BIO-AVAILABILITY OF INH IN LIQUID DOSAGE FORM*

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Summary: The amount of free isoniazid (INH) in Isokin liquid (with Sorbitol base) was estimated and the bio-availability of INH in Isokin liquid was compared with that of INH powder in ten volunteers in a cross over study. The results indicate that INH in both the forms was equally well absorbed and there was no condensation of INH in the liquid preparation containing sorbitol.

Key words: bio-availability INH

INTRODUCTION

Isoniazid (INH), is now the drug of choice in the treatment of tuberculosis in paediatric practice. Naturally it would be of great advantage if a palatable and well absorbed oral preparation of the same is available. Rao *et al.* (4) have recently shown that the absorption of INH from glucose syrups is considerably reduced due to condensation product and recommended that sugars such as glucose, fructose and sucrose should be avoided in liquid preparations of INH. Sorbitol, a stable non-carbonyl compound may be a suitable vehicle.

The present report deals with the bio-availability of INH from a commercially available preparation with sorbitol base (Isokin liquid).

MATERIALS AND METHODS

The amount of free INH in Isokin liquid was first estimated. For the second part of the study, ten healthy volunteers from the Haffkine Institute were selected. The volunteers fasted from 9 p.m. on the previous evening and reported at 9 a.m. on the following day on an empty stomach. Each volunteer was requested to empty the bladder on reporting. Initial blood sample was then collected. Each volunteer was given 300 *mg* of INH in liquid form and in the form of pure powder with a glass of water, on two separate occasions, seven days apart. The order of their administration was randomized.

The blood samples were collected at 5 min, 15 min, 30 min, 1 hr, 2 hr and 6 hr after the administration of INH. Urine samples were also collected in bottles (containing thymol) from 0 to 6 hr, 6 to 12 hr, 12 to 18 hr, and 18 to 24 hr.

The total and free INH levels in the serum and the urine were estimated by spectropho-

Isokin Liquid is supplied by Warner-Hindustan Limited.

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tometric method of Maher *et al.* (3). The results were analysed statistically by using paired 't' test.

RESULTS

Estimations of free INH in Isokin liquid showed that there was no condensation of INH in the sorbitol base. The amount of free INH was 50 *mg*/5 *ml* and it corresponded with the INH content stated on the label.

Serum levels of free INH:

Both the preparations were absorbed immediately. Within five min the serum levels of 0.97 to 1.06 $\mu g/ml$ of free INH were detected. The peak levels were obtained in 30 min following the administration of both the liquid and the powder. The peak levels of free INH were 6.20 and 6.41 $\mu g/ml$ respectively; while those of the acetylated form were 3.08 to 3.62 $\mu g/ml$ between 1/2 to 1 hr. Almost equal serum levels of total INH were observed after Isokin liquid and the powder. Peak levels were achieved in 1 hr and 1/2 an hr respectively. The difference was statistically not significant (Fig. 1).

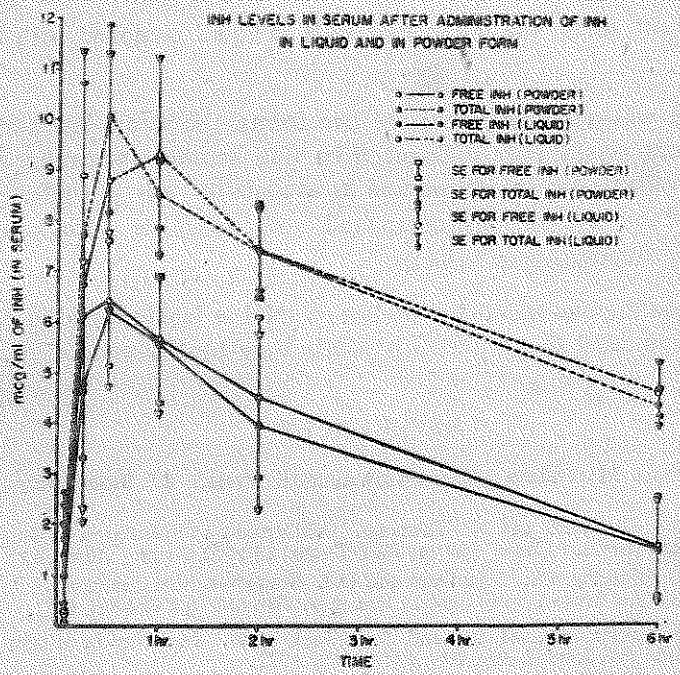

Fig. 1

Urinary excretion of INH:

The urinary excretion pattern was the same following the administration of Isokin liquid and powder.

The total amount of INH excreted in urine was as follows:

Preparation	*Amount in mg%*
Isokin Liquid	68.32 ± 4.22
INH Powder	63.96 ± 3.07

The values did not significantly (P=05) differ from one another.

DISCUSSION

INH is known to be incompatible with aldehydes and ketones (1) and this incompatibility is because of the condensation of these compounds with INH. Sugars such as glucose and fructose containing aldehydes or ketone group thus form condensation products with INH.

Kakemi *et al.* (2) found poor absorption of glucose derivatives of INH in urinary excretion studies in humans. Controlled studies in human subjects by Rao *et al.* (4) showed that absorption from the bound form was rather small, about 37% only.

In the present study, the amount of INH in liquid complied with the claim made by the manufacturer.

When INH was administered in the two forms, the serum levels attained and urinary excretions were not significantly different from one another indicating that INH in liquid form was freely available for absorption and its availability was not affected by sorbitol base. Sorbitol being a stable non-carbonyl compound is not likely to form condensation products and is thus a very suitable syrup vehicles.

In conclusion the bio-availability studies on INH in Isokin liquid in comparison to INH in powder form, indicated that both the products were equally good.

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