The effect of diclofenac on the distribution of galanin: studies in adjuvant arthritis

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Introduction
Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) with analgesic effects. NSAIDs are known to have anti-inflammatory and analgesic properties by blocking the synthesis of prostaglandins (PGs). However, other mechanisms may be involved.1,2 However, other mechanisms may be involved: COX-1- and COX-2-deficient mice still show sensitivity to the analgesic action of NSAIDs.1 Furthermore, there is a lack of correlation between the antinoceceptive effect of NSAIDs and their anti-inflammatory activities.3,4 The studies of galanin in different animal models demonstrate the inhibitory characteristics of galanin. In general, endogenous galanin has an enhanced antinoceceptive role in chronic pain with inflammatory or neuropathic origin. This study was to delineate the effect of diclofenac on galanin by applying radioimmunoassay (RIA) and immunoelectron microscopy (iEM).

Material and Methods
We used AA in Female Lewis rats as a model of inflammatory arthritis. The following four groups of rats were used:
1. AA, diclofenac injection, 10mg / kg, t.i.d.
2. AA, saline injection, 80 µl / rat, t.i.d.

Table 1 RIA analysis of galanin in DRG (pg/mg protein) and iEM analysis of galanin in cells and in fibers of DRG (Au/µm²).

<table>
<thead>
<tr>
<th></th>
<th>RIA</th>
<th>iEM in cell</th>
<th>iEM in nerve</th>
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<tbody>
<tr>
<td>Arthritis, no drug</td>
<td>47.4</td>
<td>1.9</td>
<td>4.8</td>
</tr>
<tr>
<td>Arthritis, diclofenac 10mg/kg/day</td>
<td>34.6</td>
<td>2.4</td>
<td>2.9</td>
</tr>
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Diclofenac (Novartis International AG, Switzerland) was injected subcutaneously at 8 am, 2 pm, 10 pm the day before, and at 8 am on the day of sacrifice. Radioimmunoassay (RIA) was used to determine the concentration of galanin in spinal cord, dorsal root ganglia, sciatic nerve and synovial tissue and immunoelectron microscopy (iEM) was used to analyze the distribution of galanin in the dorsal root ganglion. Statistical comparisons were made using Student’s t-test; a difference at the level of P < 0.05 was considered significant.

Results
The concentration of galanin was significantly lower in the spinal cord, dorsal root ganglion and the sciatic nerve of rats with AA after the administration of diclofenac compared to rats with AA that did not receive diclofenac injection (Figure 1a-c, table 1). In the synovial tissue of AA rats, the concentration of galanin was higher after injection of diclofenac compared to rats given saline (Figure 1d, table 1).

Immunoelectron microscopy showed specific galanin labelling within dorsal root ganglion tissues. In the dorsal root ganglion, the level of galanin labeling was decreased in myelinated nerve fibers and increased in small cells in AA as a result of injection of diclofenac (table 1). The results were expressed as Au/µm².

Discussion
In this study, the results demonstrate that the galanin level in the spinal cord, dorsal root ganglion, sciatic nerve and synovial tissue of rats with AA is affected by diclofenac. We postulate that diclofenac causes release of galanin in addition to the analgesic properties by blocking the synthesis of prostaglandins. Probably the effect is mediated via an ion channel pathway.5 Galanin may be involved in the process of pain relief from NSAIDs like diclofenac.

Figure 1. RIA results for galanin in spinal cord (a), dorsal root ganglion (DRG) (b), sciatic nerve (c) and synovial tissue (d) in the arthritic group with diclofenac injection (diclof.) and arthritic group without drug injection (saline). The data are expressed by mean+SEM.

References