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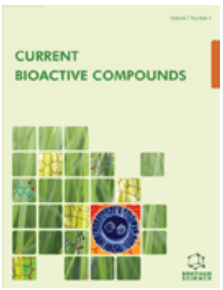

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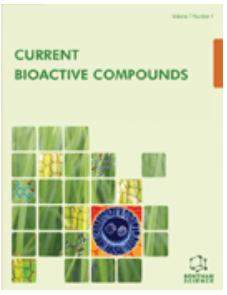

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Preface

Preface

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Perspective

Fused Heterocyclics in Medicinal Chemistry

Pp: 3-3
Author(s): Vikas Sharma*
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Mini-Review Article

A Mini Review on Recent Advancements in the Therapeutic Potentials of Benzothiazoles

Pp: 4-27
Author(s): Rubina Bhutani*, Garima Kapoor, Dharam P. Pathak, Asif Husain, Ravi Kant and Ruhi Ali
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Published on: 23 December, 2019

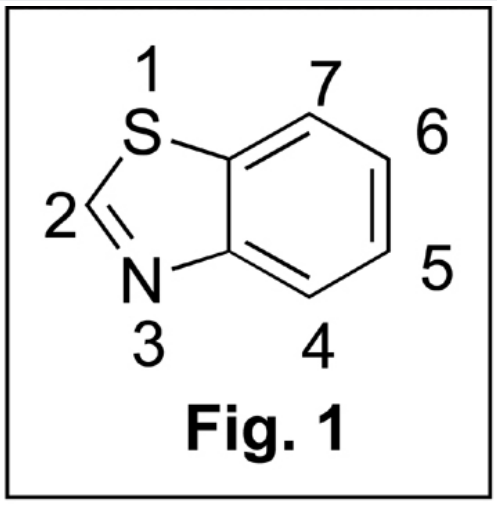

Fig. 1

Number of Atoms in the Benzothiazole Ring.

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Review Article

Natural Fused Heterocyclic Flavonoids: Potent Candidates as Anti- Inflammatory and Anti-Allergic Agents in the Treatment of Asthma

Pp: 28-40
Author(s): Rajwinder Kaur*, Kirandeep Kaur, Rashmi Arora, Balraj Saini and Sandeep Arora
DOI: 10.2174/1573407215666191120125608

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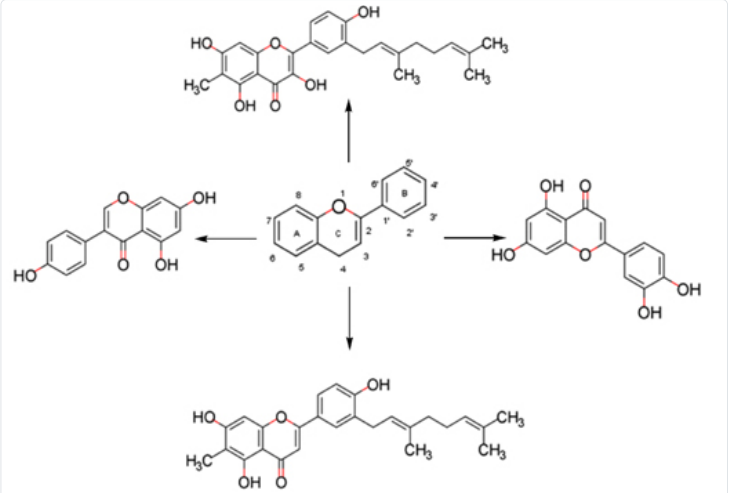

Flavonoids containing heterocyclic molecules display variety of pharmacological effects have established a new area of research in the recent past. In this review article, we highlight studies of flavonoids as potent prospective anti-allergic and anti-inflammatory agents.

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Pp: 41-58
Author(s): Lidia Baltina * and Rimma Kondratenko*
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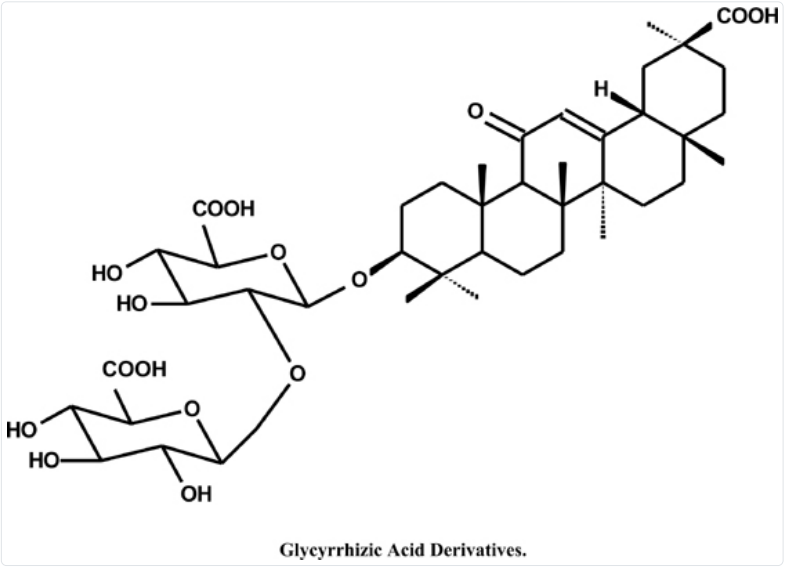
Published on: 10 February, 2020



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Pp: 59-66
Author(s): Desislava V. Stanisheva, Gjorgji Atanasov, Margarita D. Aposstolova and Ognyan I. Petrov *
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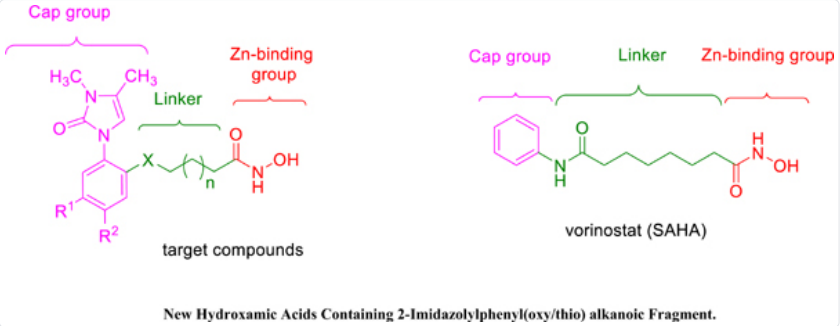

New Hydroxamic Acids Containing 2-Imidazolylphenyl(oxy/thio) alkanoic Fragment.

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Ointment Formulation and Characterization of Arum Manis Mango (*Mangifera indica* L.) Leaves' Methanol Extract as an Antibacterial Agent Against *Propionibacterium acnes*

Pp: 67-75
Author(s): Dian R. Ningsih*, Zusfahair Zusfahair , Dadan Hermawan, Wulan Anggraeni and Hassan Y. Aboul-Enein*
DOI: 10.2174/1573407216666200214100855

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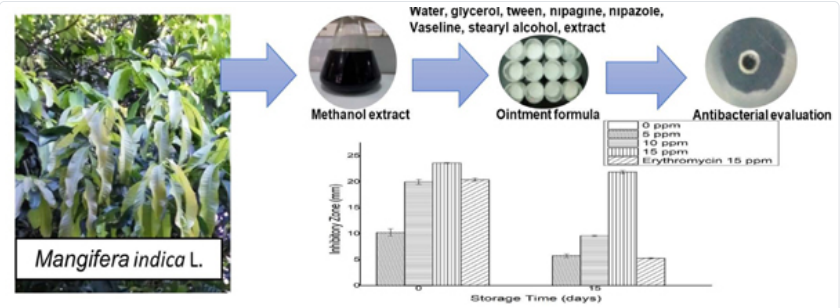

Arum Manis Mango *(Mangifera indica L.)* Leaves' Methanol Extract as an Antibacterial Agent Against *Propionibacterium acnes*.

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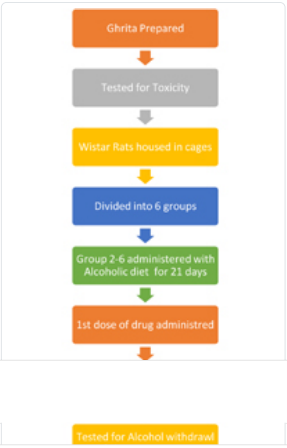

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Pp: 85-97
Author(s): Hiba N. Rajha, Gisèle El Khoury, Nada El Darra*, Karim Raafat, Espérance Debs, Richard G. Maroun and Nicolas Louka
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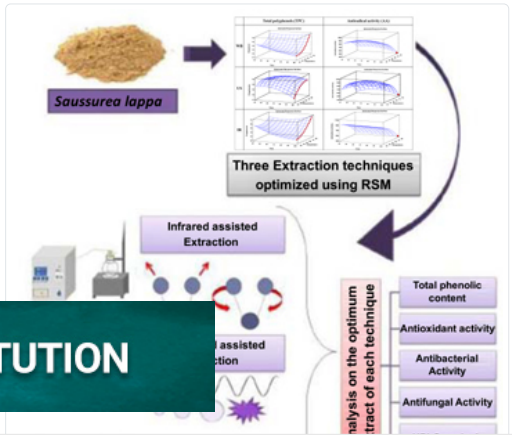

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Ointment Formulation and Characterization of Arum Manis Mango (*Mangifera indica* L.) Leaves' Methanol Extract as an Antibacterial Agent Against *Propionibacterium acnes*

Authors: Ningsih, Dian R.; Zusfahair, Zusfahair; Hermawan, Dadan; Anggraeni, Wulan; Aboul-Enein, Hassan Y.
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Abstract | References | Citations | Supplementary Data

Background: Acne is caused by several factors, including the active secretion of sebaceous sweat glands, hyperkeratosis in the hair infundibulum and the effects of bacteria. One plant which has the potential as an antibacterial agent is the extract of Arum Manis mango leaves.

Methods: The Minimum Inhibitory Concentration (MIC) of methanol extract of mango leaves was determined, which can inhibit Propionibacterium acnes activity. The antibacterial activity tests were performed using agar diffusion. The ointment formulation, the characteristics of ointment preparations, and the ointment activity against P. Acnes are discussed.

Results: MIC of methanol extract of mango leaves value is 5 ppm with an inhibition zone of 1 mm. The ointment obtained is white, has a distinctive smell, semisolid form, possesses a pH of 4.92 - 5.87, dispersive power of 5.05 - 6.30 cm, and adhesive power of 1 - 3.67 seconds, homogeneous and protective. Ointment preparations of methanol extract of mango leaves have activity on P. acnes on the 0 and 15th day of storage. The activities of ointment preparation on day 0 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 10.20 mm; 19.97 mm and 23.60 mm respectively, while the inhibition zones produced by the preparation of ointment on day 15 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 5.71 mm; 9.58 mm and 21.88 mm respectively.

Conclusion: Methanol extract of mango leaves (Mangifera indica L.) and ointment preparation can inhibit the growth of Propionibacterium acnes.

Keywords: Antibacterial agent; Arum Manis mango leaves; MIC; Propionibacterium acnes; acne; human pathogens

Document Type: Research Article

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Current Bioactive Compounds, 2021, *17*, 67-75

RESEARCH ARTICLE

Ointment Formulation and Characterization of Arum Manis Mango (*Mangifera indica* L.) Leaves' Methanol Extract as an Antibacterial Agent Against *Propionibacterium acnes*

Dian R. Ningsih[1,*], Zusfahair Zusfahair[1], Dadan Hermawan[1], Wulan Anggraeni[1] and Hassan Y. Aboul-Enein[2,*]

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Abstract: ***Background*:** Acne is caused by several factors, including the active secretion of sebaceous sweat glands, hyperkeratosis in the hair infundibulum and the effects of bacteria. One plant which has the potential as an antibacterial agent is the extract of Arum Manis mango leaves.

***Methods*:** The Minimum Inhibitory Concentration (MIC) of methanol extract of mango leaves was determined, which can inhibit *Propionibacterium acnes* activity. The antibacterial activity tests were performed using agar diffusion. The ointment formulation, the characteristics of ointment preparations, and the ointment activity against *P. Acnes* are discussed.

***Results*:** MIC of methanol extract of mango leaves value is 5 ppm with an inhibition zone of 1 mm. The ointment obtained is white, has a distinctive smell, semisolid form, possesses a pH of 4.92 - 5.87, dispersive power of 5.05 - 6.30 cm, and adhesive power of 1 - 3.67 seconds, homogeneous and protective. Ointment preparations of methanol extract of mango leaves have activity on *P. acnes* on the 0 and 15th day of storage. The activities of ointment preparation on day 0 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 10.20 mm; 19.97 mm and 23.60 mm respectively, while the inhibition zones produced by the preparation of ointment on day 15 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 5.71 mm; 9.58 mm and 21.88 mm respectively.

***Conclusion*:** Methanol extract of mango leaves (*Mangifera indica* L.) and ointment preparation can inhibit the growth of *Propionibacterium acnes*.

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Keywords: Antibacterial agent, acne, Arum Manis mango leaves, MIC, *Propionibacterium acnes*, human pathogens.

1. INTRODUCTION

Acne is an inflammatory disease of the sebaceous gland that is often found and is associated with hair follicles. The bacteria that cause acne include *P. acnes* and *Staphylococcus epidermis*. *P. acnes* cause acne by producing lipases that break down fat into free fatty acids. These fatty acids can cause tissue inflammation when associated with the immune system and support the occurrence of acne [1].

Acne treatment can be given with antibiotics, such as sulfur, resorcinol, salicylate acid, benzoyl peroxide, azelaic acid, tetracyclin, erythromycin and clindamycin. The use of these drugs as anti-acne has side effects such as irritation, while long-term use can cause resistance [2, 3].

Since ancient times people have used plants as a source of medicine. Around 80% of the general population in the world use plants to treat several illnesses [4]. One plant that has the potential as a medicine is mango leaves (*M. indica* L.). The *M. indica* L. fruit is one of the most important fruit-crops with extensive acceptance due to its succulence, exotic flavor, and nutritional value [5]. Various extracts from the seed kernel, leaves, and barks of *M. indica* is active against human Pathogens [6, 7].

The main content of mango leaf extract *(M. indica* L.) is mangiferin and has one of its functions as an antimicrobial [8]. Groups of secondary metabolites, in addition to, mangiferin contained in methanol extract of mango leaves (*M. indica* L.) based on phytochemical tests, namely alkaloid compounds, flavonoids, steroids, polyphenols, tannins, and saponins [9]. Rajan *et al*. [10] reposted that the seed kernels of *M. indica* contained secondary metabolites, such as saponin, flavonoid, glycosides, tannins, and alkaloids have

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been implicated as having antidiarrhoeal activity and inhibit the intestinal mobility.

Flavanoid compounds showed antimicrobial properties against multiresistant strains like *Staphylococcus aureus*, *Escherichia coli*, *Serratia* sp., *Klebsiellapneumonia*, and *Candida albicans* [11]. According to the research conducted by Ramesh *et al.* [12], the ethanol extract of mango leaves (*M. indica* L.) has efficacy as antianalgesic, anti-inflammatory in experiments using mice, and antimicrobials against gram-positive, gram-negative and fungi bacteria.

The use of mango leaf extract as a drug in dealing with acne can be done by making an extract of mango leaves into an easy-to-use form, such as ointment. The ointment is a semi-solid preparation that is easily applied and used as an external medicine. Ethanol extract of white frangipani leaves (*Plumeria alba L.*) can be formulated as ointment preparations that have antibacterial activity against *P. acnes* [13]. Based on the description, a formulation of ointment preparations of methanol extract of mango leaves as an antibacterial agent of *P. acnes* causing acne was carried out as shown in Table **1**.

2. METHODS

2.1. Materials and Apparatus

2.1.1. Materials

Mango leaf (*M. indica* L.) was obtained from local source (Karangwangkal Purwokerto Indonesia), distilled water (Purwokerto Indonesia), *Propionibacterium acnes* from Microbiology Laboratory Faculty of Biology Universitas Jenderal Soedirman, methanol (Darmstadt Germany), *Nutrient Broth* (NB) medium (Darmstadt Germany), *Nutrient Agar* (NA) medium (Darmstadt Germany), erythromycin, stearyl alcohol, white vaseline (China), propylparaben (Japan), methylparaben (Japan), polysorbate 80 (Darmstadt, Germany), glycerol (Darmstadt German), phenolphthalein indicator (Darmstadt Germany), KOH (Darmstadt Germany).

2.1.2. Apparatus

Test tube, Petri dishes, autoclave, analytical balance, ovens, measuring cups, Erlenmeyer, glass beakers, micropipette, glass stirrers, aluminum foil, wrapping, dilution flasks, incubator, rose needles, stirrer, spiritus burners, Genesys 20 (Thermo Scientific) Spectrophotometer, volume pipette.

2.2. Extraction

One hundred grams of mango leaf extract are macerated using 350 mL methanol, then stirred, closed, and stored for three days. It is stirred three times a day and then filtered. The residue is then macerated by adding 50 mL methanol for 3 days and filtered daily. All filtrates produced are combined and the solvent was evaporated using *vacuum rotary evaporator* until thick extract is produced and then weighed [14].

2.3. Test of Minimum Inhibition Concentration (MIC) Value

The Minimum Inhibition Concentration is the lowest concentration of the antibacterial component, which will inhibit the visible growth of bacterium after the overnight incubation period. A modified method reposted by [14] was adopted. One loop bacterial from the culture stock was taken and then incubated in 10 mL liquid Nutrient Broth (NB) medium for 18-24 hours at 37°C, then the OD of bacterial culture was measured. If the OD> 1 as much as 50 µL of culture was taken; if the OD <1 100 µL of culture was taken. It was then spread in a sterile petri dish. Suspension of test bacteria on Nutrient Agar (NA) medium was streaked using *Drugalsky* rod. After becoming solid, the Agar medium was perforated with a diameter of ± 6 mm using a crock drill. As much as 50 µL of mango leaves extract (*M. indica* L.) was inserted into the hole in various concentrations used to determine MIC in this study, namely 1; 5; 10; 15; 30; 65; 125; 250; 500 and 1000 ppm. Distilled water was used as a negative control and 1000 ppm erythromycin was used as a positive control. Incubation was carried out for 24 hours at 37 ° C. The clear zone seen around the hole indicated antibacterial activity in the sample. The clear zone formed was measured using a caliper for four measurements, and the average value was taken [14].

2.4. Water-based Ointment

2.4.1. Preparation of Water-washable Base Ointment

Ointment preparations are made with a water-washable base. The reason for such a selection of base type is that it may be cleaned easily from the skin. Thus, it will be acceptable for cosmetic applications. Ointment preparations are made by adding mango leaf extract (*M. indica* L.) as an antibacterial material against *P. acnes* at concentrations of 5 ppm, 10 ppm, and 15 ppm. 5 ppm is the Minimum Inhibitory Concentration (MIC) of methanol extract of Arum Manis mango leaves against *P. acnes*. The ointment is made using a melting method. The ointment base is made for making two preparations: preparation A and preparation B. Preparation A is made by melting stearyl alcohol of 9.98% w/w and the vaseline of 24.96% w/w at 70°C while stirring them and adding propylparaben of 0.0025% w/w. Preparation B is made by heating distilled water of 50.035% w/w and glycerol of 9.98% w/w at 70°C while stirring them and adding polysorbate 80 of 5% w/w, methylparaben of 0.005% w/w and mango leaf extract (*Mangifera indica* L.). Preparations A and B are mixed at 70°C while stirring them in a mortar until they are cooling down; thus, the oil on water ointment is produced [13].

2.5. Characterization of Ointment Preparations

The preparations for an ointment that had been made were then characterized on days 0, 5, 10, and 15 days of storage.

Table 1. Formulation of mango leaves methanol extract Ointment (*M. indica* L).

Materials	F1	F2	F3	F4	F5
Distilled water	50.035 g	50.035 g	50.035 g	50.035 g	50.035 g
Glycerol	9.98 g	9.98 g	9.98 g	9.98 g	9.98 g
Polysorbate 80	5 g	5 g	5 g	5 g	5 g
Propylparaben	0.0025 g	0.0025 g	0.0025 g	0.0025 g	0.0025 g
Stearyl Alcohol	9.98 g	9.98 g	9.98 g	9.98 g	9.98 g
Methylparaben	0.005 g	0.005 g	0.005 g	0.005 g	0.005 g
Vaseline	24.96 g	24.96 g	24.96 g	24.96 g	24.96 g
Methanol extract mango leaves	0 ppm	5 ppm	10 ppm	15 ppm	-
Erythromycin	-	-	-	-	15 ppm

2.5.1. pH Test

pH values were measured by using universal pH sticks dipped in 0.5 g of ointment diluted with 5 ml of distilled water. A good pH value of ointment is 4.5-6.5 or in accordance with human skin pH value [15].

2.5.2. Homogeneity Test

The ointment preparations at the top, middle, and bottom parts were then placed on a glass plate, then rubbed and touched. The homogeneity test was performed by pouring 1 g of ointment on the flat glass surface. The ointment homogeneity test passed when no solid substance left during hand-applying the ointment to the flat glass to mimic the normal use of ointment to the skin surface [16].

2.5.3. Dispersive Power Test

As much as 0.5 g of ointment preparations was placed on a round transparent glass with a diameter of 15 cm, the other transparent glass was placed on top of it and was left for 1 minute. The spread diameter of the ointment was measured. After that, 100 g of the load was added and was left for 1 minute, then a constant diameter was measured [2].

2.5.4. Adhesive Power Test

As much as 0.25 g of ointment preparations was placed on a given width object glass, and then another object glass was placed on the ointment. Both glasses were pressed with a load of 100 g for 5 minutes. The affixed glasses were then attached to the adhesion test equipment and were released with a load of 80 g, then the time when the two glasses disjointed was recorded [17].

2.5.5. Protection Power Test

The ointment was applied to a filter paper that has been dripped with phenolphthalein. The filter paper was then attached to the other filter paper dripped with 0.1 N. KOH solution. Observations were made at 30 seconds, 60 seconds, 90 seconds, 120 seconds, and 150 seconds after KOH was dripped by observing the red color stain appearance.

2.5.6. Test for Antibacterial Activity of Ointment Preparations

Antibacterial activity test of ointment preparations was carried out to determine whether the ointment formulations containing methanol extract of mango leaves (*M. indica* L.) has activities to inhibit the growth of *P. acnes* bacteria. The ointment activity test was carried out on day 0 and day 15th of storage using a well diffusion method as done in the MIC test. Suspension of tested bacteria on the NA medium was streaked using *Drugalsky*; then, a hole was made. Various formulations of the ointment made were then put into the hole. Erythromycin 15 ppm was used as a positive control; then incubated for 24 hours at 37°C. Antibacterial activity is obtained by measuring inhibitory zone, namely clear zone or area showing not growing bacteria around the filtrate. The clear zone was measured by using a caliper for four diagonal measurements, and their average value was then recorded [13].

3. RESULTS AND DISCUSSION

3.1. Determination of the Minimum Inhibitory Concentration (MIC)

Determination of MIC was carried out to determine the lowest concentration of methanol extract of mango leaves (*M. indica* L.), which was still able to inhibit the growth of *P. acnes* bacteria. Methanol was chosen as the solvent since it has high polarity. Based on the concept of polarization, the more polar a compound, the easier the compound dissolves in the polar solvent as well [8]. The relationship between the concentration of methanol extract of mango leaves (*M. indica* L.) and the inhibition zone is shown in Fig. (**1**).

The lowest concentration that can inhibit the growth of *P. acnes* bacteria is 5 ppm with the resulting inhibition zone of 1 mm. At the concentration of 1000 ppm methanol extract of mango leaves (*M. indica* L.), it resulted in a-6.43 mm inhibition zone. The negative control in the form of distilled water did not produce an inhibitory zone, while the positive control in the form of 1000 ppm erythromycin resulted in a-15.88 mm inhibition zone.

Based on the MIC values obtained according to [18], methanol extract of mango leaves (*M. indica* L.) has a very

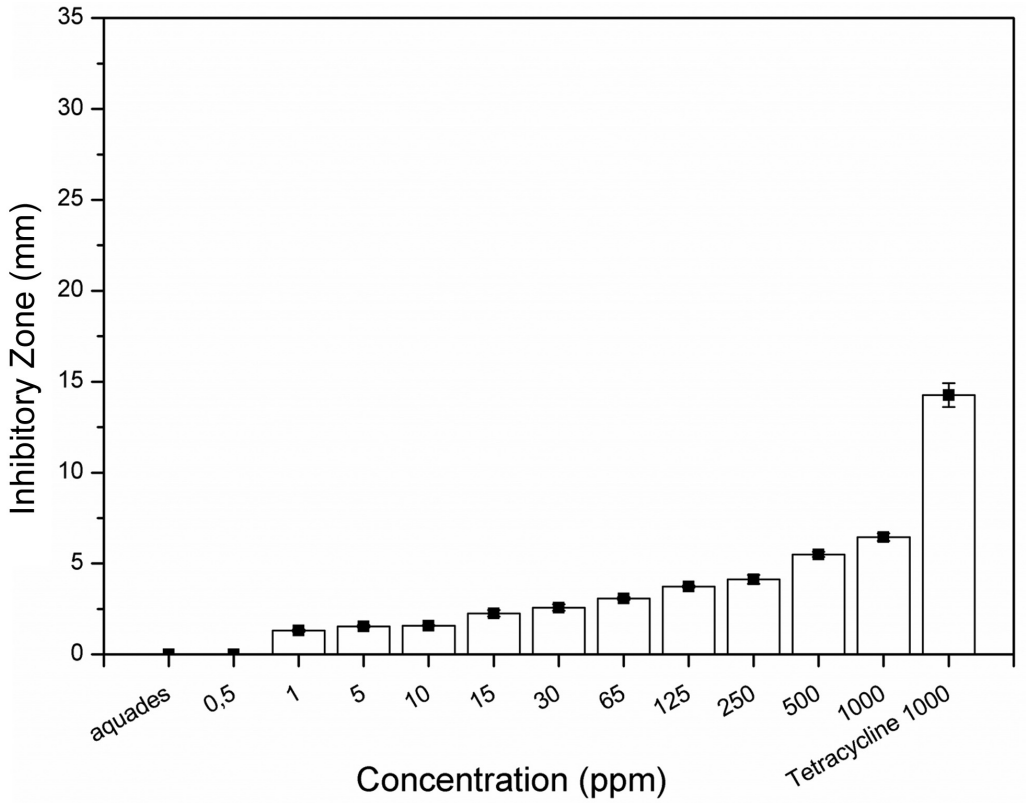

Fig. (1). Relationship between the concentration of mango leaf extract (*M. indica* L.) and inhibitory zone.

strong antibacterial activity, since the MIC value obtained is 5 ppm. The methanol extract of mango leaves (*M. indica* L.) contains flavonoids, alkaloids, steroids, polyphenols, tannins and saponins [9]. Flavonoid serves as a bacteriostatic agent, with the working mechanism of denaturing protein of bacterial cell and damaging cell membrane irreversibly. According to Cushnie and Lamb [19], flavonoids also serve to inhibit energy metabolism. These compounds will disturb energy metabolism in a way similar to inhibiting the respiration system, since sufficient energy is needed for active absorption of various metabolites and macromolecular biosynthesis. Alkaloids serve as an inhibiting mechanism by disturbing peptidoglycan composing components of a bacterial cell. Thus, the cell wall layer will not be formed completely and cause such a cell dead.

Steroid compounds inhibit bacterial growth through the inhibition of protein synthesis thus, causes changes in bacterial cell composing components [20]. Tannins' antibacterial working mechanism is expected to shrink the cell wall or cell membrane. Thus it disturbs cell permeability. As cell permeability gets disturbed, the cell cannot perform any activity, leading to its growth, thus causing its death [21]. Saponin's antibacterial working mechanism is through the reduction of the surface tension, causing an increase of cell permeability or leakage. Thus intracellular compounds discharged [22]. According to Oprica *et al.* [23], these compounds diffuse through the vulnerable cell wall and outer membrane, which then binds to the cytoplasm membrane causing a reduction in its stability. This causes cytoplasm to be discharged from the cell, causing cell death. The antimicrobial agent disturbing the cytoplasm membrane is bactericidal.

3.2. Preparation of Water-washable Base Ointment

The preparation of ointment is made on a water-removable base with oil-in-water emulsions. The choice of such base because it is easily washed from the skin, has low-fat content, does not irritate the skin, making it suitable for sufferers of sensitive or dry skin. The type of oil in water has good dispersing nature on the skin, has a cold effect and is soft. The type of oil-in-water emulsion has high water content so that it can provide the effect of hydration on the skin. The making of ointment preparations is conducted using the fusion method, in which all or some of the components of an ointment are combined by being melted together and cooled with constant stirring until congealed.

Preparation A in the form of an oil phase is made by melting stearyl alcohol, white Vaseline and nipasol into a mortar that has been previously heated in the oven to make it easier to mix solid material. Preparation B in the form of a water phase is made by heating distilled water, glycerol, polysorbate 80, nipagin at 70°C and then methanol extract of mango leaves (*M. indica* L.) is added.

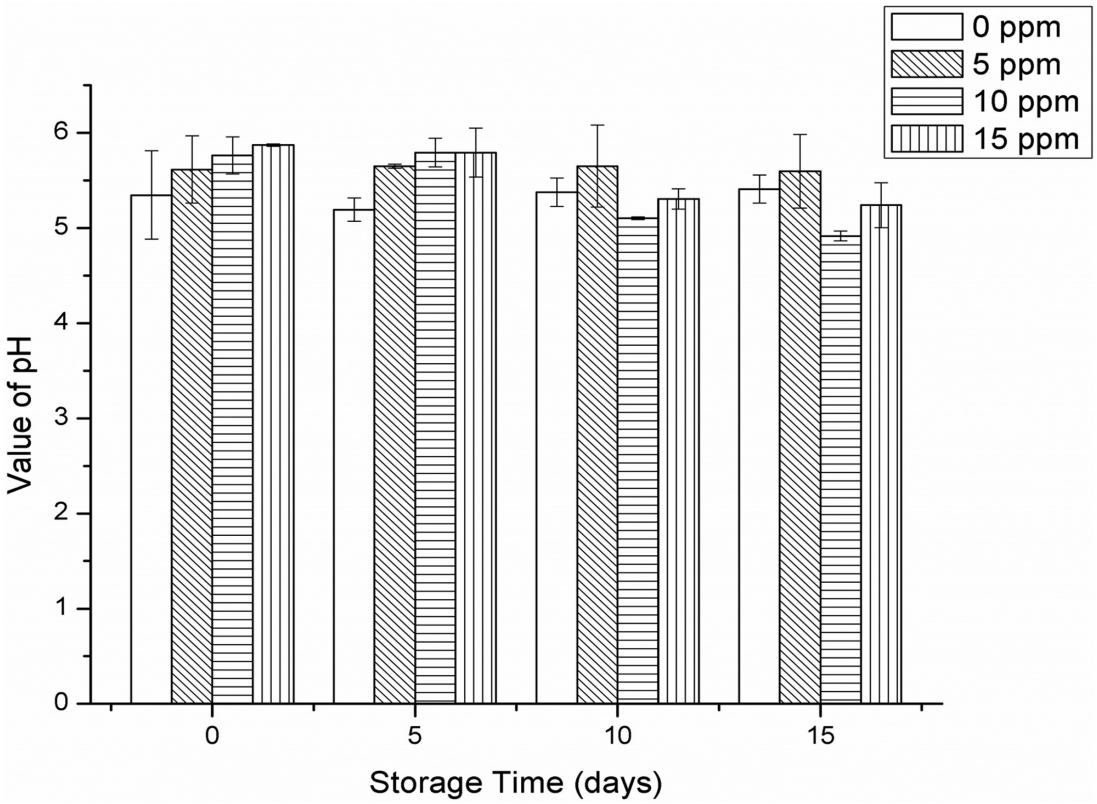

Fig. (2). Relationship between storage time and pH value of ointment of methanol extract of mango leaves (*M. indica* L).

3.3. PH Test

The pH test was carried out to determine whether the ointment preparations made had a pH that was suitable with the pH of skin, which would affect the safety of their use. The relationship between the length of storage and the pH value of mango leaves (*M. indica* L.) methanol extract ointment is shown in Fig. (**2**).

Based on the results of the study, the pH value of each ointment preparations was obtained. Ointment with a concentration of 0 ppm has a pH value ranging from 5.35 to 5.87, a concentration of 5 ppm has a pH value ranging from 5.19 to 5.79, a concentration of 10 ppm has a pH value ranging from 5.10 to 5.65 and concentration 15 ppm has a pH value ranging from 4.92 to 5.60. The pH value of ointment with concentrations of 0 ppm and 5 ppm increased from day 0 to day 15, while concentrations of 10 ppm and 15 ppm produced pH values that tended to be unstable, but the pH value of ointment is 4.5-6.5 or in accordance with human skin pH value [15]. If the pH produced is too alkaline, it can cause scaly skin, whereas if the pH is too acidic, it can cause skin irritation.

3.4. Homogeneity

A homogeneity test was carried out to determine whether the ointment preparations of methanol extract of mango leaves (*M. indica* L.) were made evenly mixed between the active substances and the base of the ointment. The homogeneous ointment is seen based on the presence or absence of lumps or coarse granules on the ointment.

Based on the research that has been carried out that ointment preparations of methanol extract of mango leaves (*M. indica* L.) with a concentration of 0, 5, 10, 15 ppm and positive control in the form of 15 ppm erythromycin is homogeneous because there are no lumps from day 0 to day 15 of storage. Homogeneous ointment preparations indicate that the ingredients of the ointment preparations and extract used have been completely mixed so that there are no lumps or granules. The homogeneity of preparation depends on the similarity of the materials used, namely the base and the active substance. If there are differences like the base and the active substance, there will be a clumping process resulting in a larger particle form [24].

3.5. Dispersive Power Test

Dispersive testing is carried out to see the ability of the preparation to disperse on the treated skin since a base of ointment should have good dispersion to guarantee satisfactory drug administration. The difference in dispersive power dramatically influences the speed of diffusion of active substances across the membrane. The relationship between storage time and dispersion value of ointment preparations of methanol extract of mango leaves (*M. indica* L.) is shown in Fig. (**3**).

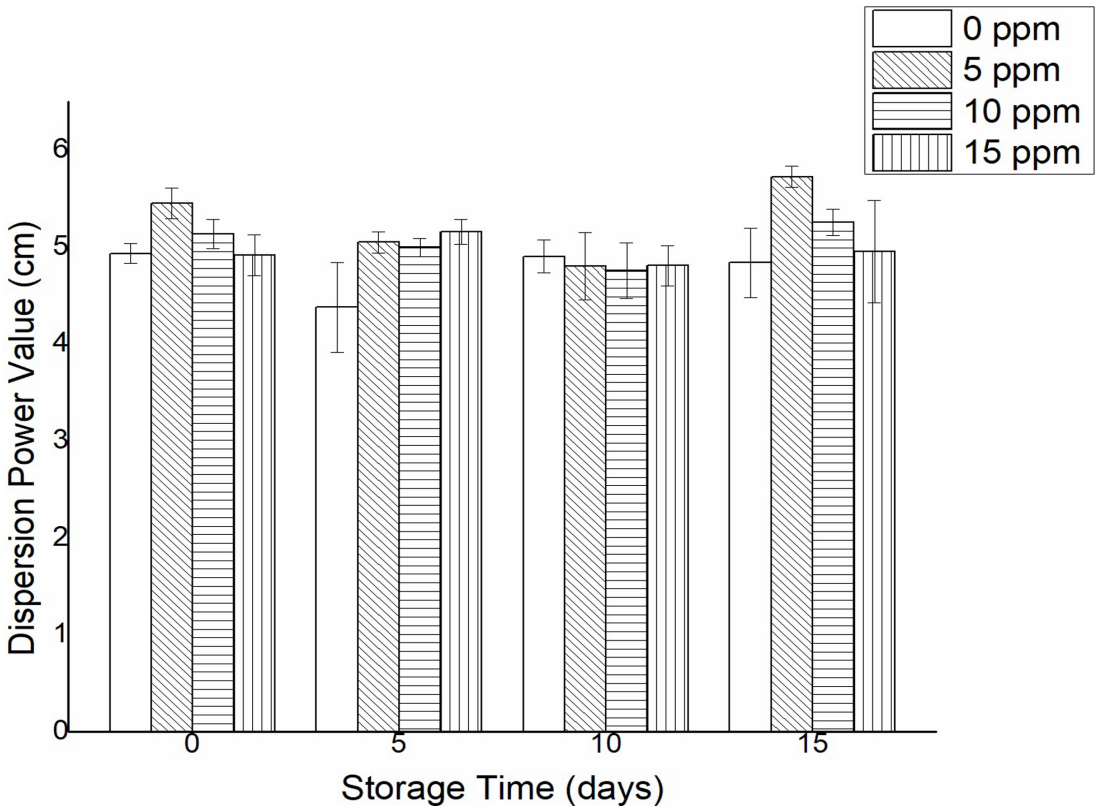

Fig. (3). Relationship between storage time and spread value ointment of methanol extract of mango leaves (*M. indica* L.).

Based on the results, increasing the concentration of the extract added in the ointment preparations produced, the lower the value of dispersive power. Increasing the storage time of the ointment preparations caused more unstable, the results tend to but is still in the range of good dispersive power value. Dispersive power that shows semi-solid consistency in providing comfort when used is 5-7 cm. Ointment with 0 ppm concentration has dispersive power value ranging from 5.57 to 6.30 cm, 5 ppm concentration has dispersive power value ranging from 5.05 to 5.96 cm, 10 ppm concentration has dispersion power value ranging from 5.55 to 5.68 cm and 15 ppm concentration has dispersion power value ranging from 5.23 to 6.21 cm. This shows that the value of dispersive power is not influenced by storage time, but is influenced by differences in the concentration of methanol extract of mango leaves (*M. indica* L.).

3.6. Adhesive Power Test

The adhesive power test was carried out to see how long the ointment can stick to the surface of the skin so that the active substance in the ointment can be absorbed. The relationship between the length of storage and the value of adhesion of the ointment preparations of methanol extract of mango leaves (*M. indica* L.) is shown in Fig. (**4**). Ointment preparations with concentrations of 0, 5, 10 and 15 ppm tend to decrease the value of adhesion from day 0 to day 15 of storage, but the value is still inside the value of good adhesion. The adhesive value of semi-solid preparations should be more than 1 second. Ointment preparations with a concentration of 0 ppm has an adhesive power value ranging from 1.33 to 3.67 seconds, a concentration of 5 ppm has a sticky power value ranging from 1.33 to 3.67 seconds, a concentration of 10 ppm has an adhesive power value ranging from 1-3 seconds and the concentration of 15 ppm has spread values ranging from 1.33 to 2.33 seconds. This shows that the value of sticky power is not affected by differences in the concentration of methanol extract of mango leaves (*M. indica L.*), but is influenced by the length of storage.

3.7. Protection Power Test

The ointment was tested for its protective power to find out how long the ointment provided protection on the treatment site against external influences. In this test, the filter paper is treated as skin to find out the protective power of the ointment when applied to the skin. The emergence of red stains was due to the phenolphthalein indicator dripped with KOH. If the stain appears, the ointment is no longer protective. The longer the color change occurs, the greater the ointment protection ability [25].

Based on the research done, the ointment preparations of methanol extract of mango leaves (*M. indica* L.) with concentrations of 0, 5, 10, 15 ppm and positive control of 15 ppm erythromycin did not cause red stains for 3 minutes after dripping with KOH. This showed that the ointment has

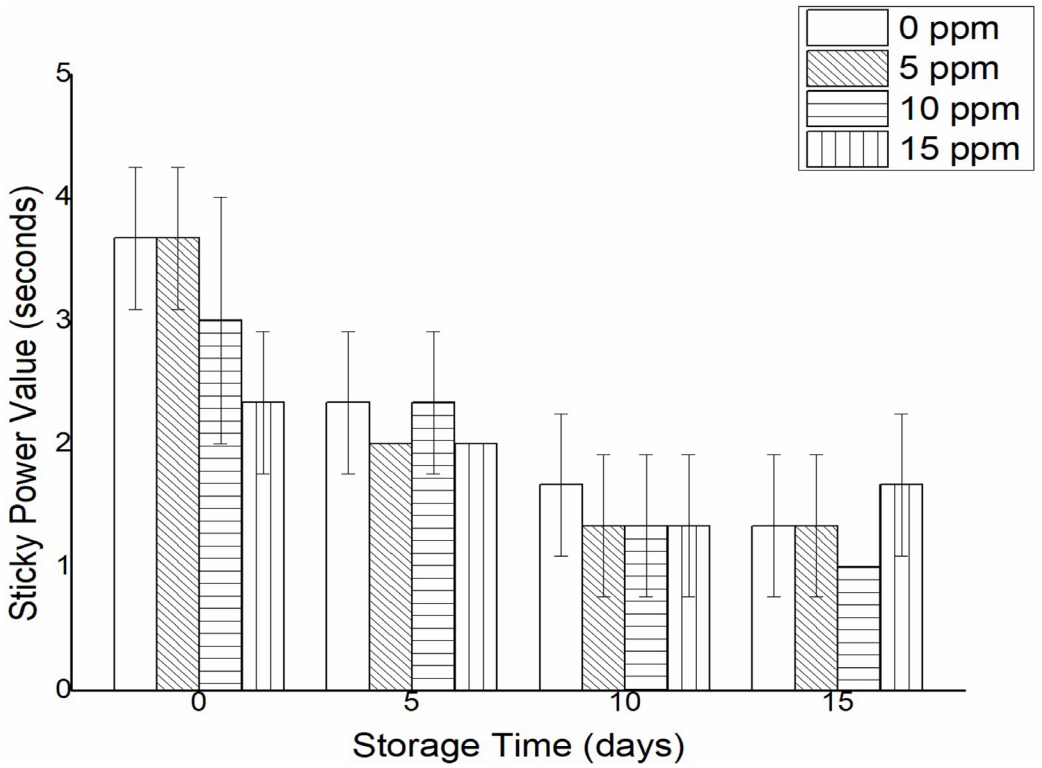

Fig. (4). Relationship between storage time and adhesive value ointment preparations of methanol extract of mango leaves (*M. indica* L.).

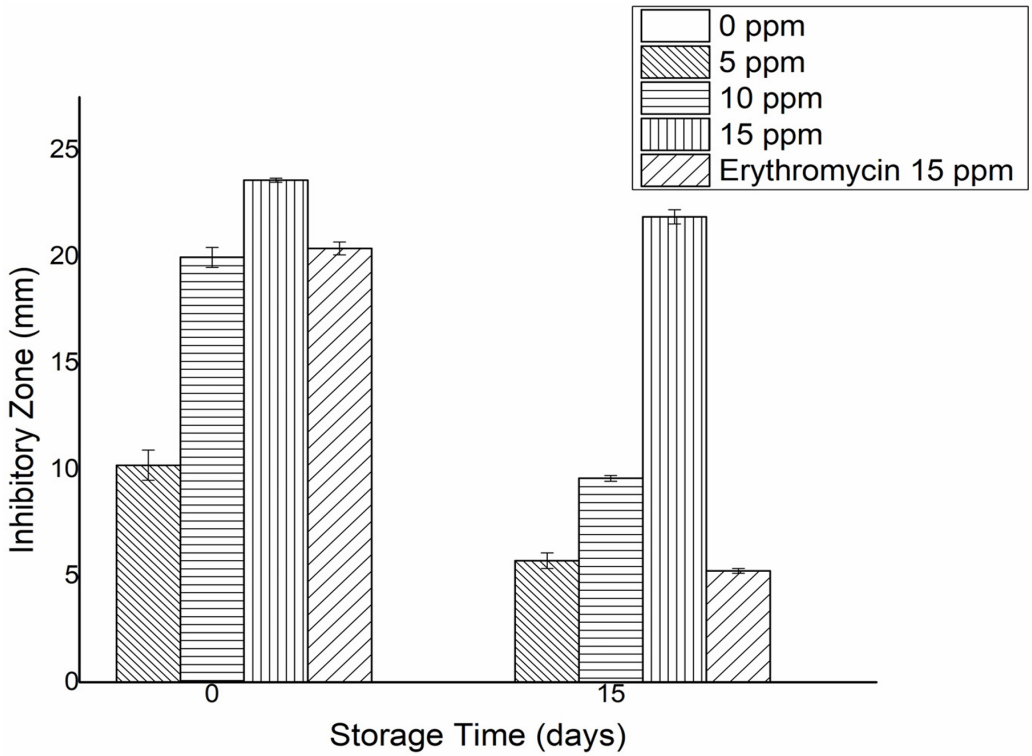

Fig. (5). Relationship between storage time and inhibition zone ointment preparations of methanol extract of mango leaves (*M. indica* L.).

protective properties. Increased levels of extract concentrations and storage time for 15 days did not affect the protective properties of the preparation.

3.8. Antibacterial Activity Test of Ointment Preparations

Based on the results of research on inhibitory zones produced by ointment preparations on day 0 with a concentration of 0, 5, 10, 15 ppm and 15 ppm positive control were 0.00 mm; 10.20 mm; 19.97 mm; 23.60 mm and 20.38 mm respectively, while the inhibition zone produced by the ointment on the 15th day of storage with a concentration of 0, 5, 10, 15 and 15 ppm positive control were 0.00 mm; 5.71 mm; 9.58 mm; 21.88 mm and 5.24 mm respectively. The relationship between storage time and inhibition zone ointment preparations of methanol extract of mango leaves (*M. indica* L.) is shown in Fig. (**5**).

Based on the results of the activity test showed that the higher the concentration of methanol extract of mango leaves (*M. indica* L.) was added, the greater the inhibition zone produced. The results of the ointment preparations activity decreased on the 15th day. This shows that the higher the concentration of extracts and the longer the storage time affects the activity of ointment preparations. The positive control ointment preparations in the form of 15 ppm erythromycin has a smaller activity compared to the preparation of ointment with the addition of methanol extract of mango leaves (*M. indica* L.).

CONCLUSION

The results showed that the methanol extract of mango leaves (*M. indica* L.) and ointment preparation able to inhibit the growth of *Propionibacterium acnes.* Minimum concentration of methanol extract of mango leaves (*M indica* L.) which is still able to inhibit the growth of *Propionibacterium acnes* bacteria with a concentration of 5 ppm with an inhibition zone of 1 mm. The ointment preparations obtained are white, the distinctive smell of ointment, semi-solid form, has a pH ranging 4.5 - 6.5 from 4.92 to 5.87, dispersive power ranging from 5.05 to 6.30 cm, adhesive power around 1 - 3.67 seconds, homogeneous and protective. The activity of ointment preparations against *P. acnes* on day 0 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 10.20 mm; 19.97 mm and 23.60 mm respectively, while the inhibition zone produced by the preparation of ointment on day 15 with concentrations of 0, 5, 10 and 15 ppm are 0.00 mm; 5.71 mm; 9.58 mm and 21.88 mm, respectively.

LIST OF ABBREVIATIONS

MIC	=	Minimum Inhibitory Concentration
NA	=	Nutrient agar
NB	=	Nutrient Broth
OD	=	Optical Density

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No animals/humans were used for studies that are the basis of this research.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared None.

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