Metabolic availability of ascorbic acid in female guinea-pigs

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Stone (1965) stated that the presence of the gene controlling the ability to synthesize ascorbic acid (AA) should be demonstrable by placing guinea-pigs on an AA-free diet and following the decrease in tissue AA content. Failure to show a uniform fall in AA before death would show that AA was being synthesized. Williams & Deason (1967) reported great individual variation in AA requirements in guinea-pigs, and suggested the possibility of endogenous AA production. Odumosu & Wilson (1970a) showed that plasma and leucocyte AA concentrations decreased after 9 days of dieting, and weight loss began after 12 days in a group of guinea-pigs of both sexes. They died between days 28 and 36. Male guinea-pigs showed severe symptoms and all died after 27–30 days (Odumosu & Wilson, 1970b). Between days 24–27, buffy coat AA values changed from 38% to 44%, and liver values from 1·3 to 1·0% of the control values. Final plasma values were 0·093±0·032 mg per 10·6 ml.

Table 1 shows the survival times and mean tissue AA values for female (Duncan-Hartley) guinea-pigs on a scorbutic diet. These animals lost weight until day 18, but maintained their food intake until they died. They were divided into two groups on day 24 on the basis of their weight loss. Those that were likely to die (D guinea-pigs) were still losing weight, but the loss of weight had ceased in the potential survivors (S guinea-pigs).

The S guinea-pigs killed on day 32 had liver AA concentrations which were 3·9 times greater than those of the D guinea-pigs which were killed on day 30.

The liver AA concentrations of S guinea-pigs were also higher than D guinea-pig values from day 36. Liver AA values were 40% of the control values in 1 S guinea-pig killed on day 72. Two guinea-pigs survived 90 days. Plasma AA increased in parallel with, but more slowly than, liver AA in the S guinea-pigs. Adrenal AA in S guinea-pigs increased from zero on day 30 in parallel with, but more slowly than,

TABLE 1. *Survival times and tissue ascorbic acid values in guinea-pigs on a scorbutic diet*

Day of diet	Number surviving S	Number surviving D	Number dead S d	Number dead S k	Number dead D d	Number dead D k	Animals analysed Group	Animals analysed No.	Tissue weight g	Analysis AA Plasma	Analysis mg% Liver
0	54	—									
1	48	—	—	6	—	—	S	6	426	0·884	20·42
1–23	46	—	—	—	—	2	D	2	306		
24	40	—	—	—	—	6	D	6	331	0·246	2·08
	17	23					—	—			
28	17	22	—	—	1	—	D	1	340		
30	16	22	1	—			S	1	526		
					—	11	D	11	314	0·122	2·16
32	15	11	—	2	—	—	S	2	524	0·171	3·90
33	13	11	—	—	3	—	D	3	307		
35	13	8	—	1	—	—	S	1	508	0·204	4·27
36	9	0	—	4			S	3	407	0·222	5·25
					2	6	D	8	303	0·084	2·97
39	8	0	1	—	—	—	S	1	448		
48	7	0	1	—	—	—	S	1	346		
54	5	0	—	—	—	—	W	2	482		
60	4	0	1	—	—	—	S	1	315		
62	3	0	—	1	—	—	S	1	465	0·571	4·69
72	2	0	—	1	—	—	S	1	380	0·178	8·17
98	1	0	—	1	—	—	S	1	504	1·400	11·04

S, Potential survivors. D, Guinea-pigs expected to die. d, Died. k, Killed. W, Withdrawn for treatment with PCMB. Tissue analysis figures are the means from the numbers of animals analysed.

plasma values. As adrenal AA increased, plasma cortisol concentrations diminished. Para-chloromercuribenzoate administration, inhibiting L-gulonolactone oxidase (Chatterjee, Chatterjee, Ghosh, Ghosh & Guha, 1960), administered to 2 S guinea-pigs (W) on day 54 caused weight loss, followed by death in 7 days when liver AA was 20% of normal, and plasma AA was zero. It is concluded that in times of deficiency, some female guinea-pigs are able to readjust their ascorbic acid metabolism and so compensate for the influence of the defective gene responsible for hypoascorbemia (Stone, 1966).

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Wy 23205, a new non-steroidal anti-inflammatory agent

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For aspirin, phenylbutazone and indomethacin a correlation exists between the tendency to elicit symptoms of gastro-intestinal intolerance in therapeutic use and

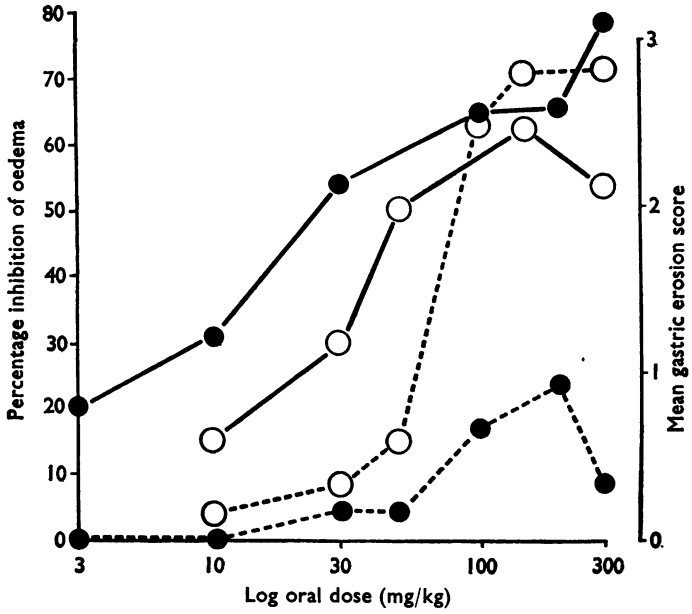

FIG. 1. Inhibition of carrageenin-induced oedema of the rat hind paw (solid lines) and gastric irritant activity (broken lines) for phenylbutazone and Wy 23205. Phenylbutazone, ○—○; Wy 23205, ●—●.