LETTER TO THE EDITOR

POTENTIATION OF ANTIPYRETIC EFFECT OF ACETAMINOPHEN BY CONCOMITANT ADMINISTRATION OF ASCORBIC ACID

Sir,

(Received on November 21, 1984)

Ascobic acid administratration has been reported to prolong the biological half-life of acetaminophen (4). In view of this, it was of interest to see if the antipyretic effect of the latter is altered by co-administration of ascorbic acid, since the two drugs are commonly used together.

Male, adult rabbits (*1.5 – 2 kg*) fasted for 24 hrs (water *ad libitum*) were divided into five groups (n=6 each). Pyrexia was induced by TAB vaccine (*0.1 ml/100 g* given through ear-vein). Normal saline (1 *ml/kg*) was administered orally (Group I). In group II, acetaminophen (*25 mg/kg – 25 mg/ml* solution) was given orally. The animals in group III and IV received ascorbic acid, in the dose of *2.5 mg/kg* and *5 mg/kg* (orally) respectively, in addition to acetaminophen. Ascorbic acid alone was administered to the animals in group V (*5 mg/kg* orally). The drugs were administered 30 min. after TAB vaccine. Rectal temperature was recorded, at 30 min intervals for 5 hrs using "Teletherm" and rectal probes. The results were analysed by Student's "t" test.

The course of pyrexia, seen in the five groups, is shown in Fig. 1. It is seen that acetaminophen alone exerted a significant antipyretic activity upto 3½ hours which began to decrease from 4 hour onwards. Co-administration with ascorbic acid resulted in a significantly lesser antipyretic effect at 1 hr but a significantly ($P<0.05$) greater antipyretic effect from 4 hr onwards. Ascorbic acid treatment alone did not affect the TAB-induced pyrexia.

Since the two drugs were given separately and are not known to be appreciably bound to plasma proteins and since the kidneys do not significantly contribute to elimination of acetaminophen, the observed interaction is not ascribed to altered absorption, distribution or elimination of acetaminophen by ascorbic acid. More than 80% of the administered dose of acetaminophen is conjugated with etheral sulfate and glucuronide (1). Ascorbic acid is metabolized in part to ascorbic acid sulfate in man as well as in some animals (2). Sulfate formation is an important pathway for biotransformation of phenolic drugs This

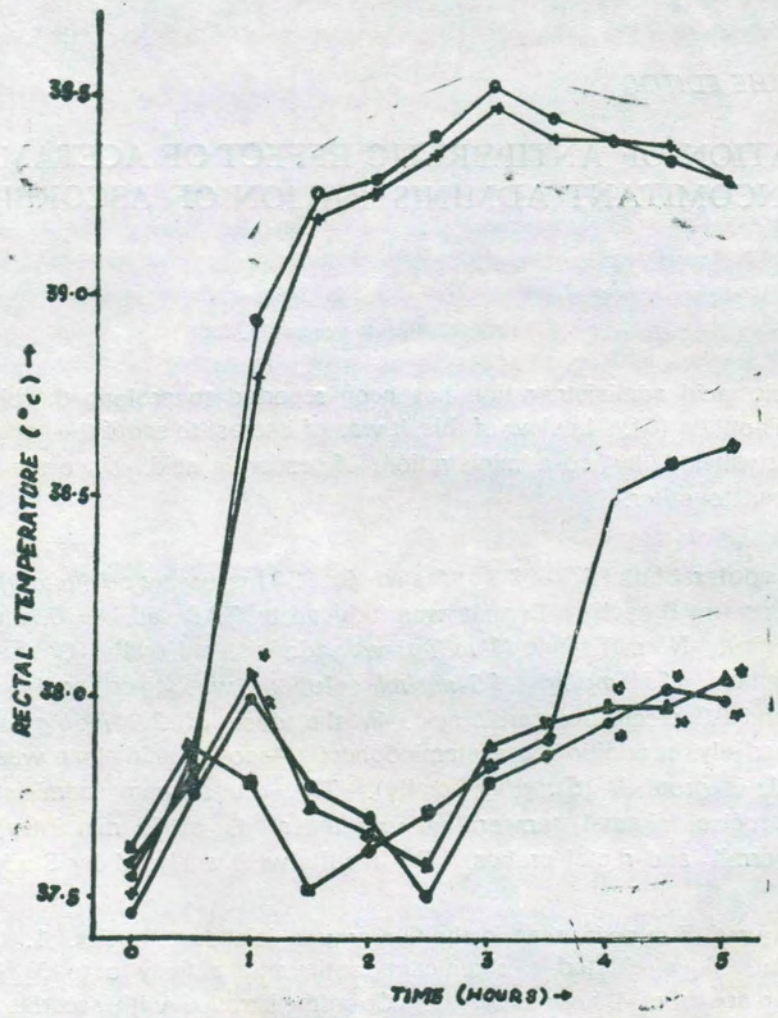

Fig. 1 : Effect of acetaminophen alone and in combination with ascorbic acid on TAB-induced pyrexia in rabbits.

I O———O Normal saline
II □———□ Acetaminophen (*25 mg/kg*)
III △———△ Acetaminophen+Ascorbic acid (*2.5 mg/kg*)
IV ⊙———⊙ Acetaminophen+Ascorbic acid (*5.0 mg/kg*)
V +———+ Ascorbic acid (5 *mg/kg*)

* $P<0.05$, Comparison of Group II with Group III and Group IV. S.E.M. was within 0.7% of each value which represents mean ($n=6$)

pathway is, however, of limited capacity in man and many species of animals (6) It is therefore, subject to saturation and competitive inhibition Concomitant administrration of ascorbic acid and salicylamide has been reported to cause a decrease in the conversion

of the latter to salicylamide sulfate (3). Reduced bio-transformation already reported (4), thus explains the potentiation of acetaminophen-antipyresis by ascorbic acid

The opposite effect at 1 hour is diffiult to explain, It may be due to reduction in the rate of abscrption of acetaminophen, resulting from inhibition of gastric emptying by ascorbic acid (5).

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