Purine base and nucleoside, cytidine and uridine concentrations in foetal calf and other sera

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Foetal calf serum, about 20% by volume, is necessary to establish and sometimes maintain cell cultures of human tissues (Harnden, 1977). The compounds responsible for its efficacy are largely unknown, but probably include macromolecular components. Consideration of the conditions used to obtain sera suggested that purine concentrations might be increased by such procedures.

Concentrations of purines, their nucleosides, uridine and cytidine were measured by methods involving high-pressure liquid chromatography (Harkness et al., 1979). The results in Table 1 show that, in foetal calf serum, the mean hypoxanthine concentration was about 40-fold higher than that from calf serum and varied from 12.4 to 108.9 μmol/litre. The availability of preformed hypoxanthine can decrease the 'energy cost' of growth.

The other results in Table 1 show a higher mean cytidine concentration in rat and mouse serum than in that from man. The other species so far studied, which were pig, rabbit, guinea pig, chicken, rhesus monkey, dog and sheep, showed detectable concentrations of cytidine. Uridine concentrations have been comparable in all species so far studied. Therefore the balance between purine and pyrimidine bases in plasma may be different in rats and mice from that in man. Experimentally a large im-balance can have 'toxic' effects (Snyder et al., 1978). However, it should be noted that the samples analysed are those used for the preparation of tissue-culture media and may differ from circulating plasma in which concentrations of hypoxanthine are probably lower.

The concentration of adenosine was also measured in trichloroacetic acid extracts of a series of human plasma samples. The method used extensive column and paper chromatography. However, co-chromatographing impurities made final high-pressure liquid chromatography difficult. Preliminary results suggest that concentrations of adenosine were approx. 1 μmol/litre, but varied widely. Such large variations may be consistent with the postulated local extracellular messenger role for adenosine (Arch & Newsholme, 1978) and with the very high concentrations of adenine nucleotides in endothelial cells (Nees et al., 1979).

Table 1. Purine, cytidine, and uridine concentrations in foetal calf, calf, rat and mouse sera

Concentrations shown are means ± s.d. The number of separate 'batches' in which the compound was detected is shown in parentheses.

<table>
<thead>
<tr>
<th></th>
<th>Hypoxanthine (μmol/litre)</th>
<th>Xanthine (μmol/litre)</th>
<th>Uridine (μmol/litre)</th>
<th>Urate (μmol/litre)</th>
<th>Cytidine (μmol/litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal calf</td>
<td>74.7 ± 11.9 (9)</td>
<td>92.0 ± 28.9 (9)</td>
<td>5.1 ± 2.1 (6)</td>
<td>130 ± 80 (7)</td>
<td>ND</td>
</tr>
<tr>
<td>Calf</td>
<td>1.8 ± 1.9 (3)</td>
<td>0.3</td>
<td>3.8 ± 2.0 (3)</td>
<td>13 ± 9 (3)</td>
<td>1.3</td>
</tr>
<tr>
<td>Rat</td>
<td>0.7 ± 0.3 (9)</td>
<td>0.4 ± 0.5 (4)</td>
<td>3.9 ± 2.3 (9)</td>
<td>75 ± 40 (8)</td>
<td>9.7 ± 3.3 (9)</td>
</tr>
<tr>
<td>Mouse</td>
<td>1.1 ± 0.8 (3)</td>
<td>0.8 ± 0.5 (3)</td>
<td>5.0 ± 3.1 (3)</td>
<td>6.1 ± 1.4 (3)</td>
<td>3.6 ± 2.6 (3)</td>
</tr>
</tbody>
</table>

Computer simulations of the rate of change of concentration of adenosine 3'-5'-cyclic monophosphate after stimulation of adenylate cyclase activity

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The concentration of free cyclic AMP within a cell responds to the rate of its formation by adenylate cyclase and its rate of breakdown by the cyclic nucleotide phosphodiesterases. I have previously reported (Fell, 1979) that the metabolism of cyclic AMP cannot be accurately represented by treating the enzymes as a homogenous system. This conclusion was based on computer simulation studies of a model, spherical cell in which adenylate cyclase and one phosphodiesterase (the low- K_m species) were located on the plasma membrane, and only a high- K_m diesterase was distributed uniformly through the cell. The same computer model has been used to study the response of the cell to a sudden change in the activity of adenylate cyclase. It is concluded that different parts of the same cell may have different rates of response to a change in cyclase activity, even though there is a single continuous pool of cyclic AMP.

The basic equation of the model is the diffusion equation in spherical polar co-ordinates, with a sink term, v_m(c), that represents the high- K_m diesterase, which is uniformly distributed throughout the sphere:

\[ \frac{\partial c}{\partial t} = \frac{D}{r^2} \left( \frac{\partial}{\partial r} (r^2 \frac{\partial c}{\partial r}) \right) - v_m(c) \]

where c is the concentration of cyclic AMP, D its diffusion coefficient and r the radial co-ordinate. The adenylate cyclase and low- K_m phosphodiesterase enter as a boundary condition on the solution of this equation, for they determine the flux of cyclic AMP at the impermeable boundary, where there is no

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