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Amycolamicin, a Novel Antibiotic as a Promising Candidate for *Clostridium Difficile* Infection: Antibacterial Activity, Mode of Action, and *In Vivo* Efficacy

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A novel antibiotic amycolamicin (AM) discovered from the culture broth of *Amycolatopsis* sp. MK575-fF5 was originally isolated as a drug which showed strong antibacterial activities against Gram-positive bacteria such as MRSA, VRE and PRSP. Mode of action study revealed that AM inhibited bacterial DNA gyrase with IC_{50} of 24.4 ng/ml, without cross-resistance to other inhibitors of DNA gyrase such as quinolones and aminocoumarins. By contrast, AM did not inhibit human DNA topoisomerase II.

Additionally, AM showed particularly strong antibacterial activity against *C. difficile* grown anaerobically. The MIC_{90}s (n=45) of AM, vancomycin, and fidaxomicin were 0.25, 1.0, 0.25 μg/ml, respectively. AM also showed strong antibacterial activity against 13 species of *Clostridiales*, some *Bacteroidales* and *Enterococcus faecalis/faecium*, whereas showed moderate or weak antibacterial activity against other enteric bacteria including *Bifidobacteriales*, *Lactobacillales* and some *Bacteroidales*. In a therapeutic experiment using for antibiotic- associated pseudomembranous colitis caused by *C. difficile* ATCC 43255 in hamsters, AM showed an equivalent therapeutic efficacy to fidaxomicin at 6, 20, and 60 mg/kg/day by oral administration (n=7).

In conclusion, AM showed to possess strong activity against *C. difficile* with novel mechanism of action. The efficacy in hamster model for pseudomembranous colitis warrants further evaluation of AM.