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(54)发明名称

由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物

(57)摘要

本发明提供了一种由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物以及含有该组合物的药物制剂。优选的，本发明所述的脂肪酶抑制剂是选自奥利司他与西替利司他中的一种；而所述的羟甲戊二酰辅酶A还原酶抑制剂是选自阿托伐他汀、瑞舒伐他汀、辛伐他汀、氟伐他汀、普伐他汀、洛伐他汀与匹伐他汀中的一种或其药学上可接受的盐。本发明所述组合物能同时产生协同的抗菌作用与协同的抑制组胺释放作用，从而能提高细菌感染致过敏性疾病患者治疗的效果与经济学特征。

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1.一种由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物。

2.根据权利要求1的组合物,其特征在于,所述的脂肪酶抑制剂是选自奥利司他与西替利司他中的一种;更优选的,所述的脂肪酶抑制剂是奥利司他。

3.根据权利要求1的组合物,其特征在于,所述的羟甲戊二酰辅酶A还原酶抑制剂是选自阿托伐他汀、瑞舒伐他汀、辛伐他汀、氟伐他汀、普伐他汀、洛伐他汀与匹伐他汀中的一种或其药学上可接受的盐;更优选的,所述的羟甲戊二酰辅酶A还原酶抑制剂是选自辛伐他汀、瑞舒伐他汀钙、阿托伐他汀钙、洛伐他汀、普伐他汀钠、匹伐他汀钙与氟伐他汀钠中的一种。

4.根据权利要求1～3中任意一项的组合物,其特征在于,所述脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂的物质的量的比在0.008:1～158.489:1之间。

5.含有根据权利要求1～4中任意一项的组合物的药物制剂。

6.根据权利要求5的药物制剂,其特征在于,所述药物制剂是口服固体制剂。更优选的,本发明所述的口服固体制剂是选自胶囊剂、片剂与颗粒剂中的一种。

7.根据权利要求1～4中任意一项的组合物或根据权利要求5～6中任意一项的药物制剂在在制备用于治疗细菌性感染的药物中的用途。

8.根据权利要求1～4中任意一项的组合物或根据权利要求5～6中任意一项的药物制剂在制备用于治疗过敏性疾病的药物中的用途。

9.根据权利要求1～4中任意一项的组合物或根据权利要求5～6中任意一项的药物制剂在制备同时用于治疗细菌性感染与过敏性疾病的药物中的用途。

10.根据权利要求7与9中任意一项的用途,其特征在于,所述的细菌性感染是由选自粘放线菌、脆弱拟杆菌、表皮短杆菌、艰难梭菌、破伤风梭菌、甲型副伤寒沙门菌中的一种所致的感染。

由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物

技术领域

[0001] 本发明属于医药技术领域，具体涉及一种由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物以及含有该组合物的药物制剂。

背景技术

[0002] 变态反应也称为过敏反应。它是机体受抗原性物质(如细菌、病毒、寄生虫、花粉等)刺激后引起的组织损伤或生理功能紊乱。属于异常的或病灶性的免疫反应。通常所说的过敏反应是指I型过敏反应，即速发型过敏反应。其机制为过敏原进入过敏者体内后产生特异性的抗体，后者结合在肥大细胞的表面，使机体呈致敏状态，当次接触过敏原时，肥大细胞脱颗粒，并释放多种化学介质，如5-羟色胺、慢反应物质、组胺、白三烯等。这些介质引发的病理改变或症状称之为速发型过敏反应的速发相。

[0003] 抑制组胺的释放是多种抗过敏药物的主要作用机制之一。

[0004] 如前所述，细菌刺激是导致变态反应的原因之一，同时具有抑制组胺释放作用与抗菌作用的药物对于改善细菌致变态反应的患者的治疗效果将带来有益的效果，尤其是能提高其治疗的经济学特征。

[0005] 以阿托伐他汀为代表的羟甲戊二酰辅酶A(HMG-CoA)还原酶抑制剂类药物是临床上常用的血脂调节药，近年来该类药物的抗菌活性屡见报告。Jerwood S等人的研究显示(J Antimicrob Chemother.2008 Feb;61(2):362-4)，辛伐他汀与氟伐他汀均具有一定的抗菌作用，其中，前者对MSSA与MRSA的平均MIC分别为29.2与74.9mg/L，而相比之下，氟伐他汀的抗菌作用显著低于辛伐他汀。Welsh AM等人报道(Pathology.2009;41(7):689-91)称阿托伐他汀与瑞舒伐他汀也具有抗菌作用，但对MRSA与MSSA的MIC值均显著高于其用于调节血脂时的典型血药浓度。Masadeh M(Ann Clin Microbiol Antimicrob.2012 May 7;11:13)等人也报道了阿托伐他汀、辛伐他汀与瑞舒伐他汀的抗菌作用，但其MIC值均>100mg/L，而且抗菌作用机制与羟甲戊二酰辅酶A无关。

[0006] Krauth MT等人的研究证实(Allergy.2006Mar;61(3):281-8.)，阿托伐他汀与cerivastatin能抑制抗IgE诱导的人肥大细胞的组胺释放。

[0007] 奥利司他与西替利司他(cetilistat)是两种脂肪酶抑制剂类减重药物，由于脂肪酶在多种细菌中均有表达并调控着细菌的生长与功能，因此奥利司他可能也具有一定的抗菌作用，本发明人在试验室工作中也证明了这一点。

[0008] 本发明人在实验室工作中还发现奥利司他与西替利司他也具有中度的组胺抑制作用.

[0009] 现有技术中暂无奥利司他与羟甲戊二酰辅酶A还原酶抑制剂联合用药同时产生协同的抗菌作用与协同的抑制组胺释放作用的技术教导。

发明内容

[0010] 本发明的目的在于提供一种由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物以及含有该组合物的药物制剂，所述组合物能同时产生协同的抗菌作用与协同的抑制组胺释放作用。

[0011] 为了实现上述目的，本发明首先提供了一种由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物。

[0012] 一方面优选的，本发明所述的脂肪酶抑制剂是选自奥利司他与西替利司他中的一种；更优选的，本发明所述的脂肪酶抑制剂是奥利司他。

[0013] 一方面优选的，本发明所述的羟甲戊二酰辅酶A还原酶抑制剂是选自阿托伐他汀、瑞舒伐他汀、辛伐他汀、氟伐他汀、普伐他汀、洛伐他汀与匹伐他汀中的一种或其药学上可接受的盐；进一步优选的，本发明所述的羟甲戊二酰辅酶A还原酶抑制剂是选自辛伐他汀、瑞舒伐他汀钙、阿托伐他汀钙、洛伐他汀、普伐他汀钠、匹伐他汀钙与氟伐他汀钠中的一种。

[0014] 另一方面优选的，本发明所述组合物中脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂的物质的量的比在0.008:1～158.489:1之间。

[0015] 本发明另一方面提供了含有如前所述组合物的药物制剂。

[0016] 优选的，本发明所述药物制剂是口服固体制剂。更优选的，本发明所述的口服固体制剂是选自胶囊剂、片剂与颗粒剂中的一种。

[0017] 本发明另一方面提供了如前所述的组合物与药物制剂在制备用于治疗细菌性感染的药物中的用途。

[0018] 本发明另一方面提供了如前所述的组合物与药物制剂在制备用于治疗过敏性疾病的药物中的用途。

[0019] 本发明另一方面提供了如前所述的组合物与药物制剂在制备同时用于治疗细菌性感染与过敏性疾病的药物中的用途。

[0020] 优选的，本发明所述的细菌性感染是由选自粘放线菌、脆弱拟杆菌、表皮短杆菌、艰难梭菌、破伤风梭菌、甲型副伤寒沙门菌中的一种所致的感染。

[0021] 本发明所述的组合物能同时产生协同的抗菌作用与抗组胺释放作用。

具体实施方式

[0022] 下面结合本发明实施例，对本发明的技术方案进行清楚、完整的描述，显然，所描述的实施例仅仅是本发明的一部分实施例，而不是全部的实施例。基于本发明中的实施例，本领域普通技术人员在没有做出创造性劳动前提下所获得的所有其他实施例，都属于本发明保护的范围。

[0023] 本发明所述的物质的量的比均为脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂的物质的量的比。

[0024] 本发明以“—”连接脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂表示两者的组合物。

[0025] 实施例1由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物的制备

[0026] 取特定物质的量的比的脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂，充分混合，即得。

[0027] 本发明试验例与实施例中的物质的量的比包括:0.008:1、0.01:1、0.013:1、0.016:1、0.02:1、0.025:1、0.032:1、0.04:1、0.05:1、0.063:1、0.079:1、0.1:1、0.126:1、0.158:1、0.2:1、0.251:1、0.316:1、0.398:1、0.501:1、0.631:1、0.794:1、1:1、1.259:1、1.585:1、1.995:1、2.512:1、3.162:1、3.981:1、5.012:1、6.31:1、7.943:1、10:1、12.589:1、15.849:1、19.953:1、25.119:1、31.623:1、39.811:1、50.119:1、63.096:1、79.433:1、100:1、125.893:1、158.489:1。

[0028] 试验例1脂肪酶抑制剂、羟甲戊二酰辅酶A还原酶抑制剂以及两者的组合物的抗菌作用

[0029] 采用滤纸片法分别测定脂肪酶抑制剂、羟甲戊二酰辅酶A还原酶抑制剂以及脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对多种细菌的抑菌活性。具体的,用移液枪吸取已经配制好的细菌混悬液(1×10^5/mL,制备方法:将供试菌种在斜面试管培养基上进行活化[37±1℃,3天],再利用接种环从斜面上轻取少量菌苔,分别添加到盛放有50mL无菌生理盐水的锥形瓶中),均匀涂抹在冷却后的琼脂平板表面,制成含菌平板。取灭菌滤纸片,分别放过6种浓度梯度的受试物甲醇溶液中浸泡1h,将浸泡过的6mm圆形滤纸片贴在上述制好的含菌平板上,每个培养皿(直径90mm)贴上3片浸过同一种质量浓度受试物甲醇溶液的滤纸片(滤纸片尽量间隔相同),以50%甲醇溶液作为空白对照。把处理过的含菌平板置于37℃恒温箱中培养24h,采用十字交叉法测定菌落直径,并按照以下公式计算抑制率(IR)。

[0030] $$IR=\frac{\text{处理组抑菌圈直径}-\text{空白对照组抑菌圈直径}}{\text{处理组抑菌圈直径}}\times100\%$$

[0031] 用抑制率(IR)对药物浓度(μM)的对数值作图,并用Excel进行线性回归,根据回归方程推算出产生fa抑制时脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂的浓度,分别为$IC_{fa(A)}$与$IC_{fa(B)}$值。对于联合用药,则用抑制率(IR)对联合用药中脂肪酶抑制剂的浓度(μM)的对数值(log(c))作图,并用Excel进行线性回归,根据回归方程推算出fa抑制时组合体系内的脂肪酶抑制剂的浓度,即$IC_{fa(mixA)}$,再根据组合体系中物质的量的比,推算出fa抑制时组合体系内羟甲戊二酰辅酶A还原酶抑制剂的浓度,即$IC_{fa(mixB)}$。

[0032] 根据下式计算产生fa抑制时的联合用药指数(CI)

[0033] $$CI=\frac{IC_{fa(mixA)}}{IC_{fa(A)}}+\frac{IC_{fa(mixB)}}{IC_{fa(B)}}$$

[0034] 当CI<1,即为协同作用,CI值越小,协同作用越强。

[0035] 结果如表1～6所示。

[0036] 表1脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对粘放线菌的协同抑菌作用

[0037]

受试物	摩尔比	最高浓度(μM) [a]	IR_{max}	fa	斜率 [b]	截距 [b]	IC_{fa}(μM) [c]	CI
ORLI		50	30.58%	27.43%	0.428	-0.408	39.323	
ATOR		80	30.33%	27.43%	0.310	-0.284	63.213	

[0038]

ORLI—ATOR	0.010	70	98.27%	27.43%	0.347	0.349	0.611	0.981
ORLI—ATOR	0.025	200	99.09%	27.43%	0.336	0.215	1.499	0.982
ORLI—ATOR	0.063	200	90.95%	27.43%	0.354	0.079	3.563	0.984
ORLI—ATOR	0.158	200	98.29%	27.43%	0.412	-0.004	4.740	0.594
ORLI—ATOR	0.398	400	97.14%	27.43%	0.341	0.083	3.626	0.236
ORLI—ATOR	1.000	100	93.92%	27.43%	0.427	0.086	2.763	0.114
ORLI—ATOR	2.512	300	96.71%	27.43%	0.426	-0.090	7.146	0.227
ORLI—ATOR	6.310	700	90.64%	27.43%	0.414	-0.269	20.566	0.575
ORLI—ATOR	15.849	1000	98.39%	27.43%	0.483	-0.478	36.044	0.953
ORLI—ATOR	39.811	1000	98.10%	27.43%	0.475	-0.470	37.036	0.957
ORLI—ATOR	100.000	2000	98.05%	27.43%	0.432	-0.407	37.622	0.963
ROSU		20	32.16%	27.43%	0.365	-0.181	17.734	
ORLI—ROSU	0.010	4	91.31%	27.43%	0.483	0.640	0.174	0.987
ORLI—ROSU	0.025	20	96.54%	27.43%	0.406	0.421	0.436	0.990
ORLI—ROSU	0.063	70	90.77%	27.43%	0.329	0.307	0.796	0.731
ORLI—ROSU	0.158	30	96.23%	27.43%	0.449	0.321	0.786	0.300
ORLI—ROSU	0.398	100	97.15%	27.43%	0.309	0.330	0.658	0.110
ORLI—ROSU	1.000	50	90.11%	27.43%	0.445	0.141	1.991	0.163
ORLI—ROSU	2.512	1000	98.67%	27.43%	0.335	-0.055	9.572	0.458
ORLI—ROSU	6.310	900	95.62%	27.43%	0.451	-0.381	28.338	0.974
ORLI—ROSU	15.849	700	90.78%	27.43%	0.480	-0.459	33.751	0.978
ORLI—ROSU	39.811	900	90.12%	27.43%	0.446	-0.421	36.302	0.975
ORLI—ROSU	100.000	3000	97.88%	27.43%	0.372	-0.310	37.415	0.973
FLUV		40	27.43%	27.43%	0.405	-0.367	38.509	
ORLI—FLUV	0.010	20	96.00%	27.43%	0.394	0.445	0.369	0.968
ORLI—FLUV	0.025	40	91.32%	27.43%	0.389	0.287	0.927	0.982
ORLI—FLUV	0.063	60	90.44%	27.43%	0.447	0.120	2.213	0.967
ORLI—FLUV	0.158	100	99.48%	27.43%	0.498	-0.082	5.187	0.982
ORLI—FLUV	0.398	100	93.22%	27.43%	0.492	-0.113	6.115	0.554
ORLI—FLUV	1.000	200	95.25%	27.43%	0.405	0.033	3.932	0.202
ORLI—FLUV	2.512	90	92.69%	27.43%	0.453	0.038	3.319	0.119
ORLI—FLUV	6.310	700	98.04%	27.43%	0.384	-0.114	10.299	0.304
ORLI—FLUV	15.849	2000	95.99%	27.43%	0.365	-0.254	28.034	0.759
ORLI—FLUV	39.811	800	92.81%	27.43%	0.491	-0.494	36.697	0.957
ORLI—FLUV	100.000	1000	96.47%	27.43%	0.452	-0.438	37.508	0.964
LORV		80	27.84%	27.43%	0.440	-0.561	79.428	
ORLI—LORV	0.010	60	94.05%	27.43%	0.349	0.314	0.768	0.987
ORLI—LORV	0.025	300	92.76%	27.43%	0.303	0.192	1.872	0.986
ORLI—LORV	0.063	200	96.85%	27.43%	0.426	0.000	4.405	0.991
ORLI—LORV	0.158	400	94.43%	27.43%	0.364	-0.010	6.047	0.634
ORLI—LORV	0.398	200	95.43%	27.43%	0.441	-0.017	4.567	0.261
ORLI—LORV	1.000	70	95.72%	27.43%	0.473	0.072	2.674	0.102
ORLI—LORV	2.512	200	97.84%	27.43%	0.474	-0.064	5.172	0.157
ORLI—LORV	6.310	400	94.27%	27.43%	0.481	-0.300	15.603	0.428
ORLI—LORV	15.849	1000	98.77%	27.43%	0.448	-0.417	34.818	0.913
ORLI—LORV	39.811	900	94.18%	27.43%	0.494	-0.506	37.885	0.975
ORLI—LORV	100.000	4000	98.77%	27.43%	0.351	-0.278	37.646	0.962
SIMV		80	32.79%	27.43%	0.445	-0.527	63.337	
ORLI—SIMV	0.010	80	94.82%	27.43%	0.320	0.342	0.615	0.987
ORLI—SIMV	0.025	30	92.54%	27.43%	0.479	0.187	1.523	0.996
ORLI—SIMV	0.063	300	91.43%	27.43%	0.334	0.087	3.626	1.000
ORLI—SIMV	0.158	200	94.97%	27.43%	0.463	-0.065	5.407	0.676
ORLI—SIMV	0.398	300	92.25%	27.43%	0.359	0.038	4.574	0.298
ORLI—SIMV	1.000	500	98.60%	27.43%	0.312	0.134	2.824	0.116
ORLI—SIMV	2.512	100	93.60%	27.43%	0.438	0.003	4.170	0.132
ORLI—SIMV	6.310	400	96.82%	27.43%	0.469	-0.238	12.360	0.345
ORLI—SIMV	15.849	2000	97.41%	27.43%	0.383	-0.283	28.586	0.755

[0039]

ORLI—SIMV	39.811	3000	94.71%	27.43%	0.354	-0.283	37.748	0.975
ORLI—SIMV	100.000	2000	96.78%	27.43%	0.434	-0.412	38.142	0.976
PITA		60	28.07%	27.43%	0.342	-0.333	59.870	
ORLI—PITA	0.010	20	90.44%	27.43%	0.397	0.369	0.578	0.979
ORLI—PITA	0.025	40	98.72%	27.43%	0.476	0.201	1.426	0.985
ORLI—PITA	0.063	90	95.32%	27.43%	0.472	0.025	3.376	0.980
ORLI—PITA	0.158	700	92.16%	27.43%	0.329	-0.012	7.402	0.968
ORLI—PITA	0.398	400	91.64%	27.43%	0.398	-0.101	8.761	0.590
ORLI—PITA	1.000	200	98.19%	27.43%	0.457	-0.059	5.365	0.226
ORLI—PITA	2.512	70	91.79%	27.43%	0.470	0.036	3.205	0.103
ORLI—PITA	6.310	400	90.34%	27.43%	0.375	-0.062	7.861	0.221
ORLI—PITA	15.849	5000	99.93%	27.43%	0.311	-0.143	21.889	0.580
ORLI—PITA	39.811	3000	92.45%	27.43%	0.336	-0.254	37.326	0.965
ORLI—PITA	100.000	3000	98.82%	27.43%	0.365	-0.301	37.692	0.965
PRAV		80	30.33%	27.43%	0.498	-0.653	72.642	
ORLI—PRAV	0.010	40	91.49%	27.43%	0.349	0.364	0.553	0.775
ORLI—PRAV	0.025	30	96.71%	27.43%	0.424	0.366	0.607	0.348
ORLI—PRAV	0.063	40	92.98%	27.43%	0.350	0.371	0.530	0.129
ORLI—PRAV	0.158	200	92.90%	27.43%	0.303	0.268	1.051	0.118
ORLI—PRAV	0.398	300	94.27%	27.43%	0.390	-0.006	5.245	0.315
ORLI—PRAV	1.000	700	92.31%	27.43%	0.411	-0.245	18.353	0.719
ORLI—PRAV	2.512	3000	91.82%	27.43%	0.324	-0.214	32.131	0.993
ORLI—PRAV	6.310	2000	98.58%	27.43%	0.426	-0.387	35.843	0.990
ORLI—PRAV	15.849	1000	98.35%	27.43%	0.476	-0.477	37.822	0.995
ORLI—PRAV	39.811	2000	91.09%	27.43%	0.365	-0.304	38.375	0.989
ORLI—PRAV	100.000	5000	94.86%	27.43%	0.324	-0.242	38.939	0.996
CETI		40	27.76%	27.76%	0.481	-0.492	39.882	
ATOR		0	30.01%	27.76%	0.342	0.680	0.066	
CETI—ATOR	0.010	0	95.51%	27.76%	0.325	1.309	0.001	0.998
CETI—ATOR	0.025	0	95.78%	27.76%	0.424	1.457	0.002	0.987
CETI—ATOR	0.063	0	91.86%	27.76%	0.375	1.170	0.004	0.993
CETI—ATOR	0.158	0	93.50%	27.76%	0.481	1.251	0.009	0.901
CETI—ATOR	0.398	2	96.68%	27.76%	0.311	0.899	0.010	0.378
CETI—ATOR	1.000	1	94.79%	27.76%	0.363	1.041	0.008	0.119
CETI—ATOR	2.512	1	96.74%	27.76%	0.442	1.021	0.021	0.125
CETI—ATOR	6.310	3	91.01%	27.76%	0.482	0.656	0.164	0.395
CETI—ATOR	15.849	50	94.98%	27.76%	0.400	0.286	0.954	0.929
CETI—ATOR	39.811	70	91.68%	27.76%	0.433	0.113	2.405	0.969
CETI—ATOR	100.000	200	91.80%	27.76%	0.399	-0.021	5.605	0.984
ROSU		30	30.84%	27.76%	0.404	-0.264	21.928	
CETI—ROSU	0.010	6	97.36%	27.76%	0.494	0.605	0.217	0.995
CETI—ROSU	0.025	90	96.30%	27.76%	0.308	0.360	0.541	0.996
CETI—ROSU	0.063	100	99.17%	27.76%	0.364	0.232	1.334	0.998
CETI—ROSU	0.158	300	91.52%	27.76%	0.323	0.115	3.191	0.998
CETI—ROSU	0.398	600	90.88%	27.76%	0.329	-0.004	7.156	0.999
CETI—ROSU	1.000	2000	99.16%	27.76%	0.320	-0.045	10.191	0.720
CETI—ROSU	2.512	300	98.95%	27.76%	0.437	-0.075	6.412	0.277
CETI—ROSU	6.310	600	98.74%	27.76%	0.321	0.102	3.526	0.114
CETI—ROSU	15.849	400	99.57%	27.76%	0.417	-0.104	8.242	0.230
CETI—ROSU	39.811	700	98.46%	27.76%	0.492	-0.401	23.901	0.627
CETI—ROSU	100.000	1000	94.03%	27.76%	0.419	-0.388	38.798	0.991
FLUV		20	32.77%	27.76%	0.410	-0.237	18.016	
CETI—FLUV	0.010	4	94.69%	27.76%	0.494	0.650	0.176	0.982
CETI—FLUV	0.025	30	97.48%	27.76%	0.372	0.412	0.436	0.974
CETI—FLUV	0.063	70	98.12%	27.76%	0.390	0.264	1.082	0.979
CETI—FLUV	0.158	100	95.11%	27.76%	0.419	0.103	2.610	0.980
CETI—FLUV	0.398	90	92.26%	27.76%	0.471	-0.006	3.993	0.657

[0040]

CETI—FLUV	1.000	200	99.41%	27.76%	0.398	0.073	3.269	0.263
CETI—FLUV	2.512	300	93.58%	27.76%	0.327	0.150	2.449	0.116
CETI—FLUV	6.310	400	95.92%	27.76%	0.374	-0.022	6.295	0.213
CETI—FLUV	15.849	1000	90.51%	27.76%	0.339	-0.160	19.474	0.556
CETI—FLUV	39.811	4000	99.14%	27.76%	0.347	-0.263	36.132	0.956
CETI—FLUV	100.000	3000	91.99%	27.76%	0.340	-0.256	37.227	0.954
LORV		20	32.20%	27.76%	0.402	-0.169	12.898	
CETI—LORV	0.010	5	95.32%	27.76%	0.419	0.656	0.125	0.973
CETI—LORV	0.025	7	90.92%	27.76%	0.480	0.517	0.317	0.987
CETI—LORV	0.063	20	90.84%	27.76%	0.460	0.329	0.774	0.971
CETI—LORV	0.158	30	92.53%	27.76%	0.484	0.228	1.265	0.651
CETI—LORV	0.398	100	96.82%	27.76%	0.351	0.240	1.277	0.281
CETI—LORV	1.000	40	94.46%	27.76%	0.426	0.269	1.046	0.107
CETI—LORV	2.512	50	92.36%	27.76%	0.480	0.101	2.336	0.131
CETI—LORV	6.310	400	92.64%	27.76%	0.389	-0.100	9.387	0.351
CETI—LORV	15.849	2000	97.69%	27.76%	0.384	-0.263	25.609	0.767
CETI—LORV	39.811	4000	96.73%	27.76%	0.334	-0.241	35.556	0.961
CETI—LORV	100.000	2000	96.46%	27.76%	0.421	-0.383	36.999	0.956
SIMV		70	29.62%	27.76%	0.463	-0.545	59.917	
CETI—SIMV	0.010	30	91.76%	27.76%	0.384	0.367	0.586	0.992
CETI—SIMV	0.025	40	96.79%	27.76%	0.470	0.204	1.432	0.987
CETI—SIMV	0.063	400	91.78%	27.76%	0.312	0.111	3.425	0.992
CETI—SIMV	0.158	100	91.28%	27.76%	0.434	-0.008	4.543	0.592
CETI—SIMV	0.398	200	99.71%	27.76%	0.421	0.037	3.718	0.249
CETI—SIMV	1.000	100	99.93%	27.76%	0.452	0.072	2.860	0.119
CETI—SIMV	2.512	300	97.93%	27.76%	0.409	-0.052	6.414	0.203
CETI—SIMV	6.310	1000	98.33%	27.76%	0.379	-0.199	18.077	0.501
CETI—SIMV	15.849	1000	92.84%	27.76%	0.426	-0.389	36.831	0.962
CETI—SIMV	39.811	2000	98.92%	27.76%	0.423	-0.392	38.188	0.974
CETI—SIMV	100.000	4000	98.13%	27.76%	0.350	-0.276	38.238	0.965
PITA		100	32.73%	27.76%	0.412	-0.515	83.548	
CETI—PITA	0.010	40	95.47%	27.76%	0.404	0.315	0.808	0.987
CETI—PITA	0.025	100	99.99%	27.76%	0.403	0.157	1.993	1.000
CETI—PITA	0.063	600	99.86%	27.76%	0.342	0.051	4.597	0.987
CETI—PITA	0.158	600	98.38%	27.76%	0.398	-0.119	9.885	0.994
CETI—PITA	0.398	200	94.35%	27.76%	0.478	-0.176	8.904	0.491
CETI—PITA	1.000	600	97.70%	27.76%	0.330	0.054	4.763	0.176
CETI—PITA	2.512	100	98.36%	27.76%	0.484	0.007	3.622	0.108
CETI—PITA	6.310	300	96.74%	27.76%	0.467	-0.202	10.598	0.286
CETI—PITA	15.849	5000	97.24%	27.76%	0.313	-0.173	27.479	0.710
CETI—PITA	39.811	3000	96.01%	27.76%	0.354	-0.282	38.297	0.972
CETI—PITA	100.000	2000	94.65%	27.76%	0.390	-0.341	38.779	0.977
PRAV		90	27.86%	27.76%	0.409	-0.524	90.849	
CETI—PRAV	0.010	90	91.85%	27.76%	0.317	0.296	0.877	0.987
CETI—PRAV	0.025	100	93.49%	27.76%	0.394	0.147	2.143	0.993
CETI—PRAV	0.063	100	94.98%	27.76%	0.499	-0.069	4.966	0.991
CETI—PRAV	0.158	600	94.34%	27.76%	0.354	-0.030	7.420	0.701
CETI—PRAV	0.398	300	90.80%	27.76%	0.380	-0.007	5.624	0.297
CETI—PRAV	1.000	300	90.38%	27.76%	0.310	0.117	3.298	0.119
CETI—PRAV	2.512	300	92.98%	27.76%	0.368	-0.001	5.729	0.169
CETI—PRAV	6.310	2000	97.48%	27.76%	0.346	-0.145	16.624	0.446
CETI—PRAV	15.849	1000	96.24%	27.76%	0.476	-0.468	36.874	0.950
CETI—PRAV	39.811	2000	99.64%	27.76%	0.412	-0.374	38.289	0.971
CETI—PRAV	100.000	1000	93.50%	27.76%	0.422	-0.394	38.817	0.978

注：

[a] 最高浓度是指抑制率进入平台期时受试物的最低浓度，对于组合物而言，所述最高浓度是指组合物中脂肪酶抑制剂的最高浓度。

[0041]

[b] 所述斜率与截距代表 IR—log(c)线性回归方程的斜率与截距。
[c] 对于组合物而言，IC_{fa}代表 $IC_{fa\,(mixA)}$.
表 2~表 7 表头的定义与表 1 相同。
简写与定义：
ORLI=奥利司他；CETI=西替利司他；ATOR=阿托伐他汀钙；ROSU=瑞舒伐他汀钙；LORV=洛伐他汀；FLUV=氟伐他汀钠；SIMV=辛伐他汀；PITA=匹伐他汀钙；PRAV=普伐他汀钠。本发明其他部分相关简写的定义与表 1 相同。

[0042] 表2脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对脆弱拟杆菌的协同抑菌作用

[0043]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		50	29.89%	28.05%	0.376	-0.335	43.186	
ATOR		50	28.05%	28.05%	0.400	-0.399	50.025	
ORLI—ATOR	0.013	20	90.76%	28.05%	0.416	0.370	0.609	0.981
ORLI—ATOR	0.032	100	96.95%	28.05%	0.382	0.212	1.514	0.992
ORLI—ATOR	0.079	200	95.29%	28.05%	0.406	0.056	3.573	0.982
ORLI—ATOR	0.200	300	95.32%	28.05%	0.376	0.017	5.028	0.620
ORLI—ATOR	0.501	200	94.60%	28.05%	0.391	0.040	4.114	0.259
ORLI—ATOR	1.259	200	99.18%	28.05%	0.379	0.121	2.637	0.103
ORLI—ATOR	3.162	100	90.18%	28.05%	0.467	-0.050	5.118	0.151
ORLI—ATOR	7.943	300	94.21%	28.05%	0.498	-0.315	15.705	0.403
ORLI—ATOR	19.953	800	92.22%	28.05%	0.471	-0.451	35.594	0.860
ORLI—ATOR	50.119	1000	93.45%	28.05%	0.474	-0.484	41.095	0.968
ORLI—ATOR	125.893	2000	97.78%	28.05%	0.445	-0.440	41.400	0.965
ROSU		80	32.33%	28.05%	0.475	-0.588	67.462	
ORLI—ROSU	0.013	30	95.58%	28.05%	0.424	0.350	0.687	0.824
ORLI—ROSU	0.032	40	95.91%	28.05%	0.396	0.342	0.700	0.344
ORLI—ROSU	0.079	10	92.48%	28.05%	0.483	0.424	0.504	0.106
ORLI—ROSU	0.200	100	92.51%	28.05%	0.321	0.266	1.113	0.108
ORLI—ROSU	0.501	200	92.84%	28.05%	0.451	-0.092	6.687	0.353
ORLI—ROSU	1.259	1000	94.64%	28.05%	0.390	-0.258	23.995	0.838
ORLI—ROSU	3.162	2000	98.01%	28.05%	0.431	-0.389	35.755	0.996
ORLI—ROSU	7.943	1000	97.22%	28.05%	0.445	-0.430	39.686	0.993
ORLI—ROSU	19.953	1000	94.30%	28.05%	0.480	-0.495	41.217	0.985
ORLI—ROSU	50.119	4000	96.67%	28.05%	0.355	-0.297	42.487	0.996
ORLI—ROSU	125.893	5000	93.55%	28.05%	0.320	-0.240	42.444	0.988
FLUV		60	32.82%	28.05%	0.393	-0.371	45.346	
ORLI—FLUV	0.013	10	90.36%	28.05%	0.443	0.395	0.553	0.981
ORLI—FLUV	0.032	100	96.31%	28.05%	0.369	0.233	1.349	0.972
ORLI—FLUV	0.079	500	95.60%	28.05%	0.303	0.126	3.243	0.975
ORLI—FLUV	0.200	500	91.72%	28.05%	0.339	-0.001	6.771	0.905
ORLI—FLUV	0.501	600	95.74%	28.05%	0.346	-0.001	6.497	0.436
ORLI—FLUV	1.259	90	95.19%	28.05%	0.497	-0.029	4.187	0.170
ORLI—FLUV	3.162	100	94.16%	28.05%	0.412	0.054	3.555	0.107
ORLI—FLUV	7.943	400	92.97%	28.05%	0.414	-0.124	9.518	0.247
ORLI—FLUV	19.953	800	97.39%	28.05%	0.463	-0.361	24.292	0.589
ORLI—FLUV	50.119	1000	98.82%	28.05%	0.472	-0.476	40.174	0.948
ORLI—FLUV	125.893	1000	92.54%	28.05%	0.430	-0.415	41.243	0.962
LORV		100	30.42%	28.05%	0.315	-0.330	85.945	
ORLI—LORV	0.013	30	97.26%	28.05%	0.482	0.273	1.035	0.980
ORLI—LORV	0.032	60	94.80%	28.05%	0.475	0.092	2.500	0.978
ORLI—LORV	0.079	200	93.86%	28.05%	0.423	-0.011	4.890	0.829
ORLI—LORV	0.200	100	93.02%	28.05%	0.446	-0.017	4.630	0.377
ORLI—LORV	0.501	300	97.52%	28.05%	0.335	0.125	2.923	0.136
ORLI—LORV	1.259	70	93.10%	28.05%	0.487	0.033	3.224	0.104
ORLI—LORV	3.162	200	91.51%	28.05%	0.489	-0.220	10.582	0.284
ORLI—LORV	7.943	6000	99.51%	28.05%	0.307	-0.161	27.380	0.674

[0044]

ORLI—LORV	19.953	7000	99.00%	28.05%	0.318	-0.231	40.421	0.960
ORLI—LORV	50.119	900	95.29%	28.05%	0.493	-0.513	40.763	0.953
ORLI—LORV	125.893	3000	99.14%	28.05%	0.390	-0.350	41.273	0.960
SIMV		50	28.96%	28.05%	0.388	-0.363	45.365	
ORLI—SIMV	0.013	30	94.26%	28.05%	0.374	0.374	0.562	0.998
ORLI—SIMV	0.032	40	99.73%	28.05%	0.480	0.214	1.378	0.992
ORLI—SIMV	0.079	200	91.77%	28.05%	0.376	0.086	3.290	0.989
ORLI—SIMV	0.200	200	94.63%	28.05%	0.450	-0.113	7.482	1.000
ORLI—SIMV	0.501	200	93.11%	28.05%	0.465	-0.134	7.814	0.525
ORLI—SIMV	1.259	100	99.73%	28.05%	0.494	-0.068	5.069	0.206
ORLI—SIMV	3.162	200	93.99%	28.05%	0.374	0.076	3.531	0.106
ORLI—SIMV	7.943	300	96.77%	28.05%	0.457	-0.149	8.687	0.225
ORLI—SIMV	19.953	3000	97.49%	28.05%	0.333	-0.174	23.200	0.563
ORLI—SIMV	50.119	3000	90.34%	28.05%	0.331	-0.255	41.431	0.978
ORLI—SIMV	125.893	3000	98.62%	28.05%	0.386	-0.345	41.798	0.975
PITA		90	28.55%	28.05%	0.315	-0.323	82.815	
ORLI—PITA	0.013	80	93.57%	28.05%	0.342	0.279	1.013	0.995
ORLI—PITA	0.032	60	92.73%	28.05%	0.477	0.095	2.452	0.993
ORLI—PITA	0.079	400	97.69%	28.05%	0.327	0.136	2.778	0.487
ORLI—PITA	0.200	200	95.49%	28.05%	0.330	0.188	1.908	0.160
ORLI—PITA	0.501	50	92.84%	28.05%	0.488	0.120	2.127	0.101
ORLI—PITA	1.259	300	91.57%	28.05%	0.445	-0.153	9.440	0.309
ORLI—PITA	3.162	800	93.47%	28.05%	0.452	-0.382	29.122	0.786
ORLI—PITA	7.943	7000	98.93%	28.05%	0.312	-0.216	39.284	0.969
ORLI—PITA	19.953	4000	95.12%	28.05%	0.334	-0.259	41.397	0.984
ORLI—PITA	50.119	2000	97.84%	28.05%	0.439	-0.432	41.971	0.982
ORLI—PITA	125.893	2000	96.41%	28.05%	0.414	-0.392	42.077	0.978
PRAV		7	30.45%	28.05%	0.479	-0.111	6.583	
ORLI—PRAV	0.013	3	96.43%	28.05%	0.439	0.758	0.082	0.988
ORLI—PRAV	0.032	5	98.25%	28.05%	0.494	0.622	0.204	0.982
ORLI—PRAV	0.079	10	93.74%	28.05%	0.472	0.418	0.511	0.988
ORLI—PRAV	0.200	30	93.02%	28.05%	0.457	0.236	1.249	0.980
ORLI—PRAV	0.501	100	97.16%	28.05%	0.440	0.068	3.040	0.992
ORLI—PRAV	1.259	100	96.22%	28.05%	0.445	0.012	4.003	0.576
ORLI—PRAV	3.162	200	96.20%	28.05%	0.392	0.093	3.002	0.214
ORLI—PRAV	7.943	100	91.58%	28.05%	0.361	0.131	2.586	0.109
ORLI—PRAV	19.953	200	93.91%	28.05%	0.468	-0.155	8.528	0.262
ORLI—PRAV	50.119	2000	95.19%	28.05%	0.370	-0.241	25.700	0.673
ORLI—PRAV	125.893	1000	92.36%	28.05%	0.452	-0.442	39.672	0.966
CETI		60	27.69%	27.03%	0.475	-0.569	58.505	
ATOR		30	28.44%	27.03%	0.438	-0.340	24.632	
CETI—ATOR	0.013	30	98.88%	27.03%	0.348	0.451	0.303	0.983
CETI—ATOR	0.032	20	94.58%	27.03%	0.470	0.327	0.759	0.987
CETI—ATOR	0.079	400	98.41%	27.03%	0.306	0.187	1.874	0.990
CETI—ATOR	0.200	100	98.69%	27.03%	0.432	0.071	2.891	0.638
CETI—ATOR	0.501	200	91.23%	27.03%	0.345	0.134	2.486	0.244
CETI—ATOR	1.259	60	96.22%	27.03%	0.486	0.098	2.262	0.112
CETI—ATOR	3.162	800	91.23%	27.03%	0.325	-0.024	8.048	0.241
CETI—ATOR	7.943	2000	90.59%	27.03%	0.359	-0.251	28.449	0.632
CETI—ATOR	19.953	5000	94.41%	27.03%	0.332	-0.297	50.703	0.970
CETI—ATOR	50.119	3000	93.77%	27.03%	0.381	-0.390	54.341	0.973
CETI—ATOR	125.893	1000	92.19%	27.03%	0.485	-0.576	55.851	0.973
ROSU		90	31.94%	27.03%	0.344	-0.361	67.924	
CETI—ROSU	0.013	40	94.33%	27.03%	0.385	0.326	0.715	0.849
CETI—ROSU	0.032	10	91.75%	27.03%	0.498	0.350	0.693	0.334
CETI—ROSU	0.079	10	92.12%	27.03%	0.492	0.419	0.499	0.101
CETI—ROSU	0.200	40	92.17%	27.03%	0.478	0.168	1.635	0.149

[0045]

CETI—ROSU	0.501	600	98.63%	27.03%	0.402	-0.136	10.264	0.477
CETI—ROSU	1.259	4000	99.75%	27.03%	0.360	-0.283	34.394	0.990
CETI—ROSU	3.162	2000	93.72%	27.03%	0.412	-0.411	45.088	0.981
CETI—ROSU	7.943	3000	93.72%	27.03%	0.389	-0.398	52.052	0.986
CETI—ROSU	19.953	5000	98.68%	27.03%	0.359	-0.354	54.964	0.980
CETI—ROSU	50.119	3000	91.51%	27.03%	0.365	-0.368	56.113	0.976
CETI—ROSU	125.893	4000	99.37%	27.03%	0.399	-0.432	57.625	0.992
FLUV		90	27.03%	27.03%	0.352	-0.410	85.364	
CETI—FLUV	0.013	40	90.10%	27.03%	0.387	0.264	1.039	0.984
CETI—FLUV	0.032	100	92.85%	27.03%	0.374	0.119	2.535	0.982
CETI—FLUV	0.079	500	97.36%	27.03%	0.365	-0.014	6.008	0.989
CETI—FLUV	0.200	400	96.13%	27.03%	0.450	-0.231	12.963	0.983
CETI—FLUV	0.501	700	91.19%	27.03%	0.417	-0.266	19.242	0.779
CETI—FLUV	1.259	500	99.30%	27.03%	0.455	-0.233	12.774	0.337
CETI—FLUV	3.162	500	91.93%	27.03%	0.328	0.029	5.459	0.114
CETI—FLUV	7.943	1000	99.50%	27.03%	0.324	0.023	5.795	0.108
CETI—FLUV	19.953	2000	99.40%	27.03%	0.367	-0.191	18.069	0.319
CETI—FLUV	50.119	3000	91.78%	27.03%	0.343	-0.292	43.233	0.749
CETI—FLUV	125.893	2000	94.94%	27.03%	0.448	-0.511	55.682	0.957
LORV		100	32.96%	27.03%	0.302	-0.308	81.664	
CETI—LORV	0.013	40	92.35%	27.03%	0.394	0.274	0.981	0.971
CETI—LORV	0.032	100	94.90%	27.03%	0.380	0.124	2.428	0.982
CETI—LORV	0.079	100	93.47%	27.03%	0.487	-0.098	5.715	0.979
CETI—LORV	0.200	400	97.85%	27.03%	0.415	-0.092	7.445	0.584
CETI—LORV	0.501	200	93.88%	27.03%	0.445	-0.057	5.442	0.226
CETI—LORV	1.259	300	96.25%	27.03%	0.382	0.035	4.121	0.111
CETI—LORV	3.162	300	92.37%	27.03%	0.483	-0.239	11.343	0.238
CETI—LORV	7.943	4000	94.08%	27.03%	0.323	-0.219	32.616	0.608
CETI—LORV	19.953	2000	93.89%	27.03%	0.412	-0.444	54.220	0.960
CETI—LORV	50.119	3000	93.41%	27.03%	0.372	-0.379	55.662	0.965
CETI—LORV	125.893	1000	90.99%	27.03%	0.491	-0.585	55.228	0.949
SIMV		90	29.77%	27.03%	0.454	-0.582	75.680	
CETI—SIMV	0.013	60	93.75%	27.03%	0.364	0.281	0.935	0.998
CETI—SIMV	0.032	200	97.63%	27.03%	0.355	0.144	2.268	0.986
CETI—SIMV	0.079	200	90.28%	27.03%	0.437	-0.050	5.401	0.991
CETI—SIMV	0.200	1000	92.38%	27.03%	0.324	-0.079	11.974	0.998
CETI—SIMV	0.501	600	97.65%	27.03%	0.447	-0.263	15.579	0.677
CETI—SIMV	1.259	400	93.28%	27.03%	0.409	-0.141	10.110	0.279
CETI—SIMV	3.162	300	95.48%	27.03%	0.407	-0.026	5.339	0.114
CETI—SIMV	7.943	400	99.08%	27.03%	0.451	-0.174	9.648	0.181
CETI—SIMV	19.953	1000	96.21%	27.03%	0.429	-0.344	27.096	0.481
CETI—SIMV	50.119	3000	97.02%	27.03%	0.401	-0.431	56.027	0.972
CETI—SIMV	125.893	2000	97.03%	27.03%	0.470	-0.554	56.510	0.972
PITA		50	32.86%	27.03%	0.317	-0.202	31.100	
CETI—PITA	0.013	40	94.14%	27.03%	0.335	0.408	0.388	0.997
CETI—PITA	0.032	20	95.18%	27.03%	0.481	0.280	0.956	0.988
CETI—PITA	0.079	300	97.95%	27.03%	0.329	0.147	2.365	0.998
CETI—PITA	0.200	1000	97.13%	27.03%	0.300	0.047	5.528	0.985
CETI—PITA	0.501	1000	99.84%	27.03%	0.348	-0.107	12.113	0.984
CETI—PITA	1.259	400	97.01%	27.03%	0.480	-0.283	14.209	0.606
CETI—PITA	3.162	500	94.39%	27.03%	0.378	-0.083	8.611	0.235
CETI—PITA	7.943	300	94.40%	27.03%	0.384	-0.019	5.660	0.120
CETI—PITA	19.953	1000	90.93%	27.03%	0.335	-0.113	13.931	0.261
CETI—PITA	50.119	7000	96.22%	27.03%	0.307	-0.212	37.073	0.657
CETI—PITA	125.893	7000	92.85%	27.03%	0.310	-0.272	55.796	0.968
PRAV		30	28.95%	27.03%	0.428	-0.357	29.287	
CETI—PRAV	0.013	9	94.93%	27.03%	0.494	0.487	0.364	0.995

[0046]

CETI—PRAV	0.032	20	91.88%	27.03%	0.444	0.331	0.730	0.801
CETI—PRAV	0.079	30	93.09%	27.03%	0.400	0.319	0.757	0.338
CETI—PRAV	0.200	30	95.76%	27.03%	0.419	0.357	0.622	0.117
CETI—PRAV	0.501	50	91.67%	27.03%	0.438	0.179	1.615	0.138
CETI—PRAV	1.259	700	98.65%	27.03%	0.385	-0.098	9.043	0.400
CETI—PRAV	3.162	2000	94.33%	27.03%	0.403	-0.339	32.402	0.904
CETI—PRAV	7.943	1000	91.58%	27.03%	0.478	-0.523	45.654	0.977
CETI—PRAV	19.953	1000	91.57%	27.03%	0.490	-0.571	52.022	0.978
CETI—PRAV	50.119	8000	96.62%	27.03%	0.319	-0.284	55.027	0.978
CETI—PRAV	125.893	2000	95.20%	27.03%	0.474	-0.559	56.206	0.976

[0047] 表3脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对表皮短杆菌的协同抑菌作用

[0048]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		80	28.82%	28.73%	0.490	-0.637	76.720	
ATOR		90	28.73%	28.73%	0.409	-0.512	90.383	
ORLI—ATOR	0.016	80	99.69%	28.73%	0.403	0.235	1.348	0.958
ORLI—ATOR	0.040	30	92.34%	28.73%	0.458	0.222	1.388	0.404
ORLI—ATOR	0.100	100	95.84%	28.73%	0.317	0.294	0.955	0.118
ORLI—ATOR	0.251	50	93.42%	28.73%	0.437	0.179	1.768	0.101
ORLI—ATOR	0.631	700	97.13%	28.73%	0.378	-0.114	11.527	0.352
ORLI—ATOR	1.585	2000	95.10%	28.73%	0.379	-0.334	43.591	0.872
ORLI—ATOR	3.981	1000	91.48%	28.73%	0.491	-0.592	61.723	0.976
ORLI—ATOR	10.000	4000	99.33%	28.73%	0.395	-0.441	69.418	0.982
ORLI—ATOR	25.119	2000	92.65%	28.73%	0.471	-0.589	72.429	0.976
ORLI—ATOR	63.096	4000	97.55%	28.73%	0.402	-0.463	73.937	0.977
ORLI—ATOR	158.489	6000	94.61%	28.73%	0.341	-0.351	74.164	0.972
ROSU		100	30.44%	28.73%	0.333	-0.370	93.916	
ORLI—ROSU	0.016	100	93.60%	28.73%	0.328	0.235	1.444	0.989
ORLI—ROSU	0.040	100	94.41%	28.73%	0.408	0.063	3.551	0.996
ORLI—ROSU	0.100	700	97.17%	28.73%	0.314	0.075	4.746	0.567
ORLI—ROSU	0.251	200	93.45%	28.73%	0.389	0.044	4.216	0.234
ORLI—ROSU	0.631	100	90.42%	28.73%	0.388	0.061	3.816	0.114
ORLI—ROSU	1.585	300	97.18%	28.73%	0.492	-0.216	10.553	0.208
ORLI—ROSU	3.981	1000	91.12%	28.73%	0.415	-0.343	32.891	0.517
ORLI—ROSU	10.000	4000	94.50%	28.73%	0.369	-0.391	68.676	0.968
ORLI—ROSU	25.119	9000	91.86%	28.73%	0.305	-0.279	72.230	0.972
ORLI—ROSU	63.096	4000	95.08%	28.73%	0.391	-0.442	73.472	0.970
ORLI—ROSU	158.489	6000	90.36%	28.73%	0.328	-0.326	73.607	0.964
FLUV		3	30.10%	28.73%	0.338	0.162	2.344	
ORLI—FLUV	0.016	1	96.08%	28.73%	0.467	0.958	0.036	0.982
ORLI—FLUV	0.040	1	90.79%	28.73%	0.444	0.876	0.047	0.508
ORLI—FLUV	0.100	3	97.58%	28.73%	0.380	0.792	0.047	0.201
ORLI—FLUV	0.251	4	90.31%	28.73%	0.343	0.689	0.067	0.115
ORLI—FLUV	0.631	10	99.26%	28.73%	0.475	0.497	0.362	0.250
ORLI—FLUV	1.585	100	91.37%	28.73%	0.350	0.171	2.144	0.605
ORLI—FLUV	3.981	800	99.35%	28.73%	0.356	-0.036	8.122	0.976
ORLI—FLUV	10.000	700	97.28%	28.73%	0.425	-0.239	17.341	0.966
ORLI—FLUV	25.119	4000	92.75%	28.73%	0.309	-0.179	32.295	0.969
ORLI—FLUV	63.096	6000	94.34%	28.73%	0.319	-0.252	49.287	0.976
ORLI—FLUV	158.489	4000	96.39%	28.73%	0.381	-0.393	61.201	0.962
LORV		30	29.29%	28.73%	0.315	-0.180	30.462	
ORLI—LORV	0.016	20	94.90%	28.73%	0.428	0.427	0.472	0.984
ORLI—LORV	0.040	40	91.18%	28.73%	0.395	0.260	1.175	0.984
ORLI—LORV	0.100	300	93.65%	28.73%	0.334	0.133	2.889	0.986
ORLI—LORV	0.251	200	90.93%	28.73%	0.422	-0.045	6.112	0.878
ORLI—LORV	0.631	500	95.61%	28.73%	0.352	0.005	6.330	0.412
ORLI—LORV	1.585	100	93.43%	28.73%	0.487	-0.034	4.557	0.154

[0049]

ORLI—LORV	3.981	100	93.98%	28.73%	0.485	-0.048	4.898	0.104
ORLI—LORV	10.000	1000	99.54%	28.73%	0.365	-0.153	16.128	0.263
ORLI—LORV	25.119	3000	91.63%	28.73%	0.335	-0.263	43.971	0.631
ORLI—LORV	63.096	12000	96.34%	28.73%	0.302	-0.270	70.323	0.953
ORLI—LORV	158.489	3000	92.87%	28.73%	0.390	-0.438	72.318	0.958
SIMV		40	31.83%	28.73%	0.380	-0.306	36.377	
ORLI—SIMV	0.016	40	94.66%	28.73%	0.362	0.375	0.572	0.999
ORLI—SIMV	0.040	50	94.73%	28.73%	0.436	0.221	1.418	0.997
ORLI—SIMV	0.100	200	95.07%	28.73%	0.401	0.071	3.470	0.999
ORLI—SIMV	0.251	100	98.19%	28.73%	0.494	-0.054	4.904	0.601
ORLI—SIMV	0.631	90	96.36%	28.73%	0.498	-0.019	4.113	0.233
ORLI—SIMV	1.585	100	92.78%	28.73%	0.401	0.068	3.509	0.107
ORLI—SIMV	3.981	500	91.14%	28.73%	0.379	-0.109	11.133	0.222
ORLI—SIMV	10.000	6000	97.81%	28.73%	0.316	-0.207	36.682	0.579
ORLI—SIMV	25.119	3000	99.95%	28.73%	0.451	-0.546	70.384	0.994
ORLI—SIMV	63.096	4000	90.12%	28.73%	0.364	-0.392	73.177	0.986
ORLI—SIMV	158.489	4000	98.04%	28.73%	0.393	-0.451	75.413	0.996
PITA		20	28.96%	28.73%	0.320	-0.133	20.596	
ORLI—PITA	0.016	20	90.86%	28.73%	0.344	0.458	0.319	0.982
ORLI—PITA	0.040	40	92.99%	28.73%	0.367	0.325	0.790	0.974
ORLI—PITA	0.100	100	98.99%	28.73%	0.411	0.168	1.949	0.972
ORLI—PITA	0.251	100	93.95%	28.73%	0.457	-0.021	4.722	0.974
ORLI—PITA	0.631	300	95.48%	28.73%	0.445	-0.142	9.229	0.830
ORLI—PITA	1.585	500	90.63%	28.73%	0.343	-0.018	7.745	0.338
ORLI—PITA	3.981	300	94.34%	28.73%	0.367	0.053	4.339	0.109
ORLI—PITA	10.000	700	99.38%	28.73%	0.359	-0.038	8.057	0.144
ORLI—PITA	25.119	700	97.16%	28.73%	0.490	-0.434	29.547	0.442
ORLI—PITA	63.096	2000	94.83%	28.73%	0.444	-0.532	69.804	0.964
ORLI—PITA	158.489	12000	98.56%	28.73%	0.313	-0.294	72.463	0.967
PRAV		10	29.89%	28.73%	0.362	-0.063	9.286	
ORLI—PRAV	0.016	9	94.98%	28.73%	0.369	0.595	0.147	0.999
ORLI—PRAV	0.040	40	93.21%	28.73%	0.306	0.457	0.280	0.760
ORLI—PRAV	0.100	30	90.48%	28.73%	0.301	0.455	0.276	0.301
ORLI—PRAV	0.251	10	90.30%	28.73%	0.358	0.500	0.255	0.113
ORLI—PRAV	0.631	50	91.42%	28.73%	0.368	0.279	1.057	0.194
ORLI—PRAV	1.585	800	96.78%	28.73%	0.325	0.018	6.741	0.546
ORLI—PRAV	3.981	3000	91.12%	28.73%	0.306	-0.139	24.684	0.989
ORLI—PRAV	10.000	3000	96.80%	28.73%	0.360	-0.296	41.605	0.990
ORLI—PRAV	25.119	6000	98.33%	28.73%	0.347	-0.322	57.216	0.991
ORLI—PRAV	63.096	12000	99.36%	28.73%	0.314	-0.287	67.049	0.988
ORLI—PRAV	158.489	2000	97.33%	28.73%	0.450	-0.548	71.466	0.980
CETI		10	30.45%	27.74%	0.367	-0.096	10.374	
ATOR		40	31.69%	27.74%	0.329	-0.211	30.514	
CETI—ATOR	0.016	10	93.27%	27.74%	0.434	0.432	0.441	0.954
CETI—ATOR	0.040	10	90.58%	27.74%	0.468	0.440	0.448	0.412
CETI—ATOR	0.100	8	93.36%	27.74%	0.472	0.516	0.313	0.133
CETI—ATOR	0.251	90	96.79%	27.74%	0.307	0.368	0.508	0.115
CETI—ATOR	0.631	60	91.13%	27.74%	0.452	0.104	2.424	0.360
CETI—ATOR	1.585	400	94.04%	27.74%	0.395	-0.066	7.397	0.866
CETI—ATOR	3.981	200	94.02%	27.74%	0.494	-0.201	9.338	0.977
CETI—ATOR	10.000	400	92.55%	27.74%	0.405	-0.125	9.884	0.985
CETI—ATOR	25.119	900	99.52%	27.74%	0.371	-0.092	9.926	0.970
CETI—ATOR	63.096	800	91.45%	27.74%	0.337	-0.062	10.175	0.986
CETI—ATOR	158.489	1000	93.64%	27.74%	0.306	-0.031	10.137	0.979
ROSU		100	31.66%	27.74%	0.440	-0.572	85.264	
CETI—ROSU	0.016	100	91.20%	27.74%	0.314	0.254	1.189	0.994
CETI—ROSU	0.040	30	95.62%	27.74%	0.472	0.253	1.129	0.442

[0050]

CETI—ROSU	0.100	50	92.36%	27.74%	0.343	0.335	0.679	0.145
CETI—ROSU	0.251	80	97.97%	27.74%	0.341	0.326	0.722	0.103
CETI—ROSU	0.631	100	96.10%	27.74%	0.409	0.098	2.748	0.316
CETI—ROSU	1.585	400	95.96%	27.74%	0.386	-0.061	7.547	0.783
CETI—ROSU	3.981	300	96.91%	27.74%	0.491	-0.211	9.870	0.980
CETI—ROSU	10.000	500	99.92%	27.74%	0.430	-0.153	10.006	0.976
CETI—ROSU	25.119	800	95.16%	27.74%	0.351	-0.075	10.106	0.979
CETI—ROSU	63.096	600	98.59%	27.74%	0.408	-0.133	10.129	0.978
CETI—ROSU	158.489	400	96.03%	27.74%	0.419	-0.145	10.144	0.979
FLUV		20	32.28%	27.74%	0.411	-0.212	15.528	
CETI—FLUV	0.016	20	90.82%	27.74%	0.322	0.505	0.196	0.817
CETI—FLUV	0.040	5	92.18%	27.74%	0.467	0.613	0.191	0.328
CETI—FLUV	0.100	9	97.31%	27.74%	0.393	0.595	0.156	0.116
CETI—FLUV	0.251	20	98.56%	27.74%	0.432	0.404	0.510	0.180
CETI—FLUV	0.631	400	99.04%	27.74%	0.330	0.139	2.624	0.521
CETI—FLUV	1.585	200	96.99%	27.74%	0.485	-0.137	7.153	0.980
CETI—FLUV	3.981	1000	98.95%	27.74%	0.328	-0.031	8.712	0.981
CETI—FLUV	10.000	300	92.79%	27.74%	0.441	-0.157	9.640	0.991
CETI—FLUV	25.119	500	95.43%	27.74%	0.394	-0.115	9.891	0.979
CETI—FLUV	63.096	300	95.04%	27.74%	0.467	-0.191	10.081	0.982
CETI—FLUV	158.489	600	96.50%	27.74%	0.387	-0.112	10.155	0.983
LORV		20	30.73%	27.74%	0.318	-0.072	12.583	
CETI—LORV	0.016	4	92.58%	27.74%	0.478	0.617	0.195	0.995
CETI—LORV	0.040	50	96.15%	27.74%	0.312	0.441	0.300	0.627
CETI—LORV	0.100	8	93.67%	27.74%	0.468	0.526	0.295	0.263
CETI—LORV	0.251	9	91.78%	27.74%	0.420	0.516	0.270	0.111
CETI—LORV	0.631	80	99.23%	27.74%	0.359	0.317	0.774	0.172
CETI—LORV	1.585	300	93.16%	27.74%	0.329	0.119	3.039	0.445
CETI—LORV	3.981	200	94.63%	27.74%	0.499	-0.173	8.000	0.931
CETI—LORV	10.000	300	92.86%	27.74%	0.425	-0.136	9.368	0.977
CETI—LORV	25.119	200	93.61%	27.74%	0.488	-0.205	9.745	0.970
CETI—LORV	63.096	600	99.48%	27.74%	0.401	-0.124	10.050	0.981
CETI—LORV	158.489	200	92.56%	27.74%	0.476	-0.201	10.148	0.983
SIMV		30	29.05%	27.74%	0.406	-0.291	25.203	
CETI—SIMV	0.016	30	91.41%	27.74%	0.350	0.423	0.383	0.996
CETI—SIMV	0.040	40	97.71%	27.74%	0.439	0.296	0.910	0.994
CETI—SIMV	0.100	300	99.60%	27.74%	0.335	0.177	1.991	0.982
CETI—SIMV	0.251	100	90.02%	27.74%	0.434	0.041	3.517	0.894
CETI—SIMV	0.631	100	96.10%	27.74%	0.385	0.134	2.356	0.375
CETI—SIMV	1.585	100	98.18%	27.74%	0.351	0.280	0.983	0.119
CETI—SIMV	3.981	100	99.56%	27.74%	0.358	0.250	1.193	0.127
CETI—SIMV	10.000	200	90.80%	27.74%	0.398	0.039	3.963	0.398
CETI—SIMV	25.119	1000	95.71%	27.74%	0.329	-0.044	9.511	0.932
CETI—SIMV	63.096	200	95.09%	27.74%	0.500	-0.220	9.906	0.961
CETI—SIMV	158.489	500	98.67%	27.74%	0.414	-0.137	9.976	0.964
PITA		70	27.74%	27.74%	0.387	-0.442	72.446	
CETI—PITA	0.016	40	93.29%	27.74%	0.409	0.273	1.025	0.992
CETI—PITA	0.040	60	93.33%	27.74%	0.462	0.115	2.251	0.997
CETI—PITA	0.100	400	93.81%	27.74%	0.306	0.130	3.047	0.714
CETI—PITA	0.251	60	96.74%	27.74%	0.476	0.138	1.968	0.298
CETI—PITA	0.631	20	94.10%	27.74%	0.477	0.286	0.961	0.114
CETI—PITA	1.585	70	97.88%	27.74%	0.428	0.197	1.539	0.162
CETI—PITA	3.981	300	99.79%	27.74%	0.400	0.019	4.428	0.442
CETI—PITA	10.000	600	90.53%	27.74%	0.352	-0.071	9.767	0.955
CETI—PITA	25.119	600	95.90%	27.74%	0.385	-0.109	10.060	0.975
CETI—PITA	63.096	400	97.42%	27.74%	0.432	-0.156	10.115	0.977
CETI—PITA	158.489	1000	99.89%	27.74%	0.348	-0.072	10.082	0.973

[0051]

PRAV		10	31.04%	27.74%	0.305	-0.022	9.595	
CETI—PRAV	0.016	5	92.83%	27.74%	0.426	0.630	0.148	0.988
CETI—PRAV	0.040	10	93.86%	27.74%	0.432	0.467	0.365	0.990
CETI—PRAV	0.100	20	90.83%	27.74%	0.488	0.308	0.866	0.986
CETI—PRAV	0.251	50	95.20%	27.74%	0.464	0.181	1.614	0.825
CETI—PRAV	0.631	40	96.43%	27.74%	0.479	0.207	1.406	0.368
CETI—PRAV	1.585	20	92.35%	27.74%	0.499	0.326	0.799	0.130
CETI—PRAV	3.981	70	97.13%	27.74%	0.366	0.293	0.905	0.111
CETI—PRAV	10.000	70	96.56%	27.74%	0.491	0.049	2.921	0.312
CETI—PRAV	25.119	400	93.69%	27.74%	0.369	-0.041	7.286	0.733
CETI—PRAV	63.096	600	91.74%	27.74%	0.364	-0.085	9.857	0.966
CETI—PRAV	158.489	500	95.58%	27.74%	0.398	-0.121	10.007	0.971

[0052] 表4脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对艰难梭菌的协同抑菌作用

[0053]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		9	32.39%	29.02%	0.304	0.029	7.193	
ATOR		30	29.02%	29.02%	0.313	-0.168	29.198	
ORLI—ATOR	0.008	20	93.20%	29.02%	0.326	0.503	0.223	0.990
ORLI—ATOR	0.020	40	93.09%	29.02%	0.338	0.383	0.533	0.990
ORLI—ATOR	0.050	20	91.41%	29.02%	0.479	0.254	1.192	0.981
ORLI—ATOR	0.126	60	93.28%	29.02%	0.453	0.119	2.384	0.980
ORLI—ATOR	0.316	70	90.13%	29.02%	0.387	0.189	1.826	0.452
ORLI—ATOR	0.794	100	95.74%	29.02%	0.314	0.326	0.770	0.140
ORLI—ATOR	1.995	20	94.49%	29.02%	0.447	0.356	0.712	0.111
ORLI—ATOR	5.012	200	92.30%	29.02%	0.333	0.158	2.496	0.364
ORLI—ATOR	12.589	400	99.43%	29.02%	0.385	-0.018	6.343	0.899
ORLI—ATOR	31.623	400	95.61%	29.02%	0.369	-0.019	6.885	0.965
ORLI—ATOR	79.433	200	97.81%	29.02%	0.453	-0.090	6.889	0.961
ROSU		40	31.71%	29.02%	0.424	-0.345	31.412	
ORLI—ROSU	0.008	20	97.04%	29.02%	0.356	0.511	0.240	0.995
ORLI—ROSU	0.020	30	99.35%	29.02%	0.403	0.388	0.573	0.994
ORLI—ROSU	0.050	40	94.39%	29.02%	0.421	0.258	1.193	0.924
ORLI—ROSU	0.126	30	94.41%	29.02%	0.465	0.268	1.115	0.437
ORLI—ROSU	0.316	60	90.03%	29.02%	0.320	0.341	0.694	0.166
ORLI—ROSU	0.794	90	96.74%	29.02%	0.312	0.353	0.628	0.112
ORLI—ROSU	1.995	70	98.05%	29.02%	0.438	0.181	1.776	0.275
ORLI—ROSU	5.012	400	99.58%	29.02%	0.364	0.053	4.503	0.655
ORLI—ROSU	12.589	200	90.42%	29.02%	0.422	-0.063	6.873	0.973
ORLI—ROSU	31.623	200	95.73%	29.02%	0.474	-0.111	7.015	0.982
ORLI—ROSU	79.433	200	92.23%	29.02%	0.432	-0.075	6.986	0.974
FLUV		2	32.40%	29.02%	0.309	0.270	1.166	
ORLI—FLUV	0.008	0	96.76%	29.02%	0.416	1.138	0.009	0.990
ORLI—FLUV	0.020	3	96.79%	29.02%	0.312	0.803	0.023	0.985
ORLI—FLUV	0.050	5	91.85%	29.02%	0.325	0.694	0.057	0.990
ORLI—FLUV	0.126	9	93.86%	29.02%	0.356	0.592	0.142	0.990
ORLI—FLUV	0.316	10	95.66%	29.02%	0.429	0.488	0.347	0.988
ORLI—FLUV	0.794	50	99.63%	29.02%	0.365	0.387	0.542	0.661
ORLI—FLUV	1.995	20	94.74%	29.02%	0.389	0.410	0.492	0.280
ORLI—FLUV	5.012	40	97.11%	29.02%	0.339	0.444	0.353	0.110
ORLI—FLUV	12.589	80	97.05%	29.02%	0.335	0.338	0.720	0.149
ORLI—FLUV	31.623	100	94.04%	29.02%	0.376	0.147	2.401	0.399
ORLI—FLUV	79.433	100	90.08%	29.02%	0.494	-0.085	5.732	0.859
LORV		100	31.81%	29.02%	0.418	-0.533	93.273	
ORLI—LORV	0.008	70	91.30%	29.02%	0.309	0.346	0.660	0.982
ORLI—LORV	0.020	30	92.14%	29.02%	0.477	0.213	1.452	0.982
ORLI—LORV	0.050	100	96.11%	29.02%	0.407	0.109	2.780	0.981
ORLI—LORV	0.126	200	98.59%	29.02%	0.410	0.028	4.366	0.979

[0054]

ORLI—LORV	0.316	200	95.35%	29.02%	0.415	-0.022	5.660	0.979
ORLI—LORV	0.794	200	99.96%	29.02%	0.397	0.091	3.180	0.485
ORLI—LORV	1.995	200	94.97%	29.02%	0.303	0.271	1.155	0.167
ORLI—LORV	5.012	20	94.81%	29.02%	0.450	0.342	0.765	0.108
ORLI—LORV	12.589	300	98.05%	29.02%	0.325	0.178	2.209	0.309
ORLI—LORV	31.623	800	98.56%	29.02%	0.321	0.052	5.521	0.769
ORLI—LORV	79.433	200	98.99%	29.02%	0.462	-0.099	6.949	0.967
SIMV		50	30.87%	29.02%	0.302	-0.196	40.754	
ORLI—SIMV	0.008	10	95.56%	29.02%	0.406	0.498	0.307	0.991
ORLI—SIMV	0.020	10	92.35%	29.02%	0.460	0.471	0.405	0.555
ORLI—SIMV	0.050	30	96.13%	29.02%	0.347	0.459	0.327	0.205
ORLI—SIMV	0.126	50	94.97%	29.02%	0.301	0.430	0.344	0.115
ORLI—SIMV	0.316	40	98.46%	29.02%	0.478	0.234	1.310	0.284
ORLI—SIMV	0.794	500	98.93%	29.02%	0.343	0.077	4.188	0.712
ORLI—SIMV	1.995	100	94.86%	29.02%	0.495	-0.110	6.431	0.973
ORLI—SIMV	5.012	500	98.92%	29.02%	0.376	-0.022	6.779	0.976
ORLI—SIMV	12.589	300	98.62%	29.02%	0.420	-0.065	7.008	0.988
ORLI—SIMV	31.623	300	95.97%	29.02%	0.405	-0.054	7.064	0.988
ORLI—SIMV	79.433	900	99.22%	29.02%	0.331	0.009	7.090	0.988
PITA		40	31.16%	29.02%	0.372	-0.280	34.249	
ORLI—PITA	0.008	6	96.73%	29.02%	0.500	0.585	0.257	0.980
ORLI—PITA	0.020	20	91.29%	29.02%	0.405	0.377	0.609	0.976
ORLI—PITA	0.050	30	95.18%	29.02%	0.498	0.225	1.354	0.977
ORLI—PITA	0.126	200	98.80%	29.02%	0.356	0.141	2.629	0.975
ORLI—PITA	0.316	300	94.47%	29.02%	0.339	0.093	3.820	0.884
ORLI—PITA	0.794	70	92.40%	29.02%	0.426	0.136	2.307	0.406
ORLI—PITA	1.995	30	94.93%	29.02%	0.462	0.294	0.980	0.151
ORLI—PITA	5.012	100	93.56%	29.02%	0.310	0.317	0.820	0.119
ORLI—PITA	12.589	50	97.17%	29.02%	0.491	0.123	2.195	0.310
ORLI—PITA	31.623	400	94.41%	29.02%	0.354	0.037	5.180	0.725
ORLI—PITA	79.433	500	93.51%	29.02%	0.354	-0.008	6.950	0.969
PRAV		100	32.25%	29.02%	0.307	-0.322	98.830	
ORLI—PRAV	0.008	30	93.15%	29.02%	0.413	0.354	0.699	0.988
ORLI—PRAV	0.020	30	95.33%	29.02%	0.477	0.279	1.054	0.681
ORLI—PRAV	0.050	70	97.88%	29.02%	0.351	0.327	0.787	0.268
ORLI—PRAV	0.126	90	99.67%	29.02%	0.306	0.394	0.459	0.101
ORLI—PRAV	0.316	30	93.66%	29.02%	0.441	0.282	1.043	0.178
ORLI—PRAV	0.794	100	91.48%	29.02%	0.384	0.091	3.304	0.501
ORLI—PRAV	1.995	300	90.48%	29.02%	0.385	-0.030	6.768	0.975
ORLI—PRAV	5.012	600	93.51%	29.02%	0.334	0.010	6.901	0.973
ORLI—PRAV	12.589	200	98.65%	29.02%	0.472	-0.108	6.959	0.973
ORLI—PRAV	31.623	700	99.01%	29.02%	0.351	-0.007	7.051	0.983
ORLI—PRAV	79.433	200	93.58%	29.02%	0.419	-0.065	7.059	0.982
CETI		60	32.08%	27.98%	0.477	-0.526	48.813	
ATOR		100	32.82%	27.98%	0.461	-0.612	85.787	
CETI—ATOR	0.008	20	99.35%	27.98%	0.487	0.366	0.664	0.988
CETI—ATOR	0.020	100	96.51%	27.98%	0.351	0.206	1.618	0.979
CETI—ATOR	0.050	50	97.57%	27.98%	0.492	0.148	1.853	0.469
CETI—ATOR	0.126	60	99.66%	27.98%	0.449	0.198	1.522	0.172
CETI—ATOR	0.316	200	95.97%	27.98%	0.356	0.182	1.876	0.108
CETI—ATOR	0.794	300	91.23%	27.98%	0.389	-0.068	7.838	0.276
CETI—ATOR	1.995	5000	96.94%	27.98%	0.304	-0.148	25.676	0.676
CETI—ATOR	5.012	3000	93.36%	27.98%	0.342	-0.277	42.495	0.969
CETI—ATOR	12.589	3000	99.41%	27.98%	0.388	-0.362	45.019	0.964
CETI—ATOR	31.623	2000	91.21%	27.98%	0.373	-0.342	46.111	0.962
CETI—ATOR	79.433	3000	96.53%	27.98%	0.388	-0.368	46.871	0.967
ROSU		70	28.71%	27.98%	0.491	-0.608	64.194	

[0055]

CETI—ROSU	0.008	50	99.51%	27.98%	0.358	0.386	0.504	0.999
CETI—ROSU	0.020	100	98.26%	27.98%	0.338	0.249	1.235	0.990
CETI—ROSU	0.050	500	97.73%	27.98%	0.302	0.158	2.535	0.840
CETI—ROSU	0.126	300	94.83%	27.98%	0.313	0.160	2.418	0.349
CETI—ROSU	0.316	200	90.08%	27.98%	0.308	0.226	1.495	0.104
CETI—ROSU	0.794	200	99.57%	27.98%	0.380	0.118	2.661	0.107
CETI—ROSU	1.995	500	95.33%	27.98%	0.416	-0.178	12.579	0.356
CETI—ROSU	5.012	3000	92.44%	27.98%	0.342	-0.252	36.105	0.852
CETI—ROSU	12.589	2000	92.40%	27.98%	0.403	-0.386	45.070	0.979
CETI—ROSU	31.623	1000	95.44%	27.98%	0.462	-0.491	46.865	0.983
CETI—ROSU	79.433	2000	94.32%	27.98%	0.418	-0.419	47.038	0.973
FLUV		50	27.98%	27.98%	0.359	-0.323	47.863	
CETI—FLUV	0.008	20	96.30%	27.98%	0.419	0.458	0.376	0.996
CETI—FLUV	0.020	20	91.85%	27.98%	0.449	0.350	0.698	0.745
CETI—FLUV	0.050	90	99.57%	27.98%	0.336	0.333	0.695	0.304
CETI—FLUV	0.126	10	96.05%	27.98%	0.491	0.410	0.543	0.101
CETI—FLUV	0.316	100	94.64%	27.98%	0.359	0.208	1.582	0.137
CETI—FLUV	0.794	700	97.16%	27.98%	0.360	-0.060	8.787	0.411
CETI—FLUV	1.995	3000	95.62%	27.98%	0.331	-0.208	29.842	0.924
CETI—FLUV	5.012	2000	96.78%	27.98%	0.416	-0.385	39.568	0.976
CETI—FLUV	12.589	4000	94.36%	27.98%	0.330	-0.263	43.949	0.973
CETI—FLUV	31.623	2000	92.72%	27.98%	0.427	-0.428	45.559	0.963
CETI—FLUV	79.433	1000	91.20%	27.98%	0.421	-0.424	46.900	0.973
LORV		10	28.13%	27.98%	0.400	-0.158	12.398	
CETI—LORV	0.008	3	97.32%	27.98%	0.473	0.779	0.088	0.896
CETI—LORV	0.020	20	97.22%	27.98%	0.309	0.584	0.104	0.421
CETI—LORV	0.050	3	96.44%	27.98%	0.461	0.749	0.096	0.156
CETI—LORV	0.126	8	95.76%	27.98%	0.393	0.598	0.155	0.103
CETI—LORV	0.316	50	92.21%	27.98%	0.373	0.290	0.941	0.259
CETI—LORV	0.794	300	96.04%	27.98%	0.392	0.001	5.135	0.627
CETI—LORV	1.995	1000	93.02%	27.98%	0.346	-0.138	16.116	0.982
CETI—LORV	5.012	800	90.85%	27.98%	0.419	-0.319	26.796	0.980
CETI—LORV	12.589	3000	94.61%	27.98%	0.344	-0.257	36.327	0.977
CETI—LORV	31.623	1000	91.15%	27.98%	0.425	-0.411	42.253	0.973
CETI—LORV	79.433	5000	92.28%	27.98%	0.322	-0.253	45.325	0.975
SIMV		100	32.42%	27.98%	0.324	-0.337	80.189	
CETI—SIMV	0.008	20	94.72%	27.98%	0.461	0.375	0.623	0.990
CETI—SIMV	0.020	80	94.68%	27.98%	0.387	0.207	1.538	0.993
CETI—SIMV	0.050	100	94.45%	27.98%	0.456	0.022	3.680	0.991
CETI—SIMV	0.126	400	96.28%	27.98%	0.376	0.006	5.353	0.640
CETI—SIMV	0.316	100	91.87%	27.98%	0.448	0.003	4.152	0.249
CETI—SIMV	0.794	100	97.49%	27.98%	0.467	0.044	3.200	0.116
CETI—SIMV	1.995	900	96.57%	27.98%	0.346	-0.050	9.012	0.241
CETI—SIMV	5.012	1000	95.14%	27.98%	0.390	-0.280	27.170	0.624
CETI—SIMV	12.589	9000	99.12%	27.98%	0.310	-0.234	45.651	0.980
CETI—SIMV	31.623	1000	94.81%	27.98%	0.489	-0.536	46.440	0.970
CETI—SIMV	79.433	3000	93.39%	27.98%	0.365	-0.332	47.289	0.976
PITA		70	31.29%	27.98%	0.409	-0.453	61.610	
CETI—PITA	0.008	30	98.55%	27.98%	0.399	0.407	0.479	0.989
CETI—PITA	0.020	30	96.15%	27.98%	0.494	0.247	1.168	0.974
CETI—PITA	0.050	200	94.47%	27.98%	0.363	0.113	2.870	0.988
CETI—PITA	0.126	400	98.07%	27.98%	0.404	-0.052	6.607	0.987
CETI—PITA	0.316	800	95.06%	27.98%	0.375	-0.132	12.555	0.902
CETI—PITA	0.794	1000	91.44%	27.98%	0.310	-0.021	9.314	0.381
CETI—PITA	1.995	200	97.24%	27.98%	0.396	0.039	4.054	0.116
CETI—PITA	5.012	200	99.76%	27.98%	0.448	-0.012	4.485	0.106
CETI—PITA	12.589	900	97.57%	27.98%	0.398	-0.201	16.173	0.352

[0056]

CETI—PITA	31.623	3000	90.21%	27.98%	0.327	-0.247	40.638	0.853
CETI—PITA	79.433	3000	97.39%	27.98%	0.385	-0.362	46.625	0.965
PRAV		60	31.86%	27.98%	0.367	-0.341	49.137	
CETI—PRAV	0.008	10	93.36%	27.98%	0.459	0.470	0.385	0.995
CETI—PRAV	0.020	20	90.41%	27.98%	0.442	0.290	0.949	0.988
CETI—PRAV	0.050	80	92.51%	27.98%	0.426	0.123	2.332	0.995
CETI—PRAV	0.126	200	91.91%	27.98%	0.442	-0.047	5.489	1.000
CETI—PRAV	0.316	300	97.83%	27.98%	0.486	-0.221	10.748	0.912
CETI—PRAV	0.794	500	94.97%	27.98%	0.392	-0.103	9.501	0.438
CETI—PRAV	1.995	300	99.43%	27.98%	0.427	-0.041	5.654	0.174
CETI—PRAV	5.012	100	95.84%	27.98%	0.470	-0.041	4.818	0.118
CETI—PRAV	12.589	1000	97.68%	27.98%	0.355	-0.107	12.320	0.272
CETI—PRAV	31.623	2000	99.63%	27.98%	0.416	-0.334	30.083	0.636
CETI—PRAV	79.433	1000	90.29%	27.98%	0.449	-0.472	47.134	0.978

[0057] 表5脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对破伤风梭菌的协同抑菌作用

[0058]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		30	31.68%	27.17%	0.387	-0.249	22.154	
ATOR		100	30.74%	27.17%	0.433	-0.570	87.784	
ORLI—ATOR	0.010	40	92.69%	27.17%	0.385	0.302	0.835	0.989
ORLI—ATOR	0.025	60	95.02%	27.17%	0.457	0.135	1.995	0.995
ORLI—ATOR	0.063	400	92.55%	27.17%	0.330	0.059	4.407	0.995
ORLI—ATOR	0.158	300	97.71%	27.17%	0.459	-0.155	8.475	0.992
ORLI—ATOR	0.398	900	90.21%	27.17%	0.348	-0.120	13.311	0.982
ORLI—ATOR	1.000	200	94.13%	27.17%	0.498	-0.209	9.238	0.522
ORLI—ATOR	2.512	300	92.00%	27.17%	0.354	0.052	4.180	0.208
ORLI—ATOR	6.310	200	96.09%	27.17%	0.386	0.118	2.501	0.117
ORLI—ATOR	15.849	700	93.52%	27.17%	0.316	0.038	5.485	0.252
ORLI—ATOR	39.811	1000	94.50%	27.17%	0.341	-0.112	13.429	0.610
ORLI—ATOR	100.000	2000	93.27%	27.17%	0.340	-0.180	21.325	0.965
ROSU		20	28.95%	27.17%	0.357	-0.135	13.868	
ORLI—ROSU	0.010	20	96.66%	27.17%	0.312	0.558	0.121	0.875
ORLI—ROSU	0.025	10	95.21%	27.17%	0.349	0.570	0.140	0.408
ORLI—ROSU	0.063	5	99.21%	27.17%	0.447	0.666	0.131	0.156
ORLI—ROSU	0.158	7	97.29%	27.17%	0.480	0.571	0.239	0.119
ORLI—ROSU	0.398	100	98.61%	27.17%	0.380	0.226	1.319	0.299
ORLI—ROSU	1.000	500	92.24%	27.17%	0.337	0.012	5.913	0.693
ORLI—ROSU	2.512	1000	91.35%	27.17%	0.332	-0.102	13.369	0.987
ORLI—ROSU	6.310	4000	99.08%	27.17%	0.307	-0.110	17.385	0.983
ORLI—ROSU	15.849	1000	98.86%	27.17%	0.414	-0.266	19.921	0.990
ORLI—ROSU	39.811	2000	93.51%	27.17%	0.321	-0.153	21.187	0.995
ORLI—ROSU	100.000	700	91.92%	27.17%	0.437	-0.311	21.622	0.992
FLUV		2	27.17%	27.17%	0.347	0.210	1.508	
ORLI—FLUV	0.010	2	96.25%	27.17%	0.332	0.880	0.015	0.977
ORLI—FLUV	0.025	1	90.60%	27.17%	0.461	0.930	0.037	0.986
ORLI—FLUV	0.063	7	94.03%	27.17%	0.362	0.645	0.093	0.986
ORLI—FLUV	0.158	30	97.96%	27.17%	0.318	0.516	0.171	0.722
ORLI—FLUV	0.398	5	94.13%	27.17%	0.472	0.628	0.176	0.301
ORLI—FLUV	1.000	10	99.13%	27.17%	0.378	0.578	0.155	0.110
ORLI—FLUV	2.512	20	96.08%	27.17%	0.458	0.418	0.480	0.148
ORLI—FLUV	6.310	200	95.03%	27.17%	0.355	0.115	2.771	0.416
ORLI—FLUV	15.849	800	94.50%	27.17%	0.354	-0.089	10.505	0.914
ORLI—FLUV	39.811	2000	91.56%	27.17%	0.306	-0.093	15.545	0.961
ORLI—FLUV	100.000	2000	98.09%	27.17%	0.343	-0.165	18.633	0.965
LORV		40	27.66%	27.17%	0.332	-0.268	42.361	
ORLI—LORV	0.010	50	99.64%	27.17%	0.344	0.403	0.415	0.998
ORLI—LORV	0.025	200	98.22%	27.17%	0.321	0.270	1.013	0.997

[0059]

ORLI—LORV	0.063	60	93.42%	27.17%	0.401	0.229	1.280	0.537
ORLI—LORV	0.158	50	99.80%	27.17%	0.436	0.246	1.144	0.222
ORLI—LORV	0.398	50	99.09%	27.17%	0.443	0.254	1.094	0.114
ORLI—LORV	1.000	70	92.43%	27.17%	0.484	0.033	3.108	0.214
ORLI—LORV	2.512	2000	94.81%	27.17%	0.306	-0.028	9.537	0.520
ORLI—LORV	6.310	500	98.20%	27.17%	0.497	-0.375	19.961	0.976
ORLI—LORV	15.849	1000	98.41%	27.17%	0.391	-0.245	20.989	0.979
ORLI—LORV	39.811	900	92.13%	27.17%	0.405	-0.267	21.425	0.980
ORLI—LORV	100.000	4000	96.88%	27.17%	0.304	-0.135	21.677	0.984
SIMV		50	32.12%	27.17%	0.444	-0.432	38.460	
ORLI—SIMV	0.010	30	95.96%	27.17%	0.376	0.431	0.377	0.997
ORLI—SIMV	0.025	30	97.04%	27.17%	0.466	0.289	0.917	0.990
ORLI—SIMV	0.063	300	99.69%	27.17%	0.348	0.155	2.168	0.991
ORLI—SIMV	0.158	300	99.07%	27.17%	0.394	0.006	4.713	0.986
ORLI—SIMV	0.398	700	99.94%	27.17%	0.337	0.035	5.031	0.556
ORLI—SIMV	1.000	200	96.46%	27.17%	0.373	0.096	2.965	0.211
ORLI—SIMV	2.512	300	94.70%	27.17%	0.314	0.174	2.052	0.114
ORLI—SIMV	6.310	200	96.54%	27.17%	0.478	-0.077	5.372	0.265
ORLI—SIMV	15.849	400	97.56%	27.17%	0.499	-0.303	14.176	0.663
ORLI—SIMV	39.811	1000	92.99%	27.17%	0.388	-0.244	21.335	0.977
ORLI—SIMV	100.000	2000	97.26%	27.17%	0.372	-0.224	21.440	0.973
PITA		20	31.80%	27.17%	0.429	-0.243	15.784	
ORLI—PITA	0.010	4	92.52%	27.17%	0.457	0.645	0.153	0.976
ORLI—PITA	0.025	10	92.43%	27.17%	0.446	0.457	0.384	0.985
ORLI—PITA	0.063	100	99.78%	27.17%	0.360	0.281	0.944	0.991
ORLI—PITA	0.158	80	97.13%	27.17%	0.445	0.117	2.224	0.989
ORLI—PITA	0.398	200	92.34%	27.17%	0.395	0.002	4.805	0.982
ORLI—PITA	1.000	200	91.99%	27.17%	0.438	-0.089	6.658	0.722
ORLI—PITA	2.512	400	95.40%	27.17%	0.335	0.065	4.130	0.291
ORLI—PITA	6.310	100	98.57%	27.17%	0.406	0.137	2.149	0.119
ORLI—PITA	15.849	700	98.39%	27.17%	0.320	0.072	4.198	0.206
ORLI—PITA	39.811	700	96.39%	27.17%	0.394	-0.152	11.849	0.554
ORLI—PITA	100.000	2000	90.35%	27.17%	0.337	-0.174	20.913	0.957
PRAV		100	28.79%	27.17%	0.425	-0.554	87.975	
ORLI—PRAV	0.010	30	94.93%	27.17%	0.455	0.308	0.831	0.982
ORLI—PRAV	0.025	300	98.13%	27.17%	0.324	0.176	1.982	0.986
ORLI—PRAV	0.063	100	92.15%	27.17%	0.441	-0.012	4.387	0.988
ORLI—PRAV	0.158	2000	98.10%	27.17%	0.302	0.007	7.528	0.880
ORLI—PRAV	0.398	700	93.06%	27.17%	0.310	0.041	5.565	0.410
ORLI—PRAV	1.000	50	90.30%	27.17%	0.497	0.052	2.769	0.156
ORLI—PRAV	2.512	100	90.70%	27.17%	0.372	0.131	2.394	0.119
ORLI—PRAV	6.310	100	90.26%	27.17%	0.493	-0.124	6.333	0.297
ORLI—PRAV	15.849	2000	91.56%	27.17%	0.302	-0.085	15.083	0.692
ORLI—PRAV	39.811	1000	93.00%	27.17%	0.379	-0.232	21.366	0.971
ORLI—PRAV	100.000	1000	99.23%	27.17%	0.429	-0.300	21.528	0.974
CETI		70	32.84%	27.04%	0.342	-0.311	50.070	
ATOR		100	31.50%	27.04%	0.392	-0.486	84.884	
CETI—ATOR	0.010	100	95.40%	27.04%	0.326	0.297	0.830	0.994
CETI—ATOR	0.025	100	92.17%	27.04%	0.359	0.160	2.030	0.993
CETI—ATOR	0.063	500	93.39%	27.04%	0.329	0.046	4.812	0.994
CETI—ATOR	0.158	500	93.42%	27.04%	0.399	-0.138	10.591	0.999
CETI—ATOR	0.398	2000	99.52%	27.04%	0.338	-0.117	14.022	0.695
CETI—ATOR	1.000	200	96.67%	27.04%	0.491	-0.196	8.888	0.282
CETI—ATOR	2.512	300	96.31%	27.04%	0.378	0.041	4.056	0.100
CETI—ATOR	6.310	300	93.18%	27.04%	0.393	-0.057	6.797	0.148
CETI—ATOR	15.849	1000	92.06%	27.04%	0.351	-0.191	20.633	0.427
CETI—ATOR	39.811	4000	94.94%	27.04%	0.351	-0.314	46.229	0.937

[0060]

CETI—ATOR	100.000	1000	93.91%	27.04%	0.499	-0.573	49.004	0.984
ROSU		20	30.77%	27.04%	0.420	-0.270	19.355	
CETI—ROSU	0.010	6	91.59%	27.04%	0.424	0.581	0.184	0.956
CETI—ROSU	0.025	10	99.12%	27.04%	0.405	0.558	0.196	0.406
CETI—ROSU	0.063	10	99.42%	27.04%	0.366	0.570	0.152	0.127
CETI—ROSU	0.158	30	97.54%	27.04%	0.368	0.442	0.342	0.118
CETI—ROSU	0.398	100	97.80%	27.04%	0.418	0.101	2.536	0.380
CETI—ROSU	1.000	500	98.61%	27.04%	0.454	-0.231	12.723	0.911
CETI—ROSU	2.512	700	91.87%	27.04%	0.446	-0.345	23.923	0.970
CETI—ROSU	6.310	5000	95.23%	27.04%	0.314	-0.214	34.803	0.980
CETI—ROSU	15.849	2000	94.26%	27.04%	0.400	-0.379	41.812	0.971
CETI—ROSU	39.811	1000	97.21%	27.04%	0.485	-0.537	46.177	0.982
CETI—ROSU	100.000	1000	92.27%	27.04%	0.480	-0.536	47.817	0.980
FLUV		80	27.17%	27.04%	0.306	-0.307	77.412	
CETI—FLUV	0.010	20	97.20%	27.04%	0.462	0.329	0.747	0.980
CETI—FLUV	0.025	100	91.65%	27.04%	0.374	0.172	1.828	0.977
CETI—FLUV	0.063	80	93.46%	27.04%	0.488	0.013	3.362	0.755
CETI—FLUV	0.158	70	92.02%	27.04%	0.470	0.051	2.933	0.298
CETI—FLUV	0.398	40	93.35%	27.04%	0.493	0.123	1.995	0.105
CETI—FLUV	1.000	200	97.08%	27.04%	0.421	-0.037	5.364	0.176
CETI—FLUV	2.512	2000	91.25%	27.04%	0.321	-0.150	20.431	0.513
CETI—FLUV	6.310	4000	96.61%	27.04%	0.358	-0.317	43.759	0.964
CETI—FLUV	15.849	1000	93.50%	27.04%	0.452	-0.485	46.802	0.973
CETI—FLUV	39.811	3000	96.75%	27.04%	0.395	-0.391	47.354	0.961
CETI—FLUV	100.000	1000	93.44%	27.04%	0.477	-0.530	47.737	0.960
LORV		60	27.16%	27.04%	0.301	-0.267	60.663	
CETI—LORV	0.010	20	96.43%	27.04%	0.450	0.371	0.599	1.000
CETI—LORV	0.025	40	93.06%	27.04%	0.411	0.266	1.024	0.692
CETI—LORV	0.063	30	94.46%	27.04%	0.467	0.278	0.962	0.270
CETI—LORV	0.158	100	96.63%	27.04%	0.328	0.277	0.951	0.118
CETI—LORV	0.398	200	92.39%	27.04%	0.363	0.059	3.825	0.235
CETI—LORV	1.000	1000	93.88%	27.04%	0.364	-0.178	17.034	0.621
CETI—LORV	2.512	6000	94.58%	27.04%	0.310	-0.216	36.954	0.981
CETI—LORV	6.310	3000	94.43%	27.04%	0.358	-0.316	43.572	0.984
CETI—LORV	15.849	1000	91.12%	27.04%	0.461	-0.499	46.825	0.984
CETI—LORV	39.811	1000	94.20%	27.04%	0.458	-0.499	47.696	0.972
CETI—LORV	100.000	4000	98.41%	27.04%	0.380	-0.370	48.633	0.979
SIMV		100	30.64%	27.04%	0.316	-0.327	77.737	
CETI—SIMV	0.010	60	96.83%	27.04%	0.367	0.314	0.759	0.992
CETI—SIMV	0.025	100	96.48%	27.04%	0.405	0.161	1.866	0.993
CETI—SIMV	0.063	100	92.39%	27.04%	0.449	-0.020	4.438	0.994
CETI—SIMV	0.158	400	93.61%	27.04%	0.415	-0.142	9.861	0.997
CETI—SIMV	0.398	4000	97.28%	27.04%	0.309	-0.124	18.791	0.982
CETI—SIMV	1.000	1000	94.93%	27.04%	0.361	-0.142	13.870	0.455
CETI—SIMV	2.512	300	90.75%	27.04%	0.397	-0.050	6.437	0.162
CETI—SIMV	6.310	700	95.59%	27.04%	0.315	0.063	4.576	0.101
CETI—SIMV	15.849	500	92.96%	27.04%	0.413	-0.191	13.138	0.273
CETI—SIMV	39.811	1000	98.40%	27.04%	0.443	-0.405	33.432	0.678
CETI—SIMV	100.000	2000	93.01%	27.04%	0.439	-0.469	48.193	0.969
PITA		60	30.27%	27.04%	0.371	-0.348	46.674	
CETI—PITA	0.010	80	97.17%	27.04%	0.312	0.379	0.449	0.971
CETI—PITA	0.025	30	99.34%	27.04%	0.490	0.247	1.117	0.975
CETI—PITA	0.063	70	98.16%	27.04%	0.497	0.053	2.738	0.985
CETI—PITA	0.158	700	97.91%	27.04%	0.349	-0.009	6.323	0.981
CETI—PITA	0.398	300	97.81%	27.04%	0.461	-0.135	7.548	0.557
CETI—PITA	1.000	300	94.21%	27.04%	0.397	-0.027	5.613	0.232
CETI—PITA	2.512	300	93.68%	27.04%	0.347	0.075	3.660	0.104

[0061]

CETI—PITA	6.310	200	91.58%	27.04%	0.465	-0.134	7.396	0.173
CETI—PITA	15.849	800	93.93%	27.04%	0.420	-0.281	20.534	0.438
CETI—PITA	39.811	3000	91.89%	27.04%	0.364	-0.327	43.853	0.899
CETI—PITA	100.000	1000	97.48%	27.04%	0.483	-0.541	47.911	0.967
PRAV		60	27.04%	27.04%	0.381	-0.419	64.568	
CETI—PRAV	0.010	20	93.19%	27.04%	0.429	0.361	0.614	0.963
CETI—PRAV	0.025	70	90.25%	27.04%	0.307	0.330	0.641	0.408
CETI—PRAV	0.063	40	90.43%	27.04%	0.322	0.379	0.460	0.122
CETI—PRAV	0.158	90	93.87%	27.04%	0.337	0.285	0.904	0.106
CETI—PRAV	0.398	200	99.54%	27.04%	0.473	-0.102	6.118	0.360
CETI—PRAV	1.000	4000	92.47%	27.04%	0.303	-0.153	24.920	0.884
CETI—PRAV	2.512	1000	93.65%	27.04%	0.421	-0.395	38.009	0.993
CETI—PRAV	6.310	1000	93.52%	27.04%	0.452	-0.474	44.387	0.995
CETI—PRAV	15.849	4000	95.72%	27.04%	0.364	-0.338	47.027	0.985
CETI—PRAV	39.811	4000	94.47%	27.04%	0.348	-0.318	49.007	0.998
CETI—PRAV	100.000	4000	96.05%	27.04%	0.355	-0.331	49.631	0.999

[0062] 表6脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂对甲型副伤寒沙门菌的协同抑菌作用

[0063]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		90	29.84%	27.22%	0.430	-0.539	77.077	
ATOR		100	32.78%	27.22%	0.463	-0.625	86.723	
ORLI—ATOR	0.013	20	90.24%	27.22%	0.473	0.257	1.075	0.998
ORLI—ATOR	0.032	300	95.48%	27.22%	0.344	0.127	2.644	0.999
ORLI—ATOR	0.079	300	95.19%	27.22%	0.424	-0.064	6.231	0.985
ORLI—ATOR	0.200	700	99.40%	27.22%	0.411	-0.181	12.675	0.897
ORLI—ATOR	0.501	1000	91.36%	27.22%	0.322	-0.075	11.958	0.430
ORLI—ATOR	1.259	400	90.72%	27.22%	0.379	-0.062	7.637	0.169
ORLI—ATOR	3.162	300	90.07%	27.22%	0.379	-0.043	6.819	0.113
ORLI—ATOR	7.943	600	93.90%	27.22%	0.448	-0.292	18.240	0.263
ORLI—ATOR	19.953	4000	93.34%	27.22%	0.348	-0.306	45.633	0.618
ORLI—ATOR	50.119	2000	94.14%	27.22%	0.473	-0.611	73.884	0.976
ORLI—ATOR	125.893	7000	99.72%	27.22%	0.372	-0.425	74.455	0.973
ROSU		50	31.76%	27.22%	0.326	-0.233	35.275	
ORLI—ROSU	0.013	40	98.19%	27.22%	0.354	0.400	0.436	0.987
ORLI—ROSU	0.032	20	95.34%	27.22%	0.451	0.335	0.728	0.662
ORLI—ROSU	0.079	20	96.80%	27.22%	0.470	0.336	0.731	0.271
ORLI—ROSU	0.200	20	99.68%	27.22%	0.495	0.362	0.659	0.102
ORLI—ROSU	0.501	60	93.29%	27.22%	0.467	0.107	2.258	0.157
ORLI—ROSU	1.259	900	99.39%	27.22%	0.387	-0.149	12.249	0.435
ORLI—ROSU	3.162	800	90.46%	27.22%	0.495	-0.534	42.642	0.935
ORLI—ROSU	7.943	11000	97.66%	27.22%	0.309	-0.273	58.237	0.963
ORLI—ROSU	19.953	3000	92.20%	27.22%	0.378	-0.419	67.040	0.965
ORLI—ROSU	50.119	10000	94.75%	27.22%	0.313	-0.306	70.514	0.955
ORLI—ROSU	125.893	2000	90.62%	27.22%	0.480	-0.624	73.399	0.969
FLUV		60	31.11%	27.22%	0.337	-0.299	49.523	
ORLI—FLUV	0.013	60	96.12%	27.22%	0.345	0.346	0.610	0.987
ORLI—FLUV	0.032	100	97.09%	27.22%	0.359	0.206	1.524	0.993
ORLI—FLUV	0.079	500	92.12%	27.22%	0.303	0.101	3.678	0.983
ORLI—FLUV	0.200	200	90.04%	27.22%	0.465	-0.114	6.757	0.772
ORLI—FLUV	0.501	600	99.07%	27.22%	0.360	-0.013	6.217	0.331
ORLI—FLUV	1.259	100	95.10%	27.22%	0.466	-0.013	4.100	0.119
ORLI—FLUV	3.162	600	97.06%	27.22%	0.367	-0.037	6.967	0.135
ORLI—FLUV	7.943	2000	95.55%	27.22%	0.363	-0.231	24.423	0.379
ORLI—FLUV	19.953	2000	98.14%	27.22%	0.495	-0.612	60.859	0.851
ORLI—FLUV	50.119	9000	94.06%	27.22%	0.315	-0.314	72.067	0.964
ORLI—FLUV	125.893	4000	99.28%	27.22%	0.411	-0.493	73.128	0.960
LORV		8	27.22%	27.22%	0.399	-0.094	8.282	

[0064]

ORLI—LORV	0.013	20	99.33%	27.22%	0.324	0.590	0.104	1.000
ORLI—LORV	0.032	8	90.79%	27.22%	0.424	0.521	0.260	0.995
ORLI—LORV	0.079	20	93.56%	27.22%	0.480	0.364	0.644	0.988
ORLI—LORV	0.200	200	93.44%	27.22%	0.318	0.206	1.611	0.996
ORLI—LORV	0.501	100	90.76%	27.22%	0.370	0.121	2.555	0.649
ORLI—LORV	1.259	100	94.68%	27.22%	0.422	0.111	2.415	0.263
ORLI—LORV	3.162	50	94.50%	27.22%	0.488	0.114	2.112	0.108
ORLI—LORV	7.943	700	96.48%	27.22%	0.338	-0.003	6.530	0.184
ORLI—LORV	19.953	2000	93.79%	27.22%	0.377	-0.259	25.795	0.491
ORLI—LORV	50.119	4000	98.26%	27.22%	0.393	-0.437	63.429	0.976
ORLI—LORV	125.893	2000	93.58%	27.22%	0.475	-0.603	69.635	0.970
SIMV		30	32.78%	27.22%	0.490	-0.405	24.168	
ORLI—SIMV	0.013	20	94.55%	27.22%	0.368	0.464	0.302	0.996
ORLI—SIMV	0.032	20	92.12%	27.22%	0.449	0.327	0.753	0.995
ORLI—SIMV	0.079	100	95.20%	27.22%	0.363	0.173	1.872	1.000
ORLI—SIMV	0.200	100	99.96%	27.22%	0.492	-0.050	4.530	0.998
ORLI—SIMV	0.501	200	98.52%	27.22%	0.453	-0.089	6.269	0.599
ORLI—SIMV	1.259	600	95.35%	27.22%	0.321	0.057	4.694	0.215
ORLI—SIMV	3.162	100	91.59%	27.22%	0.469	-0.015	4.107	0.107
ORLI—SIMV	7.943	1000	97.60%	27.22%	0.354	-0.145	15.097	0.275
ORLI—SIMV	19.953	4000	97.95%	27.22%	0.367	-0.343	47.689	0.718
ORLI—SIMV	50.119	4000	97.10%	27.22%	0.403	-0.474	70.856	0.978
ORLI—SIMV	125.893	3000	96.66%	27.22%	0.434	-0.538	73.157	0.973
PITA		20	32.09%	27.22%	0.455	-0.314	19.477	
ORLI—PITA	0.013	40	99.94%	27.22%	0.321	0.471	0.240	0.983
ORLI—PITA	0.032	20	99.69%	27.22%	0.462	0.379	0.587	0.960
ORLI—PITA	0.079	100	98.36%	27.22%	0.320	0.336	0.632	0.417
ORLI—PITA	0.200	30	90.06%	27.22%	0.370	0.383	0.503	0.136
ORLI—PITA	0.501	70	96.04%	27.22%	0.370	0.269	1.023	0.118
ORLI—PITA	1.259	100	92.92%	27.22%	0.493	-0.136	6.754	0.363
ORLI—PITA	3.162	2000	97.65%	27.22%	0.390	-0.303	29.812	0.871
ORLI—PITA	7.943	3000	94.53%	27.22%	0.389	-0.386	49.537	0.963
ORLI—PITA	19.953	2000	93.28%	27.22%	0.416	-0.472	61.300	0.953
ORLI—PITA	50.119	4000	96.22%	27.22%	0.394	-0.451	68.509	0.959
ORLI—PITA	125.893	6000	90.85%	27.22%	0.325	-0.332	71.869	0.962
PRAV		80	31.62%	27.22%	0.407	-0.468	65.584	
ORLI—PRAV	0.013	20	93.48%	27.22%	0.474	0.316	0.807	0.988
ORLI—PRAV	0.032	90	92.99%	27.22%	0.403	0.151	2.002	0.991
ORLI—PRAV	0.079	100	93.12%	27.22%	0.397	0.074	3.153	0.646
ORLI—PRAV	0.200	200	91.80%	27.22%	0.378	0.094	2.969	0.265
ORLI—PRAV	0.501	70	95.25%	27.22%	0.481	0.075	2.572	0.112
ORLI—PRAV	1.259	300	96.26%	27.22%	0.436	-0.106	7.365	0.185
ORLI—PRAV	3.162	700	91.78%	27.22%	0.461	-0.389	27.243	0.485
ORLI—PRAV	7.943	2000	96.56%	27.22%	0.443	-0.533	65.804	0.980
ORLI—PRAV	19.953	2000	95.35%	27.22%	0.496	-0.646	71.020	0.976
ORLI—PRAV	50.119	9000	99.55%	27.22%	0.343	-0.368	73.396	0.975
ORLI—PRAV	125.893	2000	92.27%	27.22%	0.427	-0.529	74.909	0.981
CETI		100	30.68%	27.09%	0.303	-0.310	82.825	
ATOR		40	27.09%	27.09%	0.348	-0.278	37.864	
CETI—ATOR	0.013	60	95.42%	27.09%	0.321	0.376	0.471	0.993
CETI—ATOR	0.032	90	92.31%	27.09%	0.342	0.248	1.166	0.988
CETI—ATOR	0.079	200	94.27%	27.09%	0.367	0.102	2.878	0.992
CETI—ATOR	0.200	600	92.64%	27.09%	0.332	0.011	6.056	0.875
CETI—ATOR	0.501	200	98.64%	27.09%	0.448	-0.077	5.995	0.388
CETI—ATOR	1.259	200	97.88%	27.09%	0.427	0.014	3.992	0.132
CETI—ATOR	3.162	800	97.85%	27.09%	0.324	0.040	5.177	0.106
CETI—ATOR	7.943	900	92.86%	27.09%	0.396	-0.245	20.112	0.310

[0065]

CETI—ATOR	19.953	2000	90.04%	27.09%	0.421	-0.464	55.518	0.744
CETI—ATOR	50.119	5000	90.07%	27.09%	0.353	-0.396	77.269	0.974
CETI—ATOR	125.893	2000	95.30%	27.09%	0.464	-0.611	79.850	0.981
ROSU		50	29.83%	27.09%	0.451	-0.461	41.943	
CETI—ROSU	0.013	20	95.00%	27.09%	0.444	0.398	0.518	0.987
CETI—ROSU	0.032	70	98.65%	27.09%	0.419	0.224	1.291	0.989
CETI—ROSU	0.079	90	95.97%	27.09%	0.472	0.035	3.158	0.986
CETI—ROSU	0.200	800	90.60%	27.09%	0.311	-0.003	7.600	1.000
CETI—ROSU	0.501	300	91.61%	27.09%	0.438	-0.144	8.843	0.527
CETI—ROSU	1.259	400	91.31%	27.09%	0.360	-0.036	7.116	0.221
CETI—ROSU	3.162	1000	99.29%	27.09%	0.316	0.028	5.861	0.115
CETI—ROSU	7.943	300	91.68%	27.09%	0.467	-0.264	13.946	0.210
CETI—ROSU	19.953	1000	98.30%	27.09%	0.499	-0.518	38.176	0.507
CETI—ROSU	50.119	3000	91.46%	27.09%	0.393	-0.472	78.014	0.979
CETI—ROSU	125.893	2000	92.34%	27.09%	0.447	-0.576	78.883	0.967
FLUV		100	32.55%	27.09%	0.367	-0.434	82.926	
CETI—FLUV	0.013	30	93.35%	27.09%	0.457	0.265	1.028	0.997
CETI—FLUV	0.032	40	91.80%	27.09%	0.449	0.177	1.620	0.637
CETI—FLUV	0.079	50	92.00%	27.09%	0.415	0.209	1.411	0.231
CETI—FLUV	0.200	40	93.54%	27.09%	0.450	0.207	1.384	0.100
CETI—FLUV	0.501	1000	92.92%	27.09%	0.301	0.021	6.767	0.245
CETI—FLUV	1.259	2000	98.67%	27.09%	0.418	-0.351	30.657	0.664
CETI—FLUV	3.162	10000	94.45%	27.09%	0.303	-0.275	62.704	0.996
CETI—FLUV	7.943	3000	98.42%	27.09%	0.451	-0.569	72.802	0.990
CETI—FLUV	19.953	3000	98.41%	27.09%	0.461	-0.603	78.406	0.994
CETI—FLUV	50.119	7000	96.07%	27.09%	0.352	-0.398	79.560	0.980
CETI—FLUV	125.893	10000	90.94%	27.09%	0.307	-0.315	81.152	0.988
LORV		100	29.63%	27.09%	0.475	-0.672	96.905	
CETI—LORV	0.013	100	95.10%	27.09%	0.334	0.244	1.201	0.999
CETI—LORV	0.032	80	96.61%	27.09%	0.427	0.163	1.791	0.606
CETI—LORV	0.079	60	92.83%	27.09%	0.422	0.169	1.742	0.247
CETI—LORV	0.200	80	99.70%	27.09%	0.449	0.153	1.835	0.117
CETI—LORV	0.501	200	94.23%	27.09%	0.425	-0.077	6.581	0.215
CETI—LORV	1.259	1000	99.13%	27.09%	0.442	-0.359	26.698	0.541
CETI—LORV	3.162	5000	99.21%	27.09%	0.381	-0.417	63.718	0.977
CETI—LORV	7.943	8000	99.69%	27.09%	0.355	-0.392	73.679	0.985
CETI—LORV	19.953	3000	98.99%	27.09%	0.472	-0.623	78.273	0.986
CETI—LORV	50.119	8000	97.95%	27.09%	0.350	-0.394	79.435	0.975
CETI—LORV	125.893	13000	95.10%	27.09%	0.306	-0.312	79.808	0.970
SIMV		10	27.39%	27.09%	0.410	-0.171	11.939	
CETI—SIMV	0.013	5	91.14%	27.09%	0.418	0.617	0.149	0.992
CETI—SIMV	0.032	10	92.47%	27.09%	0.416	0.503	0.276	0.735
CETI—SIMV	0.079	10	94.97%	27.09%	0.410	0.482	0.306	0.326
CETI—SIMV	0.200	30	98.24%	27.09%	0.357	0.469	0.279	0.120
CETI—SIMV	0.501	10	93.87%	27.09%	0.500	0.361	0.659	0.118
CETI—SIMV	1.259	300	98.05%	27.09%	0.394	0.031	4.061	0.319
CETI—SIMV	3.162	900	97.90%	27.09%	0.417	-0.260	18.768	0.724
CETI—SIMV	7.943	6000	90.91%	27.09%	0.301	-0.222	43.455	0.983
CETI—SIMV	19.953	4000	95.67%	27.09%	0.378	-0.400	59.967	0.976
CETI—SIMV	50.119	2000	91.33%	27.09%	0.474	-0.607	71.279	0.980
CETI—SIMV	125.893	2000	94.67%	27.09%	0.466	-0.609	77.220	0.984
PITA		30	31.18%	27.09%	0.333	-0.154	18.876	
CETI—PITA	0.013	8	94.97%	27.09%	0.438	0.548	0.234	0.987
CETI—PITA	0.032	40	93.70%	27.09%	0.351	0.373	0.513	0.866
CETI—PITA	0.079	20	91.14%	27.09%	0.441	0.374	0.584	0.397
CETI—PITA	0.200	40	99.62%	27.09%	0.377	0.377	0.522	0.145
CETI—PITA	0.501	100	92.80%	27.09%	0.327	0.279	0.944	0.111

[0066]

CETI—PITA	1.259	200	98.33%	27.09%	0.493	-0.093	5.456	0.295
CETI—PITA	3.162	4000	94.26%	27.09%	0.305	-0.151	24.202	0.698
CETI—PITA	7.943	5000	91.74%	27.09%	0.331	-0.296	51.606	0.967
CETI—PITA	19.953	3000	98.50%	27.09%	0.417	-0.485	64.968	0.957
CETI—PITA	50.119	11000	95.20%	27.09%	0.312	-0.313	74.047	0.972
CETI—PITA	125.893	4000	98.25%	27.09%	0.408	-0.500	77.197	0.965
PRAV		50	29.20%	27.09%	0.425	-0.435	45.751	
CETI—PRAV	0.013	50	98.09%	27.09%	0.363	0.362	0.562	0.983
CETI—PRAV	0.032	70	92.77%	27.09%	0.391	0.212	1.413	0.994
CETI—PRAV	0.079	100	93.82%	27.09%	0.411	0.051	3.434	0.986
CETI—PRAV	0.200	200	93.44%	27.09%	0.472	-0.159	8.131	0.989
CETI—PRAV	0.501	300	93.40%	27.09%	0.424	-0.138	9.220	0.513
CETI—PRAV	1.259	400	97.87%	27.09%	0.407	-0.066	6.732	0.198
CETI—PRAV	3.162	300	95.65%	27.09%	0.410	-0.053	6.156	0.117
CETI—PRAV	7.943	800	92.18%	27.09%	0.395	-0.227	18.180	0.270
CETI—PRAV	19.953	4000	98.71%	27.09%	0.378	-0.370	49.826	0.656
CETI—PRAV	50.119	4000	93.50%	27.09%	0.394	-0.474	77.760	0.973
CETI—PRAV	125.893	6000	97.40%	27.09%	0.377	-0.447	79.850	0.978

[0067] 试验例2脂肪酶抑制剂、羟甲戊二酰辅酶A还原酶抑制剂及两者的组合物抑制组胺释放的效果

[0068] 收集对数生长期的，RBL-2H3细胞，并将其浓度调整为8×10^4/mL，均匀接种于96孔板中，每孔200μL细胞悬液，于37℃、5％CO_2、饱和湿度的培养箱中培养24h，弃去培养基，200μL受试物(脂肪酶抑制剂、羟甲戊二酰辅酶A还原酶抑制剂、脂肪酶抑制剂—羟甲戊二酰辅酶A还原酶抑制剂分散于PBS中)，同时设置试剂对照组，每孔加入200μL PBS，37℃孵育30min。孵育终止后，取出细胞上清100μL置于测试荧光板中(多余的上清于-20℃冰箱中冻存，备用)，测试板各孔加入50μL、0.4mol/L NaOH后，立即加入0.1％邻苯二甲醛-甲醇溶液10μL，混匀，室温放置10min，加入50μL、0.5mol/L HCl终止反应，立即用酶标仪检测A值(入射波长360nm，发射波长450nm)，所有受试物组计为$A_{上清}$，溶剂对照组计为$A_{本底}$。

[0069] 96孔板中剩余的细胞用0.5％的Triton100-PBS溶液裂解，37℃孵育30min后，取细胞裂解液100μL置于测试荧光板中(多余的裂解液于-20℃冰箱中冻存，备用)，测试板各孔加入50μL、0.4mol/LNaOH后，立即加入0.1％邻苯二甲醛-甲醇溶液10μL，混匀，室温放置10min，加入50μL、0.5mol/L HCl终止反应，混合均匀后立即用酶标仪检测A值(入射波长360nm，发射波长450nm)，与前述的$A_{上清}$值之和计为$A_{上清+裂解}$，再根据下式计算各受试物的组胺释放抑制率(IR)：

[0070] $IR(\%)=1-(A_{上清}-A_{本底})/(A_{上清+裂解}-A_{本底})\times100\%$

[0071] 用抑制率(IR)对药物浓度(μM)的对数值作图，并用Excel进行线性回归，根据回归方程推算出产生fa抑制时脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂的浓度，分别为$IC_{fa(A)}$与$IC_{fa(B)}$值。对于联合用药，则用抑制率(IR)对联合用药中脂肪酶抑制剂的浓度(μM)的对数值(log(c))作图，并用Excel进行线性回归，根据回归方程推算出fa抑制时组合体系内的脂肪酶抑制剂的浓度，即$IC_{fa(mixA)}$，再根据组合体系中物质的量的比，推算出fa抑制时组合体系内羟甲戊二酰辅酶A还原酶抑制剂的浓度，即$IC_{fa(mixB)}$。

[0072] 根据下式计算产生fa抑制时的联合用药指数(CI)

[0073] $$CI=\frac{IC_{fa(mixA)}}{IC_{fa(A)}}+\frac{IC_{fa(mixB)}}{IC_{fa(B)}}$$

[0074] 当CI<1，即为协同作用，CI值越小，协同作用越强。

[0075] 结果如表7所示。

[0076] 表7

[0077]

受试物	摩尔比	最高浓度（μM）[a]	IR_{max}	fa	斜率[b]	截距[b]	IC_{fa}（μM）[c]	CI
ORLI		10	28.64%	27.28%	0.403	-0.150	11.184	
ATOR		100	32.93%	27.28%	0.444	-0.605	94.468	
ORLI—ATOR	0.010	30	95.04%	27.28%	0.439	0.301	0.863	0.991
ORLI—ATOR	0.025	40	91.54%	27.28%	0.486	0.134	1.932	0.987

[0078]

ORLI—ATOR	0.063	100	92.26%	27.28%	0.393	0.086	2.980	0.767
ORLI—ATOR	0.158	200	98.19%	27.28%	0.374	0.145	2.198	0.343
ORLI—ATOR	0.398	20	93.34%	27.28%	0.485	0.262	1.050	0.122
ORLI—ATOR	1.000	40	95.94%	27.28%	0.433	0.269	1.021	0.102
ORLI—ATOR	2.512	70	92.52%	27.28%	0.490	0.037	3.035	0.284
ORLI—ATOR	6.310	200	94.51%	27.28%	0.488	-0.149	7.333	0.668
ORLI—ATOR	15.849	300	93.27%	27.28%	0.442	-0.183	10.741	0.968
ORLI—ATOR	39.811	1000	93.25%	27.28%	0.314	-0.054	10.947	0.982
ORLI—ATOR	100.000	300	96.54%	27.28%	0.467	-0.212	10.882	0.974
ROSU		1	27.45%	27.28%	0.389	0.263	1.061	
ORLI—ROSU	0.010	0	95.85%	27.28%	0.454	1.172	0.010	0.984
ORLI—ROSU	0.025	2	93.00%	27.28%	0.372	0.863	0.026	0.973
ORLI—ROSU	0.063	5	92.90%	27.28%	0.352	0.690	0.065	0.977
ORLI—ROSU	0.158	5	99.32%	27.28%	0.481	0.660	0.156	0.944
ORLI—ROSU	0.398	6	90.46%	27.28%	0.405	0.577	0.178	0.437
ORLI—ROSU	1.000	7	91.17%	27.28%	0.389	0.591	0.153	0.158
ORLI—ROSU	2.512	10	92.14%	27.28%	0.394	0.526	0.227	0.105
ORLI—ROSU	6.310	40	91.51%	27.28%	0.422	0.243	1.176	0.281
ORLI—ROSU	15.849	100	91.83%	27.28%	0.428	-0.010	4.594	0.684
ORLI—ROSU	39.811	300	94.73%	27.28%	0.456	-0.151	8.508	0.962
ORLI—ROSU	100.000	300	97.04%	27.28%	0.462	-0.186	9.812	0.970
FLUV		30	27.44%	27.28%	0.465	-0.400	27.944	
ORLI—FLUV	0.010	10	90.03%	27.28%	0.398	0.498	0.272	0.998
ORLI—FLUV	0.025	20	96.79%	27.28%	0.494	0.364	0.655	0.991
ORLI—FLUV	0.063	30	95.40%	27.28%	0.490	0.214	1.316	0.864
ORLI—FLUV	0.158	30	90.41%	27.28%	0.448	0.224	1.283	0.405
ORLI—FLUV	0.398	40	99.76%	27.28%	0.446	0.307	0.840	0.151
ORLI—FLUV	1.000	20	92.13%	27.28%	0.487	0.315	0.818	0.102
ORLI—FLUV	2.512	100	95.51%	27.28%	0.396	0.114	2.510	0.260
ORLI—FLUV	6.310	500	92.19%	27.28%	0.340	-0.005	6.560	0.624
ORLI—FLUV	15.849	1000	93.31%	27.28%	0.328	-0.063	10.611	0.973
ORLI—FLUV	39.811	400	93.94%	27.28%	0.426	-0.169	10.884	0.983
ORLI—FLUV	100.000	500	95.92%	27.28%	0.407	-0.149	10.853	0.974
LORV		40	31.14%	27.28%	0.356	-0.276	34.904	
ORLI—LORV	0.010	20	92.44%	27.28%	0.373	0.449	0.336	0.993
ORLI—LORV	0.025	100	91.59%	27.28%	0.307	0.302	0.805	0.991
ORLI—LORV	0.063	40	96.04%	27.28%	0.450	0.257	1.086	0.590
ORLI—LORV	0.158	30	94.30%	27.28%	0.451	0.309	0.832	0.225
ORLI—LORV	0.398	30	99.35%	27.28%	0.435	0.361	0.627	0.101
ORLI—LORV	1.000	300	91.68%	27.28%	0.300	0.192	1.857	0.219
ORLI—LORV	2.512	100	92.55%	27.28%	0.477	-0.090	5.742	0.579
ORLI—LORV	6.310	600	98.28%	27.28%	0.399	-0.132	10.377	0.975
ORLI—LORV	15.849	200	90.26%	27.28%	0.470	-0.213	10.803	0.985
ORLI—LORV	39.811	400	91.64%	27.28%	0.418	-0.162	10.925	0.985
ORLI—LORV	100.000	700	91.94%	27.28%	0.354	-0.094	10.862	0.974
SIMV		20	32.91%	27.28%	0.378	-0.155	13.529	
ORLI—SIMV	0.010	4	90.70%	27.28%	0.431	0.653	0.131	0.981
ORLI—SIMV	0.025	20	99.64%	27.28%	0.401	0.469	0.324	0.982
ORLI—SIMV	0.063	40	98.87%	27.28%	0.415	0.317	0.782	0.986
ORLI—SIMV	0.158	100	92.82%	27.28%	0.372	0.181	1.761	0.979
ORLI—SIMV	0.398	100	94.09%	27.28%	0.425	0.039	3.547	0.976
ORLI—SIMV	1.000	300	99.94%	27.28%	0.383	0.050	3.821	0.624
ORLI—SIMV	2.512	60	96.49%	27.28%	0.462	0.145	1.890	0.225
ORLI—SIMV	6.310	100	96.18%	27.28%	0.330	0.272	1.006	0.102
ORLI—SIMV	15.849	80	90.23%	27.28%	0.427	0.088	2.712	0.255
ORLI—SIMV	39.811	1000	93.67%	27.28%	0.310	0.002	7.506	0.685
ORLI—SIMV	100.000	300	90.18%	27.28%	0.422	-0.162	10.684	0.963

[0079]

PITA		4	27.45%	27.28%	0.409	0.046	3.589	
ORLI—PITA	0.010	2	96.88%	27.28%	0.397	0.850	0.035	0.982
ORLI—PITA	0.025	9	93.61%	27.28%	0.333	0.624	0.088	0.982
ORLI—PITA	0.063	6	91.91%	27.28%	0.449	0.569	0.219	0.986
ORLI—PITA	0.158	20	96.32%	27.28%	0.418	0.389	0.527	0.973
ORLI—PITA	0.398	60	91.27%	27.28%	0.381	0.236	1.250	0.987
ORLI—PITA	1.000	50	95.06%	27.28%	0.466	0.154	1.797	0.661
ORLI—PITA	2.512	70	94.41%	27.28%	0.392	0.223	1.339	0.268
ORLI—PITA	6.310	40	92.10%	27.28%	0.388	0.304	0.832	0.111
ORLI—PITA	15.849	60	90.38%	27.28%	0.404	0.172	1.778	0.190
ORLI—PITA	39.811	400	99.71%	27.28%	0.382	-0.002	5.243	0.506
ORLI—PITA	100.000	300	90.13%	27.28%	0.449	-0.185	10.463	0.965
PRAV		20	27.28%	27.28%	0.366	-0.181	17.385	
ORLI—PRAV	0.010	8	97.16%	27.28%	0.419	0.599	0.167	0.975
ORLI—PRAV	0.025	20	98.18%	27.28%	0.405	0.429	0.412	0.981
ORLI—PRAV	0.063	100	95.92%	27.28%	0.336	0.276	0.976	0.977
ORLI—PRAV	0.158	300	93.33%	27.28%	0.314	0.168	2.157	0.976
ORLI—PRAV	0.398	300	94.30%	27.28%	0.367	0.055	3.931	0.919
ORLI—PRAV	1.000	100	95.01%	27.28%	0.398	0.109	2.577	0.379
ORLI—PRAV	2.512	40	90.14%	27.28%	0.403	0.273	1.001	0.112
ORLI—PRAV	6.310	60	97.45%	27.28%	0.415	0.236	1.226	0.121
ORLI—PRAV	15.849	300	95.89%	27.28%	0.388	0.026	4.338	0.404
ORLI—PRAV	39.811	300	94.91%	27.28%	0.447	-0.185	10.577	0.961
ORLI—PRAV	100.000	400	98.45%	27.28%	0.438	-0.176	10.580	0.952
CETI		30	28.74%	27.33%	0.306	-0.145	23.355	
ATOR		80	30.02%	27.33%	0.398	-0.446	64.451	
CETI—ATOR	0.010	20	91.90%	27.33%	0.429	0.364	0.614	0.979
CETI—ATOR	0.025	90	94.51%	27.33%	0.381	0.207	1.496	0.988
CETI—ATOR	0.063	100	90.65%	27.33%	0.408	0.056	3.408	0.984
CETI—ATOR	0.158	600	99.95%	27.33%	0.382	-0.049	6.995	0.984
CETI—ATOR	0.398	300	96.01%	27.33%	0.493	-0.259	12.049	0.985
CETI—ATOR	1.000	700	99.39%	27.33%	0.370	-0.053	7.632	0.445
CETI—ATOR	2.512	100	90.01%	27.33%	0.379	0.102	2.824	0.138
CETI—ATOR	6.310	70	96.78%	27.33%	0.481	0.082	2.501	0.113
CETI—ATOR	15.849	400	97.66%	27.33%	0.422	-0.118	8.443	0.370
CETI—ATOR	39.811	3000	98.72%	27.33%	0.341	-0.178	21.014	0.908
CETI—ATOR	100.000	600	90.81%	27.33%	0.440	-0.322	22.564	0.970
ROSU		100	28.09%	27.33%	0.326	-0.369	93.708	
CETI—ROSU	0.010	30	98.76%	27.33%	0.493	0.297	0.896	0.994
CETI—ROSU	0.025	100	93.39%	27.33%	0.366	0.170	1.922	0.899
CETI—ROSU	0.063	200	92.29%	27.33%	0.326	0.174	2.011	0.426
CETI—ROSU	0.158	300	97.54%	27.33%	0.309	0.223	1.452	0.160
CETI—ROSU	0.398	200	99.05%	27.33%	0.323	0.222	1.437	0.100
CETI—ROSU	1.000	100	99.98%	27.33%	0.487	-0.050	4.606	0.246
CETI—ROSU	2.512	500	93.18%	27.33%	0.420	-0.191	12.726	0.599
CETI—ROSU	6.310	600	92.82%	27.33%	0.466	-0.352	21.869	0.973
CETI—ROSU	15.849	6000	99.64%	27.33%	0.301	-0.131	22.176	0.964
CETI—ROSU	39.811	2000	99.29%	27.33%	0.368	-0.225	22.590	0.973
CETI—ROSU	100.000	1000	90.46%	27.33%	0.350	-0.201	22.529	0.967
FLUV		50	31.47%	27.33%	0.441	-0.447	43.022	
CETI—FLUV	0.010	10	99.41%	27.33%	0.496	0.462	0.417	0.988
CETI—FLUV	0.025	70	93.54%	27.33%	0.357	0.271	1.014	0.982
CETI—FLUV	0.063	90	93.84%	27.33%	0.429	0.110	2.398	0.986
CETI—FLUV	0.158	100	92.08%	27.33%	0.464	-0.006	4.005	0.759
CETI—FLUV	0.398	200	94.03%	27.33%	0.392	0.069	3.312	0.335
CETI—FLUV	1.000	90	96.46%	27.33%	0.412	0.169	1.790	0.118
CETI—FLUV	2.512	100	99.61%	27.33%	0.423	0.139	2.074	0.108

[0080]

CETI—FLUV	6.310	600	95.85%	27.33%	0.346	-0.009	6.547	0.304
CETI—FLUV	15.849	900	98.50%	27.33%	0.404	-0.213	15.979	0.708
CETI—FLUV	39.811	1000	99.21%	27.33%	0.429	-0.303	22.045	0.957
CETI—FLUV	100.000	2000	99.97%	27.33%	0.373	-0.228	22.221	0.957
LORV		30	28.06%	27.33%	0.432	-0.337	25.744	
CETI—LORV	0.010	40	97.43%	27.33%	0.313	0.461	0.251	0.986
CETI—LORV	0.025	20	96.74%	27.33%	0.405	0.430	0.411	0.653
CETI—LORV	0.063	20	92.77%	27.33%	0.397	0.433	0.397	0.261
CETI—LORV	0.158	10	95.36%	27.33%	0.459	0.466	0.380	0.109
CETI—LORV	0.398	60	98.76%	27.33%	0.434	0.210	1.398	0.196
CETI—LORV	1.000	300	90.25%	27.33%	0.374	-0.028	6.392	0.522
CETI—LORV	2.512	3000	98.04%	27.33%	0.324	-0.124	16.807	0.980
CETI—LORV	6.310	3000	92.91%	27.33%	0.304	-0.123	20.037	0.981
CETI—LORV	15.849	4000	99.25%	27.33%	0.311	-0.141	21.392	0.968
CETI—LORV	39.811	1000	95.44%	27.33%	0.401	-0.266	22.120	0.969
CETI—LORV	100.000	4000	93.74%	27.33%	0.302	-0.136	22.499	0.972
SIMV		100	32.64%	27.33%	0.361	-0.434	91.017	
CETI—SIMV	0.010	50	93.20%	27.33%	0.371	0.297	0.862	0.984
CETI—SIMV	0.025	100	91.94%	27.33%	0.350	0.165	2.039	0.979
CETI—SIMV	0.063	100	97.91%	27.33%	0.449	0.068	2.870	0.623
CETI—SIMV	0.158	200	95.48%	27.33%	0.344	0.141	2.431	0.273
CETI—SIMV	0.398	100	97.41%	27.33%	0.394	0.184	1.687	0.119
CETI—SIMV	1.000	500	99.08%	27.33%	0.318	0.122	2.999	0.161
CETI—SIMV	2.512	300	94.58%	27.33%	0.444	-0.139	8.482	0.400
CETI—SIMV	6.310	400	90.28%	27.33%	0.487	-0.347	18.752	0.836
CETI—SIMV	15.849	600	91.92%	27.33%	0.452	-0.333	21.967	0.956
CETI—SIMV	39.811	4000	96.68%	27.33%	0.315	-0.153	22.497	0.969
CETI—SIMV	100.000	700	97.25%	27.33%	0.476	-0.368	22.290	0.957
PITA		50	27.57%	27.33%	0.395	-0.380	45.269	
CETI—PITA	0.010	10	97.17%	27.33%	0.500	0.454	0.436	0.981
CETI—PITA	0.025	20	90.06%	27.33%	0.481	0.263	1.050	0.968
CETI—PITA	0.063	40	95.01%	27.33%	0.438	0.248	1.143	0.449
CETI—PITA	0.158	50	97.15%	27.33%	0.397	0.290	0.906	0.165
CETI—PITA	0.398	100	99.76%	27.33%	0.356	0.248	1.179	0.116
CETI—PITA	1.000	400	90.52%	27.33%	0.324	0.057	4.650	0.302
CETI—PITA	2.512	400	98.77%	27.33%	0.487	-0.284	14.004	0.723
CETI—PITA	6.310	2000	97.67%	27.33%	0.365	-0.209	21.063	0.976
CETI—PITA	15.849	600	96.41%	27.33%	0.491	-0.385	21.801	0.964
CETI—PITA	39.811	5000	98.67%	27.33%	0.301	-0.135	22.557	0.978
CETI—PITA	100.000	1000	90.49%	27.33%	0.384	-0.247	22.685	0.976
PRAV		1	27.33%	27.33%	0.428	0.369	0.596	
CETI—PRAV	0.010	0	90.97%	27.33%	0.401	1.168	0.006	0.981
CETI—PRAV	0.025	1	96.76%	27.33%	0.417	1.038	0.015	0.981
CETI—PRAV	0.063	1	95.19%	27.33%	0.431	0.894	0.036	0.971
CETI—PRAV	0.158	6	94.66%	27.33%	0.376	0.663	0.092	0.978
CETI—PRAV	0.398	7	95.77%	27.33%	0.471	0.572	0.232	0.987
CETI—PRAV	1.000	20	97.71%	27.33%	0.466	0.420	0.485	0.834
CETI—PRAV	2.512	30	90.91%	27.33%	0.366	0.394	0.469	0.334
CETI—PRAV	6.310	30	95.21%	27.33%	0.357	0.436	0.349	0.108
CETI—PRAV	15.849	20	90.08%	27.33%	0.496	0.263	1.050	0.156
CETI—PRAV	39.811	400	90.58%	27.33%	0.340	0.018	5.641	0.479
CETI—PRAV	100.000	3000	96.33%	27.33%	0.315	-0.108	16.253	0.969

[0081] 实施例2含有由脂肪酶抑制剂与羟甲戊二酰辅酶A还原酶抑制剂构成的组合物的口服固体制剂的制备

[0082] 处方(1000单位剂量)

[0083]

处 方 编号	组合物		辅料
	成分	物质的量的比	

[0084]

1.	ORLI—ATOR	0.010:1	502g 乳糖、204g 微晶纤维素、99g 交联聚维酮、99g 淀粉、78g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
2.	ORLI—ROSU	0.025:1	492g 乳糖、197g 微晶纤维素、96g 交联聚维酮、102g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
3.	ORLI—FLUV	0.063:1	477g 乳糖、199g 微晶纤维素、101g 交联聚维酮、102g 淀粉、76g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
4.	ORLI—LORV	0.158:1	483g 乳糖、200g 微晶纤维素、103g 交联聚维酮、104g 淀粉、77g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
5.	ORLI—SIMV	0.398:1	498g 乳糖、197g 微晶纤维素、101g 交联聚维酮、99g 淀粉、78g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
6.	ORLI—PITA	1.000:1	495g 乳糖、203g 微晶纤维素、95g 交联聚维酮、103g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、14g 硬脂酸镁
7.	ORLI—PRAV	2.512:1	462g 乳糖、192g 微晶纤维素、104g 交联聚维酮、95g 淀粉、75g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
8.	CETI—ATOR	6.310:1	469g 乳糖、200g 微晶纤维素、101g 交联聚维酮、96g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、14g 硬脂酸镁
9.	CETI—ROSU	15.849:1	471g 乳糖、210g 微晶纤维素、98g 交联聚维酮、103g 淀粉、77g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
10.	CETI—FLUV	39.811:1	469g 乳糖、206g 微晶纤维素、97g 交联聚维酮、98g 淀粉、72g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
11.	CETI—LORV	100.000:1	475g 乳糖、203g 微晶纤维素、104g 交联聚维酮、100g 淀粉、75g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
12.	CETI—SIMV	0.008:1	490g 乳糖、207g 微晶纤维素、104g 交联聚维酮、100g 淀粉、78g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
13.	CETI—PITA	0.020:1	464g 乳糖、193g 微晶纤维素、96g 交联聚维酮、97g 淀粉、74g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
14.	CETI—PRAV	0.050:1	489g 乳糖、202g 微晶纤维素、95g 交联聚维酮、96g 淀粉、77g 羟丙甲纤维素、29g 微粉硅胶、16g 硬脂酸镁
15.	ORLI—ATOR	0.126:1	493g 乳糖、192g 微晶纤维素、98g 交联聚维酮、98g 淀粉、79g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
16.	ORLI—ROSU	0.316:1	502g 乳糖、197g 微晶纤维素、102g 交联聚维酮、95g 淀粉、77g 羟丙甲纤维素、31g 微粉硅胶、16g 硬脂酸镁
17.	ORLI—FLUV	0.794:1	460g 乳糖、210g 微晶纤维素、97g 交联聚维酮、101g 淀粉、71g 羟丙甲纤维素、31g 微粉硅胶、16g 硬脂酸镁
18.	ORLI—LORV	1.995:1	469g 乳糖、200g 微晶纤维素、100g 交联聚维酮、97g 淀粉、75g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
19.	ORLI—SIMV	5.012:1	464g 乳糖、190g 微晶纤维素、97g 交联聚维酮、101g 淀粉、76g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
20.	ORLI—PITA	12.589:1	502g 乳糖、204g 微晶纤维素、105g 交联聚维酮、100g 淀粉、78g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
21.	ORLI—PRAV	31.623:1	494g 乳糖、208g 微晶纤维素、98g 交联聚维酮、98g 淀粉、74g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
22.	CETI—ATOR	79.433:1	466g 乳糖、207g 微晶纤维素、98g 交联聚维酮、103g 淀粉、72g 羟丙甲纤维素、31g 微粉硅胶、14g 硬脂酸镁
23.	CETI—ROSU	0.013:1	489g 乳糖、195g 微晶纤维素、96g 交联聚维酮、102g 淀粉、72g 羟丙甲纤维素、29g 微粉硅胶、14g 硬脂酸镁
24.	CETI—FLUV	0.032:1	504g 乳糖、193g 微晶纤维素、101g 交联聚维酮、98g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
25.	CETI—LORV	0.079:1	465g 乳糖、202g 微晶纤维素、95g 交联聚维酮、96g 淀粉、78g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
26.	CETI—SIMV	0.200:1	466g 乳糖、204g 微晶纤维素、99g 交联聚维酮、103g 淀粉、78g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁

[0085]

27.	CETI—PITA	0.501:1	458g 乳糖、209g 微晶纤维素、104g 交联聚维酮、99g 淀粉、77g 羟丙甲纤维素、31g 微粉硅胶、16g 硬脂酸镁
28.	CETI—PRAV	1.259:1	484g 乳糖、193g 微晶纤维素、100g 交联聚维酮、96g 淀粉、72g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
29.	ORLI—ATOR	3.162:1	457g 乳糖、192g 微晶纤维素、96g 交联聚维酮、97g 淀粉、74g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
30.	ORLI—ROSU	7.943:1	458g 乳糖、201g 微晶纤维素、104g 交联聚维酮、100g 淀粉、72g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
31.	ORLI—FLUV	19.953:1	484g 乳糖、200g 微晶纤维素、102g 交联聚维酮、100g 淀粉、72g 羟丙甲纤维素、29g 微粉硅胶、16g 硬脂酸镁
32.	ORLI—LORV	50.119:1	459g 乳糖、208g 微晶纤维素、97g 交联聚维酮、99g 淀粉、73g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
33.	ORLI—SIMV	125.893:1	466g 乳糖、200g 微晶纤维素、102g 交联聚维酮、96g 淀粉、73g 羟丙甲纤维素、30g 微粉硅胶、14g 硬脂酸镁
34.	ORLI—PITA	0.016:1	460g 乳糖、193g 微晶纤维素、100g 交联聚维酮、104g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
35.	ORLI—PRAV	0.040:1	459g 乳糖、191g 微晶纤维素、98g 交联聚维酮、105g 淀粉、71g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
36.	CETI—ATOR	0.100:1	502g 乳糖、203g 微晶纤维素、101g 交联聚维酮、101g 淀粉、75g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
37.	CETI—ROSU	0.251:1	464g 乳糖、196g 微晶纤维素、104g 交联聚维酮、104g 淀粉、75g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
38.	CETI—FLUV	0.631:1	471g 乳糖、204g 微晶纤维素、95g 交联聚维酮、105g 淀粉、76g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
39.	CETI—LORV	1.585:1	482g 乳糖、210g 微晶纤维素、103g 交联聚维酮、96g 淀粉、73g 羟丙甲纤维素、30g 微粉硅胶、15g 硬脂酸镁
40.	CETI—SIMV	3.981:1	499g 乳糖、196g 微晶纤维素、95g 交联聚维酮、103g 淀粉、73g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
41.	ORLI—ATOR	10.000:1	493g 乳糖、199g 微晶纤维素、105g 交联聚维酮、97g 淀粉、78g 羟丙甲纤维素、29g 微粉硅胶、15g 硬脂酸镁
42.	ORLI—ROSU	25.119:1	492g 乳糖、201g 微晶纤维素、99g 交联聚维酮、95g 淀粉、72g 羟丙甲纤维素、30g 微粉硅胶、16g 硬脂酸镁
43.	ORLI—FLUV	63.096:1	491g 乳糖、204g 微晶纤维素、101g 交联聚维酮、104g 淀粉、72g 羟丙甲纤维素、31g 微粉硅胶、15g 硬脂酸镁
44.	ORLI—LORV	158.489:1	501g 乳糖、193g 微晶纤维素、102g 交联聚维酮、96g 淀粉、73g 羟丙甲纤维素、31g 微粉硅胶、16g 硬脂酸镁

[0086] 制备方法

[0087] 取50g组合物与处方量辅料，均过100目筛。取组合物、乳糖、微晶纤维素、交联聚维酮与淀粉充分混匀；取处方量的羟丙甲纤维素，配制成依羟丙甲纤维素计浓度为10％的溶液，用乳酸调节pH至3.0～4.0，加入至上述混合物料中制软材，以16目筛制粒，80℃干燥3～4h。用16目筛整粒，加入处方量的微粉硅胶与硬脂酸镁混合混匀，灌装胶囊，即得胶囊；

[0088] 取50g组合物与处方量辅料，均过100目筛。取组合物、乳糖、微晶纤维素、交联聚维酮与淀粉充分混匀；取处方量的羟丙甲纤维素，配制成依羟丙甲纤维素计浓度为10％的溶液，用乳酸调节pH至3.0～4.0，加入至上述混合物料中制软材，以16目筛制粒，80℃干燥3～4h。用16目筛整粒，加入处方量的微粉硅胶与硬脂酸镁混合混匀，分装，即得颗粒剂；

[0089] 取50g组合物与处方量辅料，均过100目筛。取组合物、乳糖、微晶纤维素、交联聚维酮与淀粉充分混匀；取处方量的羟丙甲纤维素，配制成依羟丙甲纤维素计浓度为10％的溶液，用乳酸调节pH至3.0～4.0，加入至上述混合物料中制软材，以16目筛制粒，80℃干燥3～4h。用16目筛整粒，加入处方量的微粉硅胶与硬脂酸镁混合混匀，压片，既得片剂。