TP-271 is a Novel Fluorocycline Active Against Susceptible and Multidrug-Resistant Neisseria gonorrhoeae

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**Abstract**

**Background:** Gonococcal disease caused by Neisseria gonorrhoeae is a common cause of urethritis in men and endocervicitis in women. Drug resistance is a serious concern, with alarming resistance trends diminishing the effectiveness of all current standard-of-care antibiotics, including fluoroquinolones, current tetracyclines, oxacillin, erythromycin, and macrolides. TP-271, a novel and fully synthetic tetracycline analog, is a potent broad-spectrum antibiotic in preclinical development for the treatment of community-acquired respiratory infections and use against infections caused by bacterial pathogens [1]. In this study, TP-271 was tested in vitro against a panel of 20 N. gonorrhoeae isolates with various drug-resistance profiles. **Method:** Susceptibility testing was conducted by agar dilution according to CLSI guidelines. Results were interpreted using breakpoints for tetracycline, penicillin, ciprofloxacin and ceftriaxone. Strains were screened by PCR for tetracycline-resistance determinants commonly found in N. gonorrhoeae. **Results:** The minimal inhibitory concentration (MIC) range for TP-271 was 0.06 – 0.5 µg/mL, and MIC<sub>90</sub> was 0.125 µg/mL. The MIC<sub>50</sub> values for tetracycline, penicillin, ciprofloxacin and ceftriaxone were 1:8, 0.5, 0.008, and <0.008, respectively. **Conclusions:** If confirmed in vivo, these data support TP-271 as a promising new antibiotic for use against infections caused by multidrug-resistant N. gonorrhoeae.

**References**


5. CMI. 2006. CMI 14(9) 2008. Neisseria gonorrhoeae. Strains and Growth Conditions. Staphylococcus aureus was acquired from the laboratory of Dr. Ann Jerse (Uniformed Services University, Bethesda, MD) and from Eurofins-Medinet (Chantilly, VA).

**Methods**

**TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β.** Staphylococcus aureus infections from the 1970s, 1990s, and more recently 2005/2006. Strains were acquired from the laboratory of Dr. Ann Jerse (Uniformed Services University, Bethesda, MD) and from Eurofins-Medinet (Chantilly, VA). TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae. TP-271 is a novel broad-spectrum fluorocycline antibiotic with excellent potency against serious and multidrug-resistant Gram-β. Urethritis in men and endocervicitis in women are serious sexually transmitted diseases caused by Neisseria gonorrhoeae.

**Results:** The minimal inhibitory concentration (MIC) range for TP-271 was 0.06 – 0.5 µg/mL, and MIC<sub>90</sub> was 0.125 µg/mL. The MIC<sub>50</sub> values for tetracycline, penicillin, ciprofloxacin and ceftriaxone were 1:8, 0.5, 0.008, and <0.008, respectively. The activity of TP-271 was similar in strains displaying single or multiple resistance phenotypes. TP-271 showed potent activity against eight tetracycline-resistant isolates (MIC range: 0.06 – 0.5 µg/mL), of which four were confirmed to be tet(M). Fourteen isolates were also confirmed to have an additional drug-resistance phenotype by tet(A), tet(O), and tet(V) genes. These studies were funded in part by NIAID Partnership Grant #: 1R01AI093484 – 01 awarded to CUBRC and Tetraphase Pharmaceuticals; NIAID (U41 AI090455) awarded to CUBRC; and NIAID (U41 AI094714) awarded to Tetaphase Pharmaceuticals. These studies were funded in part by NIAID Partnership Grant #: 1R01AI093484 – 01 awarded to CUBRC and Tetraphase Pharmaceuticals; NIAID (U41 AI090455) awarded to CUBRC; and NIAID (U41 AI094714) awarded to Tetaphase Pharmaceuticals.

**Conclusion:** We have demonstrated the activity of TP-271 against a panel of 20 N. gonorrhoeae isolates with various drug-resistance profiles. If confirmed in vivo, these data support TP-271 as a promising new antibiotic for use against infections caused by multidrug-resistant N. gonorrhoeae.

**References**


