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论文

7-(7-氨甲基-5-氮杂螺［2,4］庚烷-5-基)-1-环丙基-6-氟-8-甲氧基-1,4-二氢-4-氧代喹啉-3-羧酸及其类似物的合成与抗菌作用7-(7-氨甲基-5-氮杂螺［2,4］庚烷-5-基)-1-环丙基-6-氟-8-甲氧基-1,4-二氢-4-氧代喹啉-3-羧酸及其类似物的合成与抗菌作用

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摘要：

目的寻找新的广谱、高效、低毒喹诺酮类抗菌药物。方法设计合成7-(7-氨甲基-5-氮杂螺［2,4］庚烷-5-基)-1-环丙基-6-氟-8-甲氧基-1,4-二氢-4-氧代喹啉-3-羧酸及其类似物,测定其体内外活性。结果共合成了20个新化合物,经^{1}HNMR,MS和HRMS确证其结构。其中5个目标化合物(22～26)有广谱活性,尤其对革兰氏阳性菌具有很强的活性。其中化合物24对所试的13株革兰氏阳性菌的MIC值均 0.03 mg·L^{-1},其活性优于对照药克林沙星和加替沙星,对所试的6株革兰氏阴性菌,其活性相当于或低于对照药。结论化合物(22～26)值得进一步评价。

关键词： 氟喹诺酮 合成 抗菌作用

Synthesis and antibacterial activity of 7-(7-aminomethyl-5-azaspiro［2,4］hept-5-yl)-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid and its analogues

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Abstract:

AimTo find new antibacterial agents of quinolone with high activity and low toxicity. MethodsTo design and synthesize 7-(7-aminomethyl-5-azaspiro［2,4］hept-5-yl)-1-cyclopropyl-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid and its analogues, and to study their antibacterial activity *in vitro* and *in vivo*. ResultsTwenty new compounds (2-11, 17-26) were obtained including five targeted compounds (22-26). The structures of the compounds were confirmed by ^{1}HNMR, MS and HRMS. Compounds 22-26 showed broad spectrum of antibacterial activity against Gram-positive and Gram-negative organisms. Especially for compound 24, the relevant MIC values for 13 strains of Gram-positive organisms were <0.001-0.03 mg·L^{-1}, including 4 strains of S.pneumoniae, 2 strains of S.pyogenes, 3 strains of S.aureus and 2 strains of Enterococci which exhibited more potent activity than contrast agents (clinafloxacin and gatifloxacin). The MIC values of 24 for 6 strains Gram-positive organisms were 0.01-1 mg·L^{-1}, which exhibited equal or lower activity than contrast agents. They were more effective than ciprofloxacin and gatifloxacin against intraperitoneal infections caused by S.pneumoniae and S.aureus in mice. Conclusion Compounds (23, 24 and 26) showed excellent antibacterial activity *in vitro* and *in vivo* and should be worth further investigation.

Keywords: synthesis antibacterial activity fluoroquinolones

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