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Safety assessment of piperine after oral administration in sirohi goats

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Abstract
The present study was planned to study the safety assessment of piperine after oral administration @ 20 mg/kg body weight in 6 healthy Sirohi goats. Blood samples were collected before administration of the piperine which served as control (day 0). After administration of piperine, blood samples were collected at day 8 and 16 from jugular vein. Serum was harvested by centrifugation of vacutainers at 4000 rpm for 10 minutes at 4ºC. On day 0, the mean value of serum aspartate amino-transferase was observed to be 116.8±3.2 IU/L, which on day 8 reaches to 130.1±16.7 IU/L and on day 16, increases upto 133.1±16.7 IU/L. On day 0, 8 and 16 of safety study, the respective mean value of alanine amino-transferase (ALT) were 42.2±1.4 IU/L, 44.0±1.7 IU/L and 41.3±3.1 IU/L, respectively. The mean value of albumin was found to be 2.5±0.1 g/dl on day 0, 2.6±0.1 g/dl on day 8 and 2.6±0.1 g/dl on day 16 of the study. In Haematological examination, the mean value of haemoglobin (Hb) on day 0, 8 and 16 were 8.0±0.1 g/dl, 8.0±0.2 g/dl and 7.6±0.2 g/dl. Packed cell volume observed on day 0 was 21.8±0.3%, whereas, same was 22.4±0.4% and 22.1±0.5% on 8 and 16 day of the study.

Keywords: Piperine, safety assessment, biochemical analyser, sirohi goats

Introduction
Piperine (1-piperoyl piperidine) is the major active pungent constituent in various species of Piper species (*Piperaceae*) [5, 3]. Among these, the black pepper (*Piper nigrum* Linn) and long pepper (*Piper longum* Linn) are well known and widely used as relish by the large number of people all over the world. They are also used as ingredient in the folkloric medicine for treatment of gastrointestinal tract disorder since ancient time [8]. The piperine contents in *P. nigrum* Linn and *P. longum* Linn are 3-9% and 3-5% (on dry weight basis) respectively [9]. It can be isolated from the oleoresin of the pepper by extraction from the powdered fruit of the plant by dichloromethane or alcohol and purified in crystalline powder [1]. Several reports have shown that piperine has anti-hypertensive, anti-oxidant, anti-microbial properties apart from other medicinal values [14].

Materials and Methods
Piperine (BIOPERINE® *Black Pepper* Extract) was received as a gift for research from Sami Labs Limited, Banglore and the same was used in this study.

a) Experimental animals
Six clinically healthy Sirohi goats of 1-2 years of age at Goat farm, Amanala, NDVSU, Jabalpur was used in this study. The average weight of goats was between 22-25 kg. All the goats were ear tagged with identification number and kept under observation for two weeks prior to start of experiment. Animals were kept in hygienic conditions and provided balance ration with *ad-lib* water. All necessary efforts were made to keep the animals free from undue stress and CPCSEA guidelines regarding care and management of animals were followed. The study was approved by Institutional Animal Ethics Committee of College of Veterinary Science and Animal Husbandry, Jabalpur, Madhya Pradesh, India (No.116/IAEC/Vety/2018). In this study, piperine was orally administered @ 20 mg.kg^{-1} for 16 days to Sirohi goats. Blood samples were collected before administration of the piperine on day 0 (control) and on day 8 & 16 after administration of piperine from jugular vein for haematological and serum biochemical analysis.

b) Sample preparation procedure

Blood smears for determination of differential leukocyte count (DLC) were prepared from fresh blood at the time of blood collection [11]. Blood samples (1ml) with anticoagulant (K_3EDTA) were utilized for haematological evaluation, whereas blood samples (1ml) collected in procoagulation vacutainer were utilized for serum-biochemical evaluation. Serum was harvested by centrifugation of vacutainer at 4000 rpm for 10 minutes at 4 ºC and obtained serum was immediately used for biochemical analysis.

From the serum, all the biochemical parameters were estimated using standard assay kits using automatic biochemical analyser (Erba Mannheim, EM 200) at Department of Veterinary Pharmacology and Toxicology, Veterinary College, Jabalpur.

Results and Discussion

These biochemical parameters were evaluated on day 0, 8 and 16 day after oral administration of piperine for 16 days @ 20 mg.kg^{-1}b.w. On day 0, the mean value of serum aspartate amino-transferase (AST) was 116.8±3.2 IU/L, which on day 8 reaches to 130.1±16.7 IU/L and on day 16, increases up to 133.1±16.7 IU/L: whereas, the respective mean value of alanine amino-transferase (ALT) on day 0, 8 and 16 of safety study were 42.2±1.4 IU/L, 44.0±1.7 IU/L and 41.3±3.1 IU/L, respectively.

No significant differences were observed in the mean value of total protein at different time interval *i.e.* 0, 8 and 16 day where, respective values of total protein were 7.6±0.1 mg/dl, 7.7±0.1 mg/dl and 7.4±0.1 mg/dl. Elevated value of total protein was observed in piperine along with *Aegle marmelos* treatment in rats by [10, 4]. Observed significant increase in total protein level by administration of silymarin along with piperine.

The mean value of albumin was found to be 2.5±0.1 g/dl on day 0, 2.6±0.1 g/dl on day 8 and 2.6±0.1 g/dl on day 16 of the study, denoting no changes in albumin level at different time interval. However [13], observed the slight but statistically non-significant reduction in albumin level on *P. nigrum* administration in rat.

Thus, it can be concluded from the biochemical study, that piperine does not produces any adverse effect on liver function as no changes were observed in AST, ALT, Albumin and Total protein values. In this study, under safety assessment of piperine, kidney parameters namely blood urea nitrogen and creatinine was studied. The level of blood urea nitrogen (BUN) as evaluated on day 0, 8 and 16 were 30.7±1.1 mg/dl, 28.9±1.2 mg/dl and 29.5±1.4 mg/dl, respectively. These values do not differ significantly at various observational periods, indicating no effect of piperine administration on blood urea nitrogen level in sirohi goats. However [6], stated that piperine significantly reduces the level of blood urea nitrogen in cationic bovine serum-albumin induced immune complex glomerulonephritis (ICGN) in BALB/c mice. Moreover [12], reported significantly decrease in blood urea nitrogen level on piperine administration in lead acetate induced nephro-toxic in rats. Creatinine level on day 0, was 1.1±0.1 mg/dl, on day 8, it was 1.1±0.2 mg/dl and on day 16, the same was 1.1±0.2 mg/dl, indicating no significant difference at various time intervals. This result on creatinine level can be interpreted as no effect of piperine administration on creatinine level in sirohi goats [12]. evaluated the effect of piperine administration on creatinine level in lead acetate induced nephro-toxic rats. Here lead acetate did not affect the creatinine level in nephrotoxic rats. However, in higher dose rate (200 mg.kg^{-1} b.w.) significantly reduction in the value of creatinine was observed [6]. Reported the significant reduction in serum creatinine level in cationic bovine serum albumin induced immune complex glomerulonephritis in BALB/c mice @ 40 mg.kg^{-1}b.w. by oral route. The studies demonstrated the nephroprotective effect of piperine on chemical induced nephrotoxicity [12, 6].

In Haematological examination , the mean value of haemoglobin (Hb) on day 0, 8 and 16 were 8.0±0.1 g/dl, 8.0±0.2 g/dl and 7.6±0.2 g/dl, which were statistically non-significant, denoting no effect on haemoglobin concentration on piperine administration via oral route. The mean value of red blood cells count (RBC count) were 8.1±0.3, 8.1±0.3 and 7.4±0.2 on day 0, 8 and 16 of piperine administration. No significant difference was observed at different time interval, indicating no effect of piperine administration on red blood cells count in sirohi goats. Packed cell volume is the measure of the ratio of volume occupied by the red blood cells to the volume of whole blood in a sample. In present study, packed cell volume observed on day 0 was 21.8±0.3%, whereas, same was 22.4±0.4% and 22.1±0.5% on 8 and 16 day of the study. On comparison, the difference among the values was found to be non-significant, depicting no effect of piperine administration on packed cell volume.

In our study, observation for total leukocyte count (TLC) was made on 0, 8 and 16 day of the study and the mean values observed were 74.00±19.14, 75.08±52.35 and 75.50±45.66, respectively. Not much difference was observed in total leukocyte count at different time interval, indicating no change in value of total leukocyte count on piperine administration.

Similarly, in neutrophil count, no significant difference was observed on day 8 and 16 in comparison to 0 day value of neutrophil count. The mean value of lymphocyte count on day 0 was 61.5±1.6%, which slightly increased on day 8 (63.8±1.3%) and further increased up to 65.8±1.1% on day 16 of the study. Significant difference was observed on day 0 and day 16 of the study, indicating piperine induced increase in lymphocyte count in goats.

In eosinophil count, statistically non-significant difference was observed on day 0 (5.8±0.9%) and day 8 (4.0±0.5%) of the study. However, on day 16, values decreased up to 3.5±0.2%. There was reduction observed in eosinophil count on day 8 and day 16 of the study. Statistically significant difference was there in the value of eosinophil count on day 0 and 16.

On day 0 and day 8, numerically similar value of monocyte count was observed in sirohi goats. However, the values increases up to 2.2±0.5% on day 16. The values of day 16 of the study were significantly different from the values of day 8 and day 0.

[13] Observed the significant reduction in packed cell volume and white blood cell count on *P. nigrum* administration in rats fed with normal and high lipid diet [2]. Administered piperine at different dose rate and observed non-significant reduction in red blood cell count, significant reduction in haemoglobin and significant reduction in white blood cell count @ 4.50 mg.kg^{-1}b.w. in mice. However, statistically non-significant increase in the value of neutrophil and eosinophil count was obtained: whereas statistically non-significant reduction in lymphocyte count and monocyte count was observed when 4.5 mg.kg^{-1}b.w. piperine was administered via oral route [7]. Reported that after benzopyrene administration, the values of

haemoglobin, packed cell volume, lymphocyte count and monocyte count were reduced and these reduced values were increased on treatment of benzopyrene with piperine.

Conclusion

The data observed in present study revealed that piperine is safe @ 20 mg.kg^{-1}b.w. No significant differences were observed in various serological and haematological values after administration of piperine to the *Sirohi* goats.

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References

1. Bhat BG, Chandrasekhara N. Studies on the metabolism of piperine:absorption, tissue distribution and excretion of urinary conjugates in rats. Toxicology 1986;40(1):83-92.
2. Dogra RKS, Khanna S, Shanker R. Immunotoxicological effects of piperine in mice. Toxicology 2004;196:229-236.
3. Finar IL. Stereochemistry and the chemistry of natural products. Organic Chemistry (5th ed.). London: Longman's UK publication, ELBS 1975
4. Javed S, Ahsan W, Kohli K. Pharmacological influence of natural products as bioenhancers of silymarin against carbon tetrachloride-induced hepatotoxicity in rats. Clinical Phytoscience 2018;4:1-9.
5. Johri RK, Zutshi U. An ayurvedic formulation 'Trikatu' and its constituents. Journal of Ethnopharmacology 1992;37(2):85-91.
6. Kakalij RM, Kumar BD, Diwan PV. Comparative evaluation of nephroprotective potential of resveratrol and piperine on nephritic BALB/c mice. Indian Journal of Pharmacology 2019;47:247-255.
7. Naseema U, Rao GVS, Pazhanivel N, Pandiyan V, Sriram P. Effect of piperine solid lipid nanoparticle on haematological alteration in benzopyrene induced lung cancer in mice. The Pharma Innovation 2018;7(4):366-368.
8. Pei YQ. A review of pharmacology and clinical use of piperine and its derivatives. Epilepsia 1983;24(2):177-182.
9. Platel K, Srinivasan K. Influence of dietary spices and their active principles on pancreatic digestive enzymes in albino rats. Nahrung 2001;44(1):42-46.
10. Rathee D, Kamboj A, Sachdev RK, Sidhu S. Hepatoprotective effect of Aegle marmelos augmented with piperine co-administration in paracetamol model. Brazilian Journal of Pharmacognosy 2018;28:65-72.
11. Schalm OW. Veterinary Haematology, 2nd Edn., Lea and Febiger, Philadelphia, USA 1967
12. Sudjarwo SA, Eraiko K, Sudjarwo GW, Koerniasari. Protective effect of piperine on lead acetate induced-nephrotoxicity in rats. Iranian Journal of Basic Medical Science 2017;20(11):1227-1231.
13. Tijjani H, Luka CD. Effects of *Afromomum melegueta*, *Zingiber officinale* and *Piper nigrum* on some biochemical and haematological parameters in rats fed with high lipid diet. International Journal of Pure and Applied Bioscience 2013;1(3):61-67.
14. Upadhyay V, Malik A, Mishra M, Singh BP, Tripathi S. Development and Validation rapid RP – HPLC method for estimation of piperine in Piper nigrum. International Journal of Herbal Medicine 2013;1(4):6-9.