

STUDIES ON METABOLISM OF SOME SULPHONAMIDES IN BUFFALO CALVES

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SUMMARY

Studies on metabolism of sulphamethoxazole, sulphadiazine and sulphadimidine were conducted to determine their extent of acetylation in blood, plasma and urine in buffalo calves following single oral administration (100 mg/kg). The acetylation percentage was highest for sulphamethoxazole and lowest for sulphadimidine in blood and plasma, while in urine the percentage of acetylation for sulphadimidine was maximum followed by sulphamethoxazole and sulphadiazine. This suggests that only sulphonamides with low degree of metabolism should be used for clinical use in buffaloes with precaution and supportive therapy to avoid chances of renal toxicity.

Key words: Metabolism, sulphonamide, buffalo calves

Sulphonamides are frequently used for the treatment of infections caused by *Streptococci*, *Staphylococci*, *Salmonella*, *E. coli* and *Pasturella* in animals (Bevill, 1988). Sulphonamides can undergo numerous structural changes following oral/parenteral administration in the body. Acetylation, oxidation, conjugation with sulphate or glucuronic acid and cleavage of the heterocyclic rings are the varied processes involved in the metabolism of sulphonamides (Nielson, 1973 a). Acetylation, one of important metabolic pathways, occurs primarily in the liver including tissues such as spleen (in cat), erythrocytes and leucocytes. Generally, the percentage of acetylated metabolites is higher in urine than blood and the acetylated sulphonamides are inactive and less soluble than the parent compounds except sulphapyrimidines (Williams, 1959). So, it is essential to measure the extent of acetylation of sulphonamides, as acetylated sulphonamides have no antibacterial activity and are more toxic than their parent compound. Therefore, the present investigation was undertaken to determine the extent of acetylated metabolites of sulphamethoxazole, sulphadiazine and sulphadimidine in blood, plasma and urine of buffalo calves.

Eighteen clinically healthy male buffalo calves aged 1 to 1½ years and weighing 100 to 120 kg, were divided into 3 groups consisting six animals in each. The animals were maintained on green fodder and concentrate mixture for one week before the start of the experiment. Water was provided *ad libitum*. Sulphamethoxazole, sulphadiazine and sulphadimidine were separately administered to each group orally at a dose rate of 100 mg/kg body weight. Blood samples were collected from the jugular vein in the dried oxalated tubes at different time intervals up to 48 h after the oral administration of sulphonamides. Plasma was collected within 20 minutes of sampling by centrifuging about 5 ml blood sample at 3000 rpm for 15 min. Specially designed urine collection bags were used for collection of urine at regular intervals up to 48 h. All the samples within 24 h were stored in deep freeze at -10°C till analysis. The samples were analyzed by the spectrophotometric method of Bratton and Marshall (1939) for free and total sulphonamides. The percentage of acetylation was calculated by the following formula:

$$\text{Per cent acetylation} = \frac{N^4}{N^4 + S} \times 100$$

Where, N⁴ and S are the concentrations of acetylated and free sulphonamides, respectively.

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Table
Overall mean percentage of acetylated metabolites of different sulphonamides in blood, plasma and urine of buffalo calves

| Drug | Overall mean acetylation percentage | | |
|-------------------|-------------------------------------|-------------|-------------|
| | Blood | Plasma | Urine |
| Sulphamethoxazole | 28.56 ± 1.9* | 48.60 ± 3.2 | 41.27 ± 2.7 |
| Sulphadiazine | 18.98 ± 1.6 | 22.73 ± 2.1 | 25.80 ± 1.8 |
| Sulphadimidine | 9.45 ± 0.9 | 14.97 ± 1.2 | 57.57 ± 4.6 |

*The values are mean ± S.E. of 6 animals

The overall mean acetylation percentage of sulphamethoxazole, sulphadiazine and sulphadimidine in blood, plasma and urine in buffalo calves is presented in the Table. The acetylation percentage was highest for sulphamethoxazole and lowest for sulphadimidine in blood and plasma, respectively. In the urine, the percentage of acetylation of sulphadimidine was maximum followed by sulphamethoxazole and sulphadiazine. The values of acetylation percentage in this study were less than those reported for sulphadiazine and sulphadimidine in the blood of cattle (Silvestri *et al.*, 1967). However, acetylation percentage of sulphadiazine in blood, plasma and urine of buffalo calves in this study was more than that reported in buffaloes (Singh and Ahmad, 1977). Further, Nielson (1973b) also reported less percentage of acetylated forms of sulphamethoxazole and sulphadimidine in the urine of goat. In general, the degree to which a sulphonamide can be acetylated, varies with the individual, the animal species and the type of sulphonamides (Williams and Parke, 1964). Factors like concentration of sulphonamide and pH of urine also determined the extent of acetylation (Baggot, 1968). On the basis of this study, it may be suggested that sulphonamides with high degree of metabolism should be avoided and sulphonamides with low degree of

metabolism should be preferred in combination which could be judiciously used for the treatment of systemic and urinary infections in buffaloes with precaution and supportive therapy to avoid risk of renal toxicity.

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