The 10th Palestinian Pharmaceutical Conference

Multidrug Resistance (MDR): A Widespread Phenomenon in Pharmacological Therapies, The experience of the (SDIPI) Institute– Birzeit University

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MDR and mortality in critically ill patients

Neutropenic patients: antibiotic prophylaxis in post-chemotherapy afebrile significantly reduced the infection-related and all-cause mortality

Diabetic patients: Polymicrobial infections are associated with an increased risk of amputations, prolonged hospital stay, increased expenses and higher infection-related mortality

Ventilator-associated pneumonia: caused by multidrug resistant (MDR) pathogens represent a common and severe problem with increased mortality.

{DOC, Culture, Dose, Duration}: Necessitated novel antibacterial strategies Due to the increasing prevalence and severity of MDR bacterial infections

Pneumonia and ways

SYMPTOMS	POINTS
Confusion	1
Urea>7mmol/l	1
Respiratory rate>30	1
SBP<90mmHg, DBP<60mmHg	1
Age>=65	1

CURB-65		
Score	Risk of Death at 30 Days (%)	Location of Therapy
0	0.7	Treat as outpatient
1	2.1	Treat as outpatient
2	9.2	Outpatient or inpatient
3	14.5	Inpatient
4	40	Inpatient (± ICU)
5	57	Inpatient (± ICU)

Risk factors for MDR organisms

i. Intravenous antibiotic therapy within the past 90 days

ii. Hospitalization of 5 days or more

iii. Septic shock at time of VAP

iv. Acute respiratory distress syndrome preceding VAP

v. Acute renal replacement therapy before VAP

The experience of the (SDIPI) Institute articles

Article #1

Urinary tract infection and Antimicrobial resistance patterns of pediatric community-acquired urinary infections: descriptive study

Hani A. Naseef, Aya H Mousa, Reem Kh Sroor, Nimeh Al-Shami, Haya O. Sultan, Yousef Sahoury, Sana'a Alkhatib, Mohammad Farraj, Abdallah D. Abukhalil.

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Article #2

Surgical Site Infections in one Palestinian Governmental Hospital Pathogen Identification and Antibiotic Sensitivity Testing: Experimental study

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Abstract:

Introduction: Surgical site infections (SSIs) are a major cause of morbidity and mortality even in hospitals with most modern facilities. The purpose of this study was to identify bacterial pathogens that cause postsurgical wound infections

Article #3----COVID-19

F1000Research F1000Research 2022, 11:30 Last updated: 17 JUN 2022

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RESEARCH ARTICLE

REVISED Bacterial and fungal co-infections among ICU COVID-19 hospitalized patients in a Palestinian hospital: a retrospective cross-sectional study [version 2; peer review: 2 approved]

Hani A. Naseef[1], Ula Mohammad[1], Nimeh Al-Shami[1], Yousef Sahoury[1], Abdallah D. Abukhalil[1], Mutaz Dreidi[2], Ibrahim Alsahouri[3], Mohammad Farraj[4]

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Therapeutic options to overcome Multidrug Resistance (MDR)-Article #4

Natural Products –Oleouropine and Metal Ions –Zinc Sulfate and Copper Sulfate antimicrobial Effect

Microorganism 10^6 CFU/ml	ATCC NO.	Day	Test dilution					Control dilution (without preservative)				
			10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}
S. aureus	6538	0	->>10^3	>10^3	>10^3	>10^3	380			525	40	
		7	0	0	0	0	0				>10^3	>10^3
		14	0	0	0	0	0				>10^3	>10^3
		28	0	0	0	0	0				750	60
P. aeruginosa	9027	0	>>10^3	>10^3	>10^3	400	120			165	10	
		7	>10^3	310	35	10	0				>10^3	>10^3
		14	0	0	0	0	0				>10^3	430
		28	0	0	0	0	0			>10^3	360	
E.coli	8739	0	>>10^3	>10^3	>10^3	>10^3	200			432	30	
		7	>10^3	500	281	120	5				>10^3	>10^3
		14	0	0	0	0	0				>10^3	580
		28	0	0	0	0	0				892	100
C. albican	10231	0	>>10^3	>10^3	620	105	10		890	100	20	
		7	>>10^3	>10^3	>10^3	>10^3	300			>10^3	>10^3	
		14	>10^3	>10^3	>10^3	600	60			>10^3	>10^3	
		28	>10^3	>10^3	>10^3	311	120				1205	
A.niger	16404	0	>>10^3	>10^3	400	75	5	>10^3	475	65	5	
		7	>10^3	300	100	25	4		85	8	1	
		14	>10^3	>10^3	200	11	2		25	3	1	
		28	477	220	10	1	0		60	5	1	

❑ Pre-Formulation stage

Anti-Microbial Efficacy Test

Best Antimicrobial Effect for addition agents:

Nanoparticles Oleuropine [0.2%, 0.4%, 0.6%]

Zinc Sulfate as Ions [1%, 1.5%, 2%]

Copper Sulfate as Ions [1%, 1.5%, 2%]

Less Concentration +best effect+ less toxicity

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Research Article

Antimicrobial Activity of Oleuropine and Thyme Extracts Against Selected Pathogenic Microorganisms and their Potential Uses as Natural Preservatives

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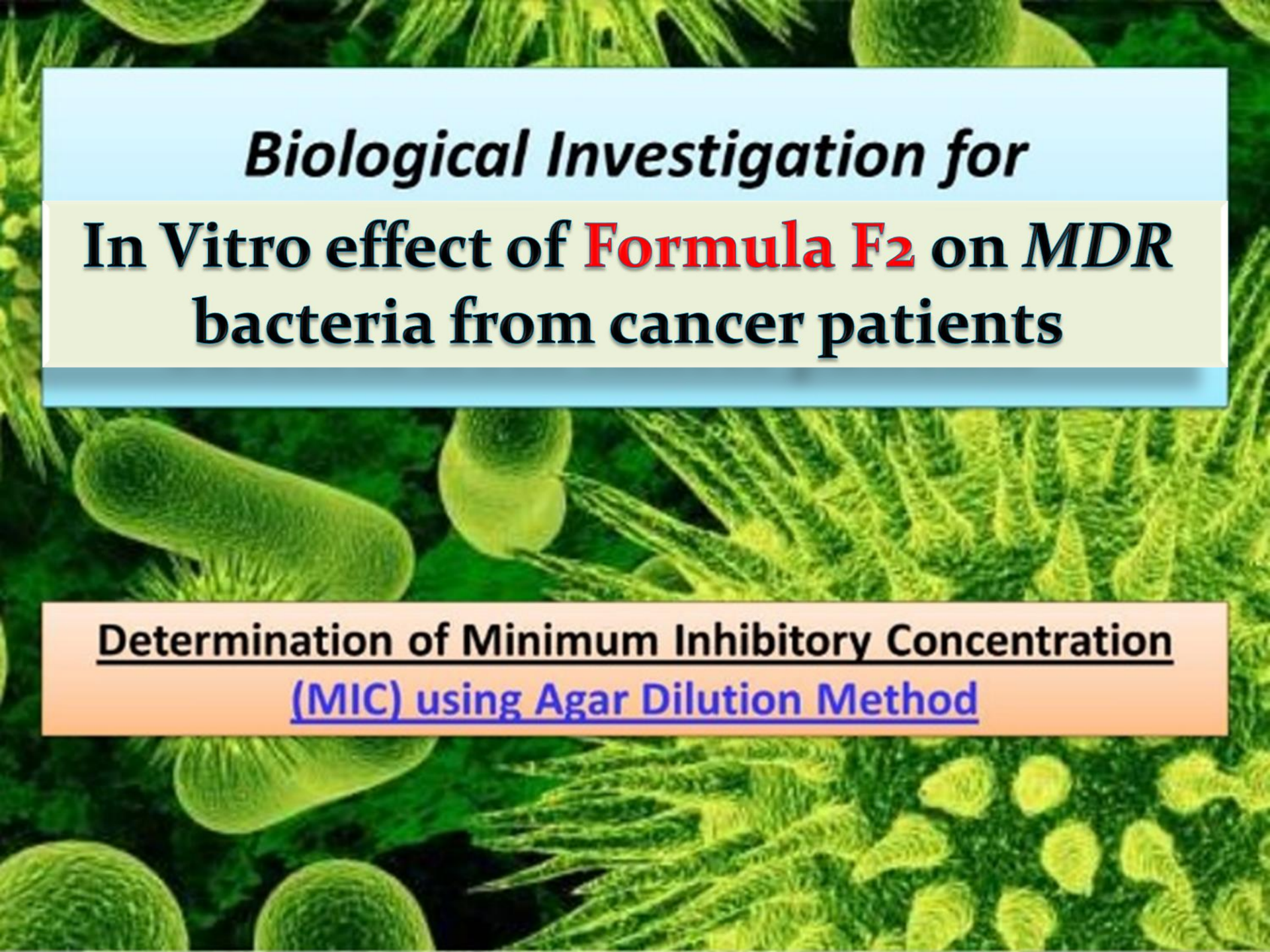
❑ Formulation stage

No.	Component	F1	F2	F3	Function
1	Fusidic Acid	2%	%2	2%	Active ingredient
2	Zinc Sulfate	1%	1.5%	2%	Antibacterial ,antiviral,
3	Copper Sulfate	1%	1.5%	2%	Antibacterial, antifungus
4	Oleuropine	0.2%	0.4%	0.6%	Antioxidant and preservative
5	Thyme oil	0.1%	0.1%	0.15%	Antioxidant and preservative
6	Cetosteroyl alcohol	7g	7g	7g	Emollient
7	Macrogol A6	1.5g	1.5g	1.5g	Emulsifying agent
8	Macrogol A25	1.5g	1.5g	1.5g	Emulsifying agent
9	Parafine oil	12g	12g	12g	Vehicle
10	Propylene glycol	8g	8g	8g	Solvent
11	Purified water	q.s	q.s	q.s	Vehicle

All formulations were evaluated at zero time, one month and after three month to describe antibacterial activity and physical stability

❖ Evaluation of different formulation at zero time(sample 1), one month (sample 2) and 3 months (sample 3) at accelerated conditions (40±2°C / 75% ±5% RH) (n=3)

Characteristic /sample	Zone of inhibition(mm)								
	F1			F2			F3		
	S.aureus	E.coli	FRSA	S.aureus	E.coli	FRSA	S.aureus	E.coli	FRSA
Control (Fucidin TM)	18.3	0	0	18.3	0	0	18.3	0	0
Sample test (1)	22.9±0.2	14.5±1.1	15.4±0.6	39.1±0.4	21.6±1.3	36.7±0.8	39.6±0.4	24.6±0.7	38.8±0.5
Sample test (2)	22.4±0.3	14.3±1.0	15.2±.5	36.8±0.5	21.4±1.4	34.5±0.7	38.2±0.2	23.8±0.9	37.6±0.8
Sample test (3)	21.2±0.2	12.6±1.4	14.1±.6	35.6±0.4	20.3±1.3	33.8±0.8	37.4±0.1	22.7±0.8	36.4±0.5
Appearance	Light green			Light green			Bold blue-greenish		
Spreadablity	Good spreadability			Good spreadability			Thick spreadability		



Biological Investigation for

In Vitro effect of Formula F2 on *MDR* bacteria from cancer patients

Determination of Minimum Inhibitory Concentration (MIC) using Agar Dilution Method

- ***In-Vitro*** **Inhibits Growth of the pathogens for F2 as compare with Fucidin TM after storage at accelerated conditions (40±2°C / 75% ±5% RH)**

E.coli MDR

C.Albicans MDR

A.Niger MDR

P.auerginosa MDR

F2 appear highly active against all microbes by inhibits growth of all pathogens as compare with fucidin TM figures

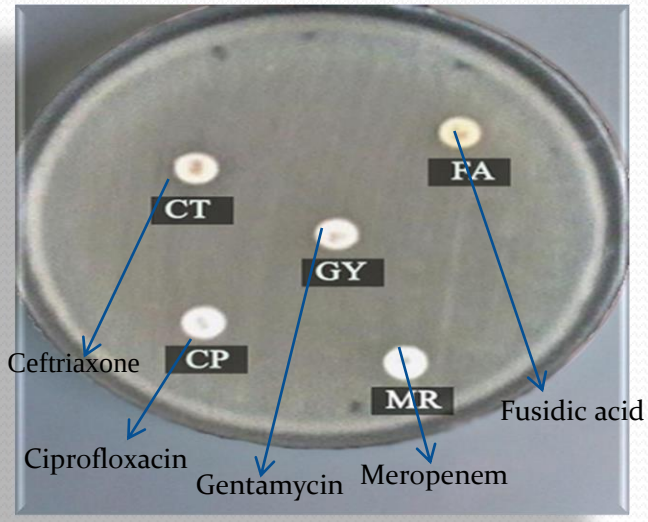
The goal has been achieved to develop formulation agent for treatment of bacterial, fungus and viral in one medical preparation

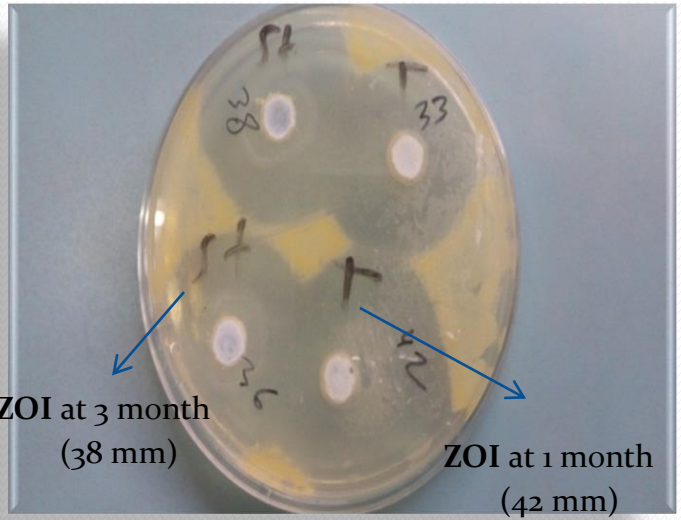
❑Determination the MICs for formula

F2 formula and its substances	Concentration of substance	MICs against pathogens
EC	*The lowest concentration of formula that prevented bacterial growth*	580 µg/ml
Zinc sulfate(ASPC)	1.5%	870 µg/ml
Copper sulfate(ASPC)	1.5%	870 µg/ml
Oleuropine(ASPC)	0.4%	232 µg/ml
Thyme(ASPC)	0.1%	58 µg/ml
Fusidic acid(AS)	2%	1160 µg/ml

- Lowest concentration of formula that prevented bacterial growth is considered to be the MIC of that formula against FRSA pathogen is 580 µg/ml = (MIC for entire cream).
- Our results showed that the strong activity was seen against FRSA sample with NCCLS acceptable range for S.aureus (MIC 0.9-875 µg/ml).
- MIC values for the active substance as part of a formulation give additive effect with active ingredient (Fusidic acid) on gram negative bacteria, FRSA, yeasts and molds.

- Result of zone of inhibition of F2 against FRSA sample (**Breast cancer and Nodular melanoma sample** case resistance to *CT*:Ceftriaxone, *FA*:Fusidic acid, *GY*:Gentamycin, CP:Ciprofloxacin, *MR*:Meropenem (Beit-Jala hospital).





(A): FRSA plate shows the resistance effect of different antimicrobial agents on S.aureus isolate

(B): FRSA plate F2 formula sensitive S.aureus shows zone of inhibition> 22 mm in diameter compared to FRSA(A) without any zone ,**T** : at first month, **st** : at third month.

❑ Stability of pharmaceutical preparation

❖ Physical parameters and assay results of **formula F2** condition at zero time and 3 month at 25°C and accelerated condition (40±2°C /75%±5% RH) (n=3)

Comparisons	Time	Precipitation	Appearance	Color	PH	Assay of Zinc sulfate	Assay of Copper sulfate	Assay of Oleuropein	Assay of Fusidic acid
F2 at 40°C	0 Time	Negative	Uniform	Light green	4.21± 0.02	99.3%± 0.73	98.5%± 1.25	98%± 0.37	101.4%± 0.12
	1Month	Negative	Uniform	Light green	4.19± 0.04	96.8%± 0.59	98.3%± 1.21	97%± 0.42	98.9%± 0.10
	3Month	Negative	Uniform	Light green	4.16± 0.03	95.4%± 0.53	92%± 1.53	95%± 0.43	97.8%± 0.12
F2 at 25°C	0 Time	Negative	Uniform	Light green	4.23± 0.05	99.8%± 0.82	98.7 %± 1.23	98.6%± 0.42	102%± 0.11
	1Month	Negative	Uniform	Light green	4.22± 0.04	99.6%± 0.79	96.4%± 1.05	97.3%± 0.26	99%± 0.13
	3Month	Negative	Uniform	Light green	4.19± 0.05	99.3%± 0.73	93.4%± 1.60	95%± 0.28	98%± 0.13

❑ Microbial stability of pharmaceutical preparation

	Period	Zone of inhibition (mm)		
		Temperature (°C)		
		4 °C	25 °C	40 °C
Plastic container	Zero time	24.42±0.06	25.35±0.21	24.8±1.41
	One month	23.54±0.05	24.55±0.28	-
	Two months	23.23±0.08	23.85±0.22	-
	Three months	22.8±0.07	22.38±0.24	-

- The antibacterial activity did not alter overtime with plastic material containers for the formula, which was observed in the diameters zone of inhibition overtime

pharmaceutics

MDPI

Article

Novel Fusidic Acid Cream Containing Metal Ions and Natural Products against Multidrug-Resistant Bacteria

Hani Naseef [1,*], Yousef Sahoury [1], Mohammad Farraj [2], Moammal Qurt [1], Abdallah D. Abukhalil [1], Nidal Jaradat [3], Israr Sabri [1], Abdullah K. Rabba [1] and Mahmmoud Sbeih [4]

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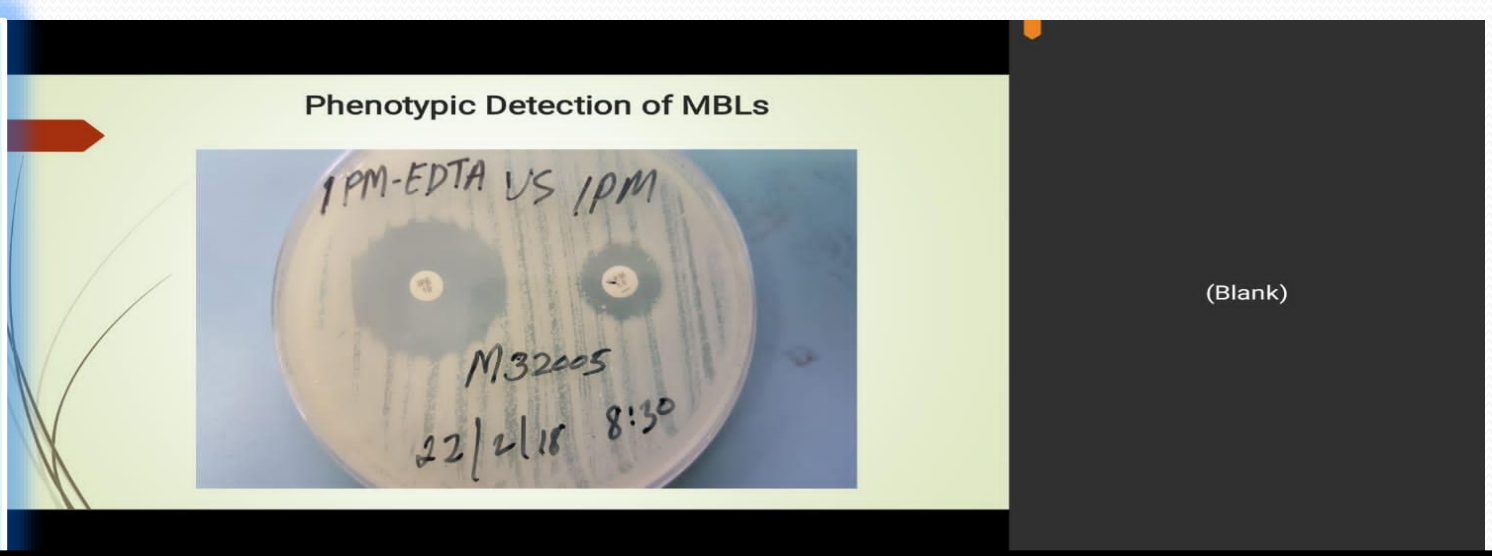
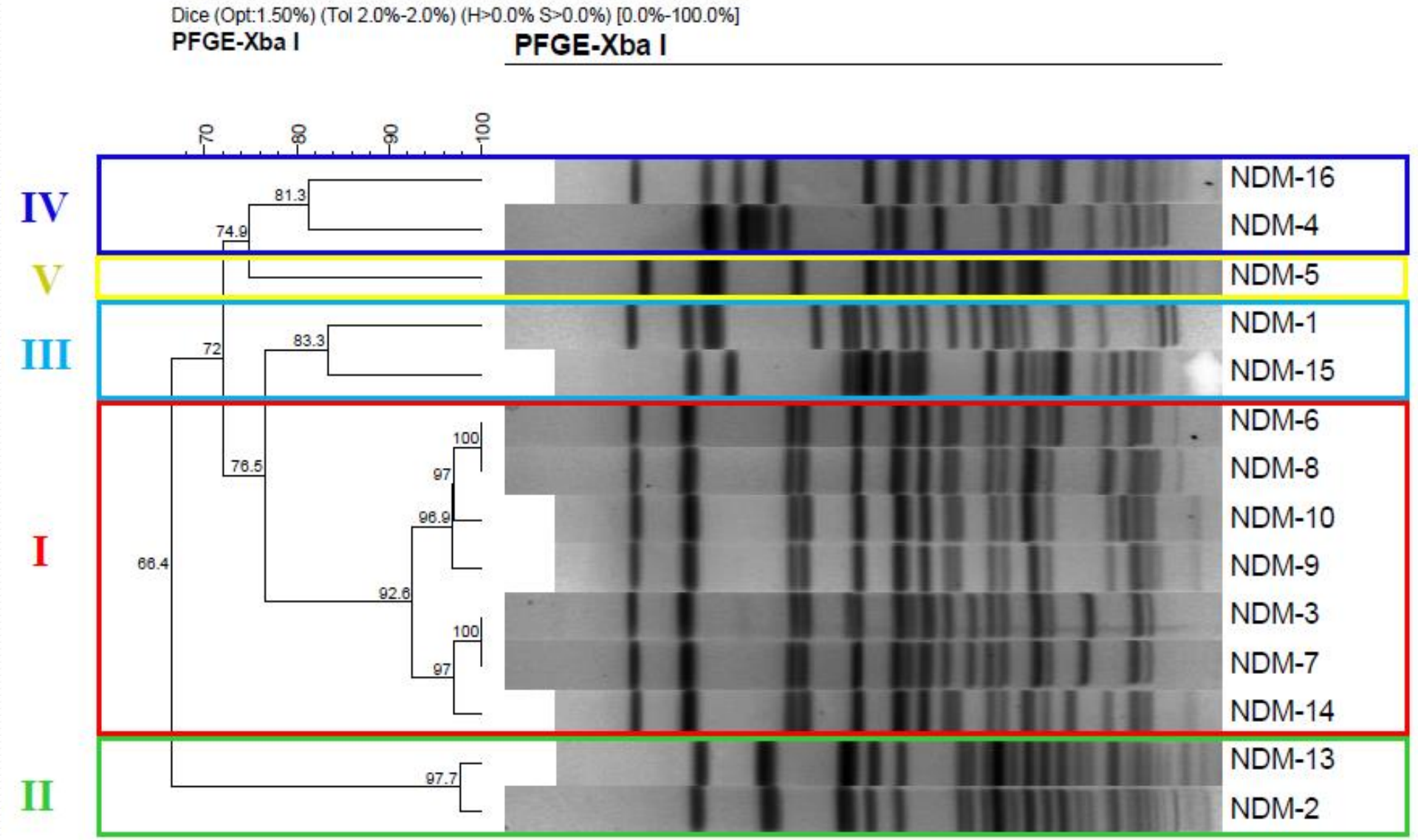
Detection of NDM-1 gene coding Producing *MDR in* cancer patients of Palestine

Future Work



Bla genes	Percentage (No. of isolates)
NDM	All country Palestine 100% (220/220)
NDM+OXA48+TEM	10% (20/220)
NDM+KPC+TEM	10%(20/220)
NDM+TEM	80%(160/220)
NDM+CTX	15%(30/220)
NDM+SHV	5%(10/220)
NDM+TEM+CTX	5% (10/220)


Dice (Opt:1.50%) (Tol 2.0%-2.0%) (H>0.0% S>0.0%) [0.0%-100.0%]
PFGE-Xba I
PFGE-Xba I
70
80
90
100
IV
V
III
I
II
81.3
74.9
72
83.3
100
76.5
97
96.9
66.4
92.6
100
97
97.7
NDM-16
NDM-4
NDM-5
NDM-1
NDM-15
NDM-6
NDM-8
NDM-10
NDM-9
NDM-3
NDM-7
NDM-14
NDM-13
NDM-2

FOR YOUR KIND ATTENTION