TRIMER OF 15-DEHYDRO-PGB1 IMPROVES RECOVERY OF MITOCHONDRIAL FUNCTION AFT. (U) OREGON HEALTH SCIENCES UNIV PORTLAND L L WIDENER ET AL. 30 NOV 87

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NL
(U) Trimer of 15-dehydro-PGB₁ improves recovery of mitochondrial function after renal ischemia

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The efficacy of (PGB₁)₃ in protecting renal mitochondrial function from ischemic reperfusion injury was firmly established in a series of experiments in rats. Renal ischemia was induced by unilateral closure of the renal artery with an arterial clip. After 48 minutes of ischemia the clip was opened to recover blood flow. At this time treated animals were given a bolus injection, I.P., of 2.5 mg/kg (PGB₁)₃. Sham controls received an injection of the vehicle. The animals were sacrificed 24 hours later, renal mitochondria were isolated and their function analyzed. (over)
Our data indicate that a bolus injection of (PGB₁)$_3$ given at the time of reflow provides significant improvement of mitochondrial function after 48 minutes of renal ischemia in the rat. 

<table>
<thead>
<tr>
<th></th>
<th>State 3 Rate</th>
<th>[Cytochrome]</th>
<th>Ca$^{2+}$ uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>moles O$_2$/mole aa$_3$/min</td>
<td>nmoles/mg Protein</td>
<td>nmoles/min/mg</td>
</tr>
<tr>
<td>Control</td>
<td>177±13</td>
<td>177±9</td>
<td>167±9</td>
</tr>
<tr>
<td>48 min Isch. +24 hrs Reperf.</td>
<td>59±19</td>
<td>45±3</td>
<td>45±13</td>
</tr>
<tr>
<td>-(PGB₁)$_3$</td>
<td>162±15</td>
<td>114±29</td>
<td>122±5</td>
</tr>
</tbody>
</table>

Cyclic mixtures of prostaglandin E2 are protective against mitochondrial functional failure after tissue ischemia. The active component of the PGE mixture is unknown. We used the trimer of 15-dehydro-PGB to test its protective effect in renal ischemia. Renal ischemia was induced by a unilateral closure of the renal artery in the rat. After a 45 min. ischemic period the arterial clip was opened to recover renal blood flow. At this time the treated animals received a bolus of 1.5 mg/kg 15-dehydro-PGB, IP. The untreated animals received an injection of the vehicle. The animals were sacrificed after 24 hours, renal mitochondria were isolated and their function analyzed. The data are shown in the Table.

<table>
<thead>
<tr>
<th></th>
<th>[CYTOCHROME] n moles/mg</th>
<th>STATE 3 RATE moles (g/mole)</th>
<th>STATE 4 RATE moles (g/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>b</td>
<td>c</td>
<td>b</td>
</tr>
<tr>
<td>CONTROL</td>
<td>0.24±.03</td>
<td>0.22±.03</td>
<td>0.63±.1</td>
</tr>
<tr>
<td>ISCH 45 MIN</td>
<td>0.13±.02*</td>
<td>0.23±.002</td>
<td>0.30±.08*</td>
</tr>
<tr>
<td>2* - PGB</td>
<td>0.17±.04*</td>
<td>0.19±.03</td>
<td>0.47±1.06*</td>
</tr>
<tr>
<td>HRS + PGB</td>
<td>0.19±.01</td>
<td>0.22±.03</td>
<td>0.51±.05</td>
</tr>
</tbody>
</table>

These data indicate that a bolus injection of the trimer of 15-dehydro-PGB given at the time of reflow provides significant improvement of mitochondrial function after 45 min. of renal ischemia in the rat. Supported by Office of Naval Research.
Oligo-PGB Program

Annual, Final and Technical Reports

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