Disposition Kinetics and Urinary Excretion of Paracetamol Following Intravenous Administration in Buffalo Calves (*Bubalus bubalis*)

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Paracetamol (Acetaminophen), a NSAID is well tolerated and lacks many side effects of aspirin. It is a widely used over-the-counter analgesic, antipyretic and weak anti-inflammatory property. The main mechanism is the inhibition of cyclooxygenase (COX) and recent findings suggest that it is highly selective for COX-2 (Henz *et al.*, 2008). The present study was aimed to study the disposition kinetics and urinary excretion of paracetamol in buffaloes.

**Materials and Methods**

Five clinically healthy female buffalo calves of (120 – 180 kg body wt.) were used in the present study. Paracetamol was administered @ 40 mg /kg i/v.in all the animals. The biological samples (plasma and urine) were collected at 2.5, 5, 10, 15,20, 30, 45 min and 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12 and 24 h, however, the samples of urine were collected up to 48 h (at 30, 36 and 48 h). Concentrations of paracetamol in plasma and urine were estimated by spectrophotometric method (Archer and Richardson, 1980). The experimental data were analysed by using two compartment open model (Notari, 1980). For two compartment open model, the concentration of the drug in plasma at any time is obtained from the formula:

\[ C_p = A e^{-\alpha t} + B e^{-\beta t} \]

Where \( C_p \) is the drug concentration in plasma at time ‘t’.

**Results and Discussion**

The drug was detected up to 2 h only with a mean of 1.87 ±0.48 µg/ml in plasma. The plasma drug concentration was higher from 2.5 min to 1 h in the present study, Sudha Kumari (1998) observed higher concentration of paracetamol from 5 to 30 min in goat after single i/v administration. In urine, paracetamol was detected for a longer period of 48 h with the mean of 10.90 ±1.14 µg/ml. The mean peak urine concentration of 2022 ±118.8 µg/ml was attained at 1.5h.

The distribution rate constant (\( \alpha \)) and distribution half –life (\( t_{1/2 \alpha} \)) were 7.148 ±1.361 h⁻¹ and 0.11 ± 0.01 h, respectively. This denoted that the drug distributed rapidly in the body of buffalo calves. Manna *et al.* (1994) reported

![Fig. Plasma – Urine – Conc.time profile curve of paracetamol @ 40 mg/kg following single i/v administration in female buffalo calves.](image-url)
approximately similar value of $t_{1/2}^\alpha$ (0.10 h) in Black Bengal goat. The elimination rate constant ($\beta$) and elimination half – life ($t_{1/2}^\beta$) of paracetamol were 0.965 ± 0.136 h$^{-1}$ and 0.77 ± 0.09 h respectively.

This denoted that the drug remained for a shorter period and eliminated rapidly from the body of buffalo calves. Almost similar value of $t_{1/2}^\beta$ was obtained by Manna et al. (loc. cit) in Black Bengal goats (0.53h) and comparatively higher $t_{1/2}^\beta$ was reported by Sidhu et al. (1993) in buffalo calf (8.69 ± 0.83h), Sharma et al. (1995) in lactating goat (3.56 ± 0.13h) and Chaudhary et al. (2002) in buffalo calves (1.91 ± 0.07h). The lower $t_{1/2}^\beta$ obtained in the present investigation denoted that the paracetamol was eliminated at a faster rate from the body of buffalo calves, which is further supported by higher values of (Kel) of 1.471 ± 0.089 h$^{-1}$ and (Cl$^B$) of 43.67 ± 3.39 ml/kg/min. This led to the lower MRT value of 1.00 ± 0.10 h. Vd$^{area}$ of paracetamol was 2.79 ± 0.14 L/kg in the present investigation. Vd$^{area}$, 1L/kg obtained in present investigation for paracetamol denoted good distribution of the drug in body fluids and tissues of buffalo calves. This is further supported by higher $T~P$ ratio of 0.59 ± 0.13 in the present study. The Cl$^B$ value of 43.67 ± 3.39 ml/kg/min was observed when paracetamol was given single i/v dose in buffalo calves in the present study.

### Table. Pharmacokinetic parameters of paracetamol in female buffalo calves following single i/v dose of 40 mg/kg (n=5).

<table>
<thead>
<tr>
<th>Kinetic parameter (units)</th>
<th>Paracetamol (Mean±S.E.)</th>
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<tbody>
<tr>
<td>A (µg/ml)</td>
<td>9.51±1.94</td>
</tr>
<tr>
<td>B (µg/ml)</td>
<td>13.11±1.08</td>
</tr>
<tr>
<td>$C_0^P$ (µg/ml)</td>
<td>22.62±1.00</td>
</tr>
<tr>
<td>$\alpha$ (h$^{-1}$)</td>
<td>7.148±1.361</td>
</tr>
<tr>
<td>$t_{1/2}^\alpha$ (h)</td>
<td>0.11±0.01</td>
</tr>
<tr>
<td>$\beta$ (h$^{-1}$)</td>
<td>0.965±0.136</td>
</tr>
<tr>
<td>$t_{1/2}^\beta$ (h)</td>
<td>0.77±0.09</td>
</tr>
<tr>
<td>AUC (mg/L.h)</td>
<td>15.59±1.07</td>
</tr>
<tr>
<td>AUMC (mg/L.h$^2$)</td>
<td>16.09±2.56</td>
</tr>
<tr>
<td>MRT (h$^{-1}$)</td>
<td>1.00±0.10</td>
</tr>
<tr>
<td>$K_{12}$ (h$^{-1}$)</td>
<td>1.672±0.142</td>
</tr>
<tr>
<td>$K_{21}$ (h$^{-1}$)</td>
<td>4.970±1.540</td>
</tr>
<tr>
<td>$K_{el}$ (h$^{-1}$)</td>
<td>1.471±0.089</td>
</tr>
<tr>
<td>T-P</td>
<td>0.59±0.13</td>
</tr>
<tr>
<td>Vd$^{area}$ (L/kg)</td>
<td>2.79±0.14</td>
</tr>
<tr>
<td>Cl$^B$ (ml/kg/min)</td>
<td>43.67±3.39</td>
</tr>
</tbody>
</table>

**Abbreviations:**
A: Zero time concentration of drug plasma at distribution phase.
B: Zero time concentration of drug plasma at elimination phase.
$C_0^P$: Theoretical zero time plasma concentration of drug.
$\alpha$: Distribution rate constant.
$\beta$: Elimination rate constant.
$\alpha$: Distribution half-life.
$\beta$: Elimination half-life.
AUC: Total area under plasma drug concentration time.
AUMC: Total area under the first moment of plasma drug concentration time.
MRT: Mean resident time.
$K_{12}$: Rate constant of transfer of drug from central to peripheral compartment.
$K_{21}$: Rate constant of transfer of drug from peripheral to central compartment.
Kel: Elimination rate constant of drug from central compartment.
T~P: Approximate tissue to plasma concentration ratio.
Vd$^{area}$: Volume of distribution based on total area under curve.
Cl$^B$: Total body clearance.
Summary

Disposition kinetics and urinary excretion of paracetamol was conducted in 5 female buf- falo calves following single i.v. injection of paracetamol @ 40 mg/kg body wt. The drug was detected up to 2 h only with the mean of 1.87 µg/ml in plasma while in case of urine the drug was detected up to 48 h with a mean of 10.90 ± 1.14µg/ml. The α and t₁/₂α were 7.148 ± 1.361h⁻¹ and 0.11 ± 0.01h, respectively. The β and t₁/₂β of 0.965 ± 0.136 h⁻¹ and 0.77 ± 0.09 h indicated that the drug was also eliminated rapidly. The rapid elimination led to the lower value value of MRT (1.00 ± 0.01h) indicating that the paracetamol remained for a shorter period in the body of buf- falo calves. AUC and AUMC were 15.59 ± 1.07 mg/L.h and 16.09 ± 2.56 mg/L.h², respectively. The good distribution of paracetamol was due to high Vd area of 2.34 ± 0.19 L/kg which was further supported by T~P value of 0.59 ± 0.13.

References


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Basal Expression of Toll-Like Receptor 18 (TLR18) mRNA in Selected Species of Food Fishes of India

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Toll-like receptors (TLRs) are pathogen recognition receptors (PRRs) that are involved in the recognition of pathogens based on pathogen-associated molecular patterns (PAMPs). TLRs play a major role in the activation of both innate and acquired immunity against the invading pathogens. About 17 different TLR types have been identified in teleost fishes (Rebl et al., 2010). Each of the TLRs has specificity in identifying the ligands of the pathogens. TLR18 has been reported to recognize Mycobacterium marinum, a gram-negative bacterial pathogen in zebra fish (Meijer et al 2004). As the reports on the study of TLR18 in tropical food fishes are scanty, this work was carried out with an objective to identify the existence of basal expression of TLR18 in selected species of food fishes of India.

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