

论文

含L-4-氧代赖氨酸和N<sup>3</sup>-(4-甲氧基富马酰)-L-2,3-二氨基丙酸寡肽类似物的合成及其抗白念珠菌活性

冯胜昔;徐修容;张鸿龙

广州白云山制药股份有限公司合成药物研究所; \*\*中国科学院上海药物研究所, 上海 200031

摘要:

运用“违法传递”概念,根据白念珠菌对寡肽的传送特点,设计并合成了8个含L-4-氧代赖氨酸(以下称I-677)和N<sup>3</sup>-(4-甲氧基富马酰)-L-2,3-二氨基丙酸(以下称FMDP)的寡肽类似物,均系新化合物。体外抗白念珠菌试验表明:I-677-FMDP-肽(I-677-FMDP,I-677-AA-FMDP,其中AA=Nva,Val,Leu,Phe,Pro,D,L-p-CI-Phe,D-Pgly)是I-677单体摩尔活性的40~770倍,是FMDP的60~1130倍,其摩尔最低抑菌浓度为6.56×10<sup>-9</sup>~3.5×10<sup>-10</sup>mol·disk<sup>-1</sup>。羧肽酶A存在时化合物I-677-FMDP体外抗菌试验表明,含FMDP的化合物I-677-FMDP能抵抗羧肽酶A的酶解。

关键词: L-4-氧代赖氨酸 N<sup>3</sup>-(4-甲氧基富马酰)-L-2,3-二氨基丙酸 违法传递 抗真菌寡肽类似物 白念

SYNTHESIS AND ANTI-CANDIDA ALBICANS PROPERTIES OF L-4-OXALYSINE-N<sup>3</sup>-4-METHOXYFUMAROYL L-2,3-DIAMINOPROPANOIC-CONTAINING PEPTIDE ANALOGUES

Feng Shengxi; Xu Xiurong and Zhang Honglong

Abstract:

In order to improve the inhibitory activity of L-4-oxalysine(abbreviated as I-677) against clinically important pathogen *Candida albicans*, double warheads peptide analogues containing I-677 and N<sup>3</sup>-4-methoxyfumaroyl-L-2,3-diaminopropanoic acid( FMDP) were designed based on the concept of “Illicit Transport” and peptide transport specificities of *C. albicans*. One compound of I-677-FMDP and seven compounds of I-677-AA-FMDP(AA=Nva, Leu, Val, Phe, Pro, D-Pgly, D,L-p-CI-Phe) were synthesized and examined for antifungal activities. The results of anti *Candida albicans* test *in vitro* of these double warheads peptide analogues containing I-677 and FMDP showed very high activities against *Candida albicans*. The molar MIC(molar minimum inhibitory concentration) ratio of free I-677 to I-677-AA-FMDP is 40~770 and that of FMDP is 60~1130. The values of molar MIC of I-677-AA-FMDP varied from 6.56×10<sup>-9</sup> mol·disk<sup>-1</sup> to 3.5×10<sup>-10</sup> mol·disk<sup>-1</sup>. The results of competitive antagonism studies indicated that I-677-AA-FMDP were transported into *Candida albicans* cells by the di tripeptide permease and subsequently hydrolyzed by intracellular peptidases, releasing free I-677 and FMDP inside cells. The result of antienzymic degradation test *in vitro* of I-677-FMDP showed that compound I-677-FMDP was resistant to the hydrolysis by carboxypeptidase A.

Keywords: N<sup>3</sup>-4-methoxyfumaroyl-L-2,3-diaminopropanoic acid(FMDP) Illicit transport Antifungal peptide analogue *Candida albicans* L-4-oxalysine(I-677)

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通讯作者: 冯胜昔

作者简介:

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