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Synthesis and Antibacterial Activity Test of Dibutyl Tin (IV) N- Ethylbenzyl Dithiocarbamate Compound Against *Salmonella Thy.Atcc.*14028 and *Propionibacterium acnes* Bacteria

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Abstract

The complex compound dithiocarbamate exhibits various biological activities, including anticancer, antibacterial, antifungal, and antioxidant properties. Dibutyl tin (IV) N-ethylbenzyl dithiocarbamate was synthesized to overview its structure and evaluate its antibacterial activity against *Salmonella typhimurium* ATCC 14028 and *Propionibacterium acnes*. This compound was synthesized via an in situ method by adding dibutyl tin (IV) dichloride, N-ethylbenzylamine, and carbon disulfide, forming a precipitate, which was then dried to yield a white powder. This powder can also be crystallized. The compound was characterized using FTIR, ^{1}H NMR and ^{13}C NMR spectroscopy, along with antibacterial activity testing using the disc diffusion method. The FTIR analysis revealed characteristic absorption bands at 1111.00 cm^{-1} (C-N), 731.02 cm^{-1} (C-S), 2954.95 cm^{-1} (C-H), 1602.85 cm^{-1} (C=C), 360.69 cm^{-1} (Sn-S), and 567.07 cm^{-1} (Sn-C). The ^{1}H NMR spectrum showed chemical shifts at 0-3.8570 ppm (δ CH_3), 5.0032-5.1472 ppm (δ N-CH_2), and 7.2780-7.3607 ppm (δ C_6H_5). The ^{13}C NMR spectrum displayed signals at 0-34.5610 ppm (δ CH_3), 48.6398-56.9247 ppm (δ N-CH_2), 127.6651-135.7665 ppm (δ C_6H_5), and 201.7568 ppm (δ CS_2). The antibacterial activity of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate was assessed, revealing inhibition zones against *Salmonella typhi* of 6.78 mm (100 ppm), 7.36 mm (120 ppm), and 7.76 mm (140 ppm), categorizing the activity as moderate. Against *Propionibacterium acnes*, inhibition zones were 1.8 mm (100 ppm), 1.88 mm (120 ppm), and 2.13 mm (140 ppm), categorizing the activity as weak. Based on these findings, it can be concluded that dibutyl tin (IV) N-ethylbenzyl dithiocarbamate can be synthesized to form an octahedral structure and exhibits antibacterial activity. However, it is not yet suitable for use as a new antibiotic.

1. Introduction

Infectious diseases are prevalent among the populations of developing countries, including Indonesia. Pathogenic bacteria are a significant cause of these diseases. Bacterial infections such as tuberculosis, typhoid fever, and pneumonia remain major health concerns in several countries, including Indonesia [1].

Typhoid fever is an infectious disease of the digestive system caused by *Salmonella typhi* bacteria. This disease is closely related to a person's hygiene because of the way this disease is transmitted through food and drinks contaminated with *Salmonella typhi* bacteria or through direct contact with the patient's feces and urine [2]. In addition to typhoid fever, infections caused by bacteria are acne. Acne is a disease that occurs in the place follicles, namely in the sebaceous glands and hair follicles. The causes of acne are multifactorial, one of which is bacterial colonization. The bacteria that causes acne is *Propionibacterium acnes* [3].

In general, the treatment of infectious diseases involves the administration of antibiotics. However, improper use of antibiotics can lead to bacterial resistance. This resistance poses a significant challenge in the healthcare sector, making infectious diseases more

difficult to treat and cure. The rise in antibiotic resistance is not accompanied by the development of new antibiotics, underscoring the urgent need for efforts to develop new antimicrobial agents [4]. One approach to new drug development is to synthesize compounds, study their structures, and analyze their therapeutic activities.

Dithiocarbamate is an important organic compound that has various activities in various fields. Recent literature indicates that organic dithiocarbamates possess biological activities, including antioxidant, antibacterial, anticancer, and antifungal properties [5].

Research conducted by Sanuddin *et al.* [6] indicates that the compound synthesized from dibutyl tin (IV) bis-methyl diiovalate exhibits significant antibacterial activity against *Salmonella typhi*, with an inhibition zone of 27.33 mm (classified as very strong) at a concentration of 90 ppm, and against *Escherichia coli*, with an inhibition zone of 26.48 mm (also classified as very strong) at the same concentration. Additionally, Anggraini *et al.* [7] reported that the complex compound diphenyltin (IV) N- benzyl methyl dithiocarbamate demonstrates antifungal activity, with the highest inhibitory effect observed at a dose of 0.050 grams.

Based on this background, researchers aim to discover new compounds as alternatives to antibiotic therapy. Consequently, a study was undertaken to synthesize and evaluate the antibacterial activity of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compounds against *Salmonella typhi* and *Propionibacterium acnes*.

2. Experimental

2.1. Materials and Tools

The materials used in this study were N- ethylbenzylamine ($C_9H_{13}N$), carbon disulfide (CS_2), dibutyl tin (IV) metal, dimethyl sulfoxide, nutrient agar, Mueller Hilton Agar (MHA), methanol, distilled water, NaCl 0.9%, *Salmonella typhi*, and *Propionibacterium acnes*.

The instruments utilized in this study included Erlenmeyer flasks, beakers, volumetric pipettes, Petri dishes, test tubes, pipette pumps, inoculating loops, cotton swabs, disc paper, filter paper, chloramphenicol discs, an analytical balance, a hotplate, detergent, an incubator, an autoclave, a laminar airflow cabinet (LAF), an FTIR spectrometer, and an NMR spectrometer.

2.2. Synthesis of Dibutyl Tin (IV) N-Ethylbenzyl Dithiocarbamate Compound

The synthesis began by preparing 3 mL (0.02 mol) of N-ethyl benzylamine and adding it to 15 mL of methanol. Subsequently, 1.2 mL (0.02 mol) of carbon disulfide was pipetted and mixed into another 15 mL of methanol. In the next step, 3.03 grams (0.01 mol) of dibutyl tin (IV) dichloride was weighed and dissolved in 15 mL of methanol. These solutions were then combined in situ slowly and stirred for approximately 2 hours. After the precipitate formed, the mixture was filtered, and the residue was placed in a vial and stored in a desiccator. The resulting samples were then analyzed using FTIR, NMR, and antibacterial activity tests [6].

2.3. Characterization using FTIR Spectroscopy

Approximately 1 mg of the synthesized compound was thoroughly mixed with KBr until a homogeneous mixture was obtained. This mixture was then compressed into pellets, and its absorption was measured at wavenumbers ranging from 4000 to 200 cm^{-1} [6].

2.4. Characterization using NMR Spectroscopy

A total of ± 10 mg of the synthesized compound was dissolved in deuterated chloroform solvent. The solution was transferred into an injection tube and subjected to analysis using an AGILENT NMR spectroscopy to obtain the ^1H NMR and ^{13}C NMR spectra [6].

2.5. Test Solution Preparation

2.5.1. Stock Solution Preparation

A stock solution of 1000 ppm was prepared by weighing 100 mg of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate, transferring it into a 100 mL volumetric flask, adding DMSO up to the mark, and ensuring thorough homogenization.

2.5.2. Dilution Series Setup

The dilution series was prepared using a stock solution initially at 100 ppm. Specifically, 1 mL of the stock solution was transferred into a 10 mL volumetric flask. Subsequently, DMSO was added until the total volume reached 10 mL, and the mixture was thoroughly homogenized. This procedure was repeated to create a dilution series at concentrations of 120 and 140 ppm, using 1.2 and 1.4 mL of the stock solution, respectively, following the same steps. This method successfully yielded a range of solutions with varying concentrations intended for subsequent antibacterial activity testing.

2.5.3. Sterilization of Tools and Materials

All equipment used in the research underwent sterilization to prevent contamination and the growth of microorganisms that could compromise the integrity of the study. Glassware was sterilized by heating in an oven at 180°C for 2 hours, while heat-sensitive instruments underwent autoclaving at 121°C for 15 minutes. Inoculation loops and tweezers were sterilized by direct exposure to a Bunsen burner flame until they reached a red-hot temperature [8].

2.5.4. Test Media Preparation

Agar-slant Preparation. A total of 2.8 grams of nutrient agar was dissolved in 100 mL of distilled water in an Erlenmeyer flask, then homogenized and heated. Subsequently, 5 mL of the nutrient agar was dispensed into each test tube. The media was then sterilized in an autoclave at 121°C and 1 atm pressure for 15 minutes [9].

Testing Media. A total of 3.8 grams of Muller-Hinton Agar powder was dissolved in 100 mL of distilled water in an Erlenmeyer flask, then homogenized and heated. The media was sterilized in an autoclave at 121°C and 1 atm pressure for 15 minutes. Once sterilization was complete, 20 mL of the media was poured into a petri dish and allowed to solidify [9].

Table 1. FTIR characterization results of the functional cluster of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compounds

Wavelength absorption area (cm^{-1}) [6]	Results of analysis of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound	
	Wavenumber (cm^{-1})	Function cluster
1300-800	1111 (s)	C-N
1563-700	731.02 (s)	C-S
3800-2700	2954.95 (s)	C-H
1900-1500	1602.85 (s)	C=C

(s): Strong

2.5.5. Bacterial Rejuvenation

Bacterial rejuvenation was performed using a sterile inoculation loop to transfer the test bacteria onto a slant agar medium. The culture was then incubated at 37°C for 24 hours in an incubator [9].

2.5.6. Making Bacterial Suspension

Rejuvenated bacteria were collected using an inoculation needle and mixed into 2 mL of a 0.9% NaCl solution. The mixture was then homogenized to achieve a turbidity equivalent to the McFarland standard of 0.5. This standard indicates a bacterial suspension concentration of 10^8 CFU/mL [10]. Subsequently, the transmittance was measured using a UV-Vis spectrophotometer at a wavelength of 580 nm until a transmittance of 25% was obtained [11].

2.5.7. Bacterial Activity Test on Sodium Butyl Tin (IV) N-ethylbenzyl Dithiokarbate

Petri dishes containing Mueller-Hinton Agar (MHA) were inoculated with a bacterial suspension using a sterile cotton swab, which was evenly spread over the medium. The plates were then left for 10-15 minutes to allow the bacteria to absorb into the agar. Discs of filter paper were prepared and soaked in a solution of the test compound, dibutyltin(IV) N-ethyl benzyl dithiocarbamate, at concentrations of 100 ppm, 120 ppm, and 140 ppm, with DMSO serving as a negative control for 10 minutes and a chloramphenicol disc as a positive control. Each disc was then placed onto the MHA medium using sterile tweezers. The Petri dishes were sealed with plastic wrap and incubated at 37°C for 24 hours. The inhibition zones that formed were subsequently measured using a caliper.

Table 2. FTIR characterization results of the metal cluster of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compounds

Wavelength absorption area (cm^{-1}) [12]	Results of analysis of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound	
	Wavenumber (cm^{-1})	Function clusters
450-350	360.69 (w)	Sn-S
605-515	567.07 (w)	Sn-C

(w): Weak

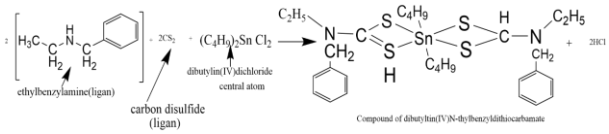

Figure 1. Reaction mechanism of synthesis of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound

3. Results and Discussion

3.1. Synthesis of Dibutyl Tin (IV) N-Ethylbenzyl Dithiocarbamate Compound

The synthesis of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate resulted in a yield of 3.5 grams of a white, odorless powder, which is capable of crystallization. The reaction mechanism for synthesizing dibutyl tin (IV) N-ethylbenzyl dithiocarbamate is depicted in Figure 1.

3.2. Characterization of FTIR Spectroscopy

Characterization using FTIR aims to identify the functional groups and bond types present in the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate, thereby predicting the compound's bonding structure. The FTIR spectroscopy analysis was conducted over a wavelength range of 4000-200 cm^{-1}.

The absorption of the C–N functional group appeared at a wavenumber of 1111 cm^{-1} in the strong spectrum, the C=S functional group appeared at 731.02 cm^{-1} in the strong spectrum, the Sn–S bond appeared at 360.9 cm^{-1} in the broad spectrum, and the Sn–C bond appeared at 567.07 cm^{-1} in the broad spectrum. These spectral peaks characterize the complex compound, enabling the prediction of its structure. The results of the FTIR spectroscopy characterization are illustrated in Figure 2. The wavelength region produced by the compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate gives rise to the spectrum shown in Tables 1 and 2.

3.3. Characterization of ^1H and ^{13}C NMR Spectroscopy

Characterization using ^1H and ^{13}C NMR spectroscopy aims to elucidate the molecular structure of the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate. The characterization data for this complex compound are presented in Figures 3 and 4.

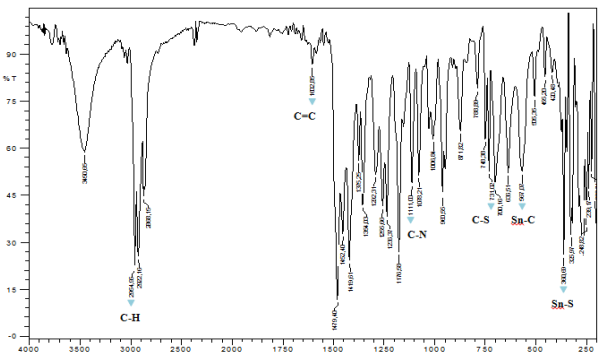

Figure 2. FTIR analysis results of dibutyl tin (IV) N- ethylbenzyl dithiocarbamate

Table 3. Results of NMR spectral measurement analysis of ^{1}H spectrum dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound

Proton shifting district ^{1}H (ppm) [12]	Analysis results of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound
δ 0-3 ppm (-CH_3)	0.9 – 2.166 (CH_3) multiplet
δ 3-5 ppm (CH_2)	3.75 – 3.85 (-CH_2) quartet
δ 5-6 ppm (β-monosubstitued aliphatic)	5.0032 – 5.1472 (CH_2-N) doublet
δ 6-9 ppm (Aromatic)	7.2780 – 7.3607 (C_6H_5) multiplet

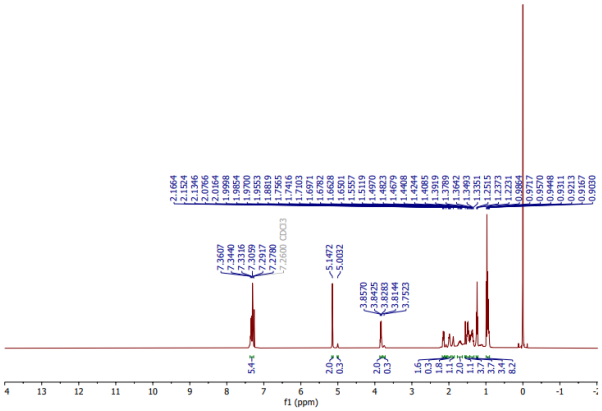

Figure 3. Results of ^{1}H NMR spectrum analysis

Based on Figure 3 and Table 3, the ^{1}H NMR characterization indicates that the CH_3 proton is in the δ shift region of 0.9 – 2.166 ppm (multiplet), the aliphatic -CH_2 proton is in the shift region of 3.75 – 3.85 ppm (quartet), the CH_2-N proton is in the shift region of δ 5.0032 – 5.1472 ppm (doublet), and the aromatic protons are in the shift region of δ 7.2780 – 7.3607 ppm (multiplet). The ^{1}H NMR spectral values align with the expected proton shift regions, where a δ value of 0-3 ppm corresponds to CH_3, a δ value of 3-6 ppm corresponds to CH_2, and a δ value of 6-9 ppm corresponds to aromatic protons [12].

According to Figure 4 and Table 4, the ^{13}C NMR characterization reveals that the CH_3 carbon resonates in the δ shift range of 0 - 34.5610 ppm, the CH_2-N carbon resonates in the δ shift range of 48.6398-56.9247 ppm, the aromatic carbon resonates in the δ shift range of 127.6651-135.7665 ppm, and the CS_2 carbon resonates at 201.7568 ppm. The ^{13}C NMR spectrum aligns with the expected carbon shift ranges as reported in the literature [12].

Table 4. Results of ^{13}C NMR spectroscopy analysis of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound

Proton shifting district ^{13}C (ppm) [12]	Analysis results of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound
δ 0-50 ppm (CH_3)	0 – 34,5610 (CH_3)
δ 40-70 ppm (β-monosubstitued aliphatic)	48,6398 – 56,9247 (CH_2- N)
δ 100-150 ppm (Aromatic)	127,6651 – 135,7665 (C_6H_5)
δ 180-220 ppm (C-S)	201,7568 (CS_2)

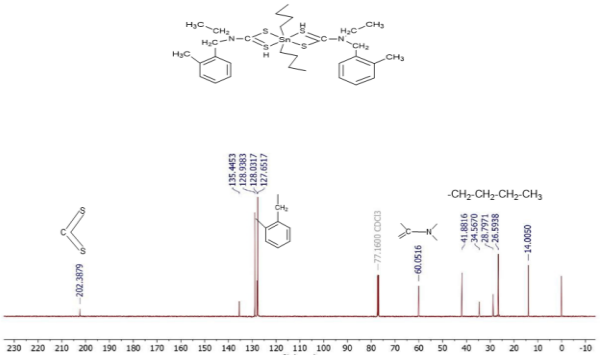

Figure 4. ^{13}C NMR spectra analysis result

3.4. Antibacterial Test of Dibutyl Tin (IV) N- Ethylbenzyl Dithiocarbamate Compound

The antibacterial activity of the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate was evaluated against *Salmonella typhi* and *Propionibacterium acnes* bacteria using the disc paper diffusion method. This method involves placing discs containing the compound onto a medium inoculated with the test bacteria, allowing for compound diffusion [13]. The test results of the dibutyl tin (IV) N-ethylbenzyl dithiocarbamate complex against *Salmonella typhi* ATCC 14028 bacteria are presented in Figure 5.

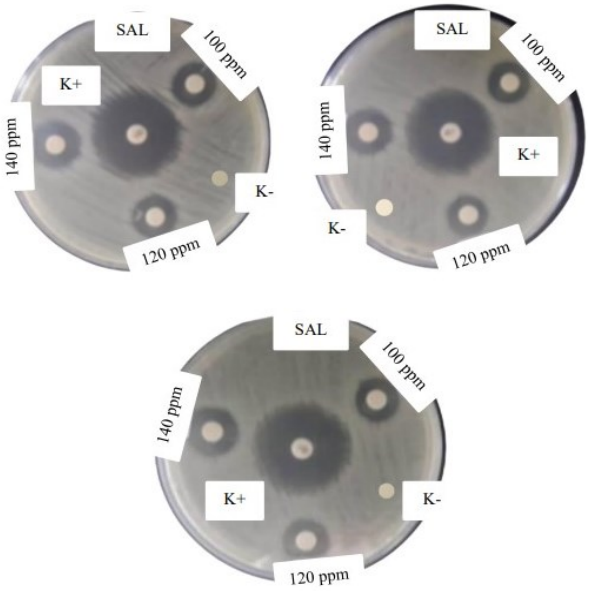

Figure 5. Results of the antibacterial activity test of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate against *Salmonella Thy*. ATCC 14028

Table 5. Inhibition zones of complex compounds at various concentrations

Concentration	Replication			Average ± Standard deviation (mm)	Category of inhibition zone
	1	2	3		
100 ppm	6.75	6.9	6.7	6.78 ± 0.08	moderate
120 ppm	7.3	7.4	7.4	7.36 ± 0.04	moderate
140 ppm	7.9	7.7	7.7	7.76 ± 0.09	moderate
K+ (Chloramphenicol)	18.8	18.8	18.8	18.8 ± 0	strong
K- (DMSO)	0	0	0	0	empty

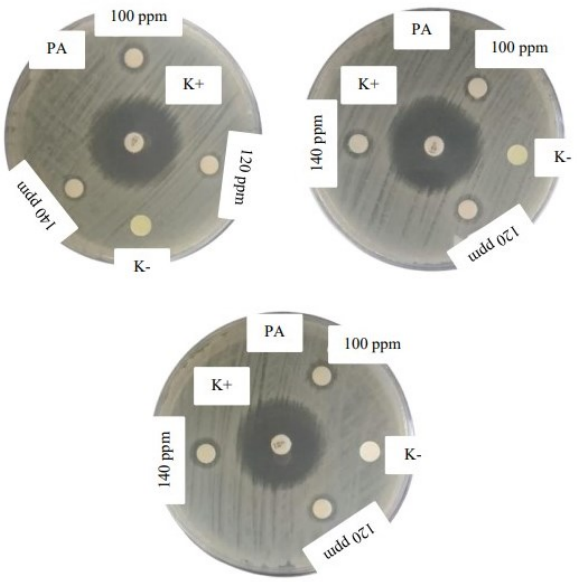

Figure 6. Test results of antibacterial activity of dibutyl tin (IV) N-ethylbenzyl dithiocarbamate compound against *Propionibacterium acnes* bacteria

The negative control employed in this study consisted of a dimethyl sulfoxide (DMSO) solution, chosen specifically to confirm its lack of antibacterial activity. DMSO was selected as a versatile solvent that dissolves polar, semi-polar, and non-polar compounds. Moreover, DMSO is non-toxic and does not interfere with experimental observations [14]. Conversely, the positive control in this study was chloramphenicol at a concentration of 30 µg per disk. Chloramphenicol is a broad-spectrum bacteriostatic antibiotic effective against both Gram-positive and Gram-negative bacteria, acting by inhibiting bacterial protein synthesis [15].

According to Table 5, the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate exhibited antibacterial activity against *Salmonella typhi* bacteria, evidenced by the formation of clear zones around the discs. The average inhibition zones at 100, 120, and 140 ppm were measured at 6.78, 7.36, and 7.76 mm, respectively. According to Davis and Stout [16], these concentrations demonstrated moderate inhibitory effects.

In comparison, the positive control, chloramphenicol at 30 µg per disk, displayed a significant inhibition zone of 18.8 mm, categorized as very strong. Conversely, the DMSO negative control showed no inhibition, confirming its lack of effect on bacterial growth. These findings support the idea that DMSO does not interfere with bacterial cultures. The test results of the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate against the bacteria *Propionibacterium acnes* can be seen in Figure 6.

According to Table 6, the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate was evaluated against *Propionibacterium acnes* at 100, 120, and 140 ppm. Clear zones were observed around the discs at these concentrations, indicating antibacterial activity with diameters of 18, 17.88, and 17.13 mm, respectively. These concentrations exhibited a weak inhibitory effect, which was categorized as weak, according to Davis and Stout [16].

The results of antibacterial testing on *Salmonella typhi* and *Propionibacterium acnes* demonstrated that higher concentrations led to larger inhibitory zones. The antibacterial activity of the dibutyl tin (IV) N-ethylbenzyl dithiocarbamate complex varied between the two test bacteria, with *Salmonella typhi* (Gram-negative) exhibiting greater resistance compared to *Propionibacterium acnes* (Gram-positive). This variance in inhibitory response is influenced by the structure of the bacterial cell walls. According to Parija [17], the cell wall of Gram-negative bacteria is thinner, comprising about 10% peptidoglycan, polysaccharides, and high lipid content.

Table 6. Inhibition zones of complex compounds at various concentrations

Concentration	Replication			Standard deviation (mm)	Category of inhibition zone
	1	2	3		
100 ppm	1.8	1.75	1.85	1.8 ± 0.01	moderate
120 ppm	1.85	1.9	1.9	1.88 ± 0	moderate
140 ppm	2.05	2.15	2.2	2.13 ± 0.01	moderate
K+ (Chloramphenicol)	18.3	18.3	18.2	18.2 ± 0.01	strong
K- (DMSO)	0	0	0	0	empty

Conversely, the cell wall of Gram-positive bacteria is thicker, consisting of 60-100% peptidoglycan and low lipid content. Gram-positive bacteria also contain teichoic acid within their thick peptidoglycan layers, whereas Gram-negative bacteria lack this acid due to their thinner peptidoglycan layer. Consequently, the cell wall of Gram-negative bacteria, such as *Salmonella typhi*, is more susceptible to physical disturbances, including the administration of antibiotics and other antibacterial agents [18].

The antibacterial activity of the complex compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate was evaluated against *Salmonella typhi* and *Propionibacterium acnes*, consistent with the research conducted by Hadijah *et al.* [19]. This research tested organotin compounds against *Salmonella typhi* and *Propionibacterium acnes*, demonstrating strong antibacterial activity in both categories. The antibacterial effect arises from the biological properties of organotin, which can integrate into the molecular structure, thereby inhibiting bacterial growth and serving as an effective pharmacophore. Additionally, dithiocarbamate compounds disrupt cell wall synthesis and decrease enzyme activity through protein denaturation [6].

4. Conclusion

Based on the results of this research, it can be concluded that the compound dibutyl tin (IV) N-ethylbenzyl dithiocarbamate can be successfully synthesized and characterized using FTIR and NMR. This compound exhibits antibacterial activity against *Salmonella typhi*, with inhibitory zones of 6.78 mm (100 ppm), 7.36 mm (120 ppm), and 7.76 mm (140 ppm), which are categorized as moderate. In contrast, for *Propionibacterium acnes*, the inhibitory zones are 1.8 mm (100 ppm), 1.88 mm (120 ppm), and 2.13 mm (140 ppm), categorized as weak. Despite these findings, dibutyl tin (IV) N-ethylbenzyl dithiocarbamate cannot yet be used as an antibiotic because its antibacterial activity at the same concentrations, when compared to the positive control chloramphenicol, remains in the moderate category.

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