the biochemical constituents viz Glutamic-oxaloacetic transaminase (GOT), Glutamic-pyruvic transaminase (GPT), Alkaline Phosphatase activity (ALP) total protein (TP), Albumin, Cholesterol, Glucose and Blood urea nitrogen (BUN) and correlation of aflatoxin B_1 with Kasni. The observations of the present study revealed that the results of the treatment T_1 and T_2 group differ significantly ($P<0.05$ and 0.01) with control. The results showed that GOT, GPT, ALP, Cholesterol, Glucose, BUN level increases more in group T_1 than T_2. Total Protein and Albumin decreased more in T_1 then T_2. Similar results were also obtained with glutathione-s-transferase activity. Kasni treatment was found beneficial as it was observed to attenuate aflatoxicosis in treated rats.

Key words: Aflatoxin · Kasni · *Cichoricum intybus* · Rat

INTRODUCTION

The historic discovery of aflatoxins was due to the death of turkeys in the United Kingdom as a result of consuming contaminated groundnut meal imported from Brazil. The harmful effects of consuming contaminated groundnut cake have been mainly observed in poultry and milch cattle [1]. Subsequently, aflatoxins have been found in other feeds especially maize and cotton seed meal [2]. A global significations survey carried out in different parts of world reveled that maize and groundnut cake are the commodities most affected by mycotoxins [3,4]. Aflatoxins have been recognized to be more harmful to malnourished than well nourished animals and humans [5]. Aflatoxins $M_1$and M_2 was frequently detected in breast milk of sudanies [6] and United Arab Emirates women [7]. The studies carried out in various countries have found a positive correlation between hepatocellular carcinoma and aflatoxin ingestion by man. The mycotoxicological etiology has been suggested for several chronic progressively disabling, polyarthritic diseases [8]. The greatest danger to human health from aflatoxins is the consumption of aflatoxins contaminated addible items [9]. Aflatoxin, the secondary fungal metabolite of the fungus *Aspergillus flavus* and *Aspergillus parasiticus* is well known for its rapid death, hepatotoxic, carcinogenic, immunosuppression, growth impairment and adverse effects in laboratory and domestic animals viz. chickens, ducklings, rabbits, guinea fowl, rats as well as in humans [10-12]. Their formation may occur when fungi grow on crops in the field, at harvest, in storage or during the processing of feed when favorable conditions for their formation prevail [13]. Cichoricum intybus or Kasni is quite effective in detoxification and prevent liver from the toxic effect of various fungal toxins [14]. The root extract of Cichoricum intybus at higher doses (i.e. 1000 mg/kg/p.o) is reported to cytotoxic to certain strains of Salmonellla [15]. The extract is also found to suitable to treat the fungal hepatic toxicity [16,17], intestinal toxicity [18] and non-ulcer dyspepsia [19]. Considering the deleterious effects of aflatoxin and ameliorative effects of Cichoricum intybus (Kasni) in fungal infections, the present study was undertaken to find out the scientific correlation of *Cichoricum Intybus*

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Linn commonly known as Kasni, with aflatoxin in rats, which could help in conclusive of chronic aflatoxicosis.

MATERIALS AND METHODS

Animals: White albino rats of either sex procured from Indian Veterinary Research Institute (IVRI) Izatnagar, Bareilly-243022, were housed in animal house provided with 12 h light and dark cycle. The research was conducted as per the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India, New Delhi.

Experimental Protocol: In the present study fifty four white albino rats were taken and randomly distributed in control and two experimental groups Viz C, T_1 and T_2. Further each group is divided in three subgroups having six rats in each. C, T_1 and T_2 diets served as experimental groups supplemented with free Diet + 0.00 ppm Aflatoxin B_1, Free diet + 7.00 ppm aflatoxin B_1 and Free diet + 7.00 ppm aflatoxin B_1+ Kasni (100 g/kg feed) replacing maize in ration. Free diet contains maize crushed, wheat crushed, wheat ban, sodium chloride, mineral mixture and casein. Each group was provided weighed quantity of respective diet daily up to end of 28 days experiment. During experimental period rats were observed for clinical sign of illness and mortality, if any and were weighed at the end of 0,7,14,21 and 28 days. The feed consumption and body weight of rats were recorded.

Aflatoxin was produced on rice substrate by following the method of Shotwell *et al.,* [20]. The extraction and estimation of aflatoxin B_1 in rice substrate as well in feed to assigned treated groups was done as per the procedure AOAC [21]. Quantitative estimation was done by using spectrophotometer and thin-Layer chromatography (TLC) by following the method of Nabney and Nesbitt [22]. At the end of experiment the blood was collected with all aseptic precautions and possible care. All the collected samples of blood were analysed to study the following biochemical constituents of the blood. The GPT and GOT were colorimetrically estimated as per the method of Reitmann and Frankel [23] as described by Woottan [24]. The alkaline phosphatase activity (ALP) was estimated by the method of Bodansky as described by Hawk [25]. The total serum protein (TP) was monitored by Biuret method of Reinhold [26]. The estimation of albumin done by the method given by Oser [27]. The cholesterol level in blood was estimated by following the method of Wybeng and Pileggi [28]. The Glucose level estimated by the method given by Hultman [29] and Blood Urea Nitrogen (BUN) estimated by the method of Schwartz [30].Glutathione-s-transferase activity was measured in the cytosol with styrene oxide as substrate as described by Baars *et al.,* [31].

Statistical Analysis: Statistical analysis was done to the test of significance by standard procedure given by Snedcor and Cochran [32].

RESULTS AND DISCUSSION

During the experimental period the albino rats did not show any clinical signs of illness and mortality except dullness and reduced feed intake in T_1 and T_2. The variations of body weight and average feed intake with time of various groups are represented graphically (Fig 1 and 2). The results are expressed as mean±standard error of mean of three replicates of six rats each. The total body weight gain and average feed intake were reduced significantly ($p<0.01$) in aflatoxin B_1 fed group, however, there was significant improvement in the weight gain and average feed intake in the animals of Kasni treated group T_2. Frape *et al.,* [33] shown that aflatoxin given at the rate of 0.5,1.0 and 5 ppm diet body weight gain, growth rate, feed intake decreased during the experiment due to consumption of aflatoxin. Result of the present study showed that the average mean values of GOT activity (IU) were 58.07^{a}±2.41, 111.20^{b}±1.92; 103.00^{c}±1.42 I.U. in C, T_1 and T_2 groups respectively .The average mean values of GOT of treatment groups are significantly different ($P<0.05$ and 0.01) with the values of control group (Table 1). An increase of 0.91 and 0.78 times in GOT activity of rats were found in treatment T_1 and T_2 with control. The average mean values of GPT activity (IU) in rats were 28.26^{b}±1.59; 83.13^{a}±3.32 and 58.33^{c}±2.06 in C, T_1 and T_2 groups respectively (Table 1). The average mean value of GPT activity of control rats differed significantly ($P<0.05$ and 0.01) with treatment T_1 and $_2$ dietary levels. In the present study aflatoxin B_1 increases GOT and GPT activity while Kasni suppressed GOT and GPT activity induced by aflatoxin B_1. The average mean values of ALP activity (units/100ml) in rats were 57.6^{a}±2.45; 100.73^{b}±1.65; 85.20^{c}±1.28 in control, T_1 and T_2 groups respectively. The average mean values of treatments groups were significantly ($p<0.05$ and 0.01) different with each other. Increment in T_2 is less than T_1. The average mean values of total protein and albumin (g/100ml) were 6.60^{a}±0.27; 4.06^{b}±0.13; 5.28^{ac}±0.27 and 4.77^{a}±0.14; 3.11^{b}±0.07; 3.74^{bc}±0.13 in C, T_1 and T_2 respectively (Table 1).

Table 1: Changes in hepatic enzymes and other blood constituents in control, aflatoxin B_1 and aflatoxin B_1+Kasni (*Cichoricum intybus* linn.) treated white albino rats. Mean with different superscripts in a column differ significantly (P<0.05 and P < 0.01). Each group has three subgroups having six rats each and data are the mean of four replicates, S.E.M

Groups	GOT (I.U.)	GPT (I.U.)	ALP (Units/100ml)	TP (g/100ml)	Albumin (g/100ml)	Cholesterol (mg/100ml)	Glucose (mg/100ml)	BUN (%)
Control (C)	56.80±3.23	29.00±1.42	57.40±2.36	6.76±0.28	5.08±0.06	49.00±1.82	84.20±1.53	11.00±1.71
	57.40±2.59	27.20±1.36	57.60±1.94	6.14±0.22	4.32±0.14	50.04±2.13	79.80±1.12	12.40±1.72
	60.00±1.41	28.60±2.01	57.80±3.04	6.90±0.31	4.92±0.29	48.60±2.44	77.00±0.89	10.40±1.57
Mean±S.E.M.	58.07^{a}±2.41	28.26^{b} ±1.59	57.6^{a}±2.45	6.60^{a}±0.27	4.77^{a}±0.14	49.21^{a}±2.13	80.33^{a}±1.18	11.27^{a}±1.67
Treatment (T_1)	104.00±1.41	80.60±3.81	96.80±0.97	4.28±0.17	3.38±0.08	91.40±1.56	126.60±1.07	36.80±1.85
	115.80±2.01	84.00±2.82	104.20±1.57	3.86±0.06	3.20±0.05	100.60±1.07	126.20±1.36	35.80±1.43
	113.80±2.94	84.80±3.31	101.20±2.42	4.30±0.16	2.74±0.08	92.60±1.78	132.20±1.02	36.00±1.52
Mean±S.E.M.	111.20^{b}±1.92	83.13^{a} ±3.32	100.73^{b}±1.65	4.06^{b}±0.13	3.11^{b}±0.07	94.87^{b}±1.47	128.33^{b}±1.15	36.20^{c}±1.60
Treatment (T_2)	101.80±1.35	54.80±1.66	83.00±0.95	5.20±0.16	3.80±0.12	64.20±2.29	102.00±2.66	25.80±1.16
	108.20±1.16	58.60±1.97	83.60±1.72	5.58±0.37	3.80±0.13	75.20±0.96	102.80±2.06	27.60±1.21
	99.00±1.74	61.60±2.56	89.00±1.18	5.06±0.28	3.62±0.14	71.80±3.08	105.40±3.06	29.80±0.66
Mean±S.E.M.	103.00^{c}±1.42	58.33^{c}±2.06	85.20^{c}±1.28	5.28^{ac}±0.27	3.74^{bc}±0.13	70.40^{c}±2.11	103.40^{c}±2.59	27.73^{b}±1.01

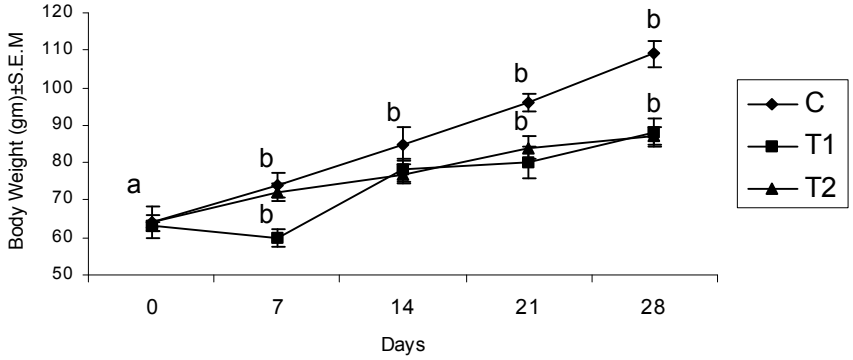

Fig. 1: Time course of body weight (gm) in rats. Results are expressed as mean±S.E.M. b=p<0.05 Vs a

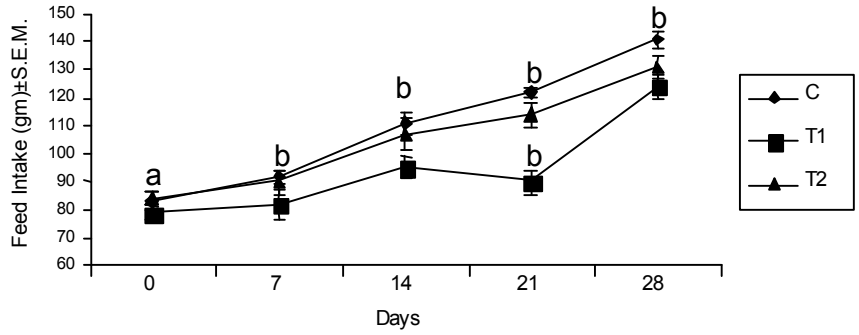

Fig. 2: Time course of feed intake (gm) in rats. Results are expressed as mean±S.E.M. b=p<0.05 Vs a

The present investigation showed that there was significant (P<0.05and 0.01) reduction in total protein and albumin in T_1 with Control. In Kasni treated group T_2 reduction in total protein and albumin is less than T_1 group. The mean values of serum cholesterol (mg/100 ml) 49.21^{a}±2.13; 94.87^{b}±1.47; 70.40^{c}±2.11 in C, T_1 and T_2which are significantly (P<0.05and 0.01) different with each other. Aflatoxin B_1 is responsible for the toxicity observed in groups fed on diet T_1 and T_2 as shown by the increase in serum enzymes. These enzymes are known to be good indicators of aflatoxin B_1 toxicity [34]. The average mean value of Glucose (mg/100ml) and Blood urea nitrogen (BUN) (%) were 80.33^{a}±1.18; 128.33^{b}±1.15; 103.40^{c}±2.59 and 11.27^{a}±1.67; 36.20^{c}±1.60; 27.73^{b}±1.01 in C and T_1 and

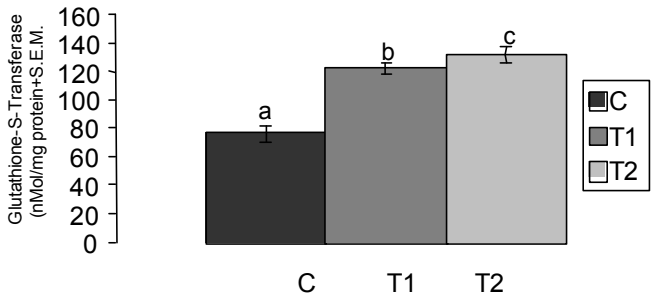

Fig. 3: C, T1 and T2, represents measurement of glutathione-s-transferase (nMol/mg proteins) in rats. Results are expressed as mean±S.E.M. b=p<0.01 Vs a, c=p<0.01 Vs b

T_2 respectively (Table 1). Enhancement in the level of glucose and blood urea nitrogen on feeding diet contains aflatoxin B_1 was observed in rats. Kasni in T_2 group suppressed the enhanced activity of glucose and BUN. Increasing trend in GPT, GOT, ALP, cholesterol, BUN and decreasing trends in total protein and albumin reported by various workers in albino rats and in other species [11,35]. Moundipa and Domngang [36] reported same type of degradation in aflatoxicosis on feeding aflatoxin B_1 with *solanum nigrum* in female rats. In 1999 Hayashi *et al.* [37] reported that chlorophyllin also have anticarcinogenic activity against aflatoxicosis. The activity of glutathione-s-transferase (Fig 3) was higher in T_1 and T_2 groups as compared with control. The activity of this enzyme increased by about 42% in T_1 and 48% in the T_2 group compared with control group. The observations of the present study revealed that the results of treatment T_1 and T_2 differ significantly (P<0.05and 0.01) with control groups. The activity of hepatic UDPGT was depressed in male rats given a low protein, energy restricted diet and cytochrome-P450 was depressed by a low protein ad lib energy diet [38]. The hepatic electron transport component and the glycogen content of female rat liver lowered by restricting food by 50% while restriction food by 25% did not alter the level of electron transport component [39]. Our findings shown that in Kasni treated groups the level of drug metabolizing enzymes were higher. The metabolite aflatoxin B_1-dihydrodiol derived from epoxide through the intervention of epoxide hydratase an enzyme whose activity has been shown to increase in female rats after chronic administration of aflatoxin B_1 [40]. This metabolite has a probable role in the toxicity of aflatoxin B_1 since its relative production by the microsomes from various species parallels their in vivo susceptibilities to aflatoxin B_1 poisoning [41]. Although epoxide hydratase yields this toxic metabolites, it also prevents the formation of AFB_1-DNA adducts, which could induce mutation. However, aflatoxin B_1-dihydrodiol could be rapidly conjugated by UDPGT and glutathione-s-transferase, which increased in the groups, fed on Kasni. Conjugation to glucuronic acid and glutathione via UDPGT and glutathione-s-transferase respectively has been established as an important pathway in the detoxification and excretion of toxic metabolites of aflatoxin B_1 [42]. The level of GOT, GPT and ALP in T_2 groups after the treatment, suggest the possible importance of Kasni in inducing excretion of the toxin.

CONCLUSION

On the bases of results it may be concluded that aflatoxin B_1 resulted in decrease in total protein and albumin and increase in GOT, GPT, ALP, Glucose, BUN and cholesterol. The improvement in glutathione-s-transferase was observed in Kasni treated rats T_2 group, which helps in excretion of aflatoxin from body. However toxicity observed in treated group even with the addition of Kasni could be due to insufficient level of Kasni. These diagnostic tools will be beneficial to control aflatoxicosis. Further studies are needed in this direction.

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