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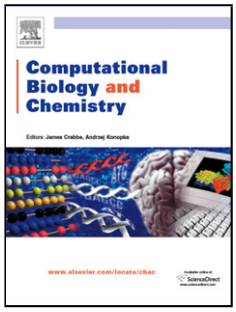

Title: Exploring the resistance mechanism of imipenem in carbapenem hydrolysing class D beta-lactamases OXA-143 and its variant OXA-231 (D224A) expressing *Acinetobacter baumannii*: An *in-silico* approach

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<AT>Exploring the resistance mechanism of imipenem in carbapenem hydrolysing class D beta-lactamases OXA-143 and its variant OXA-231 (D224A) expressing *Acinetobacter baumannii*: An *in-silico* approach

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416-2243092.

<ABS-Head><ABS-HEAD>Graphical abstract
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<ABS-HEAD>Highlights► Molecular docking and simulations are done for OXA-143 and OXA-231 CHDLs with imipenem ► Imipenem has increased binding affinity with OXA-143 CHDL than OXA-231 CHDL ► Molecular dynamics study reveals high stability of OXA-143 CHDL- imipenem complex. ► Lesser stability indicates the effectiveness of imipenem against OXA-231 CHDL

<ABS-HEAD>Abstract

<ABS-P>*Acinetobacter baumannii* (*A. baumannii)*, is a Gram negative, coccobacilli and is associated with nosocomial infections. The bacterium has developed resistance to all known classes of antibiotics. Multi-drug resistant *A. baumannii* infections have been treated with the carbapenem group of antibiotics like imipenem and meropenem. Recent reports indicate that *A. baumannii* has acquired resistance to imipenem due to the secretion of carbapenem hydrolysing class D beta-lactamases (CHDLs). Such CHDLs found in carbapenem resistant *A. baumannii* belongs to OXA-143 and its variant OXA-231, which has Alanine (A) in place of Aspartic acid (D) at sequence position 224. The mutation of the OXA-231 CHDL alters the catalytic activity of the enzyme. Hence, the present study was carried out to find the probable mechanism of imipenem resistance in OXA-143 and OXA-231 (D224A) CHDLs expressing *A. baumannii* by employing molecular docking and dynamics
<ABS-P><ST>methods</ST> Our study reveals that OXA-143 CHDL-imipenem complex has more binding affinity than OXA-231 (D224A) CHDL-imipenem complex. Our results indicate that there is a strong binding affinity of OXA-143 with imipenem when compared