Ramelteon

Cat. No.: HY-A0014
CAS No.: 196597-26-9
Molecular Formula: C₁₆H₂₁NO₂
Molecular Weight: 259.34
Target: Melatonin Receptor
Pathway: GPCR/G Protein; Neuronal Signaling
Storage:
- Powder: -20°C 3 years, 4°C 2 years
- In solvent:
  - -80°C 6 months
  - -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro
DMSO: ≥ 50 mg/mL (192.80 mM)
* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>3.8559 mL</td>
<td>19.2797 mL</td>
<td>38.5594 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.7712 mL</td>
<td>3.8559 mL</td>
<td>7.7119 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.3856 mL</td>
<td>1.9280 mL</td>
<td>3.8559 mL</td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

In Vivo
1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (9.64 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (9.64 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (9.64 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Ramelteon is a highly potent and selective melatonin receptor agonist with Kᵢ values of 14 and 112 pM for human melatonin1 and melatonin2.

IC₅₀ & Target
IC₅₀: 14 pM (melatonin1), 112 pM (melatonin2)[¹]
Ramelteon shows very high affinity for human melatonin1 and melatonin2 receptors (expressed in CHO cells), and chick forebrain melatonin receptors (consisting of melatonin1 and melatonin2 receptors) with \(K_i\) values of 14.0, 112, and 23.1 pM, respectively. The affinity of ramelteon for hamster brain melatonin3 binding sites is extremely weak (\(K_i\): 2.65 \(\mu\)M) compared to melatonin's affinity for the melatonin3 binding site \(K_i\): 24.1 nM). In addition, ramelteon shows no measurable affinity for a large number of ligand binding sites (including benzodiazepine receptors, dopamine receptors, opiate receptors, ion channels, and transporters) and no effect on the activity of various enzymes. Ramelteon inhibits forskolin-stimulated cAMP production in the CHO cells that express the human melatonin1 and melatonin2 receptors\(^1\).

Ramelteon significantly decreases wakefulness at doses of 0.001, 0.01, and 0.1 mg/kg, increases slow-wave sleep at doses of 0.001, 0.01, and 0.1 mg/kg, and increases rapid eye movement sleep at a dose of 0.1 mg/kg in freely moving cats\(^2\). Ramelteon is associated with reduced subjective sleep latency and improved sleep quality. Ramelteon is associated with improvement in latency to persistent sleep, sleep efficiency, and total sleep time\(^3\). Ramelteon (10 mg/kg, i/p), administered close to the mid-point of the dark phase of the L:D cycle, significantly reduces NREM sleep latency (time from injection to the appearance of NREM sleep). Ramelteon also produces a short-lasting increase in NREM sleep duration, but the NREM power spectrum is unaltered\(^4\).

**PROTOCOL**

**Kinase Assay \(^1\)**

cDNA encoding the human MT1 gene is introduced into CHO cells. Cells are harvested at confluence in \(Ca^{2+}\) and \(Mg^{2+}\) free Hanks' balanced salt solution containing 5 mM EDTA and collected by centrifugation. Cells are homogenized in ice-cold 50 mM Tris–HCl buffer, washed twice, pelleted, and stored at -30°C until the binding assays are conducted. Test compound and 40 pM 2-[\(^{125}\)I]melatonin are mixed with the thawed homogenate in a total volume of 1 mL and incubated at 25°C for 150 min. The reaction is terminated by addition of 3 mL of ice-cold buffer followed by vacuum filtration on a Whatman GF/B. The filter is washed twice and radioactivity is counted by a g-counter\(^1\).

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**Animal Administration \(^4\)**

Rats: Ramelteon is dissolved in DMSO at a concentration of 200 mg/mL, and diluted 100-fold in physiological saline immediately before use. A different group of six implanted rats is given vehicle or ramelteon (10 mg/kg i.p.). The EEG and EMG are recorded for 1 hr before injection and then for a further 3.5 hr. All treatments are administered at 24:00 hr (near the mid-point of the dark phase of the L:D cycle) with a minimum of 72 hr separating injections in the same animal. Each rat receives both treatments in a fully randomized, balanced cross-over design reducing the number of animals needed in the study\(^4\).

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

**REFERENCES**


Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA