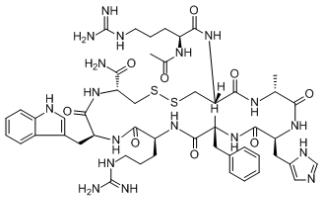
Data Sheet

Product Name:	Setmelanotide
Cat. No.:	HY-19870
CAS No.:	920014-72-8
Molecular Formula:	$C_{49}H_{68}N_{18}O_9S_2$
Molecular Weight:	1117.31
Target:	Others
Pathway:	Others
Solubility:	H_2O: ≥ 24 mg/mL



BIOLOGICAL ACTIVITY:

Setmelanotide (RM-493;BIM-22493;IRC-022493) is a melanocortin 4 receptor (**MC4R**) agonist with an **EC_{50}** of 0.27 nM for human MC4R.

IC50 & Target: EC50:3.9 nM (hMC1R), 10 nM (hMC3R), 2.1 nM (hMC4R)[1]

Ki: 5.8 nM (hMC1R), 5.3nM (hMC3R), 0.27 nM (hMC4R)[1]

In Vitro: Melanocortin receptor agonists act in the brain to regulate food intake and body weight and, independently of these actions, affect insulin sensitivity. Setmelanotide exhibits agonist activity to human and rat MC4R with K_is of 2.1 and 2.7 nM and EC_{50}s of 0.27 and 0.28 nM, respectively[1].

In Vivo: Inhibition of refeeding after an overnight fast by BIM-22493 is dependent on functional MC4R, and does not require MC3R. BIM-22493 acutely improves glucose homeostasis. Lep^{ob}/Lep^{ob} mice treated with BIM-22493 exhibits significantly improved glucose clearance when compared to controls. Chronic BIM-22493 treatment was associated with significantly lower levels of serum insulin, glucose and HOMA-IR values, suggesting an improvement in insulin sensitivity[1]. Treatment with setmelanotide results in transient decreases in food intake (35%), with persistent weight loss over 8 weeks of treatment (13.5%) in a diet-induced obese nonhuman primate model[2].

PROTOCOL (Extracted from published papers and Only for reference)

Kinase Assay: [1]Cell membranes are prepared from CHO-K1 cells stably expressing the human melanocortin receptor subtypes (MC1R, MC3R, MC4R and MC5R). They are incubated at 1-10 μg protein/well in 50 mM Tris-HCl, pH 7.4, containing 0.2% BSA, 5 mM $MgCl_2$, 1 mM $CaCl_2$ and 0.1 mg/mL bacitracin, with increasing concentrations of setmelanotide and 0.1-0.3 nM [^{125}I]-NDP-α-MSH for 90-120 min at 37°C, depending on the receptor subtype. Bound from free [^{125}I]-NDP-α-MSH is separated by filtration through GF/C glass fiber filters presoaked with 0.1 % (w/v) PEI. Filters are washed three times with 50 mM Tris-HCl, pH 7.4, at 0-4°C and assayed for radioactivity using Perkin Elmer Topcount scintillation counter[1]. **Animal Administration:** [1]Mice: Mice are weighed. Baseline blood glucose is measured and 2 g/kg body weight of D-glucose injected by i.p. BIM-22493 is administered chronically at a dose of 300 nmol/kg/day for 14 days by sc. osmotic pump. Controls are administered with 0.9% saline during the same period. Blood glucose is measured at 15, 30, 60, and 120 minutes post injection[1].

References:

[1]. Kumar KG, et al. Analysis of the therapeutic functions of novel melanocortin receptor agonists in MC3R- and MC4R-deficient C57BL/6J mice. Peptides. 2009 Oct;30(10):1892-900.

[2]. Kievit P, et al. Chronic treatment with a melanocortin-4 receptor agonist causes weight loss, reduces insulin resistance, and improves cardiovascular function in diet-induced obese rhesus macaques. Diabetes. 2013 Feb;62(2):490-7.

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

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