

# The Synergistic Effect of Combining Some Antibiotics with Powder of Silver NPs, Copper NPs and Titanium NPs

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## Abstract

Routine antibiotics susceptibility testing still relies on standardized cultivation-based analyses, including measurement of inhibition zones in conventional agar diffusion tests. The sensitivity of the bacterial isolates causing Clinical isolates test results showed that all the isolates subjected to this study showed varying resistance to the antibiotics used. The effect of nanoparticles combined with different antibiotics was investigated against multi resistant Clinical isolates bacteria using disk diffusion method. The inhibition zones diameter (mm) around various antibiotic discs (Trimethoprim, sulphamethaxazol, Azithromycin, Aztreonam, Ceftriaxone, Gentamycin, Tetracyclin, Nitrofurantoin) with/without nanoparticles against isolates were measured. The antibacterial activities of some antibiotics have been increased in the presence of nanoparticle against all isolates while others showed no effect. The highest antibacterial activities of antibiotics combined with nanoparticle were observed against *E.coli* isolates for Gentamycin, Trimethoprim-sulphamethaxazol, Azithromycin, Tetracyclin, Nitrofurantoin. while *A. baumannii* appeared sensitive to Gentamycin, Trimethoprim sulphamethaxazol and Azithromycin compared with antibiotics alone. *K.pneumoniae* became sensitive to Gentamycin, Tetracyclin and *P.aeruginosa* to Ampicillin, Trimethoprim sulphamethaxazol, Azithromycin and Gentamycin. nanoparticle showed no effect on antibacterial activities of all antibiotics except Gentamycin against gram positive bacteria *S.aureus*.

**Keywords:** Nanoparticle, Antibiotics, Toxicity; inhibition.

## Introduction

Nanoparticles: nanomaterials as a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or agglomerate; where 50% or more of the particles exhibited, one or more external dimensions in the size range 1–100 nm<sup>(1)</sup>. Silver nanoparticles have been used extensively in anti-bacterial agents, the antibacterial property of silver nanoparticles has allowed its wide range of application from disinfecting devices and home appliances to water treatment<sup>(2-3)</sup>. The nanoscale size makes them

comparable to the cellular components and proteins hence, nanoparticles can easily pass natural barriers<sup>(4-5)</sup>. Metal nanoparticles exhibit unique electronic, magnetic, catalytic and optical properties that are different from those of bulk metals. This may result in interesting new applications that could potentially be utilized in the biomedical sciences and areas such as optics and electronics<sup>(6)</sup>. Extracellular synthesis of metallic nanoparticles has extended its commercial applications in various fields. Since the main obstacle with a biological synthesis approach is polydispersity, it is important to improve these conditions toward mono-dispersity<sup>(7)</sup>. The antimicrobial activity of the nanoparticles is known to be a function of the surface area in contact with the microorganisms. The small size and the high surface to volume ratio<sup>(8)</sup>. The activity was

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**Cont... Table (1):Antibiotic Susceptibility test for Clinical isolates bacteria**

K.pneumoniae1	Si	S	Re	Re	Re	Re	Re	Re	Re
K.pneumoniae2	Si	Re	Re	Re	Re	Re	Re	Re	Re
A.baumannii1	Si	Re	Re	Re	Re	Re	Re	Re	Re
A.baumannii2	Si	Re	Re	Re	Re	Re	Re	Re	Re

F=Nitrofurantoin, IPM=Imipenem, NA=Nalidixic acid , CIP=Ciprofloxacin, CN=Gentamycin, TE=Tetracyclin ,SXT =Trimethoprim/Sulphamethoxazol ,ATM=Azteroname ,Re=Resistant ,Si=sensitive.

Bacterial isolates of *E.coli* characterized by being sensitive to the Imipenem. and resistant towards (Aztreonam, Tetracyclin). Baral *et al.*<sup>(13)</sup> reported *E. coli* included resistance to Ciprofloxacin, Gentamycin .all isolates of *K.pneumoniae* were resistant toward (Aztreonam and Gentamycin) appeared sensitive to Imipenem. Either <sup>(14)</sup> resulted in his study that some bacterial isolates of *K. pneumoniae* were resistant to Nitrofurantoin. At the same time clinical isolates of *P.aeruginosa* displayed a highly resistant to(Tetracyclin, Azteroname and Nitrofurantoin).

The synergistic effect of nanoparticles with various antibiotics was studied against multi resistant clinical bacteria using disk diffusion test. The inhibition zones diameter (mm) were measured for

each control group (Trimethoprim-sulphamethaxazol, Azithromycin, Aztreonam, Ceftriaxone, Gentamycin, Tetracyclin,Nitrofurantoin)andtestgroup(nanoparticles-antibiotics mixes). The antibacterial abilities of some antibiotics have been elevated in nanoparticle presence against all isolates while others remained unaffected. The highest antibacterial activities of antibiotics combined with nanoparticle were observed against *E.coli* isolates for Gentamycin, Trimethoprim-sulphamethaxazol ,Azithromycin ,Tetracyclin ,Nitrofurantoin. while *A. baumannii* appeared sensitive to , Gentamycin ,Trimethoprim sulphamethaxazol and Azithromycin compared with antibiotics alone. *K.pneumoniae* became sensitive to Gentamycin, Tetracyclin and *P.aeruginosa* to Ampicillin,Trimethoprim sulphamethaxazol, Azithromycin and Gentamycin. nanoparticle showed no effect on antibacterial activities of all antibiotics except Gentamycin against gram positive bacteria(*S.aureus*) as inTable-2.

**Table(2): The comparative activities of various antibiotics and antibiotic with TiO<sub>2</sub> nanoparticles against Clinical isolates bacteria.**

Bacterial isolate	(SXT)		(AZM)		(ATM)		(CRO)		(CN)		(TE)		(F)	
	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>	Ab	Ab + TiO <sub>2</sub>
E.coli 1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Si	Re	Si
E.coli 2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Si	Re	Si
A.baumannii1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	R	Re	Re
A.baumannii 2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	R	Re	Re
K.pneumoniae 1	Re	R	Re	Re	Re	Re	Re	Re	Re	Si	Re	Si	Re	Re
K.pneumoniae2	Re	R	Re	Re	Re	Re	Re	Re	Re	Si	Re	Si	Re	Re
S.aureus1	Re	R	Re	Re	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
S.aureus2	Re	R	Re	Re	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
P.aeruginosa1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re

CRO=Ceftriaxone,, AZM=Azithromycin  
 F=Nitrofurantoin, CN=Gentamycin, TE=Teteracyclin  
 ,SXT =Trimethoprim /Sulphamethoxazol,ATM=  
 Azteroname ,Re=Resistant ,Si=sensitive ,Ab:Antibiotic

in conjugation with biologically synthesized Ag nanoparticles increased the susceptibility against *E. coli*, *S. aureus*, *P. aeruginosa* and *K. pneumoniae*. Combination Ciprofloxacin and Imipenem with nanoparticles were found to be most efficient in inhibiting bacteria, if bacteria improves resistance to one of them, the other bactericidal agent would kill the bacteria <sup>(15)</sup>.

A synergistic effect of antibiotics (Imipenem, Gentamycin, Vancomycin, and Ciprofloxacin)

**Table(3): The comparative activities of various antibiotics and antibiotic with Cu nanoparticles against Clinical isolates bacteria.**

Bacterial isolate	(SXT)		(AZM)		(ATM)		(CRO)		(CN)		(TE)		(F)	
	Ab	Ab + Cu	Ab	Ab + Cu	Ab	Ab + Cu	Ab	Ab + Cu	Ab	Ab + Cu	Ab	Ab + Cu	Ab	Ab + Cu
E.coli 1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Si	Re	Si
E.coli 2	Re	Si	Re	Re	Re	Re	Re	Re	Re	Si	Re	Si	Re	Si
A.baumanii 1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	R	Re	Re
A.baumanii 2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
K.pneumoniae 1	Re	R	Re	Re	Re	Re	Re	Re	Re	Si	Re	Re	Re	Si
K.pneumoniae2	Re	Si	Re	Re	Re	Re	Re	Re	Re	Si	Re	Si	Re	Re
S.aureus1	Re	Re	Re	Re	Re	Si	Re	Re	Re	Si	Re	Re	Re	Re
S.aureus2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
P.aeruginosa1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Re	Re	Re	Re	Re

CRO=Ceftriaxone,, AZM=Azithromycin F=Nitrofurantoin, CN=Gentamycin, TE=Teteracyclin ,SXT =Trimethoprim /Sulphamethoxazol,ATM= Azteroname , Re =Resistant , Si =sensitive , Ab:Antibiotic

**Table(4): The comparative activities of various antibiotics and antibiotic with Ag nanoparticles against Clinical isolates bacteria**

Bacterial isolate	(SXT)		(AZM)		(ATM)		(CRO)		(CN)		(TE)		(F)	
	Ab	Ab + Ag	Ab	Ab + Ag	Ab	Ab + Ag	Ab	Ab + Ag	Ab	Ab + Ag	Ab	Ab + Ag	Ab	Ab + Ag
E.coli 1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Si	Re	Re
E.coli 2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	R	Si
A.baumannii 1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
A.baumannii 2	Re	Si	Re	Si	Re	Re	Re	S	Re	Si	Re	Re	Re	Re
K.pneumoniae 1	Re	R	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
K.pneumoniae2	Re	Si	Re	Re	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
S.aureus1	Re	Si	Re	Re	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
S.aureus2	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re
P.aeruginosa1	Re	Si	Re	Si	Re	Re	Re	Re	Re	Si	Re	Re	Re	Re

CRO=Ceftriaxone,, AZM=Azithromycin F=Nitrofurantoin, CN=Gentamycin, TE=Teteracyclin ,SXT =Trimethoprim /Sulphamethoxazol,ATM= Azteroname , Re =Resistant , Si =sensitive , Ab:Antibiotic, Ag: Nanoparticles.

The antibiotics-metal nanoparticles conjugates could boost the effectiveness of antibiotics against resistant pathogens. Moreover, nanoparticle–antibiotic complex reduces the amount dosage of both agents, thus increasing the antimicrobial properties and reducing risk that associated with high antibiotic doses. In addition,, due to this coupling, the concentrations of antibiotics were increased at the point of antibiotic-microbe contact and thus accelerate the antibiotic-microbe binding (16-17). Urgent and growing need for antibacterial agents to fight those pathogenic microbes that continuously developed their resistance against traditional antibiotics(18). Nanomaterials release ions, which react with the thiol group (-SH) of the proteins display on the bacterial surface due to inactivated proteins resulted decreasing the membrane permeability then cell death

(19). Moreover, (20) studied the Synergistic effect of silver nanoparticles and ampicillin were noticed against *E. faecium*, *Streptococcus mutans* and *E. coli* ATCC 25922, while Synergistic effects of Ag nanoparticles and Chloramphenicol were found only against *E. faecium* and *P. aeruginosa*. The explanation of synergistic combination of nanoparticles and Chloramphenicol exhibited increased hydroxyl radical formation which is might be an important cause of the synergism. Other studies reported that antibacterial activity of nanoparticle along with antibiotics Ampicillin and Gentamicin against *S. typhi* increased in the presence of nanoparticles(21).

### Conclusion

we would like to conclude that due to poor diagnostics and overdose and incapability of drugs, microorganisms

are commonly able to develop resistance against antibiotics. The infections caused by microorganisms are a serious global healthcare issue. Were developed nanoparticles and had proven strong efficacy against various pathogens, either individually or in combination with antibiotics.

**Ethical Clearance:** The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

**Conflict of Interest:** Non

**Funding:** Self-funding

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