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EFFECTS OF AQUEOUS EXTRACT OF *ARTEMISIA HERBA-ALBA* LEAF, *PEGANUM HARMALA* SEED AND PHYCOCYANIN AGAINST *PORPHYROMONAS GINGIVALIS*

ENAS JASIM AL- ZUBADI[1] AND DHUHA SABAH NADIR[2*]

[1]Al-Shamoukh Secondary School /Baquba Department of Education/ Diyala General Directorate of Education, Iraq
[2]Al-Fadhilat Preparatory School for Girls /Baladrus Department of Education/ Diyala General Directorate of Education, Iraq
**Corresponding author's email: dhuha.s.nader@gmail.com*

Abstract

This study tested *Artemisia herba-alba* leaf extract, *Peganum harmala* seed extract, and Phycocyanin against *Porphyromonas gingivalis*. The data showed that concentration and exposure period affected water extract and drug efficacy. This study examined the freezing and soluble antibacterial properties of the phycocyanin protein. Phycocyanin inhibited the development of natural and mutant bacteria at various doses. The results showed that a concentration of 10% for the extract of *Artemisia herba-alba* leaves and aqueous extract of *Peganum harmala* seeds and a mixture of them killed the most bacteria after 24 hours, while a concentration of 1% had the least effect, killing 62.7% and 81% of the bacteria after 120 hours. A mixture of aqueous extracts of *Artemisia herba-alba* leaves and *Peganum harmala* seeds killed bacteria 100% after 24 hours at 8% to 10%. The drug's PC protein reduced mutant strains' bacteria growth surface area.

Key words: *Artemisia herba-alba*, *Peganum harmala*, phycocyanin, *Porphyromonas gingivalis.*

Introduction

Plants have several useful chemicals. Volatile oils, antibacterial, antifungal, and other chemicals. Thus, aqueous, oily, or alcoholic extracts may treat diseases, reduce symptoms, heal wounds, etc. Different plant extracts may be effective against different bacterial strains and virulence factors or excretion toxins. *Porphyromonas gingivalis* causes severe gum inflammation (Khalil *et al*., 2019).

A. herba-alba's Sinai Desert essential oil is primarily 1,8-cineole and contains a- and b-thujone, terpinene-4-ol, camphor, and borneol. (El-Tantawy, 2015; Liu *et al*., 2021).

Moroccan and Spanish *A. herba-alba* populations include davanone, chrysanthenone, and cis-chrysanthenol. Santolina and yomogi monoterpene alcohols are discovered in several Negev desert villages (Putakala *et al*., 2017; Ibitoye & Ajiboye, 2018).

A. herba-alba's aerial parts contained many sesquiterpene lactones. Eudesmanolides and germacranolides were most common. Most flavonoids are methylated (patulin) or O-methylated (hispidulin and curvilineal). C-glycosides such as isovitexin, schaftoside, and isoschaftoside can be detected (Aguilera-Mendez *et al*., 2018).

Haram, a perennial herb in the Zygophyllaceae family, grows in Jinn, B. orba, North Africa, and West Asia Goel (Boulos, 2009). Also spread in the center and north of RAK and contains a high proportion of active compounds, especially alkaloids, which constitute 4% B-Carbolin Alkaloids and include Harmalin, Harmine, Tetrahydro Harmine, Harman, and Harmalal (Yu *et al*., 2021). The type Quinazoline includes Vasicinone and Vasicine as well as turbocharged compounds in the form of volatile oils and has proven to be effective against many plant and animal nurses as its seeds are highly toxic (Singhai & Patil, 2021).

Phycocyanin: Light-harvesting phycobiliprotein pigment-protein complex phycocyanin, and phycoerythrin. Chlorophyll's partner pigment. Unlike carotenoids, all phycobiliproteins are water-soluble. Instead, phycobiliproteins produce membrane-bound phycobilisomes (Pan-Utai & Iamtham, 2019).

Phycocyanin is light blue, absorbs orange and red light at around 620 nm, and fluoresces at about 650 nm. Blue-green algae are cyanobacteria (Laine *et al*., 1997).

Immunoassays use phycobiliprotein fluorescence. Phycocyanin comes from the Greek word "phyco," which means "algae," and cyanin comes from "cyan," which means "blue-green" (close to "aqua"), and "kyanos," which means "dark blue" (Jang & Kim, 2021). Aphanizomenon flos-aquae and Spirulina produce the natural coloring additive 'Lina Blue' or 'EXBERRY Shade Blue', which is used in confections and ice cream. Fluorescence identification of phycocyanin pigments in water samples also monitors cyanobacteria biomass (Friedewald *et al*., 2009).

Since it is stable up to 70°C and has equal light-absorbing characteristics at 20 and 70°C, cyanobacteria near hot springs commonly contain phycocyanin. Thermophiles thrive in these conditions due to their slightly different amino acid sequences (Rezaee & Hajighasemi, 2019). 30,000 Da is the molecular mass. *In vitro*, this protein is unstable at these temperatures. Photospectral analysis of pure protein after 1 minute at 65°C showed a 50% loss of tertiary structure. (Mojarrab *et al*., 2016).

PC protein: PC clotting experiments use a modified APTT reagent using Southern copperhead snake venom-derived PC activator, PC-deficient plasma, and calcium chloride. The modified APTT stimulates PC and intrinsic pathway factors. PC-deficient plasma clots in 30 s, while normal plasma takes over 100 s (Jiang *et al*., 2016), Patient plasma mixed with PC-deficient plasma prolongs clotting time proportionally to PC concentration. PC clotting tests, unlike chromogenic PC assays, detect

functional PC deficits in calcium or phospholipid binding (mutations in the Gladomain) and cofactor binding (Enersen, *et al*., 2013). Anticoagulants, factor V Leiden, LACs, elevated FVIII levels, and protein S concentration also affect them. The DRVVT may be less sensitive to the effects being researched for a functional PC activity test (Khalil *et al*., 2019; Shaheen & Issa, 2020).

Porphyromonas gingivalis: This bacterium causes periodontal infections in the mouth, upper stomach, respiratory tract, and colon. Bacterial vaginosis samples were discovered too. Collagenase enzymes in this species caused collagen relapse in chronic gum disease (Miao *et al*., 2020) laboratory study reveals that a gingival perforator can enter and stay in bubonic gingival fibers with high antibiotic doses. In gingival perforation, many bacteria and epithelial cells survive. Gingival perforation patients had elevated antibody levels (Abdallah *et al*., 2019).

Gingival perforation is linked to Alzheimer's and rheumatic arthritis. PADI4, an enzyme in this bacteria, aids sterling. Rheumatic arthritis patients have high rates of gum disease and bacteria-fighting antibodies. (Elhinnawi *et al*., 2018).

The paper aims to identify the effect of the aqueous extract of *A. herba-alba* leaves and *Peganum harmala* seeds on the bacteria activity. Also, find the effect of combining the two aqueous extracts. And find the effectiveness of phycocyanin as an antibiotic against *Porphyromonas gingivalis.*

Material and Methods

Preparation of plant extracts: Haram seeds were obtained from local markets and water extracts were attended to each plant by taking 500 grams of vegetable powder for each plant individually and placing it in a bevel containing 500 ml of distilled water, then mixing the ingredients with the mixer for 15 minutes leave the solution for 24 hours and to the degree of the laboratory. (Iqbal *et al*., 2019 a).

Filter the solution with the compliment canvas and then transfer the filter to the centrifuge at 3000 rpm for 10 minutes to get a slave solution and get rid of the remnants of Az-ZP and then sterilize the filter with a pass-through paper filter with 0.45 micrometer-diameter pores. (Atale *et al*., 2017; Li *et al*., 2018).

Bacteria strains: The isolated bacteria samples from the oral cavity were used with the first two normal strains and the second one removed the amino acid lysine from them. One ml of oral bacteria was taken and centrifuged for 5 minutes at 12,000 cycles per minute. After completion, the stranded solution was removed, after which 800 microliters of Krebs Ringer solution were added. The solution was well blended with the bacteria and then another centrifugal process was performed for 5 minutes at 12,000 cycles per minute, after which the solution was removed, and the rest kept at 37ct to be used later. (Sandoval & Jaffe, 2019). The drug's PC protein was obtained by the freezing-thaw technique (Iqbal *et al*., 2019 b).

Freeze-Thaw technique: The Freeze–Thaw approach is a "Mild" homogenization method, and it is often used in conjunction with other homogenization techniques. It consists of rapidly freezing at 85°C and thawing at 4°C in succession (the tubes may be thawed at 6–10°C in a water bath for 10 minutes and maintained at 4°C). On average, two to three Freeze–Thaw cycles are required. For optimal results, tissues are often freeze-thawed once and homogenized using a Teflon-coated pestle tissue grinder (two to four passes). (Elansary *et al*., 2020), Typically, the initial step in the formulation process is to freeze-thaw the purified bulk medicinal product. Keeping the purified medication in a frozen state permits the establishment of a large product stockpile, hence enhancing production flexibility. By decreasing the chance of microbial development and delaying degrading processes mediated by the presence of water, such as hydrolysis, storing the medicine in a frozen state may boost the product's stability. A protein kept in a frozen matrix is also less likely to interact with other proteins to form aggregates (Jiang *et al*., 2016).

Preparing liquids

Plant extract concentrations: The concentrations that were used in the experiment came from raw extract, and they were prepared as a stock solution at a concentration of 100%. The concentrations that were used in the experiment were as follows: 1%, 3%, 5%, 7%, and 10% of each 5%, 10%, 15%, 20%, and 25% of relying on the mitigation law:

$$N1 \times V1 = N2 \times V2$$

Which:
N1 = Pre-dilution extract concentration
V1 = Volume of the extract before dilution
N2 = Extract concentration after dilution
V2 = Extract size after dilution

Antibiotic concentration: A mixture 0.1 g of the antibiotic Streptomycin Sulphate together with 0.1 g of the substance and dissolved in 100 ml of distilled water. (Offenbacher, 1996).

Statistical analysis

The data were statistically examined by using the T-test via the Minitab statistical tool and comparing the averages of the various transactions with the Duncan Multi-boundary Test with the threshold of probability set at P less than 0.05. (Gokyu *et al*., 2014).

Results and Discussion

The results of the statistical analysis of (Table 1) show that there are significant differences between the used pillars and the number of hours, showing that the 10% concentration is the best at all times studied. The 7% concentration gave better results when used for 120 hours, with the rate of killed bacteria being 100%, while the lowest rate of bacteria killed was found to be 58.6% when used for 24 hours.

Table 1. *Porphyromonas gingivalis* killing percentage after exposure to aqueous extract of *Artemisia herba-alba* leaves.

Concentration	Percentage killings% Exposures (hours)					Overall average impact of concentrations
	24	48	72	96	120	
Comparative	0	0	0	0	0	0.0 f
1	17.4	25.1	33.9	51.5	62.0	37.98
3	21.0	13.4	15.0	63.7	73.5	37.32
5	27.2	40.8	58.8	80.3	90.2	59.46
7	58.6	70.1	81.0	91.7	99.5	80.18
10	100.0	100	100	100	100	100
General average with extended effect exposure	44.84d	49.88d	57.74c	77.44b	85.04a	

Table 2. *Porphyromonas gingivalis* killing percentage after exposure to Aqueous extract of *Peganum harmala* seed.

Concentration	Percentage killings% Exposures (hours)					Overall average impact of concentrations
	24	48	72	96	120	
Comparative	0	0	0	0	0	0.0 e
1	27.7	58.9	67.2	77.4	100	66.24C
3	37.9	60.3	71.9	82.3	100	70.48C
5	53.4	67.2	85.4	99.7	100	81.14B
7	86.1	96.4	99.5	100.0	100.0	96.4D
10	100.0	100.0	100.0	100.0	100.0	100A
General average with extended effect exposure	61.02d	76.56c	48.8b	91.88b	100a	

Table 3. *Porphyromonas gingivalis* killing percentage after exposure to the plant's aqueous mixture.

Concentration	Percentage killings% Exposures (hours)					Overall average impact of concentrations
	24	48	72	96	120	
Comparative	0	0	0	0	0	0.0 e
1	34.1	45.4	60.4	72.6	80.7	58.64D
3	38.4	49.5	62.8	81.1	92.4	64.84C
5	57.4	69.6	81.8	94.2	98.9	80.38B
7	100.0	100.0	100.0	100.0	100.0	100A
10	100.0	100.0	100.0	100.0	100.0	100A
General average with extended effect exposure	65.98a	72.9b	81c	89.58d	94.4c	

Table 4. PC Protein Killing Percentage.

Concentration	Percentage killings% Exposures (hours)					Overall average impact of concentrations
	24	48	72	96	120	
Comparative	0	0	0	0	0	0.0 e
1	20.9	32.8	46.1	48.4	50.8	39.8D
3	42.1	47.9	58.1	71.9	82.9	60.58C
5	55.4	79.6	93.0	99.1	99.5	85.32B
7	71.9	86.8	100.0	100.0	100.0	91.74A
10	82.9	100.0	100.0	100.0	100.0	96.58A
General average with extended effect exposure	54.64e	69.42d	79.44c	83.88b	86.64e	

The concentration of 5% was higher than 120 hours' use, with the number of bacteria killed at approximately 90.2% while the lowest rate was given when used for 24 hours and was 27.2 Concentrations of 1% and 3% were best used for 120 hours, with the number of killed bacteria significantly higher than the rest of the time, giving approximately 62.0% and 73.5% rate, respectively, when used for 120 hours, compared to 18% and 21.0%, when used for 24 hours. The reason for the effect of the aqueous extract may be that it contains a high percentage of flavonoids, glycosides, phenols, and volatile oils, which have been shown further to be toxic in multiple districts the impact of the wormwood extract L. major has been found to have a strong efficacy against this bacterium. Results agreed with (Sana'a & Ahmed, 2016).

The results of the statistical analysis showed in (Table 2) that (1%, 3%, and 5% gave the best results when used for 120 hours and a significant difference from 5%, 96 hours, 7%, 72 hours, 96 hours, and 120 hours, and 10% for all times, with a feminization rate of 100% in the three pillars while giving each the lowest rate when used for a while.

The impact of the *harmala* plant on bacteria may be due to its containment of alkaloids, soaponies, and tannins, which have a toxic effect on animal and plant intruders, found (Enersen, 2013; Abderrahim *et al*., 2019).

Also, the results show that the best pillar in controlling the bacteria population is 7% and 10% of all bacterial colonies are killed in 24 hours, followed by a concentration efficiency of 5% in which all bacteria were killed in 120 hours (Kazemi *et al*., 2018).

The effectiveness of this mixture has proven effective on *Amibia* tissue at least 98% killings (Miao *et al*., 2020).

When a mixture of water extract (Table 3) was used to kill bacteria, 100% of bacteria was killed during 24 hours when 8% and 10% of the mixture were used. However, using 6% the mixture resulted in 100% kill of bacteria during 120 hours. The lowest results 80.7% and 92.4% were obtained when the concentrations 2% and 4% were used respectively in 120 hours. This may be due to the transitic effect of chemical compounds involved in the formation of both used plants (Abbas *et al*., 2021).

High alt-core belt time with an increase in the number of hours of use of the PC protein in the crude phase gave better results and significant differences from the low-lying pillar since the use of 5% concentration and 10% gave rates of 50.8% and 82.9% respectively in 120 hours (Table 4). The Other results showed that the best way to get the best and cleanest concentration was the Aqueous Two-Phase Systems method. According to this study and the results of the current study, we can assume the use of purified protein for better results in the inhibition of *Porphyromonas gingivalis* bacteria which results in good results in control of dental health and gums in society without the need for expensive surgeries.

Health problems related to oral and dental health account for about 10% of expenditures in the health system in major economies, while in countries with less health care, they are not. Consequently, these results can be relied upon to reduce expenses as well as to prevent problems arising from the inaccessibility of oral and gum problems (Minford *et al*., 2022).

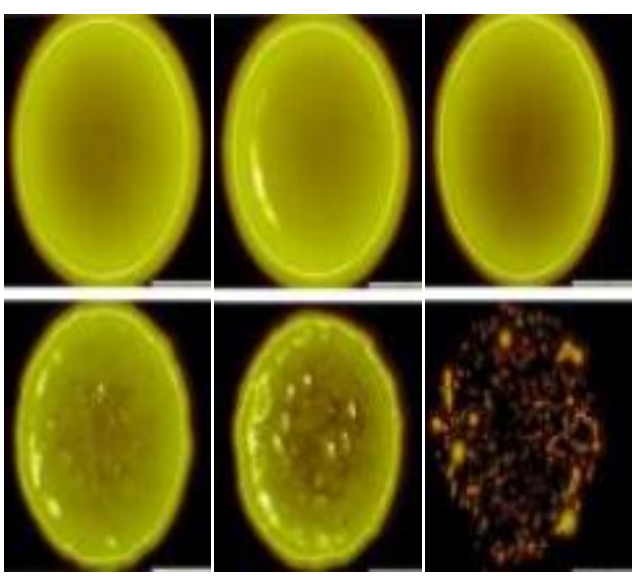

Fig. 1. Bacteria Group and Reaction with PC Protein of Phycocyanin in the range of 50- 500 µg ml^{-1} (motivative 1) and 100-500 µg ml^{-1} (motivative 2).

The results of the use of the freezing-thaw-based phycocyanin protein showed the ability of the drug to inhibit bacteria in varying proportions, and the greater inhibition ratio was when using the 2mg/ml concentration compared to 1mg/ml. Pure drug-protein extracted by freezing and soluble method can be used to treat the bacteria causing gum inflammation. We found higher phycocyanin content, 38.12 The used bacterial strains were shown different results, and the diameter of the inhibition zone increased by increasing the amount of PC protein. PC protein values were in the range of 50- 500 µg ml^{-1} and 100-500 µg ml^{-1} (Fig. 1).

The DPPH method is widely used to measure the ability of antioxidant compounds to act as free radical scavengers (Shon *et al*., 2003; Ismaiel *et al*., 2014). In this study, the antioxidant activity of phycocyanin at zero and 60 days later was 46.14 and 40.74, respectively. These results confirm that the PC protein is a potent free radical scavenger and inhibits lipid peroxidations in both temperatures.

However, the antioxidant property of PC protein decreased in 60-day time at -18°C. It is probably due to the nature of the PC protein that is changed when stored at freezing temperature.

In the study conducted by (Piñero- Estrada *et al*., 2001), the antioxidant activity of phycocyanin was lower than (24.21%) that of the present study. The results of Ismaiel *et al*., (2016) showed that had stronger antioxidant activity than the positive control (2.5µg BHT) at a wide range of pH levels from 7.5 to 11.0. The radical scavenging activity, reducing power, and chelating activities showed the highest value at a pH of 8.5- 9.0.

Protein was highly effective and pure protein was not used. This may be explained by inhibiting the growth of bacteria where raw water contains more chemicals than pure material. The results also may be obtained because the bacteria strains don't have virulence factors (Lys-X) (de Boer *et al*., 2014).

Conclusions

Artemisia herba-alba leaf extract, *Peganum harmala* seed extract, and Phycocyanin are effective materials against bacterial growth. The mixture of them eliminated the greatest number of bacteria. The efficiency of water extracts and the medicine varied with concentration and time of exposure.

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