Besause the cells were spherical in suspension, the volumes were calculated using the formula for sphere volume. Cell volumes ranged from 523 μm^3 to 3052 μm^3. The mean cell volume of pituitary cells was 742 μm^3 and 1105 μm^3 for 25- and 120-day-old rats, respectively. The adult cells showed an increase in volume 1.6 times that of cells of 25-day-old animals. Total volume of all cells in the pituitaries was calculated. The volume for adult pituitaries was 5.4 times the volume of 25-day-old rats. This value is in excellent agreement with the 5.8 times increase in pituitary weight between 25- and 120-days-of-age. Much of the weight increase between days 25 and 120 is the result of cellular hyperplasia. Definite cellular hypertrophy was demonstrated by the presence of 17 and 18 µm diameter cells which were not present in younger animals. The greater proportion of cells in the 12–13 µm range may have also developed by hypertrophic changes of smaller cells. An alternate explanation for this change in size distribution is that cells which are inherently large divide more rapidly than small cells, resulting in a significant population of large cells being formed by hyperplasia. Hypertrophy has a role, but the degree of involvement cannot be determined by this data.

Hyperplasia is the only mechanism of growth apparent in the preweanling rat pituitary. The high rate of DNA synthesis and mitosis during this period is consistent with this observation, but do not of themselves exclude hypertrophy[5,6]. Between days 10 and 25 there is a slowing in cellular multiplication and a slight shift to a population of larger cells. This may well be a critical period in postnatal development. The mean weight of rat hepatocytes increases sharply between days 21 and 41[3]. In addition, between days 21 and 103 the number of rat hepatocytes increases 3.2 times[3], while pituitary cells increase 3.6 times between days 25 and 120. It is not known if similar mechanisms control growth in these 2 organs. However, both liver and pituitary possess receptors for estrogen[7,8]. In addition, estrogenic hormones increase DNA synthesis and weight in both organs[9–11].

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Protective effect of calcium against the verapamil-induced inhibition of ionophore-mediated calcium translocation[1]

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Summary. The inhibitory effect of verapamil on A23187-mediated calcium translocation is antagonized in a competitive manner by increasing concentrations of calcium.

Organic calcium-antagonists such as verapamil, nifedipine and suloctidil are widely used both in the management of patients with cardio-vascular diseases and as a tool to interfere with calcium influx into living cells[2]. The effect of these drugs upon cellular calcium metabolism could be due to interference with native ionophoretic systems mediating the transport of calcium across the plasma membrane. Indeed, in an artificial system for the study of ionophoresis, verapamil and other organic calcium-antagonists were found to inhibit the translocation of calcium mediated by the antibiotic ionophore A23187[3]. The present study reveals that, as observed in intact cells, calcium itself protects against the verapamil-induced inhibition of A23187-mediated calcium translocation.

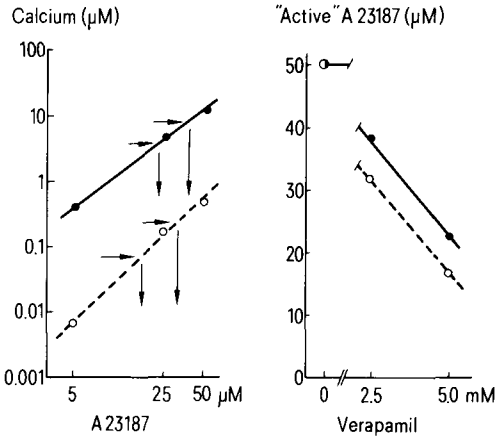
A small volume (0.2 ml) of Hepes buffer (25 mM; pH 7.0) containing Na^+ 123, K^+ 5 and Cl^- 120 mEq/l and ^{45}calcium (10 µCi/ml), with or without ^{40}calcium (1.0 mM) was vigorously mixed for 1 min at room temperature with an equal volume of a mixture of toluene-butanol (7/3, v/v) containing, as required, the ionophore A23187 (Eli Lilly, Indianapolis) and verapamil (Knoll, Ludwigshafen). The immiscible supernatant phase was then examined for its radioactive content.

The data illustrated in the table indicate that, at 2 calcium concentrations in the initial aqueous phase (8.0 µM and 1.0 mM), the amount of calcium eventually translocated in the organic phase increased as the concentration of A23187 was raised from 5 to 50 µM and, at a fixed concentration of the ionophore, decreased as the concentration of verapamil was raised to 2.5 and 5.0 mM. The dose-action relationship for the effect of increasing concentrations of A23187 (A, expressed as µM) upon calcium translocation (T, expressed as nM) was compatible with the equation $[T]=a[A]^b$ (figure, left panel), in which the factors a and b varied as a function of the concentration of calcium in the initial aqueous phase. At initial calcium concentrations of 8 µM and 1.0 mM, respectively, the factor a corresponded to a translocation of calcium, provoked by A23187 1.0 µM, of

A23187 (µM)	Verapamil (mM)	Calcium in aqueous phase 8.0 µM	1.0 mM
5	–	0.007 ± 0.001	0.396 ± 0.021
25	–	0.172 ± 0.004	4.789 ± 0.102
50	–	0.517 ± 0.029	12.565 ± 0.064
50	2.5	0.238 ± 0.010	8.603 ± 0.408
50	5.0	0.072 ± 0.001	3.902 ± 0.282

Mean values (± SEM; n = 3) for the concentration of calcium (µM) in the immiscible organic phase.

0.34 and 35.3 nM. The difference between these 2 values reflects the dose-related increase in calcium translocation at increasing calcium concentrations, saturation of the ionophore being only observed at much higher calcium concentrations in the initial aqueous phase (15–20 mM; data not shown). Factor b decreased from 1.892 ± 0.038 to $1.509 + 0.014$ as the calcium concentration was raised from 8 µM to 1.0 mM. This behaviour is due to the fact that each atom of calcium is complexed by 2 molecules of ionophore[4] so that factor b fluctuates between the extreme values of 2 (theoretical value in the presence of infinitely low calcium concentrations) and 1 (experimental value seen at saturating calcium concentrations)[5]. The exponential relationship illustrated in the figure (left panel) permitted the conversion of the amount of calcium translocated in the presence of both A23187 and verpamil into the corresponding 'active' concentration of ionophore, i.e. the concentration of A23187 which would translocate the same amount of calcium if the experiment had been performed in the absence of verapamil. When the 'active' concentrations of ionophore were plotted as a function of the verapamil concentration, it became obvious that calcium antagonizes the effect of verapamil in inhibiting calcium translocation. Under the present experimental conditions, the protective effect of calcium corresponded to a shift to the right of the dose-action response to increasing concentrations of verapamil (figure, right panel), suggesting a competitive type of antagonism. In further experiments, a series of lines parallel to those shown in the right panel of the figure were obtained when the calcium concentration was further increased to 4.0 and 20.0 mM. Control experiments indicated that the protective effect of calcium could not be attributed to any direct interference of the cation with verapamil itself.



Left panel: effect of increasing concentrations of A23187 on calcium translocation (logarithmic scales); the arrows refer to the values seen in the presence of both A23187 (50 µM) and verapamil (2.5 and 5.0 mM), and illustrate the mode of calculation for the 'active' concentration of ionophore. Right panel: effect of increasing concentrations of verapamil (logarithmic scale) upon the 'active' concentration of ionophore. The concentration of calcium in the initial aqueous phase amounted to 8.0 µM (open circles, dotted lines) or 1.0 mM (closed circles, solid lines).

The pattern of parallel lines illustrated in the right panel of the figure is superimposable on that characterizing the protective effect of calcium against the inhibitory action of verapamil upon physiological processes, such as glucose-induced insulin release[6]. This analogy reinforces the view that the modality by which verapamil affects A23187-mediated calcium translocation in the present model may be relevant to the mode of action of the organic calcium-atagonist in biological systems.

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Mean cytoplasmic protein concentration of host erythrocytes and the reticulocyte response in *Plasmodium berghei* infected mice

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Summary. The decreasing mean cytoplasmic protein concentration (MPC) of *P. berghei* host cells is paralled by an increasing parasitemia and percent reticulocyte response. The reticulocyte response parallels the percent parasitemia except during a period of accelerated reticulocytosis noted during the midpoint of the infection at which time the percent reticulocytes increases at a rate more than double the rate of increase of percent parasitemia. Although the reticulocyte population and the host cell population are usually equivalent, the disparity noted suggests the existence of unique characteristics in the reticulocyte response of *P. berghei* infected mice.

The mean cytoplasmic protein concentration (MPC) of *Plasmodium berghei* host erythrocytes has been measured in mice during patent infections[1]. The decrease in host cell MPC throughout the infection is inversely related to the percent of parasitized erythrocytes. *P. berghei* preferentially invades reticulocytes[2–4]. This study explores the relationship which exists between host cell MPC, the reticulocyte response and the percent parasitemia of the infected animal. In erythrocytes, MPC is essentially equivalent to hemoglobin concentration (%w/v), hemoglobin comprising from 95%[5] to 97%[6] of the erythrocyte dry weight.

Materials and methods. The KBG 173 strain of *Plasmodium berghei* and young female virgin Swiss mice weighing between 15 and 25 g were used in this investigation. An average of 5×10^5 parasites, suspended in 0.825% saline, was inoculated i.p. into each experimental animal with