

## BIOLOGICAL ACTIVITY STUDIES OF GUANIDINE-PHOSPHONATE COMPLEXES OF IRON, COBALT AND ZINC

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### ABSTRACT

This research work focused on biological activity studies of guanidine-phosphonate complexes of iron, cobalt and zinc for growth inhibition against *Staphylococcus aureus*. *Staphylococcus aureus* infected blood was treated with the guanidine-phosphonate complexes and their activities were examined through haematological and enzymatic analyses. Sterile water was used as negative control. The analyses results on packed cell volume, haemoglobin, white blood cell, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineaminotransferase were interpreted statistically. Guanidinophosphonatebenzothiazole compounds exhibited strongest activity followed by guanidinobenzothiazole compounds. The effectiveness trend was followed by guanidinophosphonatebenzimidazole compounds which performed better than the guanidinobenzimidazole compounds. The compounds therefore indicated that guanidinophosphonatebenzothiazole compounds gave highest antimicrobial property. This was followed by guanidinobenzothiazole compounds which were found to be higher than guanidinephosphonatebenzimidazole compounds while the least antimicrobial activity was recorded for guanidinobenzimidazole compounds.

**Keywords:** Benzimidazole, Benzothiazole, Complexes, Biological activity

### INTRODUCTION

Guanidine compounds are important materials with antimicrobial activities [1]. They are vital in diverse areas of application to life [2]. Derivatives of guanidine are early or awaited in cycle production and development of microorganism potentially [3]. Antimicrobial activities of guanidine metal complexes have made them important even in pharmaceutical and biochemical areas [4] which have increased interest in their research, hence desired for continuous investigation in pharmaceutical, academic research and industrial development. Phosphonate

guanidine compounds synthesis and their antimicrobial applications have been reported [5].

Metal complexes antimicrobial activities of guanidines, phosphonates need much to be investigated. It is therefore desired of this research works to examine antimicrobial activity of guanidinated metal complexes.

### MATERIALS AND METHODS

Blood samples of rats were used.

### ***Effect of the guanidine derivatives***

Activities of the guanidinobenzimidazole, guanidinophosphonatebenzimidazole, guanidinebenzothiazole and guanidino phosphonatebenzothiazole derivatives were assessed through blood samples of rats. The blood samples were first examined for microorganism effect on packed cell volume, hemoglobin, white blood cell, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineamino transferase according to method in literature [6]. Antimicrobial activity of the derivatives was tested and effectiveness deduced through statistical analysis.

### ***Blood Analyses***

The blood analysis was carried out to monitor treatment effect of the iron, cobalt and zinc complexes for growth inhibition against *Staphylococcus aureus* through observation of haematological data which are packed cell volume, haemoglobin, white blood cell, platelet, neutrophils and lymphocyte. Activity of the complexes was also tested for improvement investigated on the blood through enzymatic data which are aspartateaminotransferase and alanineamino-transferase according to literature method [7].

guanidinophosphonatebenzothiazole and coordinated metals compared with sterile water used as negative control were determined for effect on packed cell volume, haemoglobin, white blood cell, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineamino transferase. Packed cell volume of  $25.40 \pm 2.34\%$  decrease from  $42.60 \pm 0.81\%$  due to microorganism effect indicated improvement to  $31.40 \pm 0.68\%$  after application of guanidinobenzimidazole. Iron-guanidinobenzimidazole complex displayed effectiveness as  $24.20 \pm 0.97\%$  increase to  $33.50 \pm 1.38\%$  in expectation of  $43.40 \pm 0.93\%$  packed cell volume. Cobalt-guanidinobenzimidazole complexes gave  $34.10 \pm 1.21\%$  improvement closer to  $43.00 \pm 0.71\%$  compared to  $24.80 \pm 2.54\%$  packed cell volume. Zinc guanidinobenzimidazole complex showed effectiveness of  $35.40 \pm 2.23\%$  higher than  $25.30 \pm 0.49\%$  in expectation of  $43.00 \pm 1.41\%$ . The sterile water did not produce any antimicrobial change in the  $42.60 \pm 1.25\%$  packed cell volume compared with the derivatives which proved that the ligand and the complexes have antimicrobial potential. (Table 1). Packed cell volume has been similarly reported on malarial investigation in literature [8].

## **RESULTS AND DISCUSSION**

Antimicrobial activity of the guanidinobenzimidazole, guanidinobenzothiazole,

**Table 1: Antimicrobial activity of guanidinobenzimidazole and complexes**

S/N	Sample	PCV(%)	Hb (g/dl)	WBC (X 10 <sup>9</sup> /L)	Platelet (X 10 <sup>9</sup> /L)	Neu(%)	Lym(%)	AST (ug/L)	ALT (ug/L)
Grp 1	Ma	42.60±0.81 <sup>ef</sup>	17.34±1.34 <sup>h</sup>	12.02±0.73 <sup>b</sup>	130.00±3.42 <sup>a</sup>	29.60±3.23 <sup>k</sup>	31.30±1.57 <sup>abc</sup>	12.60±1.29 <sup>hi</sup>	22.00±1.52 <sup>ab</sup>
	Me	25.40±2.34 <sup>ab</sup>	7.46±0.43 <sup>b</sup>	28.54±0.79 <sup>de</sup>	81.80±4.02 <sup>ab</sup>	47.60±1.91 <sup>ij</sup>	46.60±2.66 <sup>fg</sup>	36.00±6.69 <sup>ef</sup>	41.80±5.98 <sup>d</sup>
	Gbm	31.40±0.68 <sup>d</sup>	10.36±1.01 <sup>def</sup>	17.86±0.97 <sup>c</sup>	92.00±2.28 <sup>bcd</sup>	39.80±2.75 <sup>def</sup>	40.50±1.64 <sup>de</sup>	32.40±2.20 <sup>i</sup>	31.90±2.11 <sup>abc</sup>
Grp 2	Ma	43.40±0.93 <sup>fg</sup>	17.86±1.01 <sup>i</sup>	12.18±2.35 <sup>ab</sup>	130.80±2.35 <sup>cd</sup>	28.70±2.16 <sup>abc</sup>	30.80±1.43 <sup>abcd</sup>	13.40±1.86 <sup>j</sup>	22.20±1.53 <sup>a</sup>
	Me	24.20±0.97 <sup>bc</sup>	7.58±0.51 <sup>bc</sup>	29.28±0.95 <sup>d</sup>	82.40±2.54 <sup>efg</sup>	49.00±2.88 <sup>h</sup>	48.20±2.27 <sup>ef</sup>	35.80±7.26 <sup>ab</sup>	42.20±6.09 <sup>de</sup>
	FeGbm	33.50±1.38 <sup>c</sup>	13.66±0.88 <sup>cd</sup>	17.14±1.95 <sup>c</sup>	99.30±3.08 <sup>hi</sup>	37.56±4.03 <sup>efg</sup>	38.40±1.84 <sup>cde</sup>	28.10±3.17 <sup>bc</sup>	27.40±1.89 <sup>bc</sup>
Grp 3	Ma	43.00±0.71 <sup>fg</sup>	17.60±1.98 <sup>hi</sup>	12.66±2.55 <sup>ab</sup>	129.80±2.20 <sup>de</sup>	29.04±2.81 <sup>ab</sup>	31.10±1.39 <sup>bcd</sup>	13.20±1.99 <sup>d</sup>	21.50±0.71 <sup>c</sup>
	Me	24.80±2.54 <sup>b</sup>	7.10±0.67 <sup>de</sup>	27.10±1.21 <sup>def</sup>	85.00±3.32 <sup>def</sup>	47.60±0.93 <sup>d</sup>	48.30±3.93 <sup>gh</sup>	35.60±7.62 <sup>a</sup>	41.70±5.98 <sup>f</sup>
	CoGbm	34.10±1.21 <sup>c</sup>	13.44±1.11 <sup>ef</sup>	17.12±0.73 <sup>cd</sup>	99.56±3.25 <sup>a</sup>	37.60±1.32 <sup>ef</sup>	38.40±3.13 <sup>e</sup>	28.40±3.32 <sup>k</sup>	27.60±1.86 <sup>cd</sup>
Grp 4	Ma	43.00±1.41 <sup>fg</sup>	17.98±0.83 <sup>i</sup>	11.42±1.32 <sup>a</sup>	131.60±0.87 <sup>abc</sup>	28.80±3.50 <sup>bc</sup>	30.50±0.80 <sup>a</sup>	12.70±1.17 <sup>jk</sup>	22.00±0.93 <sup>h</sup>
	Me	25.30±0.49 <sup>b</sup>	7.14±0.51 <sup>bcd</sup>	27.28±1.02 <sup>ghi</sup>	74.20±1.66 <sup>i</sup>	49.20±3.90 <sup>g</sup>	47.50±2.41 <sup>fg</sup>	36.30±6.23 <sup>abc</sup>	41.50±5.34 <sup>bcd</sup>
	ZnGbm	35.40±2.23 <sup>c</sup>	13.88±0.81 <sup>fghi</sup>	15.88±1.45 <sup>abc</sup>	99.60±4.67 <sup>gh</sup>	36.25±2.46 <sup>cdef</sup>	37.20±1.24 <sup>ij</sup>	26.90±2.18 <sup>ghi</sup>	27.40±1.75 <sup>g</sup>

NOTE: Same superscript results in a column means no significant different ( $p>0.05$ ), the same superscript in different columns means cross link relationship. PCV: packed cell volume, Hb: haemoglobin, WBC: white blood cells, Neu: neutrophils, Lym: lymphocyte, AST: aspartateaminotransferase, ALT: alanineaminotransferase, Grp: group, Ma: microorganism absent, Me: microorganism effect, Gbm: guanidinobenzimidazole, FeGbm: iron guanidinobenzimidazole complex, CoGbm-: cobal guanidinobenzimidazole complex, ZnGbm-zinc guanidinobenzimidazole complex.

Haemoglobin test showed  $10.36 \pm 1.01$  g/dl improvement by guanidinobenzimidazole antimicrobial activity over  $7.46 \pm 0.43$  g/dl attributed to microorganism effect whereas the haemoglobin value in absence of microorganism was  $17.34 \pm 1.34$  g/dl.  $13.66 \pm 0.88$  g/dl,  $13.44 \pm 1.11$  g/dl and  $13.88 \pm 0.81$  g/dl due to antimicrobial effects of iron, cobalt and zinc guanidinobenzimidazole complexes demonstrated good activity in comparison with the sterile water which has no effect. Haemoglobin change has been similarly reported [9]. Higher  $28.54 \pm 0.79 \times 10^9/L$  than  $12.02 \pm 0.73 \times 10^9/L$  for white blood cells due to microorganism effect that gave  $17.86 \pm 0.97 \times 10^9/L$  was attributed to activity of guanidinobenzimidazole while  $29.28 \pm 0.95 \times 10^9/L$ ,  $27.10 \pm 1.21 \times 10^9/L$  and  $27.28 \pm 1.02 \times 10^9/L$  due to effect of microorganism gave positive  $17.14 \pm 1.95 \times 10^9/L$ ,  $17.12 \pm 0.73 \times 10^9/L$  and  $14.88 \pm 1.45 \times 10^9/L$  for iron, cobalt and zinc guanidinobenzimidazole complexes close to  $12.18 \pm 2.35 \times 10^9/L$ ,  $12.66 \pm 2.55 \times 10^9/L$  and  $11.42 \pm 1.32 \times 10^9/L$  white blood cell and therefore demonstrated good effect compared with the sterile water that demonstrated no effect. Platelet and neutrophil tests which produced  $130.00 \pm 3.42 \times 10^9/L$  and  $29.60 \pm 3.23\%$  respectively dropped to  $81.80 \pm 4.02 \times 10^9/L$  for platelet and rose to  $47.60 \pm 1.91\%$  for neutrophils attributed to microorganism effect. The guanidinobenzimidazole application against microorganism showed activity because  $92.00 \pm 2.28 \times 10^9/L$  and  $39.80 \pm 2.75\%$  were recorded. Guanidinobenzimidazole complexes of the iron, cobalt and zinc yielded results between  $99.30 \pm 3.08 \times 10^9/L$  and  $99.60 \pm 4.67 \times 10^9/L$  for Platelet counts while the neutrophil occurred from

cobalt to zinc between  $36.25 \pm 2.46\%$  and  $37.60 \pm 1.32\%$ . Both the ligand and complexes demonstrated antimicrobial activity compared with the sterile water that did not show antimicrobial effect. Lymphocyte which changed from  $31.30 \pm 1.57\%$  to  $46.60 \pm 2.66\%$  due to microorganism effect turn to  $40.50 \pm 1.64\%$  when guanidinobenzimidazole was applied. Iron, cobalt and zinc complexes of the guanidinobenzimidazole application indicated  $38.40 \pm 1.84\%$ ,  $38.40 \pm 3.13\%$  and  $37.20 \pm 1.24\%$  from  $30.80 \pm 1.43\%$ ,  $31.10 \pm 1.39\%$  and  $30.50 \pm 0.80\%$  earlier raised to  $48.20 \pm 2.88\%$ ,  $48.30 \pm 3.93\%$  and  $47.50 \pm 2.41\%$  for microorganism effect. Aspartateaminotransferase and alanineaminotransferase which showed  $12.60 \pm 1.29$   $\mu\text{g/L}$  and  $22.00 \pm 1.52$   $\mu\text{g/L}$  in absence of microorganism rose to  $36.00 \pm 6.69$   $\mu\text{g/L}$  and  $41.80 \pm 5.98$   $\mu\text{g/L}$  due to microorganism effect. Guanidinobenzimidazole demonstrated antimicrobial activity with  $32.40 \pm 2.20$   $\mu\text{g/L}$  and  $31.90 \pm 2.11$   $\mu\text{g/L}$  while its Fe, Co and Zn complexes gave  $28.10 \pm 3.17$   $\mu\text{g/L}$ ,  $28.40 \pm 3.32$   $\mu\text{g/L}$  and  $26.90 \pm 2.18$   $\mu\text{g/L}$  for aspartateaminotransferase. Antimicrobial activity of the Fe, Co and Zn guanidinobenzimidazole complexes was also positive on alanineaminotransferase with  $27.40 \pm 1.89$   $\mu\text{g/L}$ ,  $27.60 \pm 1.86$   $\mu\text{g/L}$  and  $27.40 \pm 1.75$   $\mu\text{g/L}$  respectively. It was deduced from results of the sterile water that antimicrobial activity was produced by the ligand and complexes. Packed cell volume of  $42.10 \pm 0.64\%$  which decreased to  $25.20 \pm 2.14\%$  on account of antimicrobial effect gave  $31.70 \pm 1.62\%$  attributed to guanidinophosphonatebenzimidazole activity. The

guanidinophosphonatebenzimidazole demonstrated a little higher antimicrobial effect than the guanidinobenzimidazole which were also observed in the iron, cobalt and zinc complexes of the guanidinophosphonatebenzimidazole with range from  $33.80 \pm 2.12$  -  $35.90 \pm 1.42\%$ ,  $13.72 \pm 0.84$  -  $13.90 \pm 0.59$  g/dl,  $14.89 \pm 0.88$  -  $17.07 \pm 1.54 \times 10^9/L$ ,  $99.45 \pm 2.40$  -  $99.98 \pm 5.64 \times 10^9/L$ ,  $35.55 \pm 3.76$  -  $37.16 \pm 5.14\%$ ,  $36.80 \pm 3.57$  -  $38.21 \pm 3.25\%$ ,  $26.18 \pm 3.93$  -  $27.84 \pm 5.16 \mu\text{g/L}$  and  $26.80 \pm 3.03$  -  $27.10 \pm 1.50 \mu\text{g/L}$  for the pcv, hb, wbc, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineaminotransferase respectively (Table 2).

Guanidinobenzothiazole compounds were observed to be more antimicrobial active than guanidinophosphonatebenzimidazole compounds as the packed cell volume, haemoglobin, white blood cell, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineaminotransferase recorded  $32.62 \pm 1.02\%$ ,  $11.86 \pm 2.18$  g/dl,  $17.54 \pm 0.73 \times 10^9/L$ ,  $94.13 \pm 4.64 \times 10^9/L$ ,  $42.84 \pm 2.56\%$ ,  $40.50 \pm 1.74\%$ ,  $32.40 \pm 1.74 \mu\text{g/L}$  and  $31.73 \pm 1.93 \mu\text{g/L}$  improvement over  $24.25 \pm 0.81\%$ ,  $7.44 \pm 0.47$  g/dl,  $28.46 \pm 2.47 \times 10^9/L$ ,  $81.81 \pm 3.27 \times 10^9/L$ ,  $46.88 \pm 2.34\%$ ,  $47.10 \pm 1.99\%$ ,  $36.30 \pm 1.17 \mu\text{g/L}$  and  $42.40 \pm 5.14 \mu\text{g/L}$  earlier recorded due to microorganism effect (Table 3).

Guanidinophosphonatebenzothiazole and its iron, cobalt and zinc complexes reflected highest effectiveness in the benzimidazole and benzothiazole antimicrobial tests. The guanidinophosphonatebenzothiazole gave effective values to be  $32.88 \pm 0.74\%$ ,  $12.67 \pm 0.47$  g/dl,  $16.22 \pm 2.05 \times 10^9/L$ ,  $95.44 \pm 3.18 \times 10^9/L$ ,

$40.14 \pm 2.11\%$ ,  $39.30 \pm 2.19\%$ ,  $30.20 \pm 0.63 \mu\text{g/L}$  and  $30.33 \pm 1.47 \mu\text{g/L}$  for the pcv, hb, wbc, platelet, neutrophils, lymphocyte, aspartateaminotransferase and alanineaminotransferase while values due to antimicrobial activity of complexes ranged from  $34.80 \pm 1.60$  -  $37.20 \pm 2.79\%$ ,  $14.91 \pm 0.76$  -  $15.55 \pm 1.10$ g/dl,  $14.97 \pm 1.23$  -  $15.42 \pm 3.43 \times 10^9/L$ ,  $103.55 \pm 3.63$  -  $105.15 \pm 3.74 \times 10^9/L$ ,  $34.32 \pm 2.75$  -  $36.11 \pm 2.73\%$ ,  $35.88 \pm 1.91$  -  $37.13 \pm 0.97\%$ ,  $25.17 \pm 5.38$  -  $26.32 \pm 1.93 \mu\text{g/L}$  and  $25.90 \pm 1.55$  -  $26.40 \pm 1.23 \mu\text{g/L}$  (Table 4). The readings showed differences in antimicrobial activities of guanidinobenzimidazole, guanidinophosphonatebenzimidazole, guanidinobenzothiazole, guanidinophosphonatebenzothiazole and the complexes. The variation in values therefore showed differences in properties of the derivatives. The sterile water as a control did not show any antimicrobial effect. .

The high property noticed for the coordinated might be related to metal ions action [10]. Performance of the complexes over the ligands could also be due to chelated polar and nonpolar effects [10]. Ion bonding enhances biochemical ability of organic types while lipophilicity is modified by coordination associated to its ability to moderate molecules movement. The metal complexes therefore have more tendencies to indicate higher antimicrobial activities than the uncoordinated ligand and free metal ion which agrees with literature [11].

**Table 2: Antimicrobial activity of guanidinophosphonatebenzimidazole and complexes**

S/N	S	PCV (%)	Hb (g/dl)	WBC (X 10 <sup>9</sup> /L)	Platelet (X 10 <sup>9</sup> /L)	Neu (%)	Lym (%)	AST (ug/L)	ALT (ug/L)
Grp5	Ma	42.10±0.64 <sup>i</sup>	17.14±1.24 <sup>hij</sup>	12.22±0.75 <sup>c</sup>	130.10±2.04 <sup>e</sup>	28.50±3.61 <sup>a</sup>	31.10±0.97 <sup>ab</sup>	12.50±4.19 <sup>abc</sup>	22.20±1.03 <sup>i</sup>
	Me	25.20±2.14 <sup>bc</sup>	7.42±1.34 <sup>bc</sup>	28.44±3.85 <sup>b</sup>	81.81±2.95 <sup>n</sup>	47.68±8.69 <sup>ab</sup>	46.20±3.16 <sup>gh</sup>	36.10±4.06 <sup>fgh</sup>	41.70±2.62 <sup>fg</sup>
	Gpbm	31.70±1.62 <sup>d</sup>	10.65±1.12 <sup>def</sup>	17.88±0.22 <sup>a</sup>	92.03±3.08 <sup>cde</sup>	38.63±4.41 <sup>lm</sup>	40.20±1.7efg	32.47±4.24 <sup>ab</sup>	31.93±2.79 <sup>efg</sup>
Grp6	Mai	42.20±0.18 <sup>e</sup>	16.22±1.03 <sup>ghi</sup>	12.26±0.66 <sup>f</sup>	128.00±1.83 <sup>de</sup>	29.10±2.35 <sup>d</sup>	30.10±3.47 <sup>op</sup>	12.20±3.03 <sup>bc</sup>	21.00±1.36 <sup>ab</sup>
	Me	23.90±1.66 <sup>hi</sup>	7.30±0.72 <sup>b</sup>	24.68±4.37 <sup>d</sup>	82.50±5.32 <sup>ab</sup>	48.75±8.29 <sup>t</sup>	47.70±3.89 <sup>fg</sup>	36.80±2.76 <sup>efg</sup>	42.20±0.89 <sup>gh</sup>
	FeGpbm	33.80±2.12 <sup>f</sup>	13.72±0.84 <sup>de</sup>	17.07±1.54 <sup>i</sup>	99.45±2.40 <sup>c</sup>	37.16±5.14 <sup>j</sup>	38.21±3.25 <sup>yz</sup>	27.84±4.16 <sup>fg</sup>	27.10±1.50 <sup>f</sup>
Grp7	Ma	42.60±1.31 <sup>h</sup>	17.55±1.18 <sup>ij</sup>	12.62±2.13 <sup>k</sup>	129.30±1.63 <sup>def</sup>	29.00±3.07 <sup>l</sup>	31.40±2.05 <sup>xy</sup>	13.10±4.09 <sup>ef</sup>	21.40±1.50 <sup>bc</sup>
	Me	23.50±2.44 <sup>j</sup>	7.30±0.72 <sup>c</sup>	27.40±4.22 <sup>bc</sup>	85.02±5.25 <sup>s</sup>	47.46±7.04 <sup>w</sup>	48.33±3.66 <sup>z</sup>	35.50±4.49 <sup>gh</sup>	41.50±1.36 <sup>g</sup>
	CoGpbm	34.40±1.22 <sup>cd</sup>	13.84±1.03 <sup>ef</sup>	17.02±1.31 <sup>de</sup>	99.59±1.28 <sup>cd</sup>	37.46±3.02 <sup>qr</sup>	38.10±3.01 <sup>no</sup>	27.60±5.13 <sup>de</sup>	26.97±2.38 <sup>def</sup>
Grp8	Ma	42.10±1.48 <sup>k</sup>	17.78±1.72 <sup>hi</sup>	11.22±1.08 <sup>j</sup>	131.10±4.28 <sup>e</sup>	28.40±3.80 <sup>jk</sup>	30.52±2.56 <sup>n</sup>	12.50±4.25 <sup>cd</sup>	22.10±1.97 <sup>de</sup>
	Me	24.30±1.43 <sup>gh</sup>	7.11±0.94 <sup>cd</sup>	27.26±6.63 <sup>jk</sup>	74.60±3.41 <sup>b</sup>	49.10±5.54 <sup>ef</sup>	47.30±3.12 <sup>u</sup>	36.10±4.42 <sup>hi</sup>	41.30±0.40 <sup>m</sup>
	ZnGpbm	35.90±1.24 <sup>de</sup>	13.90±0.59 <sup>fgh</sup>	14.89±0.88 <sup>ab</sup>	99.98±5.64 <sup>mn</sup>	35.55±3.76 <sup>pq</sup>	36.80±3.5v	26.18±3.93 <sup>kl</sup>	26.80±3.03 <sup>q</sup>

NOTE: Gpbm: guanidinophosphonatebenzimidazole, FeGpbm: iron guanidinophosphonatebenzimidazole complex, CoGpbm-cobalt guanidinophosphonatebenzimidazole complex, ZnGpbm: zinc guanidinophosphonatebenzimidazole complex

**Table 3: Antimicrobial activity of guanidinobenzothiazole and complexes**

S/N	S	PCV (%)	Hb (g/dl)	WBC (X 10 <sup>9</sup> /L)	Platelet (X 10 <sup>9</sup> /L)	Neu (%)	Lym (%)	AST (ug/L)	ALT (ug/L)
Grp9	Ma	41.52±1.02 <sup>j</sup>	18.12±0.77 <sup>ab</sup>	12.44±0.59 <sup>abc</sup>	128.50±2.52 <sup>f</sup>	28.30±3.32 <sup>z</sup>	31.00±2.32 <sup>a</sup>	12.30±1.41 <sup>a</sup>	22.10±1.27 <sup>ab</sup>
	Me	24.25±0.81 <sup>bc</sup>	7.44±0.47 <sup>kl</sup>	28.46±2.47 <sup>hi</sup>	81.81±3.27 <sup>t</sup>	46.88±2.34 <sup>i</sup>	47.10±1.99 <sup>def</sup>	36.30±1.17 <sup>b</sup>	42.40±5.14 <sup>fg</sup>
	Gbt	32.62±1.02 <sup>gh</sup>	11.86±2.18 <sup>a</sup>	17.54±0.73 <sup>def</sup>	94.13±4.64 <sup>cde</sup>	42.84±2.56 <sup>f</sup>	40.00±1.74 <sup>b</sup>	32.40±1.74 <sup>c</sup>	31.73±1.93 <sup>st</sup>
Grp10	Ma	40.20±2.77 <sup>hi</sup>	16.54±0.84 <sup>b</sup>	12.22±0.39 <sup>a</sup>	128.40±2.58 <sup>v</sup>	28.40±1.72 <sup>ab</sup>	30.50±2.25 <sup>ab</sup>	12.10±2.99 <sup>d</sup>	21.50±1.08 <sup>bc</sup>
	Me	23.40±2.34 <sup>b</sup>	7.40±0.22 <sup>t</sup>	28.11±3.16 <sup>i</sup>	83.70±5.17 <sup>b</sup>	48.55±2.91 <sup>gh</sup>	48.20±1.44 <sup>fg</sup>	36.50±5.30 <sup>e</sup>	42.40±4.00 <sup>cd</sup>
	FeGbt	34.50±3.42 <sup>de</sup>	13.99±24.40 <sup>p</sup>	16.24±0.60 <sup>fg</sup>	99.52±2.56 <sup>c</sup>	37.16±1.64 <sup>wx</sup>	38.43±3.49 <sup>lm</sup>	27.71±3.18 <sup>f</sup>	27.40±2.32 <sup>de</sup>
Grp11	Ma	40.60±1.36 <sup>ij</sup>	17.85±2.00 <sup>yz</sup>	12.05±2.45 <sup>q</sup>	129.33±0.73 <sup>ef</sup>	28.700±2.96 <sup>m</sup>	31.60±2.31 <sup>jk</sup>	13.00±3.98 <sup>g</sup>	21.50±1.52 <sup>ef</sup>
	Me	23.20±1.29 <sup>t</sup>	7.50±0.44 <sup>s</sup>	27.45±2.74 <sup>hi</sup>	83.12±4.10 <sup>y</sup>	48.46±1.50 <sup>ghi</sup>	48.14±0.87 <sup>efg</sup>	36.00±5.56 <sup>h</sup>	42.30±4.84 <sup>fg</sup>
	CoGbt	34.80±1.16 <sup>lm</sup>	13.94±1.14 <sup>z</sup>	16.06±2.88 <sup>g</sup>	99.63±1.45 <sup>cd</sup>	37.09±0.73 <sup>pq</sup>	38.43±0.66 <sup>yz</sup>	27.60±4.45 <sup>i</sup>	27.40±2.02 <sup>gh</sup>
Grp12	Ma	40.40±2.71 <sup>xy</sup>	17.88±0.63 <sup>w</sup>	12.00±1.85 <sup>y</sup>	128.80±3.53 <sup>def</sup>	28.42±0.66 <sup>z</sup>	31.43±3.02 <sup>xy</sup>	12.00±2.97 <sup>j</sup>	22.30±1.72 <sup>hi</sup>
	Me	23.10±5.42 <sup>cd</sup>	7.17±0.51 <sup>v</sup>	27.26±2.62 <sup>i</sup>	72.20±2.79 <sup>x</sup>	47.30±4.27 <sup>uv</sup>	47.50±2.14 <sup>u</sup>	36.30±2.92 <sup>k</sup>	41.20±3.56 <sup>ij</sup>
	ZnGbt	36.25±2.65 <sup>f</sup>	14.10±0.59 <sup>m</sup>	15.98±1.88 <sup>cde</sup>	99.99±5.64 <sup>w</sup>	36.25±0.68 <sup>vw</sup>	37.00±2.34 <sup>v</sup>	26.10±4.60 <sup>l</sup>	27.20±1.88 <sup>jk</sup>

NOTE: Gbt: guanidinobenzothiazole, FeGbt: iron guanidinobenzothiazole complex, CoGbt: cobalt guanidinobenzothiazole complex, ZnGbt: zinc guanidinobenzothiazole complex.

**Table 4: Antimicrobial activity of guanidinophosphonatebenzothiazole and complexes**

S/N	S	PCV (%)	Hb (g/dl)	WBC (X 10 <sup>9</sup> /L)	Platelet (X 10 <sup>9</sup> /L)	Neu (%)	Lym (%)	AST (ug/L)	ALT (ug/L)
Grp13	Ma	41.43±1.91 <sup>efghi</sup>	18.33±1.34 <sup>ij</sup>	12.50±0.82 <sup>a</sup>	129.00±2.18 <sup>fgh</sup>	28.34±2.42 <sup>abc</sup>	31.20±2.44 <sup>abc</sup>	12.87±0.58 <sup>a</sup>	22.16±1.21 <sup>c</sup>
	Me	24.21±0.87 <sup>cd</sup>	7.40±0.53 <sup>b</sup>	28.61±9.63 <sup>b</sup>	80.65±1.91 <sup>b</sup>	46.18±2.38 <sup>de</sup>	48.00±1.63 <sup>ef</sup>	36.10±2.26 <sup>de</sup>	42.20±1.86 <sup>hi</sup>
	Gpbt	32.88±0.74 <sup>de</sup>	12.67±0.47 <sup>defg</sup>	16.22±2.05 <sup>c</sup>	95.44±3.18 <sup>c</sup>	40.14±2.11 <sup>abcd</sup>	39.30±2.19 <sup>cd</sup>	30.20±0.63 <sup>ab</sup>	30.33±1.47 <sup>d</sup>
Grp14	Ma	41.00±1.54 <sup>ghi</sup>	17.65±1.41 <sup>ij</sup>	12.12±1.50 <sup>d</sup>	128.70±3.11 <sup>fg</sup>	28.20±3.06 <sup>ab</sup>	30.30±0.93 <sup>a</sup>	12.30±1.32 <sup>b</sup>	22.10±1.20 <sup>a</sup>
	Me	22.80±0.74 <sup>bc</sup>	7.20±0.75 <sup>bcd</sup>	28.16±7.60 <sup>c</sup>	81.50±3.53 <sup>d</sup>	48.00±0.58 <sup>ef</sup>	48.10±3.02 <sup>def</sup>	36.60±4.17 <sup>de</sup>	42.20±1.70 <sup>ghi</sup>
	Fe Gpbt	34.80±1.60 <sup>efg</sup>	14.91±0.76 <sup>cde</sup>	15.42±3.43 <sup>f</sup>	103.55±3.63 <sup>cde</sup>	36.11±2.73 <sup>bcde</sup>	37.13±0.97 <sup>abcd</sup>	26.32±1.93 <sup>c</sup>	26.40±1.23 <sup>b</sup>
Grp15	Ma	40.50±2.91 <sup>hi</sup>	18.55±1.13 <sup>hij</sup>	12.31±1.48 <sup>g</sup>	129.00±3.77 <sup>g</sup>	28.10±1.07 <sup>x</sup>	31.00±1.66 <sup>b</sup>	13.13±0.71 <sup>d</sup>	21.70±0.86 <sup>e</sup>
	Me	23.00±3.12 <sup>c</sup>	7.11±0.68 <sup>bc</sup>	28.42±8.94 <sup>h</sup>	82.21±3.85 <sup>k</sup>	48.34±3.40 <sup>f</sup>	48.10±1.40 <sup>de</sup>	36.22±4.24 <sup>e</sup>	42.10±1.03 <sup>i</sup>
	CoGpbt	35.00±2.80 <sup>efghi</sup>	14.94±0.76 <sup>defgh</sup>	15.41±3.11 <sup>i</sup>	103.61±3.58 <sup>q</sup>	36.00±1.21 <sup>tu</sup>	37.10±1.74 <sup>cde</sup>	26.30±0.74 <sup>f</sup>	26.40±1.39 <sup>ef</sup>
Grp16	Ma	41.00±3.05 <sup>h</sup>	17.83±1.49 <sup>ghi</sup>	12.30±0.66 <sup>j</sup>	128.88±3.79 <sup>gh</sup>	28.22±3.18 <sup>uv</sup>	31.33±2.52 <sup>q</sup>	12.12±2.44 <sup>g</sup>	22.00±0.75 <sup>abc</sup>
	Me	23.30±2.60 <sup>cd</sup>	7.26±0.52 <sup>mn</sup>	27.10±8.83 <sup>k</sup>	82.20±4.47 <sup>y</sup>	48.10±10.35 <sup>fg</sup>	47.80±1.50 <sup>f</sup>	36.40±4.18 <sup>h</sup>	41.70±1.50 <sup>x</sup>
	ZnGpbt	37.20±2.79 <sup>efgh</sup>	15.55±1.10 <sup>def</sup>	14.97±1.23 <sup>m</sup>	105.15±3.74 <sup>defg</sup>	34.32±2.75 <sup>lm</sup>	35.88±1.91 <sup>bcd</sup>	25.17±5.38 <sup>kl</sup>	25.90±1.55 <sup>y</sup>

NOTE: Gpbt: guanidinophosphonatebenzothiazole, FeGpbt- iron guanidinophosphonatebenzothiazole complex, CoGpbt: cobalt guanidinophosphonatebenzothiazole complex, ZnGpbt: zinc guanidinophosphonatebenzothiazole complex.

## CONCLUSION

Antimicrobial activities of guanidinobenzimidazole, guanidinophosphonatebenzimidazole, guanidinobenzothiazole and guanidinophosphonatebenzothiazole derivatives were assessed. They demonstrated antimicrobial potential. They exhibited different properties. Complex high performance might result from metal ions. Activity of complexes over ligands could also be due to chelates polar and nonpolar effects that make cell accessible. Ion bonding enhances biochemical potential process while lipophilicity is modified by coordination due to its ability to control molecules movement into cell. The metal complexes therefore have more tendencies to indicate higher antimicrobial properties than uncoordinated ligand and free metal ion.

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## Data availability

All data analysed during this research are included in this article.

## Declaration

J. A. Aremu on behalf of authors states that there is no conflict of interest

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