

Dear Reviewer 1

Here you can find all the corrections you have required.

Page 1, line 41 Carbapenem antibiotics are considered the first line treatment for infections caused by the most resistant bacteria such as: *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, Enterobacteriaceae, (*Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter* spp., *Serratia* spp., *Proteus* spp.), *Enterococcus faecium*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Shigella* spp., *Mycobacterium tuberculosis*. The worldwide developing of antibiotic resistance is considered a serious healthcare problem

Page 1, Line 42: Carbapenem antibiotics are considered the first line treatment for infections caused by the most resistant bacteria such as: *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, Enterobacteriaceae, (*Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter* spp., *Serratia* spp., *Proteus* spp.), *Enterococcus faecium*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Shigella* spp., *Mycobacterium tuberculosis*. The worldwide developing of antibiotic resistance is considered a serious healthcare problem

Page 2, Line 47: These bacteria are part of ESKAPE group (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* species) which causes approximately in the United States more than 2 million people infected with antibiotic-resistant bacteria annually, with 23,000 deaths as a direct result

Page 2, Line 48: These bacteria are part of ESKAPE group (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter* species) which causes approximately in the United States more than 2 million people infected with antibiotic-resistant bacteria annually, with 23,000 deaths as a direct result

Page 2, Line 57: I've rewritten the text

Page 2, Line 58: I've rewritten the text

Page 2, Line 59: I've rewritten the text

Page 2, Line 67: I've rewritten the text

Page 2, Line 71: I've rewritten the text

Page 2, Line 72: I've rewritten the text

Page 2, Line 73: I've rewritten the text

Page 2, Line 85. Some small hydrophilic: antibiotics such as β -lactams, as well as tetracycline, chloramphenicol and fluorochinolones diffuse through aqueous channels in the outer membrane that are formed by proteins (Omp) called porins

Page 2, Line 87: . Some small hydrophilic: antibiotics such as β -lactams, as well as tetracycline, chloramphenicol and fluorochinolones diffuse through aqueous channels in the outer membrane that are formed by proteins (Omp) called porins

Page 3, Line 97: in *P. aeruginosa*, *E. coli*, and *Neisseria gonorrhoeae*.

Page 3, Line 101: I've rewritten the text

Page 3, Line 109-110: : I've rewritten the text Page 3, Line 126: heavy"

Page 3, Line 130: Changed

Page 3, Line 131: Changed

Page 3, Line 141: “: I've rewritten the text

Page 3, Line: 146-147: changed

Page 3, Line 149: The resistance to streptomycin, to quinolones, to rifampin and others antibiotic structures groups is caused by a series of mutation that can occur into the gene encoding the target protein, the protein concerned with drug transport and/or with drug activation

Page 4, Line 154: ok

Page 4, Line 157: I've rewritten the text

Page 4, Line:160: “I've rewritten the text

Page 4, Line:165 changed

Table 1. Gram-negative > Gram-positive.

Table 1. changed

Page 4, Line 174-175: done

Page 4, Line 177]. The MBLs is characterized by the ability to hydrolyze carbapenems (often considered as last resort drugs) and bacteria producing these β -lactamases including *A. baumannii*, *K. pneumoniae*, *E. coli* renders many beta-lactam class of antibiotics such as penicillins, cephalosporins, monobactams and carbapenems ineffectiv

Page 4, Line 177: ok

Page 4, Line 178: I've rewritten the text

Page 4, Line 179-182: I've rewritten the text

Page 4, Line 183: changed

Page 4, Line 188: changed

Page 4, Line 188: changed

Page 5, Line 189-190 changed

Page 5, Line 197: changed

Page 5, Line 200: changed

Page 5, Line 202: changed

Page 5, Line 206-207: changed

Page 5, Line 202-204: : I've rewritten the text

Page 5, Line 223-225: I've rewritten the text

Page 5, Line 227-237: Class A carbapenemases are chromosomally-encoded (SME, NmcA, SFC-1, BIC-1, PenA, FPH-1, SHV-38), plasmid-encoded (KPC, GES, FRI-1), or both (IMI). [38] Among these the best known KPC (*Klebsiella pneumoniae* carbapenemase) have spread all around the world and have been isolated in most of the clinical enterobacterial species such as: *P. aeruginosa* and *A. baumannii*. Generally, class A carbapenemases reduces susceptibility to imipenem for the bacteria sensitive to it and allows the hydrolysis of a broad variety of β -lactams, including carbapenems.[39]

Page 5, Line 239 changed

Page 6, Line 244: done

Page 6, Line 248-249 changed

Table 2. changed

Page 6, Line: 266: changed