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SYNTHESIS, CHARACTERIZATION, ANTIBACTERIAL AND TOXICOLOGICAL STUDIES OF HETEROLEPTIC ACETYLSALICYLIC ACID AND ANTHRANILIC ACID METAL COMPLEXES

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ABSTRACT

This present study aims at evauating the antibacterial, analgesic, and toxicological activities of new metals [Ni(II), Cu(II), Cd(II), and Zn(II)] complexes derived from acetylsalicylic acid and anthranilic acid via refluxing method in a 1:1:1 stoichiometry ratio. Characterization was executed using melting point, molar conductance, infrared and ultraviolet-visible spectroscopies. The antibacterial activities were investigated by the agar well diffusion method. The toxicological effect of the test compounds in serum and kidney homogenates of *Wister* rats was investigated. The screened complexes showed better antibacterial activities than their free ligands. The result of the analysis indicated that acetylsalicylic acid possessed a good significant analgesic activity, while toxicological studies confirmed that the complexes were toxic at the level of administered dosage.

Keywords: Antibacterial, Toxicology, Analgesics, Anthranilic acid, Acetylsalicylic acid.

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1. INTRODUCTION

More research on analgesic drugs has been developed to decrease the rate of mortality from diseases [1]. Antimicrobial resistance globally is becoming a great threat and this call for serious concern [2]. Metal complexes have now become a major concern in the development of drugs as a result of good outcomes from some chemotherapeutic drugs such as cisplatin and carboplatin [3]. This has helped to increase the database on the biological activities of complexes such as less toxicity, and an increase in antimicrobial and anticancer activities. Acetylsalicylic acid is an analgesic drug having anti-inflammatory and antipyretic activities [4,5]. From previous research, it has been discovered that biological potency improves upon coordination with transition metals [2,3].

Coordination of acetylsalicylic acid and anthranilic acid with some selected transition metals is therefore expected to have improved biological activities. Complexes resulting from the coordination between acetylsalicylic acid and central metal ions have attracted much attention as a result of their biological activities. [6] Complexes are very important as a result of their different medicinal uses. The most especially organoarsenic compound is used to cure syphilis.

Acetylsalicylic acid is a non-steroidal or anti-inflammatory drug that possessed anti-inflammatory and analgesic properties. Anthranilic acid is well known to be used in the production of azo dyes, saccharin, pharmaceuticals, corrosion inhibitors for metals, and mold inhibitors in soya sauce. Acetylsalicylic acid is used to relieve pain and prevents blood clotting.

The synthesis and antibacterial activity of mixed tributylphosphine and anthranilic acid metal complexes have been reported where it was confirmed that the deprotonated anthranilic acid coordinated through the oxygen of the carboxylate group and nitrogen of the amino group. The antibacterial activity of the ligands and their complexes revealed weak to better activity when compared with the DMSO which was employed as the control [7,8].

In continuation with our research towards the development of potential chemotherapeutic agents with various biological activities, we report the synthesis, characterization, and biological studies of mixed anthranilic acid and acetylsalicylic acid metal complexes.

2. MATERIALS AND METHODS

2.1. Material

The ligands (Acetylsalicylic acid and Anthranilic acid) used for this research work were obtained from Sigma-Aldrich chemical company. All the reagents and the hydrated metal ions (Nickel (II) chloride, Copper (II) chloride, Zinc (II) chloride, and Cadmium (II) chloride) were also collected from the Sigma-Aldrich chemical company. The melting points were performed with the use of the Gallenkamp melting point apparatus. The elemental analysis (CHN) was performed using Control Equipment CE 440 Analyzer, Egham, United Kingdom. The conductivity measurements were carried out on the HANNA instrument conductivity meter with a cell constant of 0.45. The electronic spectra of the free ligands and the coordination compounds in the DMSO solution were determined and reported within the range of 200 – 800 nm on the Aquamate V4.60 spectrophotometer. The FTIR analysis was carried out and recorded on a Happ-Genzel spectrum spectrophotometer.

2.2. Synthesis of the complexes

The complexes were prepared following the procedure reported by Ejidike et al. [8]. Anthranilic acid (0.14 g) and acetylsalicylic acid (0.18 g) were weighed separately and dissolved in 10 ml of ethanol respectively. 10 ml each aqueous solution of the metal ions, (M) = Ni^{2+} (0.24 g), Cu^{2+} (0.17 g), Cd^{2+} (0.20 g) and Zn^{2+} (0.14 g) were added to the solution of the ligands. Each of the mixed solutions was refluxed for 3 h, cooled and left to undergo slow evaporation which lasted for 20 days. The obtained precipitates were filtered, washed with equimolar mixture of ethanol and distilled water, dried and kept in sample bottles for further analysis.

2.3. Analgesic activity

The procedure presented by Kundu et al. [9] was adopted for the determination of analgesic activity using acetic acid- induced writhing model in mice. Acetic acid (0.7 %) at a dose of 0.1 ml/ 10 g was administered intraperitoneally to generate pain sensation. The ligands and the synthesized compounds were given to the mice intraperitonally after 15 min. of acetic acid injection. Immediately after 5 min., the mice were noticed for their body contraction which is also known as writhing for about 10 min [8,9].

2.4. Tail immersion test

About two-centimeter tail was measured and inserted into a warm water of temperature 57-60 ℃. The period to react is the period noted for the mice to deflect their tails. The reaction time was observed and reported as a mean of the readings. About 30 sec. of latent time was noted as a complete analgesia and then stopped in order for the animal to be harmless. The latent time was estimated at 0, 20, 40 and 60 min. after administration [8,10].

2.5. Toxicological activity

The toxicity studies were carried out to evaluate the toxic effect or toxicity level of the ligands and their metal complexes on Wister rat cellular systems. The ligands and their metal complex solutions were administered to the rats for seven days.

2.5.1. Animal handling and administration of the test agents

A previous report by Ogunniran et al. [11] was followed in determining the level of toxicity of the synthesized complexes as compared with the parent drug. About 35 Wister rats were weighed and divided into seven groups. The tested rats were obtained from the animal holding Unit of the Department of Biochemistry, University of Ilorin, Nigeria. The experimental animals were controlled following the international guidelines for the care and use of laboratory animals. They were allowed access to normal rat feeds (pelleted) and water ad libitum for two weeks during the experiment. The solutions of the parent ligands and the metal-drug complexes were orally administered to the Wister rats on daily basis for seven (7) days. After the complete administration of the test drugs, the rats were sacrificed following the international guidelines. The grouping of animals and drugs administration were as follows:

Group 1 (control): was administered 2 % DMSO

Group 2: received 20 mg/kg body weight of Acetylsalicylic acid

Group 3: received 20 mg/kg body weight of Anthranilic acid

Group 4: received 20 mg/kg body weight of Ni(II) complex

Group 5: received 20 mg/kg body weight of Cu(II) complex

Group 6: received 20 mg/kg body weight of Cd(II) complex

Group 7: received 20 mg/kg body weight of Zn(II) complex

2.5.2. Serum preparation

The serum was collected from the blood samples by centrifuging the samples for about 5 min. at 1300 RPM. The clear serum supernatant was carefully collected using a Pasteur pipette. The serum samples were stored frozen until required for analysis [11].

2.5.3. Homogenization of the kidney

Immediately after sacrificing the rats, the kidneys were collected, weighed and homogenized until a smooth texture was obtained. Ice-cold 0.25 M sucrose solution (10 ml) was added to the ground smoothen kidney. After centrifugation for about 10 min at 1500 RPM, the samples were allowed to cool. The clear serum supernatant was carefully collected using a Pasteur pipette. The serum samples were stored frozen for analysis.

2.6. Antibacterial activity

The as-synthesized complexes and the parent ligands were screened in-vitro to assess their antibacterial activity against some microbial strains: *E. coli, P. aeruginosa, K. pneumoniae, S. aureus, B. subtilis*, and *S. faecalis* using agar diffusion techniques as previously described with little modifications [8,12]. The test samples were prepared by dissolving 20 mg of each compound in 1 mL of dimethyl sulfoxide. The dispersing solvent was used as a negative control. Acetylsalicylic acid and Anthranilic acid acted as the ligands. The bacterial culture was introduced to the prepared Hinton agar plate using a sterile swab. About a 6 mm diameter disc was impregnated with a constant quantity of 100 µg/mL of the individual test compound. The prepared agar plates were then incubated for 24 h at 37 °C. The antibacterial capabilities of the examined compounds were then evaluated by measuring the zone of inhibition in diameter. The potentials of the complexes were compared to the free ligands [2,8]. The dispersing solvent used as control exhibited no inhibition zone.

3. RESULTS AND DISCUSSION

3.1. Chemistry of the compounds

The physicochemical properties of the free ligands and their derived complexes are presented in Table 1. The new metal complexes have been synthesized using the refluxing method in the ratio of 1:1:1 (Figure 1). The melting point of the ligands was typically found to be different

from those of metal complexes. This disparity in melting points may be adduced to coordination that occurred between the free ligands and the central metal ions [2, 3, 8]. The coloured powder metal complexes obtained were found to be air-stable with yields between 43 % and 75 %. The molar conductance of the complexes was in the range of 11 – 18 $\Omega^{-1}cm^2mol^{-1}$ confirming the complexes' non-electrolyte character, and insoluble in water and other common solvents but were easily soluble in polar coordinating solvents such as DMF and DMSO [2, 3]. The magnetic moment has been determined from magnetic susceptibility measurements. The elemental analysis results revealed that the experimental and calculated values were in good agreement and this consequently favoured the proposed structure [7].

Table 1. Analytical data of the ligands and the mixed complexes

Compound	**Melting Point (°C)**	**Colour**	**Conductivity ($\Omega^{-1}cm^2mol^{-1}$)**	**Elemental analysis (%) Experimental / Calculated)**			
Formula, Mol wt.				**C**	**H**	**N**	**M**
Anthranilic acid **[$C_7H_7NO_2$]**, 137.14	146-148	White	-	-	-	-	-
Acetylsalicylic acid **[$C_9H_8O_4$]**, 180.16	135-137	White	-	-	-	-	-
Ni(II) complex **[$C_{16}H_{13}Cl_2NO_6Ni$]**, 444.88	192-193	Green	14	42.52/ 42.98	3.64/ 3.36	3.41/ 3.13	13.14/ 13.55
Cu(II) complex **[$C_{16}H_{13}Cl_2NO_6Cu$]**, 449.73	230-232	Blue	13	42.22/ 42.46	3.55/ 3.32	3.50/ 3.10	14.03/ 14.04
Cd(II) complex **[$C_{16}H_{13}NO_6Cd$]**, 427.69	213-215	White	17	38.12/ 38.40	3.65/ 3.00	2.98/ 2.80	22.33/ 22.48
Zn(II) complex **[$C_{16}H_{13}NO_6Zn$]**, 380.69	226-228	White	11	42.36/ 42.28	3.28/ 3.30	3.43/ 3.08	14.00/ 14.40

Where C = Carbon, H = Hydrogen, N = Nitrogen, M = Metal.

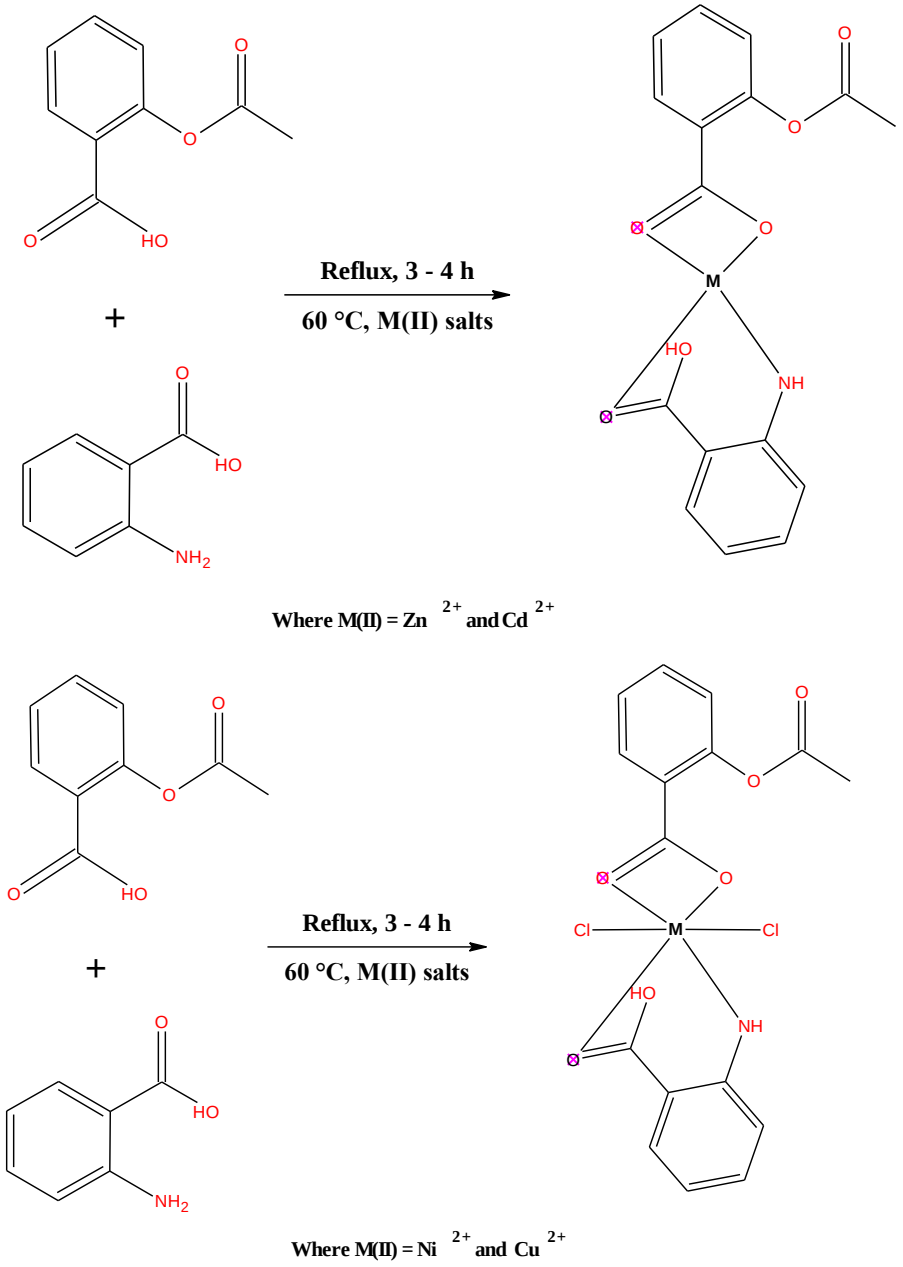

Fig.1. Proposed structures of the metal complexes

3.2. Infrared spectra of the ligands and complexes

The major FTIR data of the ligands and their synthesized metal complexes are presented in Table 2 and their comparative FTIR spectra are presented in Figure 2. The FTIR spectra of acetylsalicylic acid and anthranilic acid contain absorption bands at 1657 cm^{-1} and 1679 cm^{-1} respectively which were assigned to ν(C=O) stretching frequency. These bands shifted to higher frequencies in all the spectra of metal complexes ranging from 1716 to 1773 cm^{-1} for [Cu(II) complex] to [Ni(II) complex], suggesting that coordination occurred through a

carbonyl oxygen atom of both anthranilic acid and acetylsalicylic acid [2,8,13]. The disappearance of the absorption band of ν(N-H) observed at 3202 cm^{-1} (anthranilic acid spectrum) in the spectra of all metal complexes (Table 2), is an indication that coordination of anthranilic acid to metal ions occurred through an amino group of the acid with a band shift to higher frequency within 3239 – 3286 cm^{-1} in complexes spectra [7,8,14].

The absorption bands characterized as ν(O-H) in anthranilic acid and acetylsalicylic acid observed at 3318 cm^{-1} and 3405 cm^{-1} respectively, were shifted to a higher frequency in the metal complexes ranging from 3416 to 3496 cm^{-1} [10-13,15]. This shifting is ascribed to the deprotonation and involvement of the hydroxyl group of the ligands, bringing about bond formation with the metal center [2,14,15]. The bond formation is a result of electron transfer from oxygen to the metal ions unfilled d-orbitals, as a result, new absorption bands at 431 – 459 cm^{-1} and 518 – 533 cm^{-1} are exhibited by ν(M-O) and ν(M-N) respectively were observed and this is an indication of metal-ligand interaction [8,16,17]. The bands detected in the range of 425 – 499 cm^{-1} are due to ν(M–Cl) vibrations supportive of chlorine present in the complex coordination spheres [2,8].

Table 2. FTIR data of the ligands and the metal complexes

Ligands/ Complexes	**ν(O-H)**	**ν(C=O)**	**ν(C-N)**	**ν(N-H)**	**ν(M-O)**	**ν(M-N)**	**ν(M-Cl)**
[Anthranilic acid]	3318	1679	1123	3202	—	—	—
[Acetylsalicylic acid]	3405	1657	—	—	—	—	—
[Ni(II) complex]	3416	1773	1131	3254	456	523	482
[Cu(II) complex]	3463	1716	1126	3286	431	518	473
[Cd(II) complex]	3461	1756	1130	3239	459	533	499
[Zn(II) complex]	3496	1761	1127	3279	447	528	425

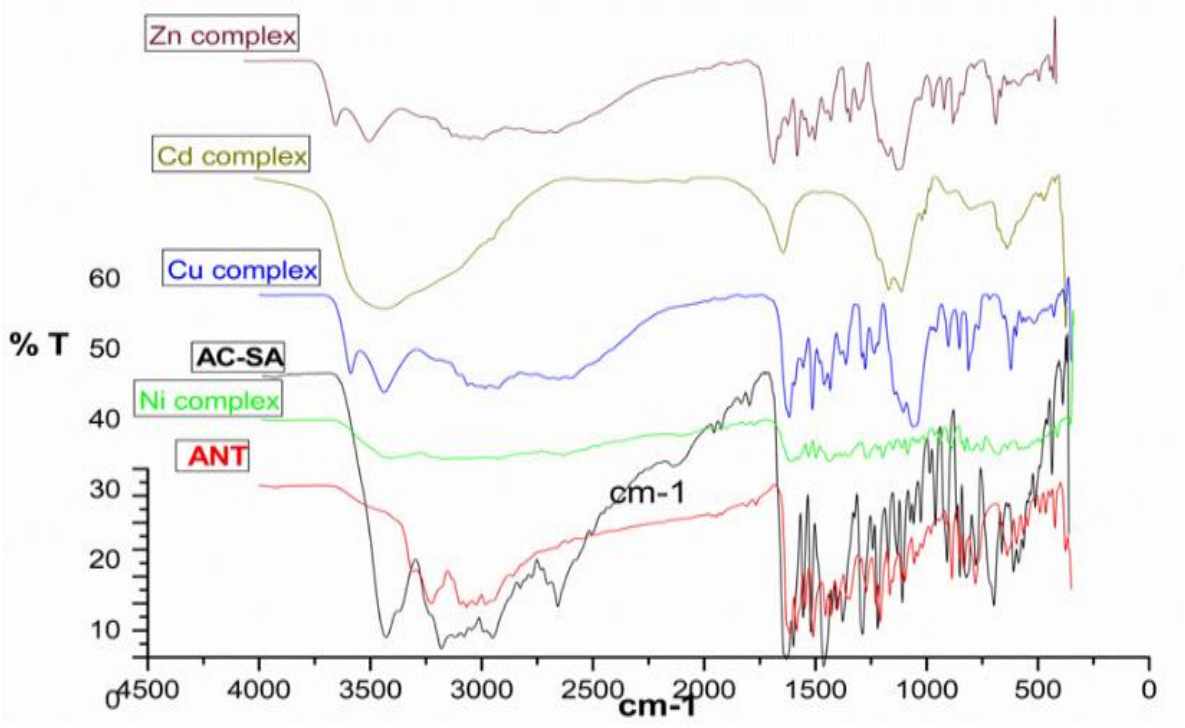

Fig.2. Infrared spectra of the ligands and complexes

3.3. Absorption spectra of the ligands and complexes

The electronic spectra of the free ligands and the complexes in DMSO are presented in Table 3. The electronic spectra of the free ligands (acetylsalicylic acid and anthranilic acid) displayed bands in the UV- region between 252 nm and 357 nm. These bands are assigned to π - π* and intra-ligand transition due to the n-π* transition of the non-bonding electrons present on the oxygen of (C=O) group and nitrogen of the amine groups [2, 8, 13]. The slight shift and disappearance of the bands in the complexes relative to the ligand are due to coordination. Ni(II) complex exhibited three bands at 339 nm, 418 nm and 610 nm assignable to $^3A_{2g}$ (F) → $^3T_{1g}$(P), $^3A_{2g}$(F)→$^3T_{1g}$(F) and $^3A_{2g}$(F) → $^3T_{2g}$(F) respectively [16]. The effective magnetic moment of 3.15 B.M obtained further confirmed the octahedral geometry proposed for Ni(II) complex of acetylsalicylic acid and anthranilic acid with two molecules of chlorine in a six-coordination sphere [18].

The electronic spectra of Cd(II) complex possessed two bands of 264 nm and 318 nm which were assigned to π - π* and intraligand charge transfer transitions as the d-d transition is not expected for Cd(II) complex [8]. This complex possesses a magnetic moment of 0.48 BM indicating that Cd(II) is in the tetrahedral geometry [19,20]. The spectrum of Cu(II) complex

possessed a broad band at 770 nm conforming to $^2E_g \rightarrow {}^2T_{2g}$ transition which is expected for Cu ion in an octahedral geometry environment. This is corroborated by the effective magnetic moment of 2.17 B.M which is within the normal range [8, 20, 21]. The electronic spectra of Zn(II) complex indicated two absorption bands at 285 nm and 351 nm which were attributed to n - π* and charge transfer (CT). The magnetic moment of zinc complex was diamagnetic and agrees with the d^{10} electronic configuration of the metal ion where *d – d* transition is not expected [16, 20].

Table 3. Electronic spectra, magnetic moments of the ligands and the mixed complexes

Compounds	**Wavelength (nm)**	**Tentative assignment**	**Magnetic moments (B.M)**
[Anthranilic acid]	330	π - π*	-
	357	n - π*	
[Acetylsalicylic acid]	236	π - π*	-
	252	n - π*	
[Ni(II) complex]	339	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$	3.15
	418	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$	
	610	$^3A_{2g}(F) \rightarrow {}^3T_{2g(}F)$	
[Cu(II) complex]	315	MLCT	2.17
	770	$^2E_g \rightarrow {}^2T_{2g}$	
[Cd(II) complex]	264	n - π*	0.48
	318	MLCT	
[Zn(II) complex]	285	n - π*	0
	351	MLCT	

3.4. Analgesic activity of the ligands and the metal complexes

The analgesic activity of the test compounds is presented in (Table 4). About 10 mg/kg of acetylsalicylic acid possessed significant analgesic activity while the synthesized complexes activities were carried out at a dosage of 10 mg/kg per body weight as shown in Table 4. The

tail flick method was used to determine the central antinociceptive response and can be differentiated by their ability to respond to nociceptive stimuli that are being produced along the neuronal as the tail insertion mediates a spinal reflex to the stimuli [8,9]. It has been observed from previous research that narcotic analgesics exhibited peripheral and central mechanisms of pain. Non-steroidal agents possessed peripheral pain [8, 9]. Data obtained are documented as mean ± SEM. The significant values are $p<0.05$ when compared with the control.

The acetic acid-induced writhing response is a method used to determine the peripherally acting analgesic and produced pain stimulus by increasing inflammatory response. The stimulus produced free arachidonic acid present in the tissue phospholipids as shown in Table 5 [10]. The metal complexes of N(II), Cu(II), Cd(II), and Zn(II) exhibited percentage writhing inhibition of 38.64, 43.68, 55.00, and 46.93 %, respectively. The data revealed good significant analgesic activity comparable to acetylsalicylic acid (standard) at an equimolar dosage of 10 mg/kg per body weight [8,10].

The analgesic activity of the test samples can be ordered as follows: Standard (Acetylsalicylic acid) > [Cd(II) complex] > [Zn(II) complex] > [Cu(II) complex]> [Ni(II) complex].

Table 4. Immersion test of the ligand and the metal complexes

Groups	**Dosage (mg/kg)**	**Average latent period in seconds during administration of the compounds**				**Increase in latent period (%)**		
		0	**20**	**40**	**60**	**20 (mins)**	**40 (mins)**	**60 (mins)**
[Standard (Acetylsalicylic acid)]	10	1.96± 0.26	1.99± 0.15	2.04± 0.38	2.26± 0.23	53.26 -	58.10 -	64.38 -
[Control]	10	0.73± 0.11	0.91± 0.18	1.06± 0.20	1.11± 0.04	-	-	-
[Ni(II) complex]	10	1.78± 0.19	1.83± 0.04	1.86± 0.12	1.88± 0.35	18.35	24.16	25.30
[Cu(II) complex]	10	1.43± 0.30	1.65± 0.16	1.73± 0.18	1.96± 0.24	25.51	28.47	33.81
[Cd(II) complex]	10	1.36± 0.15	1.40± 0.19	1.44± 0.13	1.71± 0.13	10.84	12.63	19.25
[Zn(II) complex]	10	1.50± 0.18	1.50± 0.18	1.68± 0.11	1.30± 0.63	36.20	43.86	48.14

Data obtained are documented as mean ± SEM. The significant values are $P<0.05$ when compared with the control.

Table 5. Activity of the test compounds on acetic acid induced writhing test in mice

Groups	**Dosage (mg/kg)**	**Writhing Frequency (Mean ± SEM)**	**Writhing Inhibition (%)**
[Standard (Acetylsalicylic acid)]	10	12.39±0.12	60.98
[Control]	-	58.03±0.43	-
[Ni(II) complex]	10	24.38±0.71	38.64
[Cu(II) complex]	10	27.10±0.30	43.68
[Cd(II) complex]	10	33.47±0.56	55.00
[Zn(II) complex]	10	20.62±0.31	46.93

Values are expressed as mean ± standard deviation (mean ± SEM) of three replicates (n=3).

3.5. Toxicological activity of the ligands and the metal complexes

The toxicity activities of the free ligands (anthranilic acid and acetylsalicylic acid) and their complexes are shown in Table 6, which are also presented graphically in Figures 3 and 4. The oral administration of the compounds for ALP activities in the homogenized serum and

kidney is compared with the control. According to the data obtained, it was observed that the homogenate kidney possessed very high activities when compared to the control. This suggests an increase in the enzyme activity may not be able to destroy the plasma membrane of the kidney [11].

Administrations of the test compounds also enhance the activity more than the level it can control in the kidney organ [8,22,23]. It was observed that the ALP activities of serum in the administration of the complexes to the rats were significantly different when compared to the control group after the study period at ($P< 0.05$).

This may be a result of tiredness of the organs by the administered agents or compounds which may have caused enzyme molecule waste, and this is significantly observed in the serum. This is in line with earlier reports that the administration of coordination compounds improves membrane activity, suggesting hepatic impairment of the organ function in rats [8,11,22]. The ability of the metal-drug complexes to cross a cell membrane is usually enhanced by coordination, thus, inducing oxidative stress within the cells that stages an important role in injuring biochemical polymers such as RNA, DNA, proteins, and carbohydrates [8,22,23].

The toxicological effect of the test compounds in serum homogenate are in the order: [Zn(II) complex] > [Cu(II) complex] > [Cd(II) complex] > [Ni(II) complex] > [Anthranilic acid] > [Acetylsalicylic acid] > Control.

The toxicological effect of the test compounds in kidney homogenate follows the order: [Cd(II) complex] > [Cu(II) complex] > [Ni(II) complex] > [Zn(II) complex] > [Acetylsalicylic acid] > [Anthranilic acid] > Control.

Table 6. Toxicity screening of the ligands and their mixed complexes against serum and kidney homogenates

Ligands/Complexes	**Enzyme activity (nM/min/mg protein)**	
	Serum homogenates	**Kidney homogenates**
[Control]	17	9
[Anthranilic acid]	35	20
[Acetylsalicylic acid]	30	45
[Ni(II) complex]	58	61
[Cu(II) complex]	75	66
[Cd(II) complex]	65	76
[Zn(II) complex]	88	57

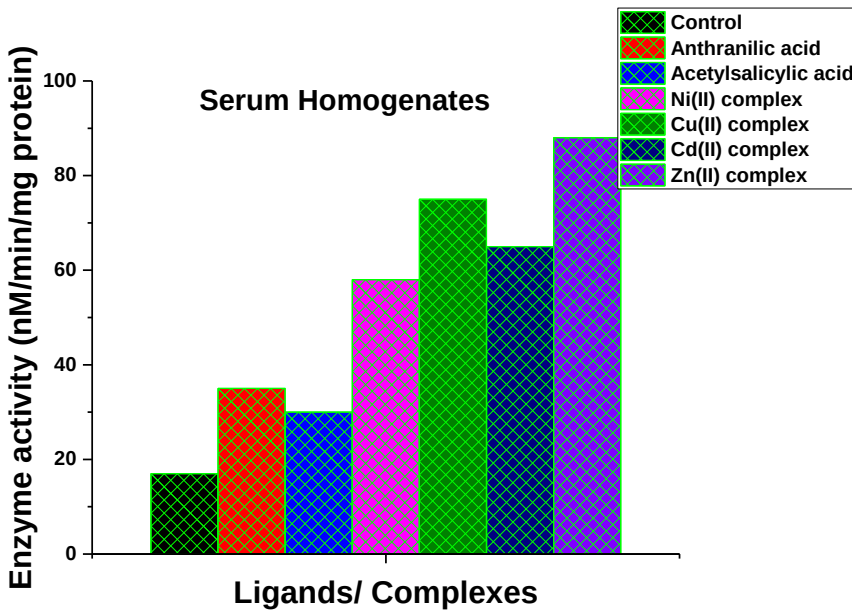

Fig.3. Toxicity screening of the ligands and the mixed complexes against serum homogenate

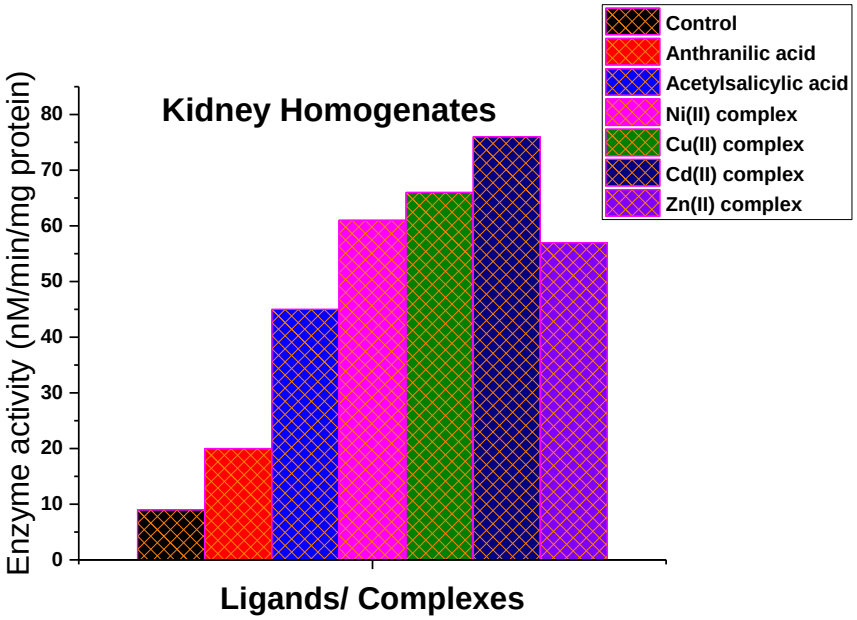

Fig.4. Toxicity screening of the ligands and the mixed complexes against kidney homogenates

3.6. Antibacterial activity of the ligands and the metal complexes

The antibacterial activities of the free ligands and their metal complexes have been carried out against some selected organisms: *E. coli, P. aeruginosa, K. pneumoniae, S. aureus, B. subtilis,* and *S. faecalis* as presented in Table 7 and Figure 5. The activities were determined by the zone of inhibition observed around the well on the agar plate. The activities of the complexes increased when compared with their ligands. This indicates that the antibacterial efficacies of metal complexes are more than their free ligands in agreement with previous studies [2,8,11-15,21-24]. [Ni(II) complex] showed the highest activity at 43.76 mm against *S. aureus* while [Cd(II) complex] possessed the lowest activity of 10.27 mm and 11.63 mm against *B. subtilis* and *E. coli*.

[Cu(II) complex], [Ni(II) complex], [Zn(II) complex], and [Cd(II) complex] exhibited better antibacterial activities with the zone of inhibitions: 35.21 and 33.39 mm; 32.66 and 38.30 mm; 39.57 and 26.15 mm; and 11.63 and 39.05 mm respectively against *E. coli* and *S. faecalis*; while [Zn(II) complex] showed good activity of 40.48 and 40.35 mm against *P. aeruginosa* and *B. subtilis*; [Anthranilic]─ 6 and 7 mm against *E. coli* and *S. faecalis*; and [Acetylsalicylic acid]─ 5 and 3 mm against *B. subtilis* and *S. faecalis*. A decrease in the activities of some complexes may be due to the substitution effect during ligation [6-8]. It has been reported that

the coordination process in complexes enhances its effectiveness when compared to the parent ligand. This can be attributed due to the partial sharing of the metal positive charge (+ve) with the donor group [8,10-15].

The zones of inhibition give information about the active role of the central metal ions present in the complexes. The increased activity of the synthesized complexes can be accounted for further based on Overtone's concept and Chelation theory of permeability [2,14-17]. The permeability of cells assists in the passage of lipid-soluble material as a result of liposolubility as one of the factors of antimicrobial activities. During complexation, the polarity of the metal decreased as a result of the overlap of the orbital of the ligand and sharing of the positive charge of the metal ion with donating atoms [21-25].

Table 7. Antibacterial activity (zone of inhibition, mm) of the ligands and their mixed complexes

Ligand /Complexes	*E. coli*	*P. aeruginosa*	*K. pneumoniae*	*S. aureus*	*B. subtilis*	*S. faecalis*
[Anthranilic]	6	-	4	-	2	7
[Acetylsalicylic acid]	2	-	-	-	5	3
[Ni(II) complex]	32.66	37.09	26.44	43.76	20.12	38.30
[Cu(II) complex]	35.21	21.37	19.00	36.65	35.00	33.39
[Cd(II) complex]	11.63	27.91	34.59	19.45	10.27	39.05
[Zn(II) complex]	39.57	40.48	22.75	13.61	40.35	26.15

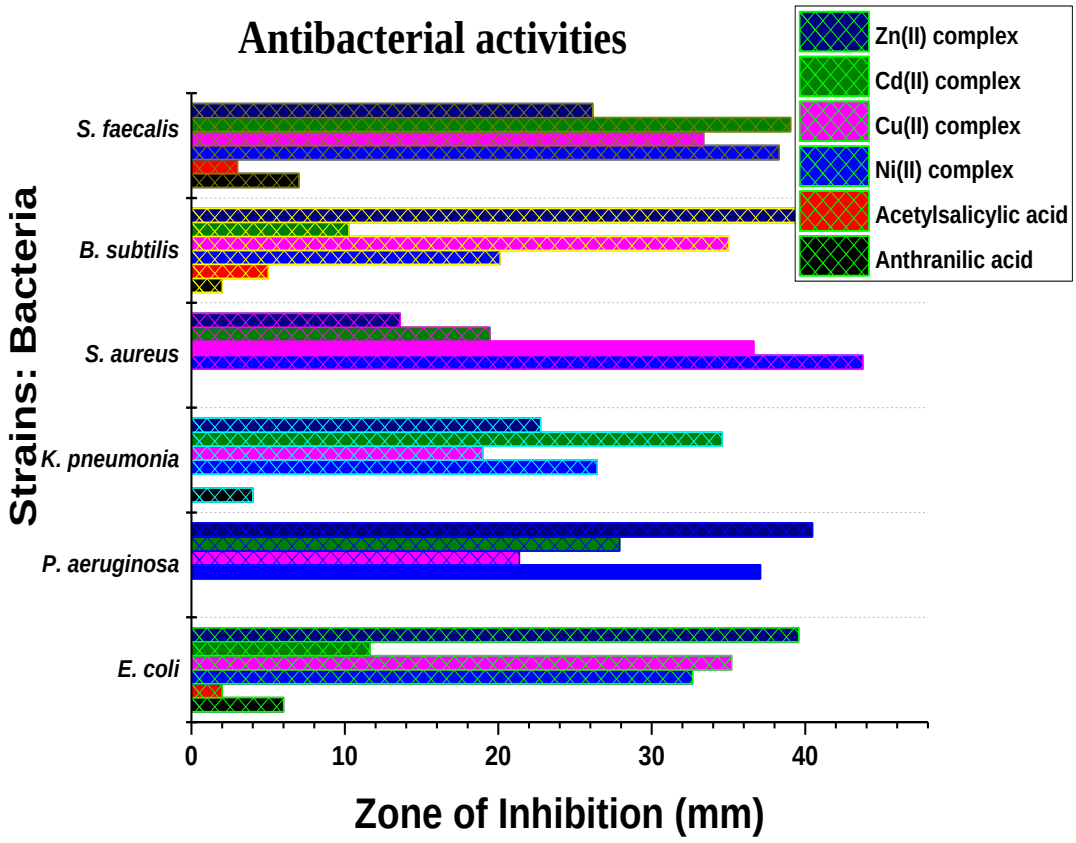

Fig.5. Antibacterial activity of the ligands and the metal complexes

4. CONCLUSION

Mixed complexes of acetylsalicylic acid–anthranilic acid have been prepared in a mole ratio of 1:1:1 and characterized through physicochemical parameter and spectroscopic studies. The synthesis resulted in good analytical yields. The ligands were found to possess good chelating properties which assured their coordination with the central metal ions through the oxygen of the carbonyl group and nitrogen of the amine group in anthranilic acid and oxygen of the hydroxyl and carbonyl group in acetylsalicylic acid. The FTIR, electronic spectroscopic, and magnetic susceptibility measurement data suggest octahedral around Ni(II) and Cu(II); and tetrahedral arrangement around Cd(II) and Zn(II) ions. Coordination of metals into the chelating ligands is a major metalloenzyme cofactor that helps to increase the inhibitory effect against organisms. The result of the analysis indicated that acetylsalicylic acid possessed a good significant analgesic activity. The toxicology studies confirmed that the complexes were toxic at the level of administered dosage. Evaluation of the ligands and their complexes

showed that the complexes exhibited good antibacterial activities when compared to the parent ligands. The data obtained were very significant and gave a promising lead towards further development of the complexes as alternatives towards combating the resistance of bacteria in the health sector.

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