hibition by PGE_1 in fresh synaptosomes could not be demonstrated when synaptosomes were ruptured by freezing and thawing, before transference to the assay medium. This raised the possibility that access to the enzyme was a limiting factor. However, when synaptosomal membranes were prepared free of cytoplasm, no inhibition of membrane Na^+-ATPase was observed under conditions which permitted maximum accessibility to the enzyme. Addition of the cytoplasm back to the membranes largely restored the inhibitory effect. This suggests that PGE_1 action depends upon the presence of a soluble factor in the synaptosome cytoplasm. Recent experiments (Gilbert & Sawas, unpublished) suggest that the actions of noradrenaline on synaptosome ATPases also depend on cytoplasmic factors.

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Hypocholesterolemic effects of vitamin C, clofibrate and diosgenin in male guinea-pigs

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Scorbutogenic diets containing 0.3 g% cholesterol were administered to 6 groups of 6 male guinea-pigs for 24 days. Bodyweight and food intakes were measured daily (Odumosu & Wilson, 1973; Ginter & Zioch, 1972). For 14 days they maintained a constant food-intake and gained weight, thereafter weight loss and reduced food-intake occurred. On day 24, plasma and hepatic ascorbic acid concentrations were reduced to 20%, and cholesterol values were 200% of their original levels (Odumosu & Wilson, 1978).

The remaining groups of 5 guinea-pigs received the scorbutogenic diet without cholesterol, with either diosgenin 1000 mg/100 g diet (DSc), or 200 mg clofibrate/kg weight by stomach tube (CSc), or supplementary vitamin C i.p. 30 mg/kg (AASc), or vitamin C with clofibrate (CAASc), or diosgenin with vitamin C (DAASc), or saline i.p. alone (Sc) (Table 1). On day 34 body weight and food intake had increased significantly in groups AASc, CAASc, DAASc; they became further reduced in the other groups (Sc, CSc, DSc). Plasma and hepatic ascorbic acid levels had fallen further in the Sc group, but the fall was arrested in the CSc and DSc groups. Ascorbic acid rose maximally in the group receiving the vitamin C supplement (AASc) and rose least in the supplemented diosgenin group (DAASc). Plasma and hepatic cholesterol did not fall in the Sc group. Cholesterol fell in the CSc and DSc groups, the hepatic fall being greater

Table 1 The effects of clofibrate and diosgenin on plasma and hepatic ascorbic acid and cholesterol levels in hypercholesterolemic scorbutic guinea-pigs in the presence or absence of supplementary Vitamin C. Control values (Day 24) before drug administration (mg%, mean ± s.d.): Ascorbic acid, plasma 0.15 ± 0.02, hepatic 2.50 ± 0.50; Cholesterol, plasma 420 ± 21, hepatic 760 ± 48. P: between control and treatment values, and between individual treatment values on day 34

	Ascorbic Acid				*Cholesterol*			
Groups	*Plasma*	*P*	*Hepatic*	*P*	*Plasma*	*P*	*Hepatic*	*P*
CSc	0.21 ± 0.02	N.S.	1.90 ± 0.16	N.S.	338 ± 36	<0.05	645 ± 38	<0.05
	N.S.		N.S.		N.S.		<0.02	
DSc	0.28 ± 0.04	N.S.	1.00 ± 0.11	N.S.	312 ± 34	<0.05	382 ± 42	<0.02
	<0.05		N.S.		<0.05		<0.02	
Sc	0.12 ± 0.03	N.S.	1.05 ± 0.11	N.S.	442 ± 21	N.S.	780 ± 30	N.S.
	<0.02		<0.02		<0.01		<0.05	
AASc	1.40 ± 0.10	<0.02	12.80 ± 0.80	<0.05	142 ± 18	<0.01	472 ± 46	<0.05
	<0.05		N.S.		N.S.		<0.05	
CAASc	0.90 ± 0.08	<0.05	10.00 ± 1.40	<0.05	120 ± 11	<0.01	340 ± 56	<0.02
	N.S.		<0.05		<0.05		N.S.	
DAASc	0.70 ± 0.03	<0.05	5.50 ± 1.20	<0.05	312 ± 32	<0.05	320 ± 42	<0.02

in the DSc group. Clofibrate and diosgenin with the supplement caused further small but significant reductions in hepatic cholesterol concentrations but diosgenin with vitamin C (DAASc) did not reduce plasma cholesterol more than diosgenin alone (DSc). Clofibrate and diosgenin therefore require ascorbic acid for their hypocholesterolemic actions and are potentiated by supplementary vitamin C. Their combination with vitamin C could have therapeutic implications in man.

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The effect of vitamin C deficiency and supplementation on the weight pattern and skin potential of the guinea-pig

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Some female scorbutic guinea-pigs are able to synthesize ascorbic acid (Odumosu & Wilson, 1971). Since females only were able to do this, the sexes might respond differently if similarly tested when availability of vitamin C is the determining factor. Ten male and 10 female mongrel guinea-pigs were housed separately and fed with rabbit pellets containing 25 mg vitamin C/100 g, with free access to drinking water containing vitamin C, 53 mg/100 ml. After 7 days, 5 males and 5 females were transferred to a scorbutogenic diet and Vitamin C free drinking water. The other 2 groups continued on the supplemented diet. For 29 days weight changes, plasma ascorbic acid levels, and skin potential values were recorded. The group diets were then alternated and measurements continued. Plasma and dietary ascorbic acid were measured with 2,4-dinitro-phenylhydrazine (Roe & Kuether, 1943). Skin potential was measured with a millivoltmeter and AgCl electrodes (Edmonds & Cronquist, 1970) using depilated skin areas.

Females maintained higher plasma ascorbic acid and skin potential values in the scorbutic state (Table 1). Body weights initially increased more rapidly in the scorbutic than in the supplemented guinea-pigs. They began to fall in the scorbutic groups before the diet change was introduced. Skin potential values rose in the supplemented groups and fell in the scorbutic groups together with plasma ascorbic acid changes. When the diets were alternated, plasma ascorbic acid values moved in the opposite directions. Skin potential values also immediately reversed their directions of change. These results indicate the changes produced by the essential electron donor in the semi-dehydroascorbate-ascorbic acid system (Ghirretti & Ghirretti-Magendie, 1977) and suggest it may be essential for maintaining basal body energy.

Table 1 Mean values for plasma ascorbic acid (AA, mg/100 ml), body weights (g) and skin potentials (mV) of guinea-pigs receiving vitamin C supplemented or scorbutogenic diets before and after alternation of their diets on day 29.

	Males			*Females*			*Males*			*Females*		
Day of Diet	*Plasma AA*	*Body Wt*	*Skin Pot*	*Plasma AA*	*Body Wt*	*Skin Pot*	*Plasma AA*	*Body Wt*	*Skin Pot*	*Plasma AA*	*Body Wt*	*Skin Pot*
	Supplemented Diet						Scorbutogenic Diet					
0	0.58	532	—	0.47	532	—	0.53	556	—	0.66	550	—
7	0.59	546	7.4	0.50	545	7.4	0.48	569	6.4	0.59	562	8
15	0.64	558	9.2	0.58	650	9.8	0.21	565	6.2	0.64	571	7.2
29	0.67	582	12	0.75	595	12	0.04	541	0.2	0.45	565	3.6
	Scorbutogenic Diet						Supplemented Diet					
7	0.72	593	9.8	0.72	607	10.6	0.12	554	2.6	0.54	576	4.1
14	0.48	566	7.8	0.73	607	9.4	0.2	562	5	0.72	602	6.6
28	0.12	522	2.4	0.36	609	7	0.45	582	10	0.93	621	10