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Efficacy of Selected Antibiotics Against *Porphyromonas Gingivalis* Isolated from Periodontal Infections: In Vitro Study

Sarah Falah Noori [1], Huda Abbas Mohamed [2], Zeyad Nazar Majeed [3]

1 Microbiology \College of Dentistry, University of Babylon, sara39169@gmail.com , Babylon, Iraq

2 Microbiology \College of Dentistry \University of Babylon, hoda.jerawi@uobabylon.edu.iq , Babylon, Iraq, https://orcid.org/0000-0003-0939-319X

3 Department of Periodontology, College of Dentistry, University of Babylon, dent.zeyad.nazar@uobabylon.edu.iq or ziyadnm@yahoo.com , Babylon, Iraq.

***Corresponding author email:** sara39169@gmail.com; mobile: 07819574630

(فعالية بعض المضادات الحيوية ضد بكتريا *P. gingivalis* المعزولة من التهابات اللثة: دراسة مختبرية)

ساره فلاح نوري[1]، هدى عباس محمد[2]، زياد نزار مجيد [3]

1 احياء مجهرية كلية طب الاسنان، جامعة بابل، sara39169@gmail.com، بابل، العراق

2 احياء مجهرية كلية طب الاسنان، جامعة بابل، hoda.jerawi@uobabylon.edu.iq or https://orcid.org/0000-0003-0939-319X ، بابل، العراق

3 أمراض اللثة كلية طب الاسنان، جامعة بابل، dent.zeyad.nazar@uobabylon.edu.iq or ziyadnm@yahoo.com، بابل، العراق

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ABSTRACT

Background:

Porphyromonas gingivalis is a key pathogen associated with periodontitis, a chronic inflammatory disease of the supporting structures of the teeth. Due to the rising resistance to conventional antimicrobial agents, *P. gingivalis* is resistant to many antibiotic treatments. The study aimed to describe in vitro susceptibility of *P. gingivalis* to 10 registered antibiotics.

Materials and Methods:

Bacterial samples were collected from patients diagnosed with periodontitis. The study was conducted in vitro using Antimicrobial Susceptibility Testing (AST) including (Amoxicillin, Clindamycin, Penicillin, Ciprofloxacin, Nalidixic Acid, Amikacin, Imipenem, Gentamicin, Oxacillin, and Tetracycline) and was assessed using the disc diffusion method.

Results:

The sensitivity of 15 *Porphyromonas gingivalis* isolates to ten antibiotics was evaluated using the disk diffusion method. The results showed a clear variation in the response of the isolates to the antibiotics, with Imipenem and Tetracycline recording the highest mean inhibition zones respectively, indicating their high effectiveness against the studied isolates.

In contrast, some antibiotics showed weak or no efficacy, such as penicillin and oxacillin, with most isolates showing complete resistance to them. These results reflect the widespread prevalence of acquired resistance mechanisms in *P. gingivalis*, particularly against traditional antibiotics such as penicillin.

Conclusion:

The widespread use of antibiotics has led to significant resistance in key periodontal pathogens, underscoring the importance of susceptibility testing and careful consideration of resistance profiles in clinical practice to optimize treatment strategies.

Key words: *Porphyromonas gingivalis*, Periodontitis, Antimicrobial activity, Resistance, Antibiotics.

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INTRODUCTION

Periodontitis is a chronic inflammatory disease affecting the supporting structures of the teeth, primarily caused by pathogenic microorganisms. Among these, *Porphyromonas gingivalis (P. gingivalis*) is recognized as a key pathogen due to its significant role in biofilm formation and its contribution to the progression of periodontal disease. Its virulence factors enable it to evade host immune responses and disrupt periodontal tissues, making it a critical target in periodontal therapy[1].

Porphyromonas gingivalis is a Gram-negative anaerobic bacterium and one of the key pathogens linked to the onset and progression of periodontal disease. Multi-species communities form and become stable with the help of interspecies cooperation, which can result in chronic inflammation of periodontal tissues and, if untreated, can lead to tooth loss from local tissue destruction. In some cases, these chronic infections become systemic and contribute to a variety of comorbidities [2].

Antibiotic susceptibility testing (AST) is an essential laboratory service in the clinical microbiology laboratory, primarily to inform the clinician whether a specific isolate is resistant or sensitive to a drug [3]. Bacteria have developed strategies to survive in the face of host immunological pressure. A better understanding of the mechanism of action and survival strategies of important pathogens will lead to the development of effective therapeutics. The periodontal pathogen *P. gingivalis* has various survival strategies, including use-of-blebbing the mediated filamentous structures as predatory weapons, the use of food preferences and lactic acid metabolism to make anaerobic pockets/capsules, entry to oral normal tissue and the brain, and use of molecular mimicry to avoid immune surveillance.[4]

The majority of AST methods have been developed for aerobic bacteria. However, many of the morphologically complex bacteria are slow-growing and/or anaerobic, with *Porphyromonas gingivalis* as one of the most frequently isolated taxa in the oral cavity. This bacterium can cause bone resorption and periapical lesions as a result of inflammation at the level of the periodontal and peri-tissue complexes. A game of necrotic/suppurative microorganisms, including *P.gingivalis*, contributing to the endodontic infection may predispose to infected root-based cysts. *P.gingivalis* is resistant to many antibiotic treatments, including beta-lactams, tetracyclines, macrolides and phenicol's.[3]

MATERIALS AND METHODS

- **Subjects**

This in vitro experimental study was conducted after obtaining ethical approval and informed consent from all participants. A total of 100 patients diagnosed with periodontitis (both males and females, aged (18–70 years) were recruited from the College of Dentistry, University of Babylon, between November 2024 and February 2025. Excluded criteria are Patients which have been taking antibiotic therapy in the last 6 months, patients with systemic diseases, pregnant women, and smoker. Clinical periodontal parameters were notarized before the start of periodontal treatment, containing PD, clinical attachment loss (CAL), plaque index (PI), and bleeding on probing (BOP). All members in this study were employed to participate in this study, based on clinical and serological criteria according to the 2010 ACR/EULAR criteria.

From each patient, four subgingival plaque samples were collected, totaling 370 viable samples. Sampling targeted sites with evident clinical attachment loss and maximum probing pocket depth.

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After removal of supragingival plaque and isolation using cotton rolls, sterile 30 mm paper points were inserted into periodontal pockets for 30 seconds. Contaminated paper points containing blood were discarded. Each collected sample was transferred into sterile tubes containing 4 mL of nutrient broth as a transport medium, then stored at –20°C until were isolate the bacteria and biochemical tests were performed.

• The PCR mixture was formed in PCR tubes prepared with the components from the(abm) kit, and added components were introduced into the reaction mixture affording to the manufacturer's specifications [5], as exposed in table (1).

Table (1): Stuffings of the PCR reaction mixture used in this test

NO.	Subjects of reaction mixture	Amount
1.	PCR master mix	12.5 µl
2.	DNA template	5 µl
3.	Forward Primer 10pmol	1.5 µl
4.	Reverse Primer 10pmol	1.5 µl
5.	Nuclease free water	4.5 µl
Total		25 µl

- **Ethical Approval**

The study was to agree with the ethical principles of the Declaration of Helsinki. Patients obtained verbal and analytical consent prior to sample collection. A local ethics committee reviewed the study protocol, patient information, and consent form and approved them.

Antimicrobial Susceptibility Testing (AST)

Fifteen strains of *P. gingivalis* were sub cultured and inoculated on Muller-Hinton agar. The table 2 showed the antibiotics (OxoidTM, Fisher Scientific) were tested using disc diffusion Plates, were incubated anaerobically for 2–5 days. Inhibition zones were measured in millimeters (mm) [6].

Table 2. Antibiotic disc which is used

NO.	Antibiotics	Symbol	Concertation
1.	Clindamycin	CD	2 µg
2.	Amikacin	AK	30 µg
3.	Imipenem	IMP	10 µg
4.	Penicillin	P	10 µg
5.	Amoxicillin	AML	25 µg
6.	Oxacillin	OX	1 µg
7.	Gentamicin	CN	10 µg
8.	Niladic Acid	NA	30 µg
9.	Ciprofloxacin	CIP	5 µg
10.	Tetracycline	TE	30 µg

RESULTS AND DISCUSSION

- Diagnosis of *P. gingivalis*.

In this study, biochemical tests are used to identify bacterial strains such as the catalase test, oxidase test, Indole test and motility. Table 3 shows the isolated bacteria that were identified by microscope examination of colony characteristics and biochemical testing.

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Table 3. Biochemical tests used in this study.

Biochemical tests	Result of biochemical tests
Gram stain and shape On microscope	G -ve coccobacilli
Catalase test	–
oxidase test	–
Indole	+
Motility	–

P. gingivalis, a non-motile, strictly anaerobic, and encapsulated Gram-negative, rod-shaped, black-pigmented microorganism. The primary etiological agents of periodontal diseases are generally Gram-negative rods such as *P. gingivalis*. The human oral cavity contains approximately 700 species of bacteria. *Porphyromonas gingivalis* is a Gram-negative anaerobic bacterium and a member of the black-pigmented Bacteroides species. That has a negative indication for catalase test which does not make bubbles because of hydrogen peroxide breakdown. The indole test is positive (greenish color) and negative (no color change). Since *P. gingivalis* failed in the oxidase test and does not turn purple (does not change color). These findings validate the outcomes of prior research [7,8].

Table 3. shows the diameter (mm) of inhibition using 10 antibiotics on 15 bacterial isolates. The highest resistance rate was observed against Oxacillin (OX 1), with 15 out of 15 isolates showing clear resistance (figure 2), indicating low efficacy of this antibiotic against the studied isolates. Penicillin (P 10) also recorded a high resistance rate of approximately (12 resistant isolates). Niladic Acid (NA 30) was the next most resistant isolate with 7 out of 15 isolates. These results are agreed with the results [9].

In contrast, there were high susceptibility rates to antibiotics such as Imipenem (IPM 10), Tetracycline (TE30), and Ciprofloxacin (CIP 5), with most isolates showing broad inhibition zones, indicating their high efficacy against these isolates (figure 3). Clindamycin (CD2), and Amoxicillin (AML 25) showed relatively good efficacy (figure 4), with most isolates being susceptible to it, except for some limited resistant cases These results are consistent with those reported by Ardila [10]. Other antibiotics, such as Gentamicin (CN 10), and Amikacin (AK 30), were moderately to highly effective (figure 5), depending on the bacterial isolate.

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A study by Conrads *et al*. which mentioned that all isolates were 100% sensitive to (clindamycin, amoxicillin, and imipenem) while resistance was evident only against tetracycline [11]. While the study by Larsen reported resistance of up to 10% of *P. gingivalis* isolates to tetracycline [12] this is contrary to the results of the current study.

Table 3. Inhibition zone to antibiotics that are used in this study.

Bacterial Isolates	IPM 10	CD 2	P 10	NA 30	CIP 5	AK 30	AML 25	OX 1	CN 10	TE 30
1.	32	19	0	10	20	14	13	0	14	30
2.	26	20	0	10	20	15	13	0	15	38
3.	29	20	0	14	24	16	14	0	14	35
4.	35	26	17	17	31	26	0	0	28	32
5.	28	23	0	0	20	14	0	0	14	30
6.	30	25	0	0	21	15	14	0	14	35
7.	28	0	0	0	20	16	13	0	12	33
8.	28	20	0	12	17	13	11	0	11	30
9.	36	27	22	22	34	26	19	0	27	35
10.	29	14	0	0	20	16	0	0	13	28
11.	26	24	0	0	18	16	12	0	15	29
12.	32	25	0	0	20	17	11	0	18	32
13.	35	0	0	0	29	19	0	0	13	29
14.	35	0	0	14	22	26	19	0	13	30
15.	37	8	15	27	22	20	22	0	12	32

The table 4 showed variation in the response of the isolates to antibiotics, with Imipenem and Tetracycline recording the highest mean inhibition zones (31.07±3.75 mm) and (31.87±2.85mm),

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respectively, indicating their high effectiveness against the studied isolates. In contrast, some antibiotics showed weak or no efficacy, such as penicillin (3.6±7.576 mm), Nalidixic Acid (8.4±9.179), and oxacillin (0.0±0.0mm), with the majority of isolates showing complete resistance to them. These results reflect the widespread prevalence of acquired resistance mechanisms in *P. gingivalis*, particularly against traditional antibiotics such as penicillin, which is consistent with previous reports confirming the resistance of this bacterium to beta-lactam antibiotics. which indicated high resistance of *P. gingivalis* to penicillin and its derivatives, and higher efficacy of antibiotics from the carbapenem and tetracycline groups [13, 14].

These results are consistent with clear resistance by *P. gingivalis* to penicillin, due to its possession of the beta-lactamase enzyme, these results are agreed with the results [15]. Figure 1 shows some antibiotics have weak efficacy. Susceptibility testing revealed the sensitivity of *P. gingivalis* to CD (16.73±9.932), CIP (22.53±4.926), AML (10.73±7.382), CN (15.53±5.125), AK (17.93±4.543). Mult resistant oral isolates could resist most conventional antibiotics which are agreed with prior research [16, 17].

Table 4. Mean and standard deviation of antibiotics

No. isolates	Antibiotics	Mean ± S. D
15	Imipenem	31.07±3.75
15	Clindamycin	16.73±9.932
15	Penicillin	3.6±7.576
15	Nalidixic Acid	8.4±9.179
15	Ciprofloxacin	22.53±4.926
15	Amikacin	17.93±4.543
15	Amoxicillin	10.73±7.382
15	Oxacillin	0.0±0.0
15	Gentamicin	15.53±5.125
15	Tetracycline	31.87±2.85

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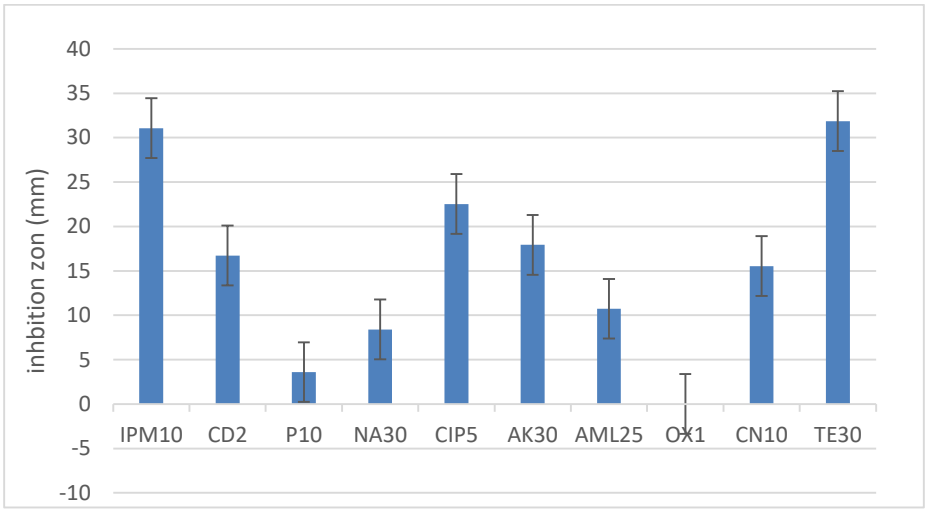

Figure 1. scheme shows means to antibiotics

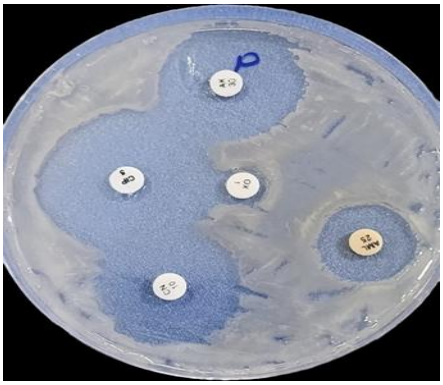

Figure (2): effect of some antibiotic dick against *P. gingivalis*

Figure (3): effect of some antibiotic dick against *P. gingivalis*

Figure (4): effect of some antibiotic dick on isolate number 13

Figure (5): effect of some antibiotic dick on isolate number 15

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CONCLUSION:

This study confirms the potent antibacterial effects of antibiotics against *P. gingivalis*, a key periodontopathogen. Tetracycline (TE) and Imipenem (IPM) showed the highest mean inhibition zone, indicating high efficacy against the bacterial isolates. Penicillin and Oxacillin demonstrated clear resistance, with most values being zero or low, indicating the presence of acquired resistance. The high standard deviation of some antibiotics (such as Clindamycin and nalidixic acid) indicates significant variability among isolates, which may reflect the presence of different resistance patterns. Variation in susceptibility between isolates should be considered, indicating the importance of individual diagnosis before prescribing treatment.

Conflict of interest.

There are non-conflicts of interest.

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الخلاصة

المقدمة:

تُعدُّ بكتيريا بورفيروموناس اللثة مُمْرِضًا رئيسيًا مُرتبطًا بالتهاب دواعم السن، وهو مرض التهابي مزمن يُصيب البنى الداعمة للأسنان. ونظرًا لمقاومتها المتزايدة للمضادات الحيوية التقليدية، تُقاوم بكتيريا بورفيروموناس اللثة العديد من العلاجات بالمضادات الحيوية. هدفت الدراسة إلى وصف حساسية بكتيريا بورفيروموناس اللثة لعشرة مضادات حيوية مُسجلة في المختبر.

طرق العمل:

جُمعت عينات بكتيرية من مرضى شُخِّصوا بالتهاب دواعم السن. أُجريت الدراسة في المختبر باستخدام اختبار حساسية مضادات الميكروبات (AST)، وشملت (أموكسيسيلين، كليندامايسين، بنسلين، سيبروفلوكساسين، حمض الناليديكسيك، أميكاسين، إيميبينيم، جنتاميسين، أوكساسيلين، وتتراسايكلين)، وتم تقييمها باستخدام طريقة انتشار القرص.

النتائج:

تم تقييم حساسية 15 عزلة من بكتيريا بورفيروموناس لثوية لعشرة مضادات حيوية باستخدام طريقة انتشار القرص. أظهرت النتائج تباينًا واضحًا في استجابة العزلات للمضادات الحيوية، حيث سجل الإيميبينيم والتتراسيكلين أعلى متوسط منطقة تثبيط على التوالي، مما يدل على فعاليتهما العالية ضد العزلات المدروسة.

في المقابل، أظهرت بعض المضادات الحيوية فعالية ضعيفة أو معدومة، مثل البنسلين والأوكساسيلين، مع إظهار معظم العزلات مقاومة تامة لها. تعكس هذه النتائج الانتشار الواسع لآليات المقاومة المكتسبة لدى البكتيريا اللثوية، وخاصةً ضد المضادات الحيوية التقليدية مثل البنسلين.

الاستنتاجات:

لقد أدى الاستخدام الواسع النطاق للمضادات الحيوية إلى مقاومة كبيرة لمسببات الأمراض اللثوية الرئيسية، مما يؤكد أهمية اختبار الحساسية والتفكير الدقيق في ملفات المقاومة في الممارسة السريرية لتحسين استراتيجيات العلاج.

الكلمات المفتاحية:

بكتيريا بورفيروموناس اللثوية، التهاب دواعم السن، النشاط المضاد للميكروبات، المقاومة، المضادات الحياتية.

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