WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 4, 1885-1888. Review Article ISSN 2277– 7105

STUDY OF NEW ANTIBACTERIAL MECHANISM AGAINST GRAM NEGATIVE BACTERIA

[1]*Sd. Abdul Jabbar Basha, [2]K. Venkata Ramana., [3]K. Kalyan Chakravarthi, [4]E. Pragna

[1]Professor, ASN Pharmacy College, Tenali.

[2]Professor & Principal, ASN Pharmacy College, Tenali.

[3,4]Asst. Professor, ASN Pharmacy College, Tenali.

Article Received on
20 Feb. 2021,

Revised on 12 March 2021,
Accepted on 01 April 2021

DOI: 10.20959/wjpr20214-20243

***Corresponding Author**
Sd. Abdul Jabbar Basha
Professor, ASN Pharmacy College, Tenali.

ABSTRACT

Many life threatening bacteria's are responsible of dangerous diseases and they are increasing their resistant to existing antibiotics which is a matter of global concern. At present the Gram Negative bacteria like *Acnetobacter baumanii*, *Pseudomonas Aeruginosa and Enterobacteriaceae* are resistant to *carbapenam* and *cephalosporin* antibiotics. Now the report of Advancement studies of Swiss research teams headed by the Zurich University and polyphorAG discovered the characterization of new family of synthetic antibiotics that possess broad spectrum anti-gram-negative antimicrobial activity.

INTRODUCTION

Bacterial cells are generally surrounded by two protective coverings: an outer cell wall and an inner cell membrane. Certain bacteria, like the mycoplasmas, do not have a cell wall at all. Some bacteria may even have a third, outermost protective layer called the capsule. Whip-like extensions often cover the surfaces of bacteria — long ones called flagella or short ones called pili — that help bacteria to move around and attach to a host.

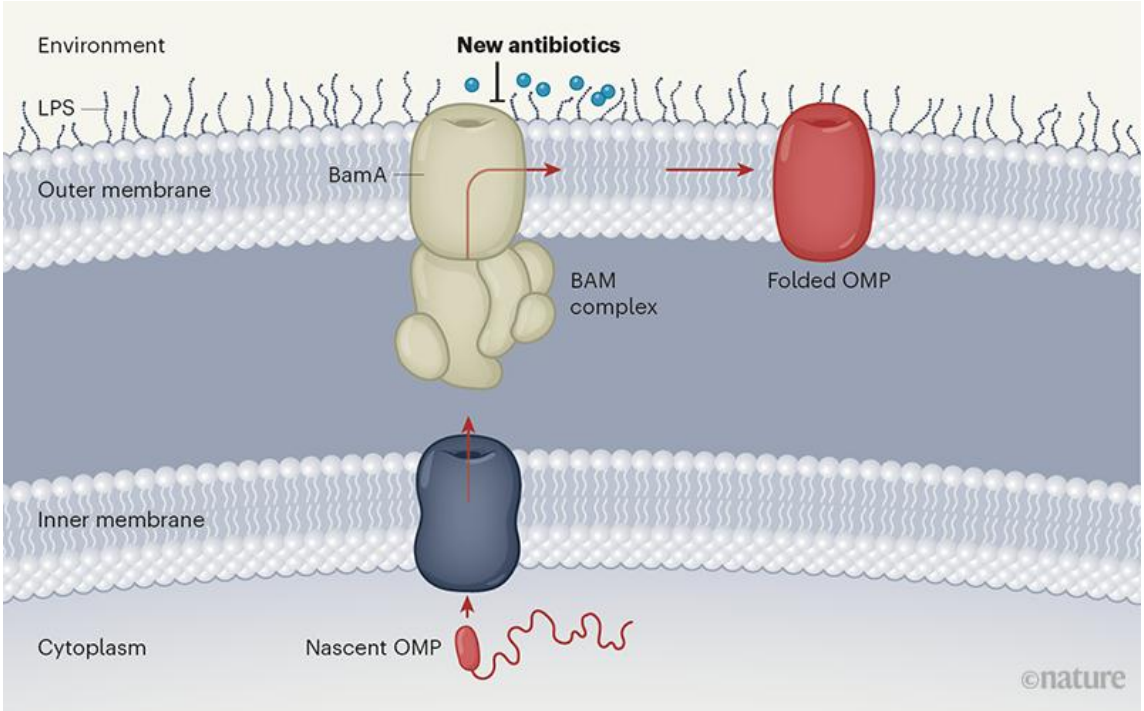
The Gram stain is a test used to identify bacteria by the composition of their cell walls, named for Hans Christian Gram, who developed the technique in 1884. The test stains Gram-positive bacteria, or bacteria that do not have an outer membrane. Gram-negative bacteria don't pick up the stain. For example, Streptococcus pneumoniae (S. pneumoniae), which causes pneumonia, is a Gram-positive bacterium, but Escherichia coli (E. coli) and Vibrio cholerae, which causes cholera, are Gram-negative bacteria.

ANTI BACTERIAL ACTIVITY

Antibiotics are typically used to treat bacterial infections. However, in recent years, improper and unnecessary use of antibiotics has promoted the spread of several strains of antibiotic-resistant bacteria. Antibacterial action generally falls within one of four mechanisms, three of which involve the inhibition or regulation of enzymes involved in cell wall biosynthesis, nucleic acid metabolism and repair, or protein synthesis, respectively. The fourth mechanism involves the disruption of membrane structure. Many of these cellular functions targeted by antibiotics are most active in multiplying cells. Since there is often overlap in these functions between prokaryotic bacterial cells and eukaryotic mammalian cells, it is not surprising that some antibiotics have also been found to be useful as anticancer agents.

Gram Negative Bacteria

The outer membrane of Gram-negative bacteria contains lipopolysaccharide (LPS) molecules in its outer leaflet, with outer-membrane proteins (OMPs)8 spanning the entire outer membrane. OMPs are folded into the membrane by a protein complex called the β-barrel assembly machine (BAM), the central component of which, BamA, is an OMP itself (Fig. 1). Because BamA is exposed to the extracellular space, it could be an Achilles heel in the bacterial shield — inhibitors that access BamA would not need to penetrate the cell. Indeed, a proof-of-concept study9 has shown that this approach inhibits OMP folding and compromises membrane integrity, albeit by an unknown mechanism.



Novel family of antibiotics against dangerous bacteria

Swiss research teams headed by the University of Zurich (UZH) and Polyphor AG now report the discovery and characterization of a new family of synthetic antibiotics that possess broad-spectrum anti-Gram-negative antimicrobial activity. "The new antibiotics interact with essential outer membrane proteins in Gram-negative bacteria," says John Robinson from the UZH Department of Chemistry, who co-headed the study. "According to our results, the antibiotics bind to complex fat-like substances called lipopolysaccharides and to BamA, an essential protein of the outer membrane of Gram-negative bacteria," Robinson adds. BamA is the main component of the so-called ß-barrel folding complex (BAM), which is essential for outer membrane synthesis. After targeting this essential outer membrane protein, the antibiotics destroy the integrity of the bacterial membranes and the cells burst. The outer membrane of Gram-negative bacteria has the important function to protect the cells from toxic environmental factors, such as antibiotics. It is also responsible for the uptake and export of nutrients and signaling molecules. "Despite its critical importance, so far no clinical antibiotics target these key proteins required for outer membrane biogenesis," says. The research was carried out in close collaboration with Polyphor AG, a former UZH start-up Robinson company that was founded in 1996. The clinical stage biopharmaceutical company based in Allschwil now plans to progress one compound into human clinical trials. "POL7306, a first lead molecule of the novel antibiotics class, is now in preclinical development," says Daniel Obrecht, chief scientific officer at Polyphor and co-head of the work.

1. Darobactin displayed antibiotic activity against multiple Gram-negative bacteria, both in vitro and in infected mice, including against several drug-resistant human pathogens such as polymyxin-resistant Pseudomonas aeruginosa and β-lactam-resistant Klebsiella pneumoniae and Escherichia coli. Darobactin was not toxic to human cells at the concentrations at which it was an effective antibiotic. The authors provided evidence that darobactin and BamA bind to each other directly, using a technique called isothermal titration calorimetry, which measures the heat changes associated with physical interactions between molecules.

2. Murepavadin displays potent but narrow antibiotic activity against P. aeruginosa10. The authors therefore screened for murepavadin analogues that had antibiotic activity against other Gram-negative species.

3. In the third study, Hart et al.7 identified a compound, MRL-494, that had similar antibiotic potency against both wild-type E. coli and a mutant defective in outer-membrane integrity and efflux mechanisms, suggesting that this antibiotic might not need to penetrate the cell to exert its activity. In vitro, MRL-494 exhibited moderate potency against Gram-negative pathogens, including K. pneumoniae and P. aeruginosa. The efficacy of MRL-494 in animal models remains to be tested.

These studies describe new antibiotics that are active against difficult-to-treat Gram-negative bacteria. Given the compounds' size and chemistry, they are likely to act at the cell surface, bypassing the need to breach the permeability barrier. Imai et al. provided compelling evidence that BamA is the target of darobactin, including a putative binding site, to be confirmed by demonstrating reduced binding to resistant mutants. The chimaeric compounds both seem to bind BamA and LPS. But, as is also the case for MRL-494, further experiments will be required to determine whether their activity is caused by direct effects on BamA.

REFERNCES

1. Antibiotics with novel mechanism of action discovered article published by the zhurich university, oct 23, 2019.
2. What are bacteria by aparna sagar and life science contributor, April 25, 2019.
3. New antibviotics target the outer membrane of the bacteria, Marcelo c souza, December 09, 2019.