LETTER TO THE EDITOR

STUDIES ON THE EFFECT OF ASCORBIC ACID, ZINC SULPHATE AND THEIR COMBINATION ON CARRAGEENAN-INDUCED OEDEMA IN RATS

Sir,

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Ascorbic acid besides having wound healing properties has value in conditions such as gastro-intestinal disorders (1, 6), rheumatic fever, rheumatoid arthritis, acute and chronic infections, allergies and bleeding gums (7). Further, the combination of proteolytic enzymes, flavonoids and ascorbic acid showed a more complete spectrum of action than non-steroidal anti-inflammatory substances against initial symptoms of inflammation (10) and ascorbic acid and zinc exerted protective effects in ethanol - intoxicated rodents (12).

Since zinc sulphate (equivalent to 150 *mg* of zinc) is benificial in the treatment of rheumatoid arthritis (9) and stimulates the rate of healing of granulating wounds (8), leg ulcers (4), gastric ulcers (3) and ulcerative colitis (2), it appeared worthwhile to investigate the anti-inflammatory effect of zinc sulphate and its modification, if any, by ascorbic acid using carrageenan-induced oedema model.

Wistar rats of either sex weighing 150-300 *g* were used each group comprised of a minimum of 6 rats.

Indomethacin (10 *mg/kg*, p.o.), ascorbic acid (100 *mg/kg*, p.o.), zinc sulphate (20 *mg/kg*, p.o.), a combination of ascorbic acid (100 *mg/kg*) with zinc sulphate (20 *mg/kg*), ascorbic acid (100 *mg/kg*) with indomethacin (10 *mg/kg*), and zinc sulphate (20 *mg/kg*) with indomethacin (10 *mg/kg*) were administered separately by oral route 1 hr prior to carrageenan injection.

TABLE I : Effect of ascorbic acid, zinc sulphate and indomethacin and their combination on carrageenan-induced rat paw oedema at different time intervals. Each value represent the mean ± SEM of *ml* of Hg displaced by the rat paw.

Sr. No.	*Treatment*	*Dose, mg/kg, p.o.*	*n=*	*Time (hr)*				
				0	0.5	1	2	3
1.	Control	—	9	0.01±0.01	0.22±0.02	0.325±0.06	0.445±0.033	0.53±0.03
2.	Ascorbic acid	100	6	0.0±0.0	0.242±0.03	0.208±0.031	0.258±0.041*	0.308±0.04*
3.	Zinc sulphate	20	6	0.008±0.009	0.225±0.044	0.2±0.016	0.233±0.03*	0.225±0.031*
4.	Indomethacin	10	6	0.0±0.0	0.158±0.030**	0.092±0.036*	0.067±0.023*	0.05±0.025*
5.	Ascorbic acid + Zinc sulphate	100 20	6	0.017±0.012	0.125±0.039***	0.125±0.034**	0.175±0.019**	0.117±0.012*
6.	Ascorbic acid + Indomethacin	100 10	6	0.0±0.0	0.05±0.012*	0.066±0.016*	0.04±0.015*	0.075±0.021*
7.	Zinc sulphate + Indomethacin	20	6	0.0±0.0	0.066±0.016*	0.075±0.01*	0.1±0.026*	0.15±0.034***

*P < 0.001 when compared between 1:2, 1:3; 1:4, 2:5, 3:4, 3:5, 2:4, 2:6, 4:6, 3:7
**P < 0.05 when compared betwecn 2:5, 3:5, 4:2
***P < 0.025 when compared between 2:5, 3:7.

Carrageenan (0.1 *ml* of 1.0% w/v) was injected into the plantar region of the hind paws and the paw volume was recorded as the *ml* of Hg displaced at 0, 0.5, 1, 2 and 3 hr of carrageenan injection (11). The mean increase in paw volume of different groups at different time intervals were calculated and compared (Table I).

Statistical analysis was done using student *t*-test.

The results are summarised in Table I. All the agents investigated i.e. ascorbic acid, zinc sulphate and indomethacin exhibited significant anti-inflammatory effect against carrageenan-induced paw oedema. When the combined effects of drugs were compared with individual drug treatment, zinc sulphate and indomethacin combination showed significantly more inhibition of paw oedema at all time intervals as compared to zinc sulphate alone but at only 0.5 and 1 hr intervals as compared to indomethacin alone. On the other hand ascorbic acid significantly modified the effects of both zinc sulphate and indomethacin. Since zinc sulphate and indomethacin combination showed exaggerated anti-inflammatory effect, the combined use may be beneficial as zinc sulphate might reduce the gastric effects of indomethacin by lowering its dose.

A preliminary study was done wherein the effect of zinc sulphate (20 *mg/kg*, p.o.), and its combination with ascorbic acid (100 *mg/kg*, p.o.) on ulcerogenic effect of indomethacin was investigated in the pylorus ligated rats (5). Indomethacin (40 *mg/kg*, p.o) was administered in pylorus ligated rats just after ligation. The rats were sacrificed after 4 hr of pylorus ligation and the gastric ulcers were scored as 0— normal stomach, 0.5— red colouration, 1.0— spot ulcer, 1.5— streaks, 2.0— spot ulcers no. ≥ 3 but < 5, 3—spot ulcers ≥ 5. Indomethacin (40 *mg/kg*) given orally at ligation produced extensive gastric ulcers (4.7 ± 0.51). Zinc sulphate (20 *mg/kg*, p.o.) alone showed a gastric ulcer protective effect in indomethacin-induced gastric ulcers (2.5 ± 0.54, $P < 0.02$). Simultaneous administration of ascorbic acid (100 *mg/kg*) with zinc sulphate (20 *mg/kg*) orally showed enhanced protective effect (1.8 ± 0.2, $P < 0.001$) when compared to controls.

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