GUANIDINE DERIVATIVES OF CO(II), NI(II), CU(II) COMPLEXES AND HEPATITIS ACTIVITIES STUDIES

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ABSTRACT

This study determined hepatitis B and hepatitis C effectiveness of guanidine derivative, cobalt(II), nickel(II) and copper(II) complexes using rats as test animal. Histopathological analysis was carried out. The derivatives demonstrated effectiveness at 2 mg kg^{-1} (w/w) for 5 ml kg^{-1} (v/w) concentration. Phosphonate compounds of benzothiazole demonstrated highest treatment, guanidine compouds of benzothiazole.were found to be next effective. The effectiveness trend was followed by phosphonate compounds of benzimidazole which performed better than the benzimidazole compounds of the guanidine. The derivatives compete favourably with the vaccine contre hepatitis recombinant standard which gave similar results of the analysis. The treatment properties of the derivatives therefore demonstrated that benzimidazole compounds of the guanidine < phosphonate compounds of benzimidazole < guanidine compounds of benzothiazole < phosphonate compounds of benzothiazole

Keywords: Guanidine derivatives; Treatment, Hepatitis; Test animals

INTRODUCTION

Derivatives of guanidine make up a significant group of drug substances fit to cure many ailments [1]. Guanidine is critical for normal function of living organisms [2]. They have ability to perform fast or delay in virus development cycle to prevent yielding of antigenic viral protein [3].

Guanidine derivatives possess many biochemical and pharmaceutical activities [4] and are believed to have antimicrobial abilities [5],[6]. The important roles of guanidine and phosphonate derivatives therefore encourage continuous interest in academic research and industrial development. Synthesis and uses of phosphonate-containing entities have been noticeable for decades [1], [2], [7].

Despite the fact that guanidines, phosphonates and thiazoles possess biochemical and pharmaceutical importance, their activities and those of their metal complexes have been scarcely reported about hepatitis B and hepatitis C. Hence, the significance of this research works to determine effectiveness of the derivatives for treatment of the hepatitis diseases.

MATERIALS AND METHODS

Blood samples screened for hepatitis B and C were obtained from Abeokuta, Nigeria. Male rats were used.

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Blood sample treatment

Treatment effectiveness of the guanidine derivatives of the Co(II), Ni(II) and Cu(II) complexes were examined against hepatitis B and hepatitis C diseases through adult male rats ranging from 220 g to 250 g. The rats were divided into groups A, B and C after acclimatization for thirty days. Raw blood samples of the rats were tested to be free of the hepatitis B and hepatitis C diseases. Group B rats were infected with hepatitis B while group C were infected with hepatitis C. Group A rats were not infected because they were only used to monitor physical activity and comparison with those infected groups. The blood samples were examined again after fifteen days according to method in literature [8] which showed evidences of infection. Treatments were carried out for ninety days through administration at 5 ml / kg at 2 mg / kg in line with literature procedure [9]. One group was treated with standard vaccine contre hepatitis recombinant while one group was left untreated both as control. The blood samples were further tested after ninety days of treatments and treatment effectiveness deduced.

Liver histopathological examination

Effects of the hepatitis disease on the livers were examined by histopathological study [10] and the treatment demonstrated effectiveness of the derivatives. Processed tissues were treated by using haemotoxyline and eosin staining techniques [11]. The livers were observed for changes under microscope. Levels of degeneracy were discovered in some sections of the livers as comparison was made with the uninfected, treated and untreated rats which led to inferences drawn about the treatment activities of the derivatives.

RESULTS AND DISCUSSION

Ninety days treatment carried out which reflected ability of the guanidine derivatives was established through the analysis results. Histopathological study revealed effects of the hepatitis B and hepatitis C diseases in the livers expressed as fat degeneracy: accumulation of fat in hepatocyte-liver cells [12], congestion of blood vessel: blood over filled vessels, necrosis of hepatocytes: liver dead cells, sinusoid: small blood vessels in the passages/drainages of the liver and perivascular infiltration by inflammatory cells: space around blood vessel infiltrated by inflammatory cells [12] which were observed under microscope. Levels of degeneracy were discovered in some sections of the livers as comparisons were made with the uninfected, untreated and the treated infected rats which led to inferences drawn about the treatment activities of the compounds.

Plate 1 indicated histopathological picture for liver of an hepatitis B free rat while plate 2 displayed effect of the hepatitis B before commencement of treatment which was compared with plate 3 for hepatitis B treated with guanidinobenzimidazole and plates 4-6 showed

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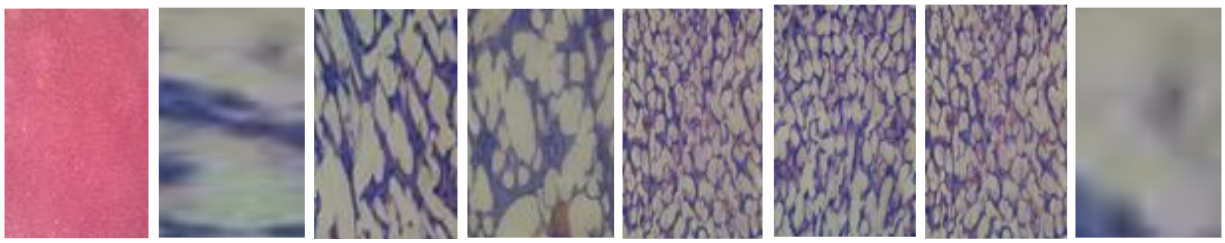
histopathology of rats treated with Co-guanidinobenzimidazole, Ni-guanidinobenzimidazole and Cu-guanidinobenzimidazole complexes along with plate 7 for rat treated with the standard vaccine contre hepatitis recombinant while plate 8 gave result for infected but untreated rat throughout the period of the experiment.

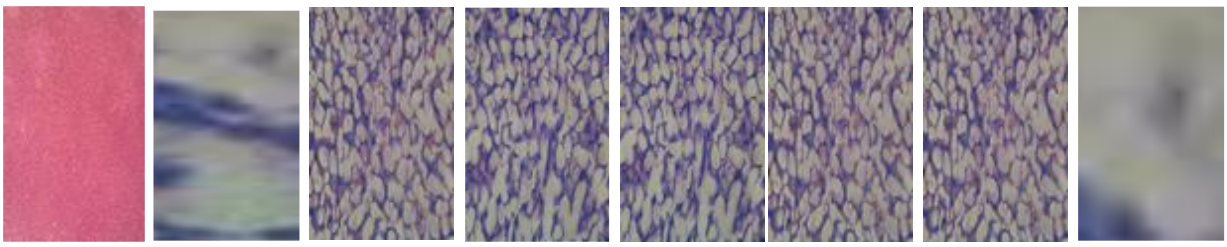


1 2 3 4 5 6 7 8

Plates 1 - 8: Histopathological pictures for livers of rats

Fat degeneracy, congestion of blood vessel, necrosis of hepatocytes, sinusoid and perivascular inflammatory infiltrated cells were observed for plates 2 to 8. The defects were more severe in plates 2 and 8 which stood for untreated rats that demonstrated accumulation of excess fat globules, blood vessel congestion and perivascular infiltrated inflammatory cells that were less prevalent in plates 3 to 7 due to treatment effect.

Similarly, plate 1.1 gave histopathological picture for liver of an uninfected rat, plate 2.1 represented liver with effect of hepatitis B before commencement of the treatment which was compared with liver of rat in plate 3.1 for hepatitis B treated with guanidinophosphonatebenzimidazole and plates 4.1 to 6.1 where histopathological results for livers of rats treated with Co-guanidinophosphonatebenzimidazole, Ni-guanidinophosphonatebenzimidazole and Cu-guanidinophosphonatebenzimi dazole complexes were demonstrated while plate 7.1 was obtained for rat treated with the standard vaccine contre hepatitis recombinant and plate 8.1 indicated result for rat infected with the hepatitis B but untreated throughout the period of experiment. Evidence of positive treatment therefore showed between livers of the treated rats 3.1 - 7.1 and livers of the untreated rats 2.1 and 8.1. This agreed with literature [13] that phosphonate compounds are potentially active.



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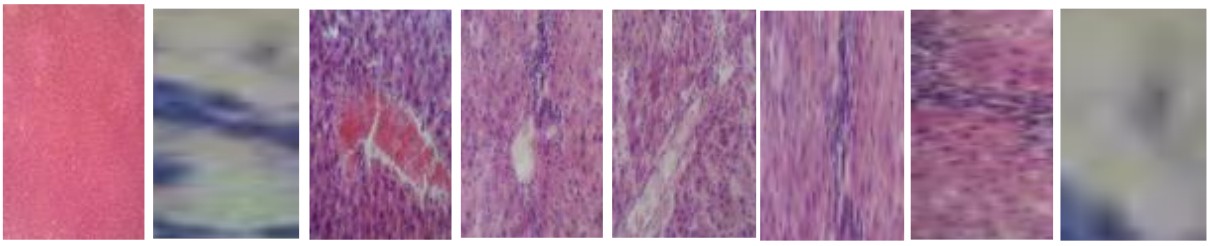
1.1 2.1 3.1 4.1 5.1 6.1 7.1 8.1

Plates 1.1 - 8.1: Histopathological pictures for livers of rats

Plates 1.2 to 8.2 in the same manner showed histopathological pictures of liver of an uninfected rat, liver of hepatitis B infected rat before commencement of the treatment, liver of rat for hepatitis B treated with guanidinobenzothiazole, histopathological results for livers of rats treated with Co-guanidinobenzothiazole, Ni-guanidinobenzothiazole and Cu-guanidinobenzothiazole complexes, liver of rat treated with the standard vaccine contre hepatitis recombinant and liver of rat with untreated hepatitis B. Treatment effectiveness of the compounds was observed to be progressively increasing since guanidinobenzothiazole produced better treatment than guanidinophosphonatebenzimidazole in the same pattern of better results of guanidinophosphonatebenzimidazole compounds over guanidinobenzimidazole compounds. Apart from livers on plates 2.2 and 8.2 which were not treated and demonstrated severe fat degeneracy, blood vessel congestion, necrosis of hepatocytes and perivascular infiltration by inflammatory cells, livers 3.2 to 7.2 responded to treatment as evident in comparison with the histopathological pictures for liver of the uninfected rat.



1.2 2.2 3.2 4.2 5.2 6.2 7.2 8.2

Plates 1.2 – 8.3: Histopathological pictures for livers of rats

1.3 to 8.3 displayed products of guanidinophosphonatebenzothiazole compounds due to treatment in the same order of plates described earlier. The compounds did not only show excellent treatment potential but also showed reduced manifestation of the hepatitis B effects as more healthy livers were observed when compared with 1.3 for the liver of uninfected rat except 2.3 and 8.3 that represented livers of untreated rats.

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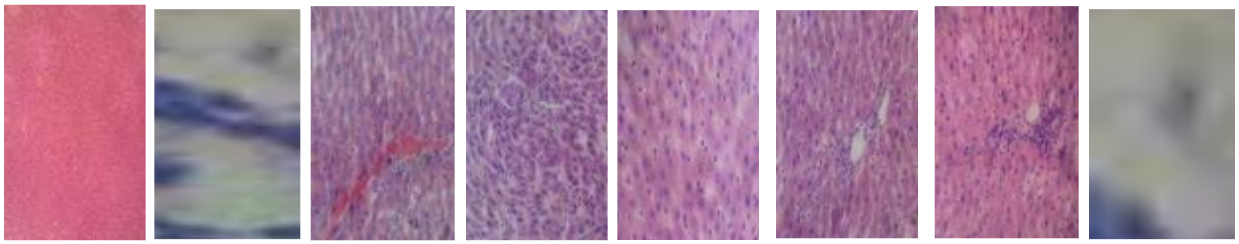
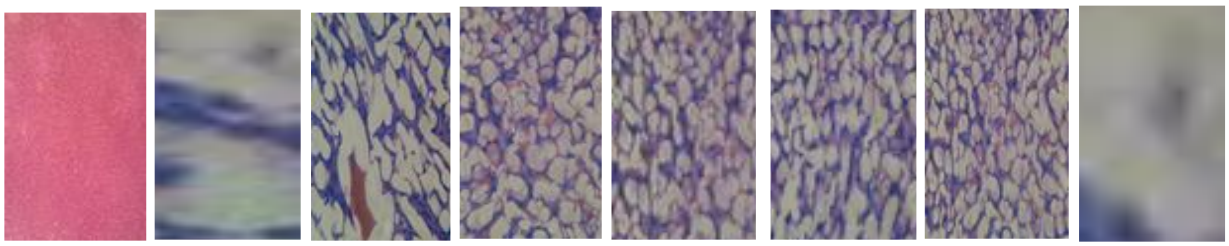


1.3 2.3 3.3 4.3 5.3 6.3 7.3 8.3

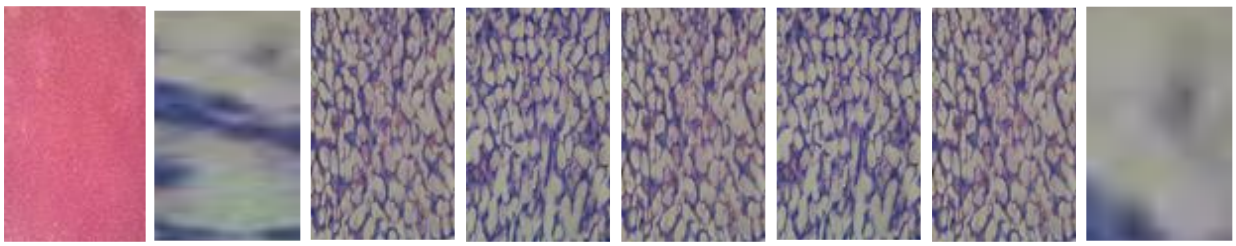
Plates 1.3 - 8.3: Histopathological pictures for livers of rats

Histopathological pictures of livers 1.4 - 8.4 in relation with guanidinobenzimidazole compounds, 1.5 - 8.5 with guanidinophosphonatebenzimidazole compounds, 1.6 - 8.6 with guanidinobenzothiazole compounds and 1.7 - 8.7 with guanidinophosphonatebenzothiazole compounds gave results for treatment of hepatitis C by following the same process carried out for hepatitis B. Observation of the histopathological pictures revealed that both hepatitis B and C responded to treatments.



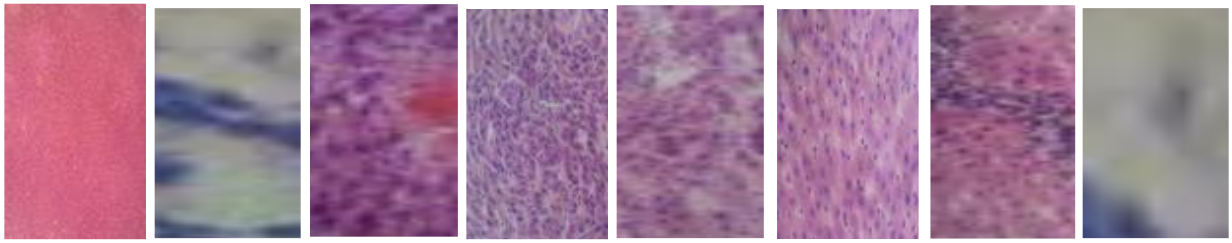
1.4 2.4 3.4 4.4 5.4 6.4 7.4 8.4

Plates 1.4 – 8.4: Histopathological pictures of livers of rats



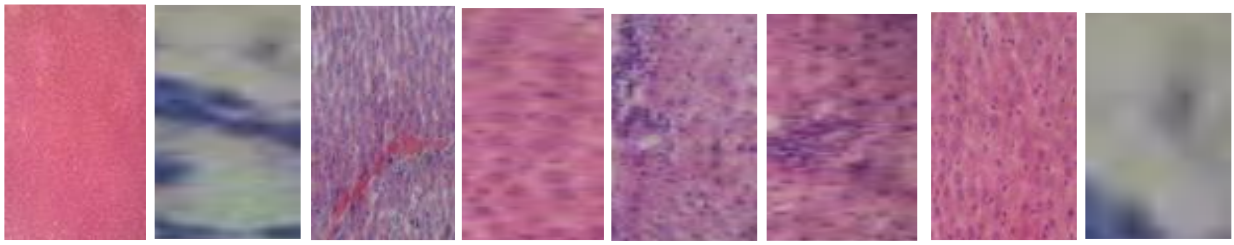
1.5 2.5 3.5 4.5 5.5 6.5 7.5 8.5

Plates 1.5 – 8.5: Histopathological pictures for livers of rats



1.6 2.6 3.6 4.6 5.6 6.6 7.6 8.6

Plates 1.6 – 8.6: Histopathological pictures for livers of rats



1.7 2.7 3.7 4.7 5.7 6.7 7.7 8.7

Plates 1.7 - 8.7: Histopathological pictures for livers of rats

Fat degeneracy, congestion of blood vessel, necrosis of hepatocytes, sinusoid and perivascular infiltration by inflammatory cells observed under microscope for hepatitis B were also detected for hepatitis C.

The treatment showed that guanidinophosphonatebenzothiazole derivatives > guanidinobenzothiazole derivatives > guanidinophosphonatebenzimidazole derivatives > guanidinobenzimidazole derivatives.

The high property due to coordination might related to metal ions action on cell membrane [14],[15]. Performance of the complexes over the ligands could also be due to chelated polar and nonpolar effects that make cells and tissues accessible [15]. Ion bonding enhances biochemical ability of organic types while lipophilicity is modified by coordination associated to its ability to moderate molecules movement into cell. The metal complexes therefore have more tendencies to indicate higher antimicrobial activities than the uncoordinated ligand and free metal ion. This agrees with literature [15],[16].

CONCLUSION

Treatment activities of the guanidine derivatives were assessed against hepatitis B and hepatitis C diseases. They demonstrated potential for the treatment**.** They exhibited different treatment properties. The treatment effectiveness was deduced through histopathological studies. The derivatives compete favourably with the standard; vaccine contre hepatitis recombinant. Complex high performance might resulted from metal ions on cells. Activity of complexes over ligands could also be due to chelates polar and nonpolar effects that make

cells and tissues accessible. Ion bonding enhances biochemical potential process while lipophilicity is modified by coordination due to its ability to control molecules movement into cells. 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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