Review

PHARMACOLOGY OF BENZYDAMINE

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ABSTRACT


Benzydamine is a topical anti-inflammatory drug which is widely available and used topically for the
treatment of the mouth. It is also used as a gel for application to inflamed joints. It has physicochemical
properties and pharmacological activities which differ markedly from those of the aspirin-line non-
steroidal anti-inflammatory drugs. Benzydamine is a weak base unlike the aspirin-like drugs which are
acids or metabolized to acids. A major contrast with the aspirin-like drugs is that benzydamine is a
weak inhibitor of the synthesis of prostaglandins but it has several properties which may contribute to
its anti-inflammatory activity. These properties include inhibition of the synthesis of the inflammatory
cytokine, tumour necrosis factor-α (EC50, 25 μmol/L). Inhibition of the oxidative burst of neutrophils
occurs under some conditions at concentrations of 30 to 100 μmol/L, concentrations which may be
produced within oral tissues after local application. A further activity of benzydamine is a general
activity known as membrane stabilization which is demonstrated by several actions including inhibition
of granule release from neutrophils at concentrations ranging from 3 to 30 μmol/L and stabilization of
lysosomes. Lack of knowledge of the tissue concentrations of benzydamine limit the correlation
between pharmacological activities in vitro and in vivo. The concentration of benzydamine in the
mouthwash is 4 mmol/L but the concentrations in oral tissues have not been studied adequately.
Limited data in the rat indicates that concentrations of benzydamine in oral tissues are approximately
100 μmol/L.

Keywords: benzydamine, NSAIDs

INTRODUCTION

Benzydamine hydrochloride is a local anti-inflammatory drug which has analgesic and
antipyretic properties. Formerly administered as tablets for systemic use, it is currently
available only for local application: for the relief of sore throats, a mouth gargle or
pump spray is available; gel ointment preparations are applied to the skin to treat
inflammation of the soft tissues, skin and joints. It is widely used and has negligible
side-effects when used locally [1]. The mode of action of benzydamine has not been
established although many pharmacological effects are known.
CHEMISTRY

Anti-inflammatory drugs are commonly organic acids or metabolized to acids but benzydamine is a base usually formulated as its hydrochloride salt. It is highly lipid soluble in the unionized form (log partition coefficient - octanol/water = 3.71) [2].

Benzydamine is fluorescent (excitation 306 nm; emission 362 nm) [3] and is detected fluorometrically in HPLC assays [4]. This absorbance and fluorescence in the ultraviolet region may be associated with a possible pharmacological effect. It has been suggested that benzydamine and related compounds may reduce the formation of cataract due to absorbance in the UV region or, by a molecular interaction with lens protein, reduce the UV damage [3].

PHARMACOKINETICS

When administered as a mouthwash, the recommended dose of benzydamine is 15 ml of a 4-mmol/L solution of the hydrochloride salt in water [4]. This high concentration is transient as the benzydamine solution is only used to rinse the mouth and the remaining material is diluted by saliva. Following a mouthwash administration of benzydamine to rats (1 mg/kg), tissue concentrations in the oral tissues are reported to be as high as 100 μmol/L [5]. The depth of diffusion of the drug into oral tissues is not known but it is probable that surface concentrations are higher than 100 μmol/L. Commercially available benzydamine mouthwash is typically pH 4.5–5.0 but is unbuffered, so should rise quickly to salivary pH which is about 7. Judging from the uptake of other weakly basic, lipid-soluble drugs into buccal tissue, only a limited amount should be absorbed into buccal tissue during the recommended 30 s of mouthwash application [6,7]. The predicted small amount of absorption into buccal tissue is confirmed by the poor systemic availability (5%). Peak plasma concentrations are obtained at about 3 h and reach 0.5 μmol/L (Table 1) [4].

**TABLE 1**

Pharmacokinetic parameters of benzydamine in man

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic clearance</td>
<td>170 ml/min</td>
<td>[8]</td>
</tr>
<tr>
<td>Volume of distribution</td>
<td>10 L</td>
<td>[8]</td>
</tr>
<tr>
<td>Terminal half-life</td>
<td>7.7 h</td>
<td>[8]</td>
</tr>
<tr>
<td>Peak plasma concentrations from mouthwash</td>
<td>0.05 μmol/L</td>
<td>[4]</td>
</tr>
<tr>
<td>Local oral concentrations from mouthwash</td>
<td>4 mmol/L</td>
<td>[4]</td>
</tr>
<tr>
<td>Peak plasma concentrations from oral dosage</td>
<td>1.5 μmol/L</td>
<td>[4]</td>
</tr>
<tr>
<td>Gastrointestinal absorption</td>
<td>Rapid and complete</td>
<td>[8]</td>
</tr>
<tr>
<td>Drug bound to plasma proteins</td>
<td>&lt;20%</td>
<td>[13]</td>
</tr>
</tbody>
</table>