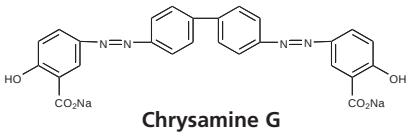
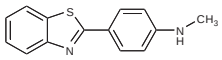
Chrysamine G and BTA-1: New probes for β-amyloid aggregates

Prod. Nos. **C 1115** and **B 9934**



Chrysamine G



BTA-1

The pathological signature of Alzheimer's disease is the deposition of β-amyloid protein (Aβ). Its cleavage products, such as Aβ40 and Aβ42, form amyloid fibrils and plaques in the brains of affected individuals. Compounds that have affinity for Aβ have the ability to prevent neurotoxicity by inhibiting aggregation of amyloid fibrils. In addition, these molecules can also serve to quantify amyloid deposits *in vivo* and thus may serve as diagnostic tools [1].

Chrysamine G is a lipophilic analog of **Congo red** (Prod. Nos. **C 6767** and **C 6277**). The compound displays a K_i value of 25.3 nM [2] and labels both high- (K_d = 0.2 μM; B_{max} = 1.13 moles per mole of Aβ40) and low- (K_d = 39 μM) affinity binding sites for synthetic Aβ [1]. At concentrations of 0.1 to 1 μM, Chrysamine G increases the number of surviving neurons following exposure to both Aβ25-35 and Aβ40 [3].

BTA-1 is a fluorescent **Thioflavin-T** (Prod. No. **T 3516**) derivative. The compound exhibits high affinity for synthetic aggregated Aβ40 fibrils, displaying a K_i value of 11 nM vs. 580 nM for Thioflavin-T [4]. In addition, BTA-1 crosses the blood-brain barrier and displays 50-fold higher affinity than Thioflavin-T. It selectively stains cerebral plaques and cerebrovascular amyloid deposits in the brains of PS1/APP transgenic mice, as well as Aβ fibrils in postmortem brain tissue obtained from Alzheimer's disease patients [4].

Both Chrysamine G and BTA-1 are high affinity probes for Aβ that cross the blood-brain barrier. They will thus serve as useful tools in the study of Aβ-induced neurotoxicity, as well as in the development of *in vivo* imaging tools to detect formation of amyloid fibrils and plaques.

References

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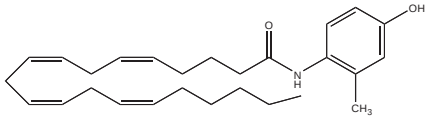
VDM 11: Potent and selective anandamide membrane transporter inhibitor

Prod. No. **V 3264**



Anandamide (Prod. No. **A 0580**) is a putative endogenous agonist at CB_1 cannabinoid and TPRV1 vanilloid receptors [1]. Its physiological effects are terminated by a two-step process that involves reuptake via the anandamide membrane transporter (AMT), followed by hydrolysis catalyzed by the enzyme fatty acid amide hydrolase [2]. A derivative of anandamide, VD M11 has recently been described as a potent and selective AMT inhibitor [3].

VDM 11 inhibits AMT activity, displaying IC_{50} values of ~10 μM in C6 glioma and RBL-2H3 cells [3]. However, although equipotent to another AMT inhibitor, **AM404** (Prod. No. **A-262**) VDM 11 exhibits negligible agonist activity at the human TRPV1 vanilloid receptor, as well as CB_1 and CB_2 cannabinoid receptors [3].

VDM 11 is therefore a new and potentially superior pharmacological tool for studying the role of AMT in the physiological termination of the effects of anandamide.

References

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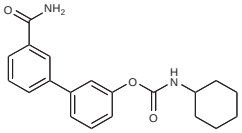
URB597: Potent and selective fatty acid amide hydrolase (FAAH) inhibitor

Prod. No. **U 4133**



The enzyme fatty acid amide hydrolase (FAAH) has been shown to hydrolyze endogenous cannabinoids, such as **anandamide** (Prod. No. **A 0580**), **2-arachidonylglycerol** (Prod. No. **A 8973**) and **oleamide** (Prod. No. **O 2136**). In mice lacking FAAH, it has been shown that a decrease in FAAH activity leads to reduced sensation of pain and enhanced signaling by endogenous cannabinoids [1]. Blocking FAAH may thus serve to enhance the analgesic effects of endogenous cannabinoids [2].

URB597 has recently been described as a potent and selective FAAH inhibitor, displaying IC_{50} values of 4.6 nM and 0.5 nM in rat cortical neuron membranes and intact neurons, respectively [3]. This compound does not interfere with the binding of anandamide to CB_1 and CB_2 cannabinoid receptors (IC_{50} > 100 mM), but has been shown to exhibit anxiolytic effects in rats (ID_{50} 0.15 mg/Kg) [3].

URB597 is thus a promising tool with which to explore the development of novel anxiolytic and analgesic drugs.

References

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