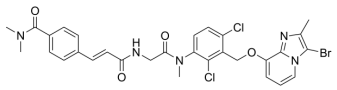
FR167344 free base

Cat. No.:	HY-100301
CAS No.:	215258-13-2
Molecular Formula:	$C_{30}H_{28}BrCl_2N_5O_4$
Molecular Weight:	673.38
Target:	Bradykinin Receptor
Pathway:	GPCR/G Protein
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	FR167344 free base is an orally active, nonpeptide bradykinin receptor B2 antagonist. FR167344 free base shows a high affinity binding to the B2 receptor with an IC_{50} value of 65 nM and no binding affinity for the B1 receptor.
IC_{50} & Target	Bradykinin B2 Receptor (B2R)
In Vitro	In competitive experiments using membranes prepared from Chinese hamster ovary cells expressing the bradykinin receptor subtypes, FR167344 shows a high affinity binding to the B2 receptor with IC_{50} values of 65 nM, and no binding affinity for the B1 receptor. FR167344 inhibits the B2 receptor-mediated phosphatidylinositol (PI) hydrolysis and produces a concentration-dependent rightward shift in the dose-response curve to bradykinin. This shift is accompanied by a progressive reduction of maximal response. Estimated pA2 values for the antagonism of bradykinin induced PI hydrolysis by FR167344 is 8.0. FR167344 shows no stimulatory effects on PI hydrolysis[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of FR167344 inhibits carrageenin-induced paw oedema in rats with an ID_{50} of 2.7 mg/kg at 2h after carrageenin injection. Oral administration of FR167344 inhibits kaolin-induced writhing in mice with an ID_{50} of 2.8 mg/kg in 10 min writhing and 4.2 mg/kg in 15 min writhing. Oral administration of FR167344 inhibits caerulein-induced pancreatic oedema with an ID_{50} of 13.8 mg/kg as well as increases in amylase and lipase of blood samples with ID_{50} of 10.3 and 7.4 mg/kg, respectively, in rats[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Binding assays for the B1 and B2 receptor are carried out by using [^{3}H]des-Arg10-kallidin and [^{3}H]bradykinin, respectively. Cell membranes (12.5-75 mg/mLl) are incubated with various concentrations (saturation experiments) or 500 pM (displacement experiments) of [^{3}H]des-Arg10-kallidin or [^{3}H]bradykinin for 90 min in 0.25 mLof the binding solution containing 20 mM HEPES, pH 7.4, 125 mM N-methyl-D-glucamine, 5 mM KCl, 0.1% BSA, 1 mM 1,10-phenanthrolin monohydrate, 1 mM dithiothreitol, 1 mM captopril and 140 mg/mLbacitracin (for the B1 receptor) or 25 mM trimethylaminoethanesulfonic acid, pH 6.8, 0.1% BSA, 1 mM 1,10-phenanthrolin monohydrate, 1 mM dithiothreitol, 1 mM captopril, and 140 mg/mLbacitracin (for the B2 receptor). All experiments are carried out at least three times in duplicate. The specific binding is calculated by subtracting the nonspecific binding, determined in the presence of 1 mM unlabeled des-Arg10-kallidin (for the B1 receptor) or bradykinin (for the B2 receptor), from the total binding. The specific binding

	activity amounted to 90–92% of the total binding activity[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Rat: Male Sprague-Dawley rats (8 weeks old) are deprived of food overnight and treated orally with FR167344, 15 min before carrageenin is injected into the right hind paw intraplantar. Paw volume is measuredby water plethysmometer before and 1, 2, 3 and 4 h afterthe injection of carrageenin. FR167344 is dissolved in 0.05N HCl and administered orally at a volume of 5 mL/kg. Carrageenin is made up as 1% solution in saline. Each rat received 0.1 mL of the irritant. As saline-control, saline is administered in the same manner as carrageenin. Mouse: Male ICR mice (Slc:ICR, 5 weeks old) are fasted overnight and used. Writhing responses are induced by an intraperitoneal injection of kaolin(250 mg/kg, 50 mL/kg). The responses are counted over a 10 or 15 min period by a trained observer. FR167344 dissolved in 0.05N HCl or vehicle (10 mL/kg) is administered orally 30 min before the intraperitoneal injection of kaolin. As saline-control, saline is administered in the same manner as kaolin[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Aramori I, et al. Novel subtype-selective nonpeptide bradykinin receptor antagonists FR167344 and FR173657. Mol Pharmacol. 1997 Feb;51(2):171-6.

[2]. Asano M, et al. Effects of a nonpeptide bradykinin B2 receptor antagonist, FR167344, on different in vivoanimal models of inflammation.Br J Pharmacol. 1997 Dec;122(7):1436-40.

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