Short Communication

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In vitro Activities of RD-3 and Other Antimicrobial Agents against *Ureaplasma urealyticum* Isolates

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About the Study

RD-3 is a quinoline derivative with the formula bis(4,9,9a,10-tetrahydro-9-phenyl-3bH-pyrrolizino-(1,2b)quinolin-7-) methane12 (**Figure 1**) and has shown broad spectrum of activity against different microorganisms [1,2]. Currently this drug is under consideration for development by a pharmaceutical company. *Ureaplasma urealyticum* is known to cause a variety of urogenital infections [3]. It is known to cause systemic infections in newborns. Tetracycline is the treatment of choice in adults and erythromycin is used in the case of children and neonates [4]. Resistance to fluoroquinolones due to mutations in *parC* and *parE* genes, and resistance to macrolides due to mutations in 23SrRNA have been increasing in these isolates worldwide [5]. In this study we examined the activity of RD-3 and other antimicrobial agents against clinical isolates of *Ureaplasma urealyticum.*

Organisms included 32 isolates of *Ureaplasma urealyticum* strains collected since 2008. Organisms included 18 isolates resistant to tetracyclines, macrolides, fluoroquinolones, alone or in combination.

The comparator agents, tetracycline, azithromycin and moxifloxacin were from Sigma-Aldrich (St. Louis, MO,USA).

Antimicrobial powders were used according to the manufacturer's protocol. Working dilutions of the drugs were prepared fresh on the day of the assay.

Antimicrobial Susceptibility testing was performed by the standard agar-dilution method as described in accordance with Clinical and Laboratory Standards Institute (CLSI) guideline [6]. Inoculum was prepared and MICs were determined and interpreted. Organisms were stored frozen at -80° until thawing for testing.

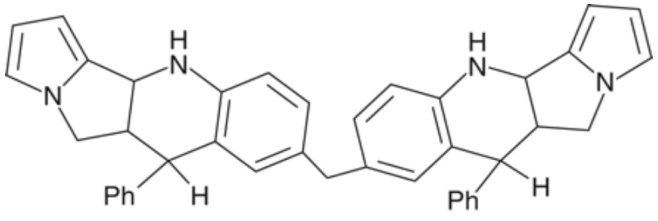

Figure 1 Chemical structure of RD-3.

The MICs of *U. urealyticum* against different drugs are given in (**Table 1**). RD-3 was most active with an MIC_{90} of 0.032 mg/L (range 0.016-0.032 mg/L). Moxifloxacin showed better activity than azithromycin and tetracycline with an MIC_{90} of 2 mg/L. Tetracycline and azithromycin had an MIC_{90} several fold higher than RD-3 at 4 mg/L and 8 mg/L respectively.

Among the 32 isolates, 8 isolates were resistant to tetracycline (MICs 16 to >32 mg/L, 5 isolates were resistant to macrolide, azithromycin (MICs>32 mg/L), and 2 isolates were resistant to fluoroquinolone, moxifloxacin (MICs 4 to 8 mg/L). 2 isolates of *U. urealyticum* were resistant to both azithromycin and tetracycline. One isolate was resistant to tetracycline and moxifloxacin. RD-3 was highly active against these resistant isolates with MICs

Table 1: Activities of RD-3 and other antibiotics against clinical isolates of *U. urealyticum.*

Organism or drug (n= 32)	MIC range	MIC50 (mg/L)	MIC90 (mg/L)
RD-3	0.016-0.032	0.016	0.032
Tetracycline	0.125-16	0.25	4
Azithromycin	0.25-32	4	8
Moxifloxacin	0.125-4	0.25	2

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ranging from 0.016 to 0.032 mg/L. This shows that resistance to moxifloxacin, azithromycin and tetracycline did not affect RD-3's activity. Since there are no CLSI breakpoints for *Ureaplasmas*, susceptibility testing to different antibacterials was difficult to compare. Previous studies showed that RD-3 was highly active against *M. pneumoniae* and *M. hominis* (2). These studies suggest that RD-3 could be used as an alternative drug to treat upper respiratory tract infections and urogenital infections caused by human *Mycoplasmas* and *Ureaplasma*, requiring further clinical studies.

Conclusion

Rise in antimicrobial resistance to microorganisms had led researchers to look for new strategies and novel mechanisms to combat this microbial resistance. Some novel methods have been to use antimicrobial peptides, new drug classes etc. *Ureaplasma* sp causes a variety of urogenital infections in humans. Treatment of *Ureaplasmas* has been complicated by resistance to macrolides and fluoroquinolones. Tetracycline resistance occurs due to ribosomal protection mediated by the term transposon. Urogenital *Mycoplasmas* and *Ureaplasmas* have different antimicrobial resistance patterns. The reasons like this have prompted researchers to look for new antimicrobials that are not affected by cross-resistance to other drugs. Even in the absence of resistance genes *Ureaplasmas* have higher MICs than other organisms for fluoroquinolones and tetracycline. quinoline derivatives are drugs that have shown broad spectrum activity. These drugs have also shown potent antimicrobial activity against *Mycoplasmas*, *Chlamydias* etc. Earlier work demonstrated that RD-3 inhibited gyrase supercoiling with activity that was comparable to ciprofloxacin and down-regulated gyrase A expression in *Escherichia coli*. These *in vitro* data suggests that RD-3 may show considerable promise in treating genital and respiratory infections.

Acknowledgement

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