

LETTER TO THE EDITOR

EFFECT OF SODIUM ASCORBATE ON RAT UTERUS AND
GUINEA PIG ATRIA *IN VITRO*

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Sir,

Sodium ascorbate, an antioxidant, has been reported to have a complex stimulating action on guinea pig ileal longitudinal smooth muscle (3,5-7). Acetylcholine-induced contractions are augmented (3,6) in small concentrations. Larger concentrations inhibit spasmogenic responses induced by acetylcholine, histamine and 5-hydroxytryptamine (2,3,5), potentiate the effect of DMPP on guinea pig ileum but potassium induced contractions are not altered (5). Large doses also inhibit the bronchospasm induced by histamine, bradykinin, 5-hydroxytryptamine (5-HT) and acetylcholine in guinea pigs and have been found to exert a beneficial effect in anaphylaxis (1,3).

We found that ascorbate also inhibits action of spasmogens on rat uterus and inhibits isolated guinea pig heart. Virgin Wistar albino rats (150-180 g) and English albino guinea pigs (350-450 g) of either sex were used.

Solution of sodium ascorbate (2M, ph; 7.2) was buffered, with 2M ascorbic acid solution (ph; 2.3 to 2.5) and final pH was adjusted to 5.7.

Rat uterus was set up according to the method of Gaddum *et al.* (4). Submaximal dose of agonists viz. 5-HT (2.47×10^{-8} mol), carbachol (1.09×10^{-6} mol) and potassium (2.01×10^{-2} mol) were used as spasmogen. The effect was elicited again 10 min after addition of ascorbate.

Isolated atria of guinea pigs were mounted in a 60 ml bath containing oxygenated Ringer-Locke Solution at $37 \pm 0.5^\circ\text{C}$. The force (amplitude) and rate of the atria were recorded through a high sensitivity transducer (Type DY0) on the recording microdynamometer (Ugo Basile, Italy). In each experiment, effect of ascorbate was reassessed 10 min after its addition to the bath. Effect of ascorbate on stimulant responses to histamine (6.51×10^{-6} mol) was also studied.

Sodium ascorbate (5×10^{-3} to 8×10^{-2} mol) antagonised the contractions induced by 5-HT, carbachol and K^+ on rat uterus in a dose-dependent manner (Table I), however, it did not have any effect *per se* on this preparation. EC₅₀ (and fiducial limits) were 3.8×10^{-2} (1.8×10^{-2} to 8.3×10^{-2}), 3.4×10^{-2} (1.8×10^{-2} to 6.5×10^{-2}) and 1.7×10^{-2} (8.1×10^{-2} to 3.6×10^{-2}) mol, respectively. Recovery always took place in 5-10 min after two washes.

TABLE I : Effect of Sodium ascorbate on isolated rat uterus.

Sodium ascorbate (mol)	% Inhibition (Mean \pm SEM) of the contractions*		
	5-HT	Carbachol	Potassium
5×10^{-3}	5.14 \pm 2.98	5.27 \pm 2.54	14.64 \pm 2.38
1×10^{-2}	12.24 \pm 3.20	8.71 \pm 2.67	32.45 \pm 3.98
2×10^{-2}	29.21 \pm 3.52	26.90 \pm 3.27	51.20 \pm 5.46
4×10^{-2}	50.69 \pm 7.42	59.26 \pm 4.81	77.20 \pm 3.54
8×10^{-2}	86.42 \pm 3.56	99.64 \pm 0.36	100.00 \pm 0.00

No. of experiments : 6 except in case of carbachol where 5 experiments were performed for each result.

*Each spasmogen was used in a concentration which produced a submaximal response.

Spontaneous rate of beating of isolated atria was 232 ± 6.5 /min ($n = 6$). Sodium ascorbate inhibited the rate and force/amplitude of the atria. Effect was not appreciable upto 1×10^{-2} mol, but 3×10^{-2} ($n = 6$) and 1×10^{-1} ($n = 6$) had marked effect (% inhibition of rate, 14.16 ± 1.02 and 46.29 ± 3.33 ; % inhibition of force, 32.96 ± 9.21 and 76.63 ± 5.74 , respectively). Histamine-induced stimulation of rate and force of beating atria was not altered by ascorbate (upto 1×10^{-2} mol, $n = 6$).

Dawson *et al.* (2,3) have shown that the high concentrations (5×10^{-3} to 10^{-2} mol) of sodium ascorbate directly inhibit the spasmogenic responses of acetylcholine, histamine and 5-HT on guinea pig ileum. Further, Hayashi *et al.* (5) confirm these findings; however, potassium (4×10^{-2} mol)-induced contractions were not altered by ascorbate in concentrations upto 5×10^{-3} mol. Our results using isolated rat uterus are in accordance with these findings. However, the drug had no spasmogenic effect *per se* and inhibited K^+ - induced contractions. The present data show that the inhibitory action of sodium ascorbate extends to drug induced spasm of isolated rat uterus and to spontane-

ously beating guinea pig atria, inhibitory effect being more on force. It appears that the drug has a direct cardiac depressant effect since histamine-induced stimulation was not altered.

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