33rd Internal REPORT TO MACLAB: More on Lyprinol

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This report consists of 2 pages and 1 table (No. 73).

**Summary**

A pilot study to assess the duration of Lyprinol’s efficacy, indicated Lyprinol was effective for at least 3 days after ceasing dosing. Naproxen and Celebrex were not.

**Background**

Nearly all the previous assessments of mussel lipid preparations have been conducted in rats with pre-established arthritis, beginning treatment when the first signs of paw inflammation were evident (usually day 10 after giving the arthritigen). This gives the best opportunity to assess anti-inflammatory (AI) activity when comparing drugs and test compounds, which may have different mechanisms of action, against chronic (i.e. non-transient) disease. However, it does not distinguish different types of AI drugs which may act primarily upon different stages of disease development or expression – with differing durations of action.

Here we began treating the rats on day 7 for four days only i.e. ceasing dosing on day 10.

**Results (Table 73)**

The severity of arthritis was scored on day 13: it would normally be on day 14 but we had a ‘galloping’ disease this time (not very common but it does happen) and we were required to terminate the controls = untreated animals at this earlier time. Table 73 indicates that Naproxen (an OTC Cox-1 inhibitor) and Celebrex were virtually ineffective, given on this early pre-arthritic dosing schedule, in preventing subsequent expression of arthritis.

However Lyprinol did have a significant effect in reducing the severity of the subsequent arthritis (reducing the arthritis score >50%).
### TABLE 73: COMPARING LYPRINOL WITH NAPROXEN & CELEBREX ON AN EARLY DOSAGE REGIMEN FOR RATS DEVELOPING POLYARTHRITIS

Treatment given on Days 7 → 10 polyarthritis measured on Day 13.

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>Mg/kg</th>
<th>Rear paw Swelling</th>
<th>Front paw inflamm.</th>
<th>△Wt (days 7→13)</th>
<th>Arthr. Score</th>
<th>% Inhibition of:</th>
<th>Arthr. Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>-</td>
<td>1.59mm</td>
<td>4.1+</td>
<td>+04gm</td>
<td>3.5+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lyprinol</td>
<td>16</td>
<td>0.28</td>
<td>2.5+</td>
<td>+10</td>
<td>1.5+</td>
<td>84</td>
<td>39</td>
</tr>
<tr>
<td>Naproxen</td>
<td>25</td>
<td>1.60</td>
<td>3+</td>
<td>+11</td>
<td>3+</td>
<td>(-01)</td>
<td>27</td>
</tr>
<tr>
<td>Celebrex</td>
<td>15</td>
<td>1.39</td>
<td>4.3+</td>
<td>+16</td>
<td>2.8+</td>
<td>13</td>
<td>(-05)</td>
</tr>
</tbody>
</table>

N = 4 rats/gp

Conclusions:  
(i) Lyprinol has an enduring effect in retarding arthritis development.  
(ii) 2 NSAIDs did not.

Report by M Whitehouse (E.749)
Comment:

This result is certainly interesting but must be confirmed – perhaps comparing Lyprinol next time to Vioxx and Diclofenac (Voltaren), which are also big selling COX-2 and Cox-1 inhibitors respectively. After this repeat experiment (including a dose-response study for Lyprinol) with early dosing i.e. Days 7-10 only, it should be possible to write a short article for publication in a mainline pharmacology journal (other than Inflammopharmacology), with guaranteed wider readership.

Test is on email and hardcopy in the mail.

Report by M Whitehouse