What is the problem?

Some chemicals, at concentrations that are normally harmless, can react with sunlight to cause painful phototoxic reactions in susceptible people if they get into their skin or eyes (below left). Sunlight can pass through glass, so people can be affected indoors or in their cars (below right). At the moment, it is difficult to predict what chemicals are likely to cause phototoxic reactions.

Phototoxicity of Non-Steroidal Anti-Inflammatory Drugs

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What we did

The NSAIDs were studied in human cells grown in culture. To find out if they were phototoxic we exposed them to full spectrum ultraviolet light. We also split the light into different wavelengths using a monochromator (Figure 3).

Phototoxicity and photoallergy of nonsteroidal anti-inflammatory drugs

Catriona Neil, supervised by Dr Julie-Ann Woods, Dermatology & Photobiology, Dundee University Medical School.

The monochromator splits up light (a bit like a prism). The cells with or without the NSAID are stirred in a small quartz cuvette placed at the front of the instrument. Non-irradiated cells are treated exactly the same way, but are wrapped in foil. After the cells have been irradiated with light they are split into culture plates and allowed to grow for several days. Neutral red dye is then applied. Live cells retain the dye and become stained pink, but dead cells do not retain the dye.

What we found

By measuring the dye retained within cells using a spectrophotometer, we calculated the IC50 value (Concentration of drug that inhibited dye uptake by 50%). The light and dark samples allowed us to compare the cytotoxicity (% cell death with NSAID alone) and phototoxicity (% cell death with NSAID and light).

IC50 Value (µM)

<table>
<thead>
<tr>
<th>NSAID</th>
<th>Without UVA</th>
<th>With UVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoprofen</td>
<td>GT 39.3</td>
<td>19.6</td>
</tr>
<tr>
<td>Carprofen</td>
<td>GT 36.5</td>
<td>32.3</td>
</tr>
<tr>
<td>Etofenamate</td>
<td>32.5</td>
<td>LT 16.9</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>GT 314.0</td>
<td>GT 314.0</td>
</tr>
<tr>
<td>Naproxen</td>
<td>GT 434.0</td>
<td>GT 434.0</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>GT 302.0</td>
<td>GT 302.0</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>GT 46.5</td>
<td>GT 46.5</td>
</tr>
</tbody>
</table>

LT: IC50 value was less than; GT IC50 value was greater than. A small IC50 value is associated with more toxicity; a large IC50 value is associated with less toxicity.

The data in this Table show that carprofen, ketoprofen and etofenamate were the most phototoxic NSAIDs. Diclofenac, naproxen, ibuprofen showed no phototoxic reaction. Etofenamate was also cytotoxic to the cells.

When the light was split into wavebands using the monochromator, a more detailed picture emerged.

At shorter, ultraviolet, wavelengths (335nm), ketoprofen was the most phototoxic drug, whereas at longer visible wavelengths (430 nm), etofenamate was more phototoxic.

What this means

The test we used identified NSAIDs that are known to be phototoxic, but not those that are less likely to induce phototoxic reactions in patients, so our test is less likely to identify NSAIDs where phototoxicity is idiosyncratic. By splitting up the light we identified clinically-important ultraviolet and visible light phototoxicity. This is essential for patient education, because activities, even when indoors, could put them at risk of phototoxicity depending on the chemical they are exposed to.

Catriona Neil is a 4th year medical student at Dundee University. This project began when I elected to do a four-week Student Selected Component in laboratory research. I applied to Medical Research Scotland and was awarded an eight-week Vacation Scholarship that allowed me to continue my research. I hope to graduate from medical school and then follow a career combining clinical work and research.

What is the problem?

Phototoxicity and photoallergy of nonsteroidal anti-inflammatory drugs

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