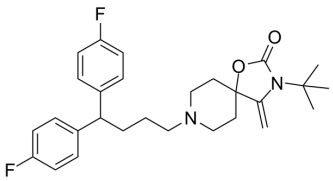
TDN345

Cat. No.:	HY-101669
CAS No.:	134069-68-4
Molecular Formula:	$C_{28}H_{34}F_2N_2O_2$
Molecular Weight:	468.58
Target:	Calcium Channel
Pathway:	Membrane Transporter/Ion Channel; Neuronal Signaling
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	TDN345 is a Ca^{2+} antagonist, used for the treatment of vascular and senile dementia including Alzheimer's disease.
In Vitro	TDN-345 (10 μM) significantly increases the intracellular NGF content in the time-course study. TDN-345 induces NGF synthesis/secretion at the concentrations of 0.1 μM; statistically significant at 1 μM. The ED_{50} is 0.88 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	TDN-345 (0.1-1.0 mg/kg, p.o.) dose-dependently decreases the mortality and ischemic neurological deficit score when administered orally twice, 60 min before ischemia and 90 min after recirculation. Additionally, TDN-345 (0.2 or 1.0 mg/kg, p.o. once daily for 3 weeks after the onset of stroke) decreases the mortality and recurrence of stroke in SHRSP[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [2]	Male Mongolian gerbils (50-70 g body weight) are anesthetized lightly by ether inhalation. A 1-2 cm midline throat incision provided access to both carotid arteries, which are clamped with microaneurysm clamps immediately after recovery from anesthesia. Sixty minutes before occlusion, TDN-345 (0.3 or 1.0 mg/kg suspended in a 5% gum arabic solution or 0.1 or 0.3 mg/kg with 1% NaHCO3 suspended in a 5% gum arabic solution) or vehicle is administered orally. After 15 min of bilateral carotid artery occlusion, the clamps are removed. Ninety minutes after reperfusion, TDN-345 or vehicle is again administered orally. The body temperature is maintained at 37°C during the experimental period using a heating pad. The experiments are performed in nine to 15 animals in each group. Animal survival is observed 8 h and 7 days after reperfusion, and neurological signs are evaluated according to the scoring system as an ischemic neurological score for 5 h after the ischemic insult from an area under the time-neurological deficit score curve ($AUC_{reperfusion\ (0\text{-}300\ min)}$) (hair roughed up or tremor, obtunded, paucity of move, 1; ptosis, seizure, 2; head cocked, eyes fixed open, splayed out hind limbs, extreme rotation, circling behavior, rolling seizure, 3; coma, 6; death, 34). Nine to 15 animals are used in each experimental group. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Fukumoto H, et al. The novel compound TDN-345 induces synthesis/secretion of nerve growth factor in C6-10A glioma cells. Brain Res. 1997 Nov 7;774(1-2):87-93.

[2]. Nakayama T, et al. Beneficial effects of TDN-345, a novel Ca2+ antagonist, on ischemic brain injury and cerebral glucose metabolism in experimental animal models with cerebrovascular lesions. Brain Res. 1997 Jul 11;762(1-2):203-10.

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