INTRODUCTION

This study was aimed at exploring the feasibility of conducting simultaneous dissolution testing of two actives, using a multi-channel UV-Vis fiber optic system and second derivative spectra, as an analytical technique to support real-time in vitro release profiling.

MATERIALS AND METHODS

Extended release compositions were prepared containing varying proportions of meloxicam (Fig. 1, a) and bupivacaine (Fig. 1, b) in proprietary Heron Therapeutics Biochronomer® formulations) [1-3]. Drug release was assessed for ~100 mg depots in 100 mL of phosphate buffer saline (pH 7.4) at 37°C. UV absorbance data in the range of 200 – 720 nm were collected using a Spectra™ fiber-optic instrument (Pion Inc.). Collected data were imported into the Au PRO™ software, revision 5.1 (Pion Inc.) where deconvolution of the spectral data was done using the Zero Intercept Method (ZIM) [4-6].

RESULTS AND DISCUSSION

ZIM Analysis; (Figure 3) the 2nd derivative of the meloxicam spectrum intercepts zero at 279.4 nm, and does not contribute to the UV absorbance from the mixture. The 2nd derivative of the bupivacaine spectrum has a high value at this wavelength (Figure 3). An example of the standard curve for bupivacaine built using 2nd derivative values at 279.4 nm is shown on Figure 4.

Dissolution of Different Dual Component Formulations

Meloxicam absorb in the range 200-450 nm and bupivacaine absorb in the range 200-290 nm. To calculate the concentration of meloxicam, the area under the second derivative profile in the range 340-380 nm was used since bupivacaine has no UV absorbance above 290 nm. For bupivacaine, the second derivative value at 279.4 +/- 0.2 nm was used, as the second derivative spectrum of meloxicam has zero value at this wavelength (ZIM point), thus not contributing to the combined spectra of the mixture.

This analytical approach was then applied to four extended release formulations of dual actives present in varying proportions (Table 1). It was possible to follow dissolution curves of both components in real time (Figure 5) although the molar amounts differed by up to forty-fold.

Table 1: Dual Component Formulations: Ratios of Active Ingredients

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Bupivacaine to Meloxicam Molar Ratio</th>
<th>Max Conc. of Bupivacaine, µg/mL</th>
<th>Max Conc. of Meloxicam, µg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lot 154</td>
<td>2:1</td>
<td>27.1</td>
<td>1.6</td>
</tr>
<tr>
<td>Lot 156</td>
<td>4:1</td>
<td>54.1</td>
<td>1.6</td>
</tr>
<tr>
<td>Lot 158</td>
<td>4:1</td>
<td>50.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Lot 177</td>
<td>8:1</td>
<td>49.9</td>
<td>10.5</td>
</tr>
</tbody>
</table>

REFERENCES