The effect of *Lactobacillus acidophilus as* a probiotic against *Pseudomonas aeruginosa* growth and biofilm formation

Thesis

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༺ List of Abbreviations ༻

A	**AHLs**	Acylated homoserine lactones
	AIDs	Acquired immunodeficiency syndrome
	AME	Aminoglycoside modifying enzymes
	AMPs	Antimicrobial Peptides
	ATPase	Adenosine triphosphatase
C	**°C**	Degrees Celsius
	C.albicans	*Candida albicans*
	CF	cystic fibrosis
	CFU	Colony forming unit
	CTAs	Cancer-testis antigens
D	**Dept**	Department
	DNA	Deoxyribonucleic acid
	DNAses	Deoxyribonucleases
E	**eDNA**	Extracellular DNA
	EDTA	Ethylenediaminetetraacetic acid
	EPS	Extracellular polymeric substances
	E-coli	*Escherichia coli*
	ESBLs	extended-spectrum β-lactamases
F	**FAO**	Food and Agriculture Organization
G	**GALT**	Gut-associated immune cells
	G. vaginalis	*Gardenella vaginalis*
	Gm	Gram
H	**HAI**	Health care associated infections
	H_2O_2	Hydrogen peroxide
	HDL	High density lipoprotein
	HGT	Horizontal gene transfer

	Hrs	Hours
	HSL	Homoserine lactone
I	**ICUs**	Intensive care units
	IgA	Immunoglobulin A
	IL	Interleukin
	IFN-γ	Interferon gamma
k	**KD**	Killo Dalton
L	**LAB**	Lactic acid bacteria
	L.acidophilus	*Lactobacillus acidophilus*
	LDL	low density lipoprotein
M	**MBC**	minimum bactericidal concentration
	MDEPs	multidrug efflux pumps
	MDR	Multi drug resistance
	MMRS	methyl- directed mismatch repair system
	Mg	Milligram
	µg	Microgram
	MIC	Minimum inhibitory concentration
	Min	Minute
	Ml	Milliliter
	µL	Microliter
	Mub	Mucus-binding protein
	MTP	Microtitre plate
N	***N. gonorrhoeae***	*Nisseria gonorrhoeae*
O	**Opr**	Outer membrane protein
P	***P.aeruginosa***	*Pseudomonas aeruginosa*
	PVC	polyvinylchloride
Q	**QS**	Quorum sensing
	QSIs	Quorum sensing inhibitors

R	ROS	radioactive oxygen species
S	***S. agalactiae***	*Streptococcus agalactiae*
	S.aureus	*Staphylococcus aureus*
T	**T_{reg}**	Regulatory T cells
	Th2	T helper 2
u	**UC**	Urinary catheter
W	**WHO**	World Health Organization

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Abstract

The emergence of antibiotic-resistant microorganisms as *Pseudomonas aeruginosa* has pushed efforts to find safe alternatives of antibiotics as probiotics which include Lactobacilli strains with a large antibacterial and anti- biofilm effects against different pathogenic strains. Antibiotic susceptibility test and antibiogram were done for 35 isolated *P. aeruginosa* strains from ICU patients followed by assessment of *Lactobacillus acidophilus* as antibacterial and antibiofilm formation/removal against them by using different methods. The results showed that among the 35 *P. aeruginosa* strains, 1 (2.8%), 2 (5.7%), and 32 (91.4%) were PDR, XDR, and MDR, respectively. The effective antibiotics against them was Aztreonam. *L.acidophilus* with ATCC 4356, showed powerful inhibition and anti-biofilm effects against all isolated *P. aeruginosa* strains. It significantly inhibits biofilms by 68.52% with mean optical density reading 0.72 ± 0.44 and removes already formed biofilms by 43.8 % with mean optical density reading 1.28 ± 0.65. It was concluded that *L.acidophilus* can be used in bio-control of different antibiotic resistant biofilm producing *P.aeruginosa* strains.

Key words:
Antibiotic resistance. *Lactobacillus-acidophilus*. Probiotic.*Pseudomonas-aeruginosa*

Introduction

Bacterial biofilms are complex structured communities of bacterial cells enclosed in a self-produced polymer matrix that is attached to a surface. Biofilms protect and allow bacteria to survive and thrive in hostile environments. Bacteria within biofilms can withstand host immune responses and are much less susceptible to antibiotics and disinfectants when compared to their planktonic counterparts. Diseases associated with biofilms require great methods for their prevention, diagnosis and treatment ***(Tremblay et al., 2014)***.

P. aeruginosa causes a threatening diseases world wide especially in compromised immunity . it's one of the most common causes of recurrent UTI. The emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) strains of *P. aeruginosa* that are treated difficulty with current antibiotics causes wide efforts for finding an alternative approach for treatment ***(Gomila ,et al., 2013 ; Ha D, O'Toole ,2015)***

Probiotics are defined as live nonpathogenic microorganisms that when administered in adequate amounts confer a health benefit on the host, The use of probiotics especially *L.acidophilus* as safe and natural live microorganisms against other microorganisms are considered as an alternative to antibiotics ***(Hill, et al.,2014; Chatterjee , et al., 2015)***

As a probiotic, *L.acidophilus* can be active as microbial barriers against pathogens by competition with them for binding sites, enhancement of the host's immune responses and production of antimicrobial substances as hydrogen peroxide , organic acids like lactic, formic, acetic, propionic and butyric acids together with proteinaceous compounds as bacteriocins, bacteriocin-like components ***(Marianelli et al, 2010).***

L.acidophilus has potent activity of biofilm inhibition/removing, in addition to its antibacterial effect. This proposes it as potential probiotics for bio-control of antibiotic-resistant *P. aeruginosa* strains as alternative to antibiotics ***(Shokri et al ., 2018).***