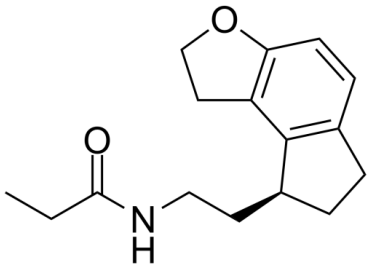
Data Sheet

Product Name:	Ramelteon
Cat. No.:	CS-0382
CAS No.:	196597-26-9
Molecular Formula:	C16H21NO2
Molecular Weight:	259.34
Target:	Melatonin Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : ≥ 50 mg/mL (192.80 mM)



BIOLOGICAL ACTIVITY:

Ramelteon is a highly potent and selective **melatonin** receptor agonist with **K_i** values of 14 and 112 pM for human melatonin1 and melatonin2. IC50 & Target: IC50: 14 pM (melatonin1), 112 pM (melatonin2)[1] **In Vitro:** 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 μM) 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]. **In Vivo:** 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 (Extracted from published papers and Only for reference)

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 icecold buffer followed by vacuum filtration on a Whatman GF/B. The filter is washed twice and radioactivity is counted by a g-counter[1]. **Animal Administration:** [4]Rat: 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].

References:

[1]. Kato K, et al. Neurochemical properties of ramelteon (TAK-375), a selective MT1/MT2 receptor agonist. Neuropharmacology. 2005 Feb;48(2):301-10.

[2]. Miyamoto M, et al. The sleep-promoting action of ramelteon (TAK-375) in freely moving cats. Sleep. 2004 Nov 1;27(7):1319-25.

[3]. Kuriyama A, et al. Ramelteon for the treatment of insomnia in adults: a systematic review and meta-analysis. Sleep Med. 2014 Apr;15(4):385-92.

[4]. Fisher SP, et al. Acute sleep-promoting action of the melatonin agonist, ramelteon, in the rat. J Pineal Res. 2008 Sep;45(2):125-32.

CAIndexNames:

Propanamide, N-[2-[(8S)-1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl]ethyl]-

SMILES:

O=C(NCC[C@H]1C2=C(C=CC3=C2CCO3)CC1)CC

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