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Disposition kinetics of sparfloxacin under different pathological condition in Black Bengal goat following single intravenous administration

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ABSTRACT

Clinically healthy 9 black Bengal female goats (1–1.5 year age) weighing between 9–12 kg were divided into 3 equal groups. Group 1 served as control and the animals of group 2 and 3 were considered to be experimental. In experiment no. 1 sparfloxacin was administered intravenously to the goats of group 1 and disposition kinetics and protein binding studies were conducted in plasma. Liver of each goat of group 2 and 3 were damaged by subcutaneous administration of carbontetrachloride and considered as experiment no.2. Sparfloxacin was administered intravenously to group 2 for disposition kinetics and protein binding study. In experiment no.3 rejuvenation of liver of animals of group 2 were done by oral administration of a commercial medicine for consecutive 21 days period. Animals of group 3 were considered as untreated control for the commercial medicine. The results of icterus index, bromosulphophthalein clearance, serum transaminase activity suggested that carbontetrachloride at the recommended dose level produced hepatopathy of goats. The commercial medicine treatment brought all the altered values of plasma kinetic parameters to base level and regenerated the damaged tissue of liver. Disposition kinetic study of sparfloxacin showed that carbontetrachloride –induced damage liver retained Sparfloxacin for same period with almost equi concentration.

Key word: Carbontetrachloride, Disposition kinetics, Goats, Hepatopathy, Sparfloxacin

Liver is the main metabolizing organ where drugs undergo hydrolytic, oxidative, reductive and or conjugative reaction. Hepatic microsomal oxidative system is the major metabolic pathway for lipid soluble drugs. The factors affecting hepatic tissues as well as hepatic function can affect drug disposition. Study of the biotransformation of drugs in the diseased liver may be approached by two ways, either by measuring the activity of drug metabolizing enzymes in hepatic tissue or by determining the disposition kinetics of drugs. Different drugs including carbontetrachloride can induce hepatopathy which is reliable, effective and reproducible (Kumar *et al*. 2009). An ayurvedic preparation (AP) is extensively used as hepatoprotective and hepatostimulatory drug. Sparfloxacin, a potent, long acting bactericidal fluroquinolone derivative is metabolized and excreted through urine. In field condition the most clinical cases are complicated, and a combination of bacterial infection with hepatopathy is not uncommon.

Therefore the present research work was carried out to determine any modification of pharmacokinetics in goats of induced hepatopathy for judicious application of antibacterial agents.

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MATERIALS AND METHODS

Sparfloxacin (purity >98%) and all the chemicals of analytical grade and ayurvedic preparation were obtained commercially. The ayurvedic preparation (AP), a polyherbal compound is composed of *Solanum nigrum*, *Holarrhena antidysterica*, *Tephrosia purpurea*, *Berbaris aristata, Alostania scholaris, Hygrophila auriculata, Cichorium intybus*.

Clinically healthy 9 black Bengal female goats (1–1.5 year age) weighing between 9–12 kg were caged individually in custom made metabolic cage (stainless steel). Before starting the experiment, the animals were dewormed twice with albendazole (7.5mg/kg) at 21 days interval. After one month of last dosing of anthelmintic, animals were acclimatized for 7 days before starting the experiment. The present study was approved by CPCSEA.

The animals were divided into 3 equal groups. Group 1 served as experimental control and the animals of groups 2 and 3 were considered to be experimental. In experiment no. 1, sparfloxacin was administered intravenously to the goats of group 1 and disposition kinetics and protein binding activity were conducted in plasma. Liver of each goat of

Groups 2 and 3 were damaged by subcutaneous administration of carbontetrachloride at (0.75 ml /kg) mixed with equal volume of liquid paraffin following over night fasting on three occasions at an interval of 48 h (Jamir *et al*. 2005) and considered as experiment 2. Sparfloxacin was administered intravenously to group 2 for disposition kinetics and protein binding study. In experiment 3 rejuvenation of liver of animals of group 2 were done by oral administration of AP for consecutive 21 days period. Animals of group 3 (hepatopathy) were considered as untreated control for AP.

Experiment 1

A single dose of sparfloxacin @20 mg/kg body weight was administered intravenously to each animal of group 1.

Collection of samples

Blood: Blood samples were collected from jugular vein at 0,0.08, 0.16, 0.33, 0.5, 0.66, 1, 2, 4, 6, 8, 10 and 12 h interval. About 3.5 ml of blood was collected at the above mentioned time except at 0.08, 0.16, 1 and 2 h samples where 8 ml blood was collected for protein binding study of sparfloxacin.

Plasma (2 ml) was utilized for the analysis of sparfloxacin concentration while 2 ml of plasma collected at 0.08, 0.16, 0.33 and 0.5 h were used for estimation of plasma protein binding of sparfloxacin.

Plasma protein binding

Equilibrium dialysis technique as described by Sisodia *et al*. (1965) and modified by Mandal *et al.* (1995) was used in this experiment to determine plasma protein binding of sparfloxacin. The dialysis tube containing 2 ml of plasma was suspended in a test tube containing 2 ml of phosphate buffer (pH 7.4) and placed into the incubator in standing position for 24 h at 37°C. The protein content of plasma of each sample was also estimated by Biuret method (Wooton 1974). The protein content was expressed as percentage. The binding capacity, dissociation and association constants were also calculated by the method of least regression technique described by Pilloud (1973).

Induction of liver damage

Liver damage was induced experimentally in the animals of groups 2 and 3 with subcutaneous administration of carbontetrachloride (at 0.75ml /kg) on 3 occasions at an interval of 48 h. The intensity of liver damage was assessed by performing serum bromosulphophthalein clearance test, icterus index, serum aspartate and alanine aminotransferase.

Experiment 2

Sparfloxacin was administered intravenously to each animal of group 2 animal at 20 mg/kg after 48 h of third dose of carbontetrachloride.

Collection of sample: Blood samples were collected in the same procedure as in experiment no. 1 except plasma protein binding.

Rejuvenation of liver: Ayurvedic preparation (AP) was administered orally at 20 ml twice daily to each goat of group 2 consecutive for 21 days period and liver function test was monitored weekly to observe the intensity of rejuvenation.

Experiment 3

Sparfloxacin was administered intravenously to each animal of group 2 at 20 mg/kg after rejuvenation of liver with AP.

Collection of samples: Blood samples were collected in the same procedure as stated above.

Statistical analysis

The results were analysed using general linear model with invariable data in SPSS 10.0 version of software. The results were expressed as mean±standard error (SE). Pharmacokinetic parameters were determined for each animal individually.

Pharmacokinetic parameters: Pharmacokinetic parameters of sparfloxacin were determined from computerized curve fitting programme 'PHARMKIT' supplied by the Department of Pharmacology, Institute of Postgraduate Medical Education and Research, Pondicherry, India.

Estimation of sparfloxacin in plasma: Concentration of sparfloxacin was measured by modified method of Frazier *et al*. (2000). To a test tube 2 ml of plasma, 5 ml of acetonitrile and 0.05 M sodium phosphate buffer (NaH_2PO_4, H_2O, pH3.5) 80: 20 was added and vigorously shaked for 5 min. It was centrifuged at 3,000 rpm for 35 min. The supernatant was collected and the absorbance was read in double beam UV-VIS spectrophotometer at 295 nm wavelength against blank prepared with plasma collected at 0 h. Concentration of sparfloxacin present in each blood sample was then calculated from standard curve earlier and expressed as µg/ml.

Estimation of sparfloxacin in urine: To urine (2 ml), 2 ml of distilled water and 10 ml of dichloromethane (DCM) were added. The mixture was then shaken for 3 min and let to settle down for 5 min. The lower phase was filtered through sodium sulphate. The total filtrate was reduced to 5 ml using boiling water bath and absorbance was read using double beam UV-VIS spectrophotometer at wavelength of 295 nm against the blank collected at 0 h. Concentration of sparfloxacin present in each blood sample was then calculated from standard curve earlier and expressed as µg/ml.

Recovery of sparfloxacin from plasma: Recovery of saparfloxacin from goat plasma was carried out *in vitro* to ascertain the reliability of analytical method after fortifying 2, 4, 5, 8, 10 µg/ml of sparfloxacin (analytical grade). The absorbance maximum was found to be at 295 nm. The absorbance against several concentration of sparfloxacin at 298 nm was plotted linearity was found to be maintained. The recovery was 85–90%. The limit of detection of sparfloxacin was 1 µg/ml.

Blood chemistry

Bromosulphophthalein (BSP clearance test): Bromosulphophthalein (BSP) was injected intravenously at 5 mg/kg body weight as 5 % aqueous solution. The blood samples (3 ml) were collected at 0, 3, 6, 9, 12, 15 and 30 min. The concentration of the dye present in serum was measured spectrophotometrically according to Oser (1965). A standard curve with quantity of dye in serum was prepared for calculation of unknown samples, The quantity of dye (µg/ml) was plotted on semilogarithmic paper against time and t½ value was calculated (Cornelius 1989) and expressed as mean. The test was carried out in the serum of goats before administration of carbontetrachloride and 48, 96, 120 h and 7, 14, 28 day following administration of first, second and third dose respectively.

Icterus index: The test was carried out in the serum of goats according before administration of carbontetrachloride and 48, 96, 120 h and 7, 14, 28 day following administration of third dose of carbontetrachloride and was expressed as unit according to the method of Oser (1965)

Estimation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities in serum: Serum AST and ALT activities were measured as per Yatizidis (1960).

RESULTS AND DISCUSSION

Icterus index: The values of icterus index of goats of group 2 were significantly higher except 28th day than that of control goats (Table 1). The peak value of icterus index was obtained at 120 h and thereafter the value was started to decrease and return to the base level on 28th day of AP treatment. Pandey *et al*. (1983) observed that carbontetrachloride induced higher icterus index unit started to decrease from fourth day onwards till 10th day in goats when treated with AP, a polyherbal liver stimulant. AP, a polyherbal drug showed some delayed time of response on liver which might be due to difference in composition as well as dose level and intensity of liver damage.

Table 1. Serum icterus index (unit) of goat following induced liver damage with carbontetrachloride
(mean values of 3 replicates with SE)

Time	Carbon tetrachloride-induced liver damage		
	Control (group 1)	Treated (21 days) with AP (group 2)	(Group 3)
0 h	5.02±0.120^{a}	4.64±0.266^{a}	4.10±0.130^{a}
48 h	4.91±0.114^{a}	9.77±0.290^{c}	8.92±0.209^{b}
96 h	4.87±0.141^{a}	14.180±0.483^{c}	12.72±0.291^{b}
120 h	4.97±0.173^{a}	20.36±0.490^{b}	19.03±0.496^{b}
7 day	4.96±0.113^{a}	19.43±0.516^{c}	14.74±0.202^{b}
14 day	4.89±0.179^{a}	12.78±0.489^{b}	13.16±0.248^{b}
28 day	5.19±0.124^{a}	4.68±0.498^{a}	7.71±0.264^{b}

Mean values in the row bearing different superscripts differ significantly (P<0.05).

Table 2. Bromosulphophthlein clearance (t½ values, minutes) from serum of goat following carbon tetrachloride-induced liver damage
(mean values of 3 replicates with SE)

Time	Carbontetrachloride-induced liver damage		
	Control (group 1)	Treated (21 days) with AP (group 2)	(Group 3)
0 h	3.32±0.358^{a}	3.36±0.271^{a}	3.05±0.150^{a}
48 h	3.24±0.250^{a}	5.92±0.788^{b}	5.92±0.055^{b}
96 h	3.24±0.298^{a}	11.48±0.308^{b}	14.06±0.042^{b}
120 h	3.20±0.341^{a}	21.65±0.281^{b}	21.11±0.228^{b}
7 day	3.20±0.317^{a}	17.90±0.342^{b}	19.14±0.323^{b}
14 day	3.21±0.271^{a}	11.25±0.388^{b}	12.22±0.498^{b}
28 day	3.17±0.314^{a}	3.36±0.280^{a}	3.07±0.150^{b}

Mean values in the row bearing different superscripts differ significantly (P<0.05).

Bromosulpophthalein clearance test: The mean values of BSP (t½) with S.E of all goats of all three groups are presented in Table 2. The values of group 2 and group 3 goats at 0, 48, 96 and 120 h were significantly higher compared to control goats but the difference of value between group 2 and group 1 at 28 days was not significant but the same was significant (P<0.01) when compared between group 2 and group 3 goats. Cornelius (1989) stated that t½ values of BSP clearance exceeding 4 min indicate liver damage in goats. In this experiment carbontetrachloride increases the t½ value above 5 min from 0 hr onward post administration. In carbontetrachloride treated groups the peak value in serum reached on 120 hr and thereafter the value started to decrease. In AP treated groups (group 2) the t½ returned to the base level on 28th day.

Serum transaminase activity

Aspartate transaminase: The mean values with SE of AST activity in goats of all three groups are presented in Table 3. The difference in enzyme activity in between

Table 3. Serum AST activity (unit/ml) in goat following carbontetrachloride induced liver damage
(mean values of 3 replicates with SE)

Time	Carbon tetrachloride-induced liver damage		
	Control (group 1)	Treated (21 days) with AP (group 2)	(Group 3)
0 h	343.33±11.01^{a}	348.32±7.51^{a}	346.67±10.43^{a}
48 h	340±6.60^{a}	638.33±17.72^{b}	638.33±8.79^{b}
96 h	345.00± 13.86^{a}	815.00±21.80^{b}	821.67±16.42^{b}
120 h	341.00±11.85^{a}	1066.67±14.38^{c}	963.33±12.85^{b}
7 day	355.67±6.81^{a}	889.43±15.44^{b}	951.33±16.89^{b}
14 day	377.67±1.20^{a}	576.00±20.95^{b}	620.67±17.07^{b}
28 day	380.68±.85^{a}	274.67±17.09^{b}	426.00±9.45^{a}

Mean values in the row bearing different superscripts differ significantly (P<0.05).

control and group 3 goats was highly significant (P<0.05).The increased activity returned to the base level on 28th day in the serum of group 2 goats treated with AP. Arsul *et al.* (2011) observed increase of serum AST activity after carbontetrachloride administration in rats following administration of a polyherbal formulation, AP.

Alanine transaminase: The mean values with S.E. of ALT activity in all three Groups of goats have been presented in Table 4. Group 3 goats treated with carbontetrachloride showed significant increase in enzyme activity from 96 hr onwards, group 2 goats showed a peak increase of enzyme activity on 120 h, thereafter the activity started to decline in serum of goats of group 2 and 3 but the activity reached the base level only in group 2 goats treated with AP. The difference of enzyme activity between group II and 1 was not significant from 21st day onward. Chaudhari *et al.* (2009) reported similar trend increase of serum ALT activity after carbontetrachloride administration in rats following a polyherbal drug AP administration.

The parameters like icterus index, half-life of BSP, AST and ALT showed that carbon tetrachloride has damaged liver cells. The treatment of goats having liver damage with AP showed a tendency to return all the above parameters to base level. Therefore it may be concluded that AP may be a comprehensive treatment for rejuvenation of liver.

Disposition kinetics of Sparfloxacin: Blood concentration and disposition kinetics of sparfloxacin in healthy (group 1) and carbon tetrachloride induced liver damaged (group 2) goats after single dose intravenous administration at 20 mg/kg body weight.

The mean plasma concentration of sparfloxacin with SE in healthy (group 1) and carbon tetrachloride induced liver damage (group 2) goats at different time interval after single dose intravenous administration have been incorporated in Table 5. Both the values of C^{P}_{max} and C^{p}_{min} in group 1 were non significantly higher than that of liver damaged group 2 goats. The concentrations of sparfloxacin were higher from 0.08 to 10 h in healthy goats compared to liver damaged goats. Disposition kinetics of sparfloxacin in group 1 and group 2 liver damaged goats after single dose intravenous administration at 20 mg/kg body weight derived from computerized semilogarithmic plot of plasma level time profile have been presented in Table 5. The results showed the biphasic declination of the concentration in both the groups of animal suggesting two compartment open model of sparfloxacin in healthy and damaged goats (Fig. 1). The lower values of t½ ß along with higher values of Cl_B in both the groups indicate sparfloxacin has a shorter duration of action in goats. The values of Vd_{area},Vd_B and Vd_C were not significantly changed between two groups. However, higher values of apparent volume of distribution in both groups suggested wide distribution of sparfloxacin including water space in the body. Values of K_{21} and K_{12} were higher in healthy compared to damaged goats. This also suggested that sparfloxacin may not have affinity to accumulate in tissue compartment in both goups of animals. The protein binding study of sparfloxacin in groups 1 and 2 animals revealed that percentage of binding of sparfloxacin was about 70% but the elimination half life is shorter. This is possible when the drug is excreted through active tubular secretion. Seth (2000) studied that fluoroquinolones are primarily excreted via the kidneys by glomerular filtration and tubular excretion.

Blood concentration and disposition kinetics of sparfloxacin in healthy groups (group 1) and AP treated (group 2) goats after single dose intravenous administration at 20 mg/kg body weight.

The mean plasma concentration of sprfloxacin with SE in healthy (group 1) and AP treated (group 2) goats at different time intervals after single dose intravenous administration have been incorporated in Table 5. It would

Table 4. Serum ALT activity (unit/ml) in goat following carbon tetrachloride induced liver damage (mean values of 3 replicates with SE)

Time	Carbon tetrachloride-induced liver damage		
	Control (group 1)	Treated (21 days) with AP (group 2)	(Group 3)
0 h	73.49±2.08[a]	75.89±4.04[a]	72.97±6.42[a]
48 h	111.33±4.61[a]	134.45±12.08[b]	127.00±5.77[b]
96 h	95.33±7.50[a]	180.33±8.41[b]	178.00±13.78[b]
120 h	88.60±4.62[a]	288.67±9.94[b]	309.33±11.93[b]
7 day	85.67±4.04[a]	258.67±9.20[b]	282±8.66[b]
14 day	101.33±3.51[a]	160.00±14.47[b]	231.33±4.50[b]
28 day	93.67±2.31[a]	83.00±5.29[a]	139.33±8.08[a]

Mean values in the row bearing different superscripts differ significantly (P<0.05).

Table 5. Plasma Sparfloxacin concentration (µg ml^{-1}) after single dose intravenous administration at 20 mg/kg body weight in plasma of goat following carbon tetrachloride-induced liver damage (mean values of 3 replicates with SE)

Time (h)	Carbon tetrachloride-induced liver damage		
	Control (group 1)	Group 2 (Treated with AP)	Group 3
0.08	8.88±1.12[a]	7.86±0.369[b]	11.24±0.191[c]
0.16	7.52±0.79[a]	7.30±0.449[a]	9.97±0.080[b]
0.25	6.81±0.66[a]	6.87±0.48[a]	8.76±0.166[b]
0.33	6.40±0.62[a]	6.49±0.508[a]	7.32±0.255[b]
0.5	5.55±0.53[a]	5.88±0.526[a]	6.42±0.278[b]
0.66	5.20±0.42	5.45±0.556	5.89±0.316
1	4.66±0.28	4.69±0.487	5.08±0.516
2	3.45±0.10	3.36±0.385	3.79±0.463
3	2.75±0.02	2.40±0.257	3.22±0.292
4	2.23±0.05[a]	1.68±0.361[b]	2.70±0.249[c]
6	1.37±0.05[a]	1.02±0.136[ab]	1.66±0.185[b]
8	0.81±0.08[a]	0.53±0.088[b]	0.95±0.150[a]
10	0.53±0.05	0.32±0.005	0.58±0.94

Mean values in the row bearing different superscripts differ significantly (P<0.05).

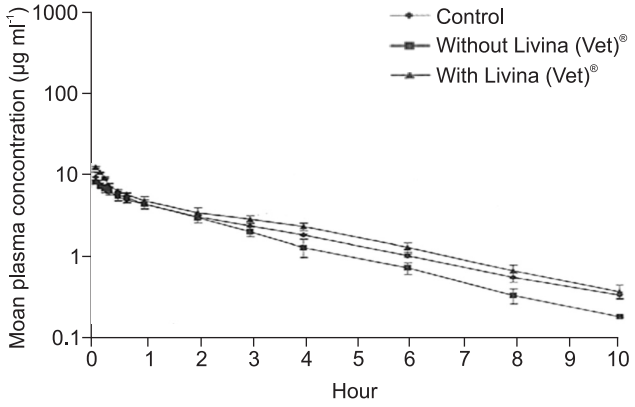

Fig 1. Semilogarithmic plot of mean plasma concentration of sparfloxacin against time after single doseintravenous administration at 20 mg/kg body weight in healthy and carbon tetrachloride –induced liver damage.

be evident from Table 6 that the concentration of AP treated animals were somewhat higher nonsignificantly than that of healthy animals suggesting gradual improvement in liver function of group 2 goats. Disposition kinetics of sparfloxacin in group 1 and group 2 AP treated goats after single dose intravenous administration at 20 mg/kg body weight derived from computerized semilogarithmic plot of plasma level time profile are shown in Table 5 and Fig. 1. The computerized plot of plasma level time profile of sparfloxacin showed biphasic decay in both groups of animals and confirmed two compartment open model of sparfloxacin.The α and $t_{½\alpha}$ values were unaltered between the two groups. It indicates the rejuvenatinaion of Liver by AP treated goats. The values of $t_{½\beta}$ and Cl_B in AP treated goats suggesting smaller half life of sparfloxacin in both

Table 6. Values of pharmacokinetic parameters after single dose intravenous administration at 20 mg/kg body weight in goats following carbon tetrachloride-induced liver damage (mean values of 3 replicates with SE)

Parameters	Carbon tetrachloride-induced liver		
	Group 1	damage Group 2	Treated (21 days) with AP, group 2)
C^0_B (µg ml^{-1})	10.47±1.47^b	8.45±0.318^a	13.12±0.183^c
A (h^{-1})	5.52±0.58^c	2.67±0.364^a	4.07±0.361^b
$t_{½\alpha}$ (h)	0.13±0.015^a	0.27±0.034^b	0.17±0.015^c
β (h^{-1})	0.25±0.02^a	0.30±0.006^b	0.25±0.011^a
$t_{½\beta}$ (h)	2.85±0.24	2.29±0.050	2.78±0.13
AUC (µg h L^{-1})	25.06±0.335^{ab}	21.19±2.30^a	29.48±2.59^b
Vd_{area} (L kg^{-1})	0.365±0.205^b	0.317±0.263^{ab}	0.274±0.136^a
Cl_B (L kg^{-1}h^{-1})	0.009±0.09^b	0.010±0.096^c	0.007±0.056^a
K_{21} (h^{-1})	3.35±0.487^c	1.98±0.144^a	2.27±0.297^b
K_{12} (h^{-1})	1.99±0.259^c	0.588±0.194^a	1.59±0.088^b
K_{el} (h^{-1})	0.41±0.058^a	0.40±0.033^a	0.453±0.032^b
f_C	0.60±0.054^a	0.753±0.046^b	0.554±0.048^{ab}

Mean values in the row bearing different superscripts differ significantly (P<0.05).

Table 7. Protein binding activity of sparfloxacin after single intravenous administration at 20mg/kg in the plasma of goat following carbon tetrachloride –induced liver damage (mean values of 3 replicates with SE)

Time (h)	Control	Carbon tetrachloride-induced liver damage	
	Control (group 1)	AP treated for 21 days (group 2)	Without AP Group 2
0.08	72.25 ±0.61^a	73.43 ±0.40^a	69.93±0.21^b
0.16	72.29±0.69^a	73.61±0.39^a	70.29±0.55^b
0.25	71.73±0.46^a	73.34±0.33^b	71.08±0.52^a
0.33	71.47±0.70^a	73.36±0.34^b	71.08±0.52^a

Mean values in the row bearing different superscripts differ significantly (P<0.05).

Table 8. Plasma protein binding capacity (β_i), dissociation rate constant (K'_a) and association rate constant (K_β) of sparfloxacin in goats following carbon tetrachloride-induced liver damage (Mean values of 3 replicates with SE)

Time (h)	Carbon tetrachloride-induced liver damage		
	Control (group 1)	AP treated for 21 days (group 2)	Without AP Group 2
β_i (mol g^{-1})	1.75×10^{-8} ±0.21×10^{-8}	1.50×10^{-8} ±0.09×10^{-8ns}	1.44×10^{-8} ±0.05±10^{-8ns}
K_β (L mol^{-1})	1.63×10^{-6} ±0.27×10^{-6}	1.61×10^{-6} ±0.06×10^{-6ns}	2.06×10^{-6} ±0.09×10^{-6ns}
K'_a (mol L^{-1})	0.65×10^6 ±0.13×10^6	0.62×10^6 ±0.02×10^{6ns}	0.55×10^6 ±0.04×10^{6ns}

Mean values in the row bearing different superscripts differ significantly (P<0.05).

the groups of animals. The values of Vd_{area},Vd_B and Vd_C were not significantly lower in AP treated goats (Table 7). However, in both the groups the values of suggested wide distribution of sparfloxacin in goats. The value of K_{21} and K_{12} in AP treated animals are lower than healthy goats. This also suggested that sparfloxacin may not have affinity to accumulate in the tissue compartment in both the group of animals.

Blood concentration and disposition kinetics of sparfloxacin in carbon tetrachloride induced liver damaged (group 2) goats and AP treated animals of group 2 after single dose intravenous administration at 20 mg/kg body weight.

Pharmacokinetics of sparfloxacin in group 2 (AP treated) and group 2 carbon tetrachloride induced liver damaged goats after single dose intravenous administration at 20 mg/kg were summarized in Table 5. The biphasic declination of the concentration in both the groups of animal suggested 2 compartment open model kinetic in both the groups of goats. It would be apparent that sparfloxacin in blood at all time intervals showed no significant difference between 2 groups. The values of $t_{½\beta}$ and Cl_B in both groups of goats suggested similar half life of sparfloxacin. The values of

Vd_{area}, VdB and Vd_C indicate wide distribution of sparfloxacin in both groups of animals. Values of K_{12} and K_{21} in liver damaged goats were lower compared to healthy and AP treated goats. This also suggested that sparfloxacin may have slow rate of entry as well as rapid back diffusion of sparfloxacin from the cell in damaged goats. From the above study it is quite clear that hepatic damage had very lesser effect on sparfloxacin kinetics. The recovery percentage of from urine of all the groups (Table 6) suggested the similar rate of metabolism in goats irrespective of the different stress condition in liver. This may further indicative negative metabolism of sparfloxacin in liver of goats.

Plasma protein binding of sparfloxacin: The mean values with SE of plasma protein binding of groups 1, 2 (liver damaged) and 2 treated with AP are presented in Table 7. The binding capacity, association constant and dissociation constant of sparfloxacin with plasma protein in goats are summarized in Table 8. It revealed that equilibrium association constant was greater compared to dissociation constant in groups 1 and 2 animals respectively.

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