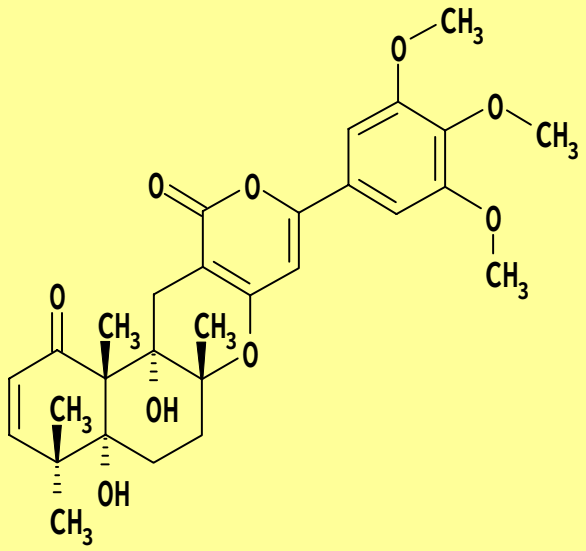
Territrem B, synthetic

Cat.# BLS0600

Structure



Origin: synthetic originally from *Asperigillus terreus*

CAS Registry Number: 70407-20-4

CA Index Name: (4aR)-4a,6,6a,12,12a,12b-Hexahydro-4aβ,12aβ-dihydroxy-4,4,6aα,12bα-tetramethyl-9-(3,4,5-trimethoxyphenyl)-4*H*,11*H*-naphtho[2,1-*b*]pyrano[3,4-*e*]pyran-1,11(5*H*)-dione

Appearance: white solid

Molecular Formula/ Weight: $C_{29}H_{34}O_9$=526.58

Melting Point: >300℃ | **Purity:** 95.0% by HPLC

Solubility: Soluble in MeOH, chloroform
Insoluble in water

Background Information:

Territrem B was isolated from *Asperigillus terreus* as a tremorgenic mycotoxin[1)]. Futhrmore, the very similar compounds, arisugacins A and B were isolated from *Penicillium* sp. FO-4259 in the course of screening for selective acetylcholinesterase inhibitors[2)].

Their structures are comprised of a highly oxygenated trans decalin system and an α-pyrone moiety which belong biogenetically to the mixed polyketide-terpenoid group (meroterpenoid) (Figure 1)[3)]. The first total synthesis of arisugacins was achieved by Sunazuka –Ōmura[4)].

Arisugacins A, B and territrem B possess inhibitory activities against AChE (from human erythrocyted) in vitro, with IC50 values of 1, 26, and 8 nM, respectively (Figure 2)[5)]. And the activity against AChE was more than 20,000 times higher than that against butyrylcholinesterase (BChE, from horse serum) (Table 1). The studies on the effects of arisugacin A on an animal model of scopolamine-induced amnesia showed that arisugacin A protected against amnesia and exhibited very weak effects on mouse salivation and hypothermia, a peripheral cholinergic response and central cholinergic response[6)].

Effects of territrem B on the central neuron of the snail Achatina fulica were studied electrophysiologically[7)]. It was predicted that an optimal territrem B-AChE binding would position a narrowing connection of the territrem B structure at a constricted area near the entrance of the gorge, thereby providing a structural basis for the observed irreversible binding (Figure 3, 4). Territrem-B potentiated the acetylcholine (ACh) induced current of the neuron, while it had no effect on GABA or L-glutamate elicited currents. Territrem B increased the peak amplitude of the response elicited by the first perfusion of ACh and depressed the increase in current produced by a second perfusion[7)]. They could be potentially excellent drugs for the treatment of AD

Handling and Storage:

Store at -20℃.

References:

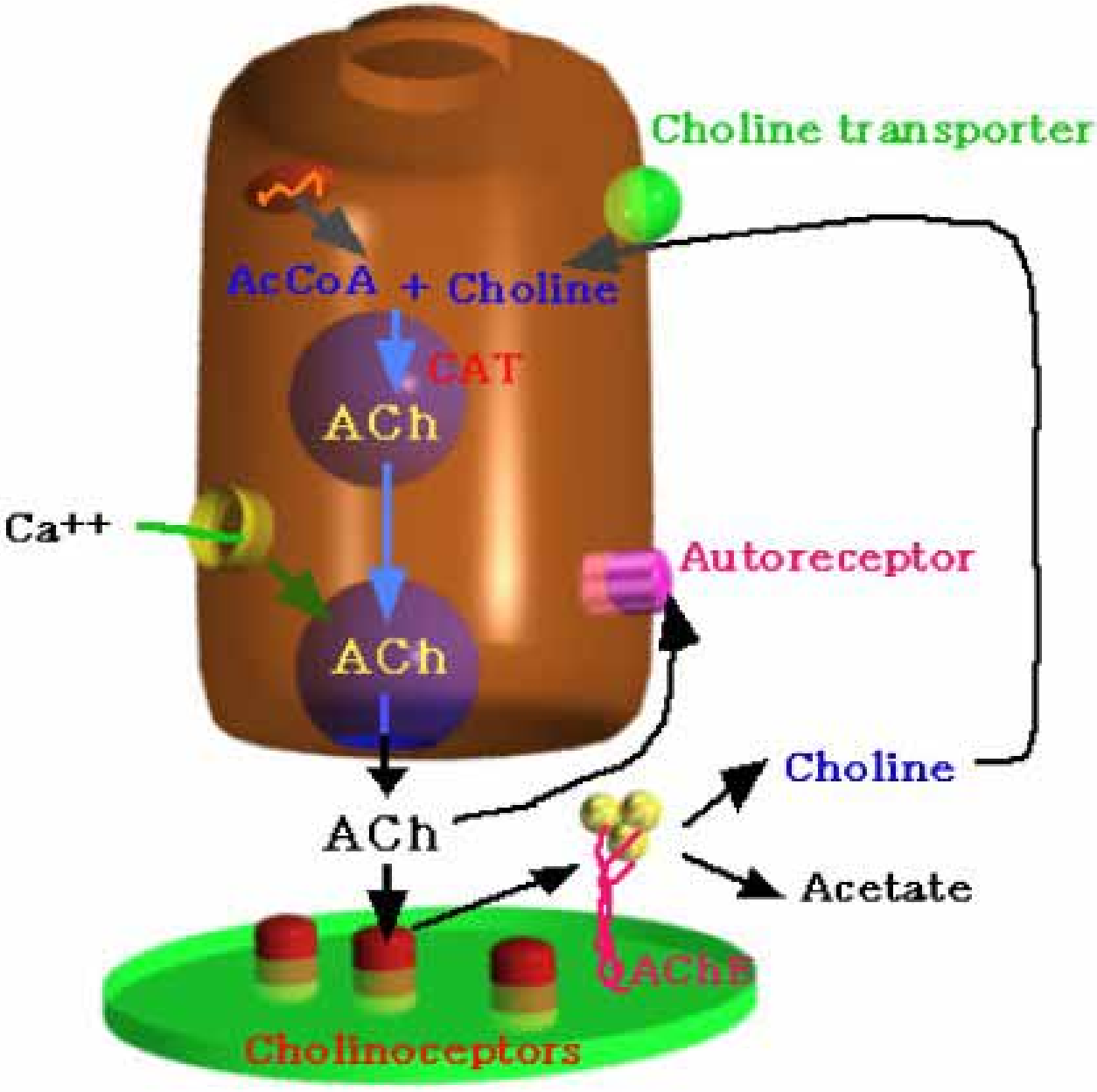
1. K. H. Ling et al., Appl. Environ. Microbiol. **37**, 355 (1979).
2. S. Ōmura, et al., J. Antibiot. **48**, 745 (1995).
3. T. Simpson et al., J. Chem. Soc. Rev. **16**, 123 (1987).
4. T. Sunazuka et al., Org. Lett. **4**, 367 (2002).
5. F. Kuno et al., J. Antibiot. **49**, 742 (1996).
6. K. Otoguro et al., Pharmacol. Ther. **76**, 45 (1997).
7. J. W. Chen et al., J Biol Chem. **274**, 34916 (1999).

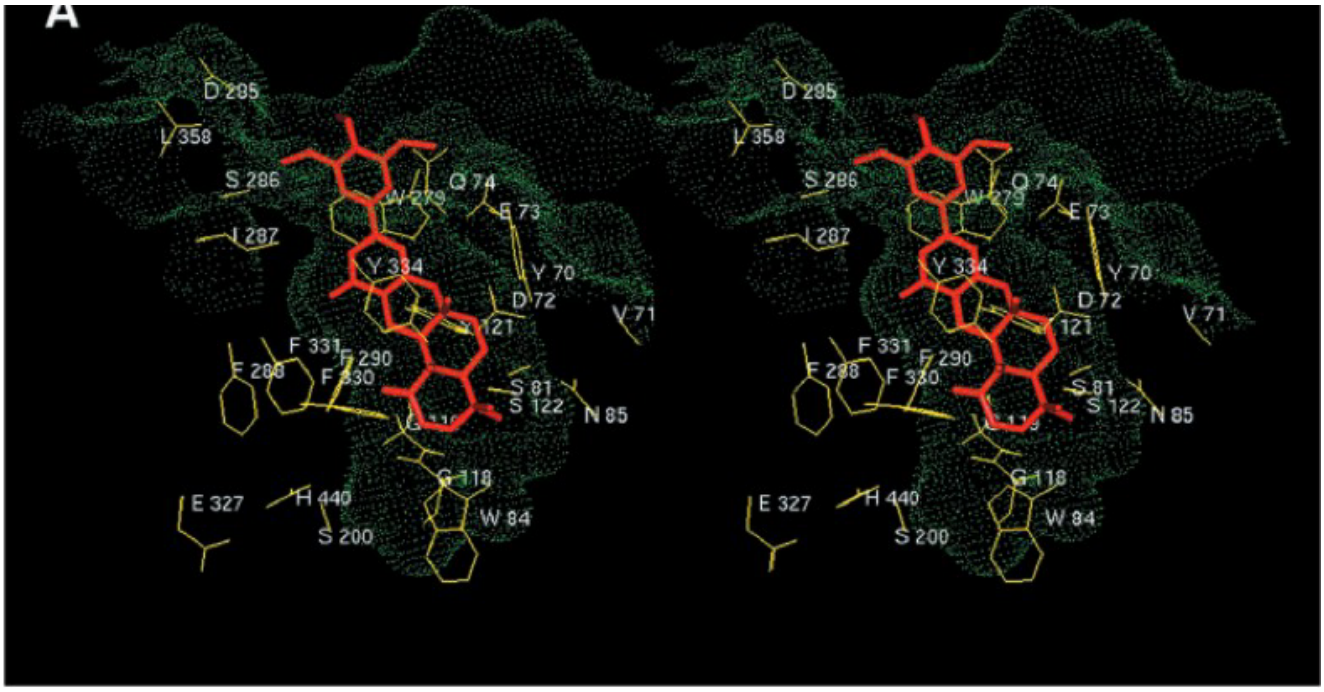
Synthesized by Organic Chemistry Group, The Kitasato Institute.

Table 1

Inhibition of AChE and BuChE by Arisugacins and Territrem B

Compound	IC50 (nM) AChE	BuChE	(BuChE/AChE)
Arisugacin A	1.0	>21,000	>21,000
Arisugacin B	25.8	>516,000	>20,000
Territrem B	7.6	>20,000	>2,632




A
D 285
I 358
S 286
Q 74
W 279
E 73
I 287
Y 334
Y 70
D 72
V 71
121
F 331
F 290
F 288
F 330
S 81
S 122
N 85
G 118
E 327
H 440
W 84
S 200