Combating Metallo- carbapenemase in *E. coli* & *K. pneumoniae* isolates

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Introduction

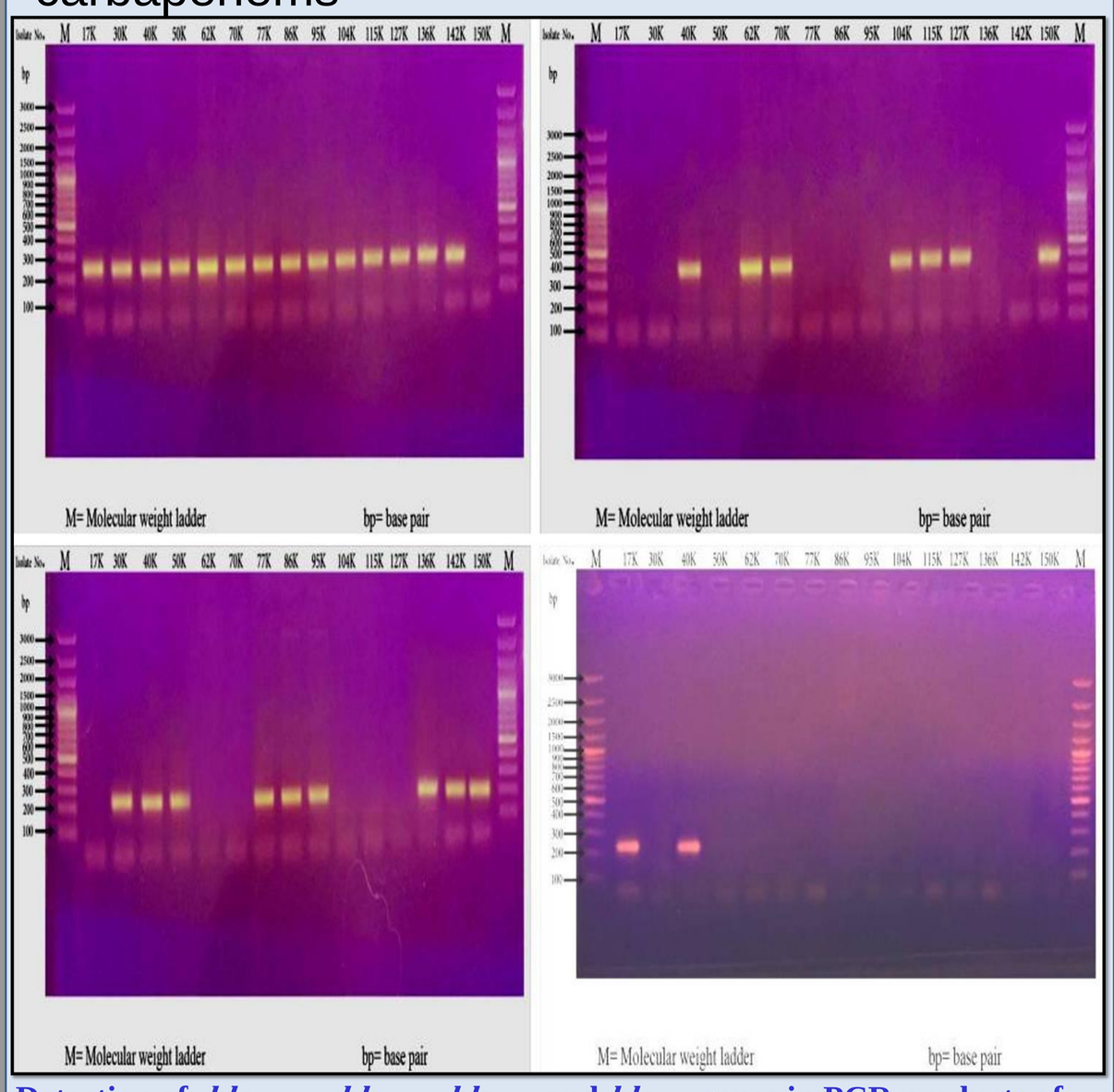
Carbapenems are the last choice in treating serious infections (Zhanel et al., 2007). β-lactamases, include class B metallo-enzymes (MBLs), require Zn ion for substrate hydrolysis (Walash et al., 2007), resist β-lactamase-Is, inhibited by metal ion chelators & hydrolyze carbapenems, penicillins & most cephalosporins. (Queenan et al., 2007). NDM1 , VIM & IMP, are common MBLs incorporated as gene cassettes within integron structures. The transfer between bacteria is facilitated when these integrons become associated with plasmids or transposons (Drawz et al., 2014).

Materials and Methods

Escherichia coli and Klebsiella pneumoniae carbapenem resistant isolates were recovered from 300 clinical isolates.

They were subjected phenotypically for detection of class B metallo-carbapenemase (MBL) producers (by carbapenem disks with or without EDTA), and were subjected for confirmation genotypically by PCR.

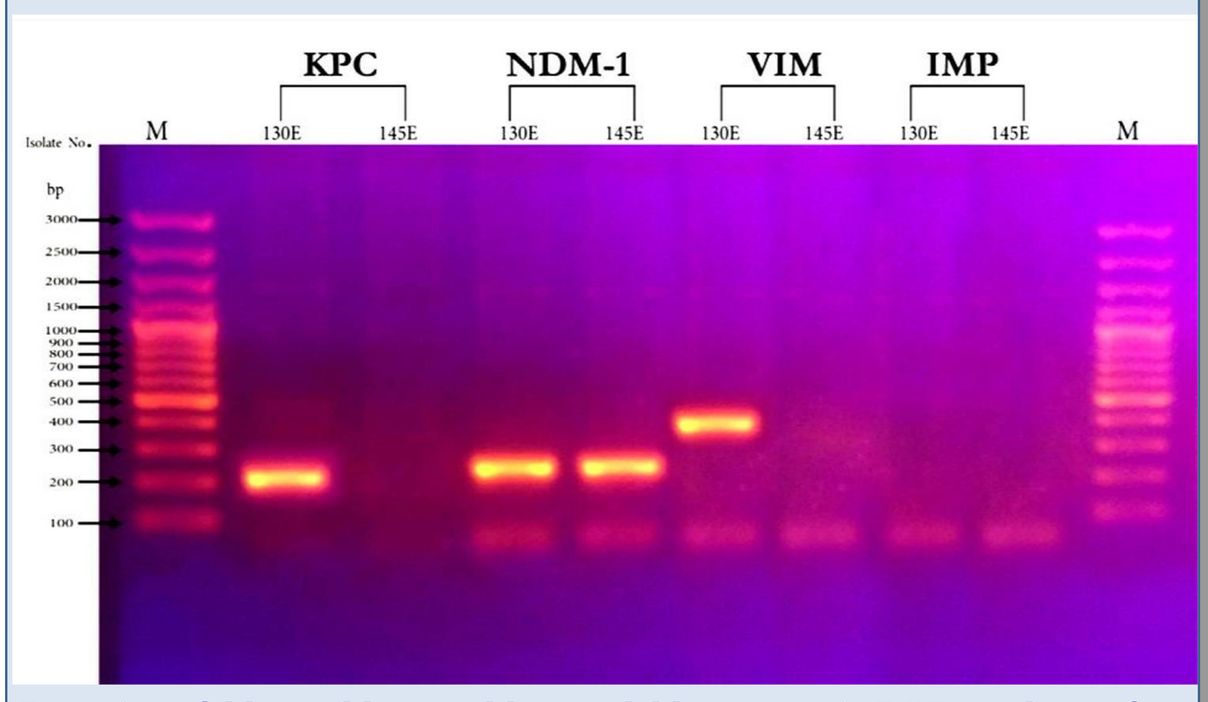
In addition, the synergistic activities of MBL-inhibitors like malic acid, citric acid and ascorbic acid in combination with carbapenems



Detection of *bla*$_{NDM-1}$, *bla*$_{VIM}$, *bla*$_{KPC}$ and *bla*$_{IMP}$ genes in PCR products of carbapenem resistant *K. pneumonia* isolates.

Results

Two *E. coli* & 15 *K. pneumoniae* isolates produced metalo- carbapenemases. The genes encoding *bla*$_{NDM-1}$ carbapenemase were detected in 16/17 isolates, or collaboratively with either *bla*$_{VIM}$, or *bla*$_{IMP}$ or both in all carbapenem resistant isolates, by PCR method. The *NDM-1* gene was detected in 94.1% of carbapenem resistant isolates, *VIM* and *IMP* genes were detected in 47% and 11.8% of MBL-isolates, respectively. A previous Egyptian study reported a higher rate of *bla*$_{VIM}$ gene in clinical isolates of *E. coli* (66.6%) and *Klebsiella pneumonia* (80%) (Mohammed *et al*., 2016). Sub-inhibitory concentrations of citric acid, malic acid and ascorbic acid in combination with imipenem or meropenem exerted synergistic activities against metallo-carbapenemases. Their activities are probably attributed to the chelation of zinc ions which is required for the active site of metallo-carbapenemase



Detection of *bla*$_{KPC}$, *bla*$_{NDM-1}$, *bla*$_{VIM}$ and *bla*$_{IMP}$ genes in PCR products of carbapenem resistant *E. coli* isolates.

Conclusions

We successfully used the combinations of carbapenems with malic acid, citric acid and ascorbic acid to inhibit carbapenemase-producing K. pneumoniae and E.coli.

Further studies will be conducted to elucidate the inhibitory mechanism of the previous combinations on resistance due to KPC-producing isolates on the molecular level

References

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