بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

The Combined Antimicrobial Activity of Citrus Honey and Fosfomycin on Multidrug Resistant *Pseudomonas aeruginosa* Isolates

Thesis

Submitted for Partial Fulfillment of M.D. Degree
in ***Medical Microbiology and Immunology***

By

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Amira Saied Mohammed Abdelhady

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List of Abbreviations

Abb.	Full term
AIDS	*Acquired immunodeficiency syndrome*
ATCC	*American type culture collection*
°C	*Celsius*
CDC	*Centre for Disease Control and Prevention*
CF	*Cystic fibrosis*
CLSI	*Clinical laboratory standards institute*
DNA	*Deoxyribonucleic acid*
E. coli	*Escherichia coli*
ECDC	*European Centre for Disease Prevention and Control*
ESBL	*Extended spectrum beta-lactamases*
E-test	*Epsilometer test*
ETT	*Endotracheal tube*
EUCAST	*European Committee on Antibiotic Susceptibility Testing*
ExoU	*Exoenzyme U*
G-6-P	*Glucose 6-phosphate*
HAIs	*Hospital acquired infections*
ICUs	*Intensive care units*
IDSA	*Infectious Diseases Society of America*
MDEPs	*Multidrug efflux pumps*
MDR	*Multidrug resistant*
µg	*Microgram*
MHA	*Muller Hinton agar*
MIC	*Minimal inhibitory concentration*
min	*Minute*
ml	*Milliliter*

List of Abbreviations cont...

Abb.	Full term
MRSA	*Methicillin resistant Staphylococcus aureus*
P. aeruginosa	*Pseudomonas aeruginosa*
PCR	*Polymerase chain reaction*
PDR	*Pandrug resistant*
PEP	*Phosphoenolpyruvate*
RNA	*Ribonucleic acid*
s	*Second*
S. aureus	*Staphylococcus aureus*
SD	*Standard deviation*
sig.	*Significance*
SPSS	*Statistical package for Social Science*
T3SS	*Type III secretion system*
UDPMurNAc	*Uridine diphosphate N-acetylmuramic acid*
UK	*United Kingdom*
USA	*United states of America*
UTIs	*Urinary tract infections*
V/V	*Volume per volume*
VAP	*Ventilator associated pneumonia*
VRE	*Vancomycin resistance Enterococci*
XDR	*Extensively drug resistant*

Introduction

Development and spread of antibiotic resistance is an alarming threat to effective treatment and prevention of bacterial infections in humans and animals. Solving this problem necessitates searching for natural antimicrobial alternatives. Currently, more researchers are turning their attention to traditional medicines as a potential source of antimicrobial agents ***(Wasfi et al., 2016).***

The medicinal effects of honey date back to the days of Aristotle (384–322 BC) for the treatment of sore eyes and wound infections. This reputation has continued up to the present day, leading to the emergence of a relatively new branch of alternative medicine, called "apitherapy", which focuses on medical applications of honey and other bee products. Different types of honey have been used in many countries as an alternative to pharmaceutical products for treating infected burn wounds. This is attributed to the effectiveness of these honeys in inhibiting or killing different types of bacteria ***(Vandamme et al., 2013 and Almasaudi et al., 2017).***

Pseudomonas aeruginosa is a common opportunistic micro-organism that causes various infections in human beings. It is often associated with different types of health care associated infections. Because it possesses a battery of virulence genes, *Pseudomonas aeruginosa* can cause both acute and chronic diseases. *Pseudomonas aeruginosa* antimicrobial resistance is due to its

potential ability to acquire new antimicrobial resistance genes and is enhanced by its ability to form biofilm ***(Camplin and Maddocks, 2014 and Hassuna, 2016).***

Type III secretion system has been identified as a major virulence determinant in the pathogenesis of acute *Pseudomonas aeruginosa* infections. Type III secretion system allows the delivery of various effector toxins as *exoenzyme S, exoenzyme U, exoenzyme Y,* and *exoenzyme T* into host cells, which can facilitate the pathogen cellular invasion. Various studies suggest that *exoenzyme U*-producing strains are associated with poor outcomes, resistance to many antibiotics and high mortality rates ***(Hassuna, 2016).***

As the use of novel antimicrobial agents became limited, the re-evaluation of older antibiotic agents seems to be an appealing option. Fosfomycin is an old and decommissioned antibiotic that inhibits the initial steps of cell wall synthesis and was previously used mainly as oral treatment for uncomplicated urinary tract infections. It currently attracts clinicians' interest worldwide due to its reported activity against pathogens with advanced resistance and treatment of difficult infections ***(Matthew et al., 2016).***

The use of antibiotics exerts selection pressures that favor the emergence of mutants with antibiotic resistance determinants. Experiments with honey indicate that bacteria failed to manifest resistance to honey in the laboratory. It can

be postulated that combinations of antibiotic and honey would be less likely to encourage the emergence of multidrug resistant bacteria than antibiotics alone ***(Jenkins and Cooper, 2012).***

Aim of the Work

The aim of the present study was to evaluate the synergistic antibacterial effect of citrus honey and fosfomycin on multidrug resistant *Pseudomonas aeruginosa*.