Possible Anthelmintic Use of Piperazine Acetate & Lactate

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Possibility of anthelmintic use of piperazine acetate and lactate in place of the commonly used piperazine citrate has been investigated by comparing the urinary excretion of piperazine and ketone bodies for the three salts during 72 hr after oral feeding in albino rats. Results indicate a fair possibility of the replacement of piperazine citrate by piperazine acetate for anthelmintic use.

Dosage forms of piperazine salts1 are extensively used as practically non-toxic anthelmintics in the treatment of Ascaris lumbricoides and Enterobius vermicularis infections, the phosphate and adipate being used as tablets and the citrate as syrup, after a comparative excretion study by Rogers2. Taraeva et al.3 demonstrated comparable anthelmintic properties for the acetate, sulphate and hydroxy glutarate etc. In view of the shortage and high price of citric acid and its almost exclusive dependence on import, possibilities of the use of alternative salts which would make the product cheaper and independent of imported components, such as acetate4 or lactate5 were thought worth investigating.

This communication reports the results of preliminary investigations on the possibility of using piperazine acetate and lactate in place of citrate by a comparative urinary excretion study in albino rats after oral feeding.

Syrups were prepared with piperazine citrate, piperazine diacetate4 and piperazine dilactate5 and standardized as per syrup piperazine citrate I.P.6. These syrups were used for urinary excretion studies in albino rats.

A group of 6 albino rats of 200–250 g. each, bred and housed in our own animal house, was taken for excretion study of each salt. Before use the rats were fasted overnight but were allowed water. A measured quantity of one of the syrups was fed to each member of a group so as to administer 75 mg/kg of anhydrous piperazine (maximum clinical dose—66 mg/kg) followed by 10 ml of water. They were allowed usual food and water after 1 hr. Thereafter, the rats were kept on usual diet and water, administering orally two 10 ml portions of water to each rat every day at the interval of 12 hr. Each animal cage was placed on urine collection set with arrangement to prevent loss by evaporation and urine was collected. Urinary excretion of piperazine and ketone bodies were determined after 24, 48 and 72 hr collection. For piperazine, cumulative excretion for 72 hr were noted and for ketone bodies cumulative excretions during each 24 hr were observed separately. Ketone bodies in urine were determined immediately after collection of urine and piperazine was determined thereafter, storing urine under toluene and refrigeration whenever necessary. Piperazine in urine was determined by Rogers5 method and ketone bodies by the method of Behre and Benedict6.

Cumulative excretion rates of citrate, acetate and lactate during 72 hr following administration of the salts, expressed in terms of percentage of piperazine administered are shown in Fig. 1. Excretion (24 hr) of ketone bodies during the same period are shown in Fig. 2. The pattern of urinary excretion of citrate, acetate, and lactate was very much similar (Fig. 1). For all the 3 salts maximum excretion was 100% during 72 hr after the drug administration, while the minimum was 47, 52.5 and 44% respectively for citrate, acetate and lactate. The mean excretion values were 72, 85.5 and 72% respectively for citrate, acetate and lactate during the period. During the first 24 hr 37 to 79% of the citrate, 49–84% of the acetate and 18 to 78.5% of the lactate were excreted. The rates of excretion, diminished in order as acetate, citrate and lactate.

It may be mentioned that Rogers5 found minimum individual variations with citrate as compared to phosphate and adipate which might have resulted in better acceptance of the citrate presumably due to better uniformity of clinical results. In our experiments with citrate, acetate and lactate, we obtained significantly lower individual variations with acetate, compared even to citrate. This suggests that comparatively better uniformity of clinical results is more likely to be obtained with the acetate than with citrate. It may also be observed that the acetate has somewhat faster rate of excretion than the citrate which is likely to reduce incidence of untoward
reactions of the drug without reducing clinical efficacy. Another possible point in favour of apparently better acceptability of citrate is the direct fitting into the physiological citric acid cycle of the system. Any other organic acid, if administered, has to be metabolized to fit in with the citric acid cycle ultimately. Systemic limitations for such transformations is likely to be reflected in a higher ketone body excretion. As evident from the results represented in Fig. 2, the pattern of excretion of ketone bodies is similar for acetate and citrate; the acetate resulting in a consistently lower ketone body excretion than the citrate indicating absence of any added stress and strain to the system on this account, while with the lactate, a conspicuously higher ketone body excretion suggests increased stress and strain to the system indicating poor systemic acceptability for this salt. It may also be noted that in keeping with piperazine excretion, individual variations of ketone body excretion, both in respect of pattern and quantum are also conspicuously minimum with the acetate and maximum with the lactate presumably due to comparatively narrow and widely varying limitations of the systems in metabolising lactic acid to fit in with the physiological citric acid cycle. No adverse effect on body weight was noted in the treated animals. The work carried out so far leads us to infer that piperazine acetate is probably a good substitute for piperazine citrate in clinically effective dose. Further work is in progress. The authors thank Sri A. Kaviraj for his assistance.

References
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