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Editorial

# Oxazolidinones as Inhibitors of Protein Synthesis

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The ribosome is the largest and most complex enzymatic system present in organisms, acting as the machinery of protein synthesis in cells. Even in simple organisms such as bacteria, the ribosome consists of approximately 54 proteins and ribosomal RNA components (rRNAs; 16S, 23S e 5S) [1,2]. In all organisms, ribosomes are at the heart of the translation process, converting coded genetic information from messenger RNA (mRNA) into extensive chains of amino acids (polypeptides or proteins) with distinct structural and / or catalytic properties. This process is performed on two large ribonucleoprotein particles of different sizes, the ribosomal subunits. The small subunit (30S in prokaryotes and 40S in eukaryotes) has the function of decoding, while the large subunit (50S in prokaryotes and 60S in eukaryotes) catalyzes the formation of peptide bonds, being referred to as peptidyl transferase [3,4]. Significant differences between the prokaryotic and eukaryotic ribosomes allow the development of antibacterial drugs with surprising selectivity [4-6], making the ribosome a particularly versatile target for drug development [7]. Many of the drugs that are used in clinical medicine for the treatment of bacterial infections (e.g. macrolides, ketolides, lincosamides, oxazolidinones, chloramphenicol, aminoglycosides and tetracyclines) specifically inhibit the bacterial as opposed to the eukaryotic ribosome [7]. The oxazolidinones should be highlighted, since they are the only fully synthetic class of antibiotics that acts on the ribosome. Linezolid, the first representative of this class, was discovered in the mid 1990s and was approved for commercial use as an oral available antimicrobial in the 2000. It is active against several gram-positive bacteria and *Mycobacterium tuberculosis* [8]. Following the success of linezolid as antibacterial, several other oxazolidinone derivatives and consequently analogs of linezolid have been developed or are in clinical developmental stages, including radezolid, torezolid, sutezolid, posizolid, eperezolid, ranbezolid, and tedizolid. The increasing incidence of antibiotic resistance and the toxicity associated with some of the available drugs constitutes a challenge to be overcome through the development of new compounds. Currently, several oxazolidinone derivatives have been reported with potent antimicrobial activity. Many of these compounds have activity superior to that of linezolid against different strains of bacteria. For instance, Ang et al. reported a series of bis-oxazolidinone derivatives with $MIC_{90}$ of 0.125 µg/mL against *M. tuberculosis* H37Rv, two times lower than that of linezolid [9]. In another work, Kaushik., *et al.* described a new oxazolidinone derivative 4-fold more active than linezolid against *Staphylococcus aureus* and *Enterococcus faecalis*, with $MIC_{90}$ values of 0.5 and 0.25 µg/mL, respectively [10]. Sumesh and coworkers reported a series of hybrid quinoline-oxazolidinone derivatives with potent activity against several gram-positive and gram-negative bacteria. The most active compound showed $MIC_{90}$ values in range of 0.1 to 0.8 µg/mL [11]. Importantly, the peptidyltransferase center is the active site of oxazolidinones in ribosome. This subdomain catalyzes the process of peptide bond formation [12]. The class of oxazolidinones represents one of the very few success stories of antibiotic development and these examples described above demonstrate the therapeutic potential that oxazolidinones have in the clinical medicine.

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