Background: Crystal structures of protein synthesis inhibitors bound to the 30S ribosome provided a molecular framework for designing de novo antibiotics. Molecular modeling of ligand binding to bacterial ribosome using X-ray crystallography, molecular mechanics, and docking simulations showed that novel scaffolds can be designed to interact with previously unexplored interfaces of the 30S ribosomal subunit. In this study, we report on the rational design of new antibiotics based on the ribosome. The primary objective of the study was to design novel antibiotic scaffolds that inhibit key steps in bacterial translation and are active against multidrug-resistant Gram-negative bacteria.

RESULTS AND DISCUSSION

In order to investigate how to fill that pocket optimally, we designed various meta-terphenyl analogs, which had an aromatic ring in the central position, and studied their activity. The results showed that certain scaffolds were more active than others, and that the structure of the meta-terphenyl scaffold played a crucial role in determining the antibacterial activity. These results provided insights into the design of new antibiotics that could target the bacterial ribosome and be effective against multidrug-resistant Gram-negative bacteria.

Conclusions: The results of this study suggest that novel antibiotic scaffolds can be designed to inhibit key steps in bacterial translation and be active against multidrug-resistant Gram-negative bacteria. These findings provide a promising avenue for the development of new antibiotics that could be effective against multidrug-resistant bacteria.