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Original Research Article

In vitro Antioxidant Activities of Some Re(I) Metal Carbonyls Synthesized from Isatin DerivativesAdebomi A. Ikotun¹, Esther E. Babajide¹, Tolulope O. Omolekan², Chijioke J. Ajaelu^{1*}¹Industrial Chemistry Programme, College of Agriculture, Engineering and Science, Bowen University, Iwo, Nigeria²Biochemistry Programme, College of Agriculture, Engineering and Science, Bowen University, Iwo, Nigeria

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ABSTRACT

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Isatin is a natural indole found in some plants, brains, and human tissues, which possesses numerous medicinal applications. Rhenium complexes of different Schiff bases have multiple biological applications like anti-tumour, anti-microbial and antioxidant activities. Little information exist in literature on the Re(I) metal carbonyls of isatin derivatives and their biological significance. Therefore, the aim was to determine the antioxidant capacities of Re(I) complexes of the Schiff bases of isatin with aniline (C₁₄H₁₀N₂O) and isatin with sulphanilamide (C₁₄H₁₁N₃O₃S) using three antioxidant assays to facilitate further plausible biological and medicinal applications. 2,2-diphenyl-1-picrylhydrazyl (DPPH) and hydrogen peroxide radical scavenging activities of the Re(I) isatin derivative complexes and their reducing power were evaluated. Complex 1 was [Re(C₁₄H₁₀N₂O)(CO)₃Cl], Complex 2 was [Re(C₁₄H₁₀N₂O)(CO)₃Br] and complex 3 was [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br]. It was observed that Complexes 2 and 3, which contain bromine in their coordination spheres, had better DPPH scavenging activities than Complex 3, which had chlorine in its coordination sphere. Although [Re(C₁₄H₁₀N₂O)(CO)₃Br] has better DPPH and hydrogen peroxide radical scavenging abilities than [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br], it was observed that [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] was a better reducing agent than [Re(C₁₄H₁₀N₂O)(CO)₃Br]. These results showed good antioxidant properties of the complexes, recommendable for further applications such as anti-tumor or cell imaging known with isatin derivatives and Re(I) compounds. Also, this might arouse the interest to study the structure to function relationships in aniline and sulphanilamide-containing complexes, which could be of great medicinal significance.

Keywords: Rhenium complexes, Antioxidant activities, Isatin, sulphanilamide.

Introduction

Transition metal complexes have therapeutic potential and biological activities.¹⁻³ Rhenium complexes coupled with different Schiff bases have multiple biological applications which include anti-tumour activity.⁴ One of the main mechanisms for eliciting these properties is their antioxidant capacity. Antioxidant compounds attenuate the initiation and progression of stress due to oxidation which has caused several diseases within living systems. Molecules that possess antioxidant abilities in biological systems are also capable of displaying therapeutic abilities on human diseases. Isatin is an indole found naturally in some plants, some human tissues, as well as the brains of mammals.⁵ The preparation of many Schiff bases of isatin and its derivatives with N-benzyl has been reported with their metal complexes, as they also possess some anticonvulsant, antimicrobial, antiviral activities, anti-HIV and anticancer properties.^{6,7} Schiff bases have high cytotoxicity.⁸ Cytotoxic isatin derivatives' modes of action are very dependent on the type of substitution that exists there. While isatin analogues derivatized at the C2 position display Cyclin Dependent Kinase (CDK) 1, CDK2, and glycogen synthase kinase 3 kinase inhibition, N-alkylation produces cytotoxic chemicals with nanomolecular activity that cause morphological change by interfering with tubulin polymerization.

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Similar to isatin derivatives, those functionalized at the C position exhibit kinase inhibition activity, inhibiting the vascular endothelia growth factor receptor-2, platelet-derived growth factor receptor-β, fibroblast growth factor receptor, and endothelia growth factor receptor. The common result of ring-centered derivation is isatin analogues that cause cancer cells to die through high-micromolar-range necrosis and mid- to low-micromolar-range apoptosis.⁸ Microwave synthesized Co(II) complex prepared from the Schiff base of N-benzylisatin and p-toluidine has been reported.¹ This complex possessed better free radical scavenging properties than its isatin Schiff base.¹ N-alkylation significantly enhanced the cytotoxic effect of brominated isatins in human cancer but not normal cell lines compared with the parent isatin.⁸ More importantly, N-alkylated isatin Schiff base complexes are used in fluorescence microscopy as a highly efficient 'turn-off' fluorescence sensor and they have received much attention recently.⁹ Although the synthesis of rhenium tri- and dicarbonyl complexes suitable for diagnostic and therapeutic antitumor applications¹⁰ is fast gaining more attention, there is little or no literature on such bioactive compounds consisting of isatin Schiff bases coordinating to the rhenium metal through oxygen and nitrogen donor atoms. This research was geared towards that. Recently, we reported the synthesis, characterization and antimicrobial activities of some Re(I) metal carbonyls prepared from the Schiff bases of isatin with aniline, as well as isatin with sulphanilamide.^{11,12} It was discovered that Re(I) metal coordinated through the oxygen and nitrogen donor atoms in those complexes. Furthermore, in this work, we evaluated the scavenging abilities of DPPH radical, hydrogen peroxide radical and the reducing power abilities of three of those Re(I) metal carbonyls of isatin derivatives.^{11,12} This is the first report of the antioxidant activities of Re(I) metal carbonyls of isatin Schiff bases of aniline, as well as that of sulphanilamide. The good results from this preliminary study could lead to several other biological studies and medicinal applications.

Materials and Methods

Chemicals

ReCO₅Cl, isatin, aniline and sulphanilamide were bought from Aldrich, while Re(CO)₅Br was synthesized in the laboratory from Re₂(CO)₁₀ as previously reported.²² All solvents used; N,N-dimethylformamide (DMF), methanol, ethanol and chloroform were purchased from SAARChem and Sigma-Aldrich.

Instrumentation

Room temperature recordings of the NMR spectra (¹H & ¹³C; 400 MHz) were carried out using a Bruker Spectrometer. Shimadzu IRAffinity-1 spectrometer possessing a pike MIRacle ATR system (diamond crystal) was used for running the Infrared spectra within the range of 4000 to 400 cm⁻¹. A Shimadzu UV-1800 spectrometer was used to record the UV-Visible spectra. A MicromassZabspec instrument (FAB) was used to determine the mass spectra. A Johnson Matthey Magnetic Susceptibility balance was used to determine the room temperature magnetic susceptibility measurements. The purity of the compounds alongside the endpoints of all reactions was ascertained through Thin Layer Chromatography (TLC) using Silica Gel 60 F₂₅₄ alumina plates (E Merck) involving solvent mixtures (chloroform: diethyl ether, either 5:5 or 6:4 v/v), which were viewed in a UV chamber (365 nm). A Gallenkamp variable heater apparatus was used to determine the melting points of compounds.

Preparation of the isatin Schiff base

The isatin Schiff base was prepared as previously reported by Ikotun *et al.*,^{12,13} Isatin (5 g; 0.03398 mol) was dissolved completely in 180 ml methanol. Aniline (3.1 ml; 0.03398 mol) was added with 8 drops of conc. sulphuric acid, as stirring was done at room temperature for 2 h. The filtered yellow precipitate weighed 4.32 g (0.01945 mol; 57% yield). It was recrystallized in a mixture of ethanol : chloroform (70 : 30) and weighed 3.08 g (41% yield). This was characterized as C₁₄H₁₀N₂O.¹⁰ Isatin (5 g; 0.03398 mol) was completely dissolved with 200 ml methanol and sulphanilamide (5.85 g; 0.03398 mol) was also added, while room temperature synthesis was being carried out. After which 8 drops of concentrated H₂SO₄ was also added and stirred for 1½ h. Filtration of the yellow product was followed with recrystallization in ethanol: chloroform (70: 30). It weighed 9.43 g (0.03149 mol; 92 %). This has been fully characterized as C₁₄H₁₁N₃O₃S.¹²

Preparations and Spectroscopic Characterization of Re(I) metal carbonyls

The Re(I) metal carbonyl complexes have been prepared according to literature.^{12, 13, 14} C₁₄H₁₀N₂O (0.03 g; 0.00014 mol) as well as Re(CO)₅Cl (0.05 g; 0.00014 mol) were stirred at 100 °C for 3 h in 20 ml of toluene. After cooling in oil, the filtered light purple solids, Complex 1; [Re(C₁₄H₁₀N₂O)(CO)₃Cl], weighed 0.07 g (0.00013 mol; 96 % yield). Also, Re(CO)₅Br (0.45 g; 0.00111 mol) was added to C₁₄H₁₀N₂O (0.25 g; 0.00111 mol) and 45 mL toluene and refluxed for 1 h. The filtered purple solids, Complex 2; [Re(C₁₄H₁₀N₂O)(CO)₃Br], weighed 0.57 g (0.00099 mol; 90 %). Re(CO)₅Br (0.2 g; 0.00049 mol) was also stirred with C₁₄H₁₁N₃O₃S (0.14 g; 0.00049 mol) in hot toluene (20 ml; 100 °C; 20 h). [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] precipitated as the product having colour purple (complex 3), filtered after cooling. Its weight was 0.2797 g (0.00043 mol; 92 % yield). The physical and spectroscopic characterization of the prepared rhenium (I) tricarbonyl complexes 1, 2 and 3 have been extensively reported by Ikotun and coworkers.^{12, 13}

Scavenging activities

DPPH radical

The principle of the scavenging activities of DPPH radical has been established.^{15, 16} Methanol solution of DPPH (4 ml) was mixed with 1 ml of different concentrations (0.1, 0.3, 0.6 mg/ml) of [Re(C₁₄H₁₀N₂O)(CO)₃Cl],¹⁷ Complex 1 solution. This was also repeated for [Re(C₁₄H₁₀N₂O)(CO)₃Br] and [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] solutions which are complexes 2 and 3, respectively. The solutions were shaken thoroughly and placed in the dark for 35 minutes, after which the absorbance was taken at 520 nm. The standard used was ascorbic acid, while the results were expressed as percentage (%) DPPH radical scavenging activity.

H₂O₂ radical

H₂O₂ (2 mM) was prepared in 50 mM phosphate buffer (pH = 7.4). 0.3 ml of the solution was added to 0.6 mL of different concentrations (0.1, 0.3, 0.6 mg/mL) of [Re(C₁₄H₁₀N₂O)(CO)₃Br] solution. This was also repeated separately for [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] solution. Each mixture was vortex with the reading of the absorbance done at 230 nm against a blank after 10 minutes. The results have been reported as percentage (%) H₂O₂ scavenging activity.

Reducing power activities

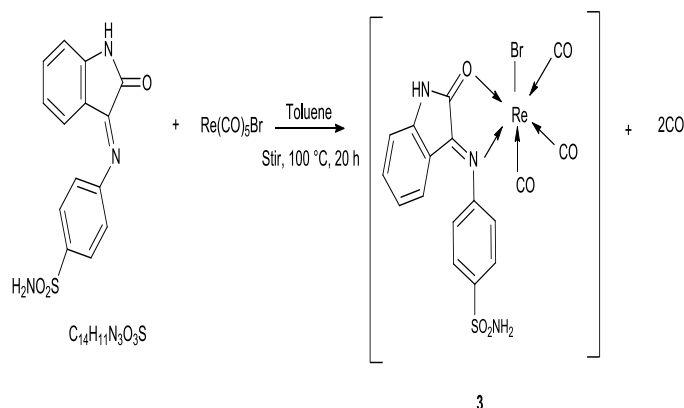
1 ml each of both phosphate buffer, 0.2 M, pH 6.6 and 10 mg/ml of K₃[Fe(CN)₆], were added to 1 ml of different concentrations (0.1, 0.3, 0.6 mg/ml) of [Re(C₁₄H₁₀N₂O)(CO)₃Br] and solution. This was also repeated for different concentrations (0.1, 0.3, 0.6 mg/ml) of [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] solution. The solutions were incubated for 20 minutes at 50 °C followed by the addition of 1 ml trichloroacetic acid (100 mg/ml). Each of the solutions was centrifuged for 10 minutes (at 3000 rpm) and the upper layer of the solution was collected. 2 ml distilled water and 0.1 % ferric chloride was mixed with 2 ml from each solution. After 10 minutes, the absorbance was recorded at 700 nm. The high reducing power of the reaction mixture was due to the elevated absorbance value.¹⁸

Results and Discussion

The preparation of the metal carbonyls can be represented by the general scheme of reaction in Scheme 1. Antioxidants are reducing agents. Their ability to donate electron or hydrogen atom enables them to scavenge free radicals and reduce elements with higher valence to their lower valence state.^{19, 20} Their reducing power is an important indicator of their antioxidant efficacy. Their structure influences their functions. Many natural and synthetic nitrogen-containing compounds possess antioxidant activities.^{21, 22} However, to an extent, multiple ring systems and the degree of electron delocalization around the nitrogen and oxygen atoms of these compounds hinder their antioxidant capacity.

DPPH radical scavenging activities

The percentage DPPH radical scavenging activities of the metal carbonyls and their inhibitory concentration at 50 % DPPH radical are presented in figure 1 and table 1. The three Re(I) complexes were more effective than ascorbic acid in scavenging singlet DPPH radical.



For Complex 1, SO₂NH₂ = H; C₁₄H₁₀N₂O + Re(CO)₅Cl, Toluene, Stir, 100 °C, 3 h

For Complex 2, SO₂NH₂ = H; C₁₄H₁₀N₂O + Re(CO)₅Br, Toluene, Reflux, 100 °C, 1 h

Scheme 1: The general scheme for the reaction for preparing the metal carbonyls

Complex 2 [Re(C₁₄H₁₀N₂O)(CO)₃Br], Complex 3 [Re(C₁₄H₁₁N₃O₃S)(CO)₃Br] and Complex 1 [Re(C₁₄H₁₀N₂O)(CO)₃Cl] were 43, 27 and 13 times better scavenger of singlet DPPH radical than ascorbic acid.

H₂O₂ scavenging activities

The percentage H₂O₂ scavenging activities of the metal carbonyls and their inhibitory concentration at 50 % H₂O₂ are presented in Figure 2

and Table 2. Figure 2 demonstrates that an increase in sample concentration increases the percentage hydrogen peroxide scavenging ability of ascorbic acid, Re(I) complex 2 and Re(I) complex 3. Re(I) complex 2 is more effective in scavenging hydrogen peroxide than both ascorbic acid and Re(I) complex 3.

Complex 2 $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Br}]$ is six times more effective than ascorbic acid, while the effectiveness of complex 3 $[\text{Re}(\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S})(\text{CO})_3\text{Br}]$ is approximately the same as that of ascorbic acid in scavenging H_2O_2 .

Reducing power activities

The percentage-reducing power abilities of the tested Re(I) complexes and their inhibitory concentration in comparison with ascorbic acid are presented in Figure 3 and Table 3. The two Re(I) complexes have very high reducing power capability than ascorbic acid. Complex 2; $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Br}]$ and complex 3; $[\text{Re}(\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S})(\text{CO})_3\text{Br}]$ have 14 and 53 times capacity than ascorbic acid as reducing agents. As such they could prevent lipid peroxidation and limit cell membrane disruption as well as prevent cell lysis. The presence of bromine in Complexes 2 and 3 improved their ability to scavenge singlet radicals like DPPH better than Complex 1. This also corroborates the fact that bromine possesses stronger lone pair dispersion forces than chlorine. This is consistent with expectations because chlorine has a higher electronegativity value than bromine and it would readily withdraw electrons more towards itself from other ions or atoms around. Hence, bromine's electron clouds can easily be distorted to become asymmetric and instantaneously form dipoles compared to chlorine because its valence electron is also farther away from its nucleus. This conferred better antioxidant capacity on the bromine-containing Re(I) tricarbonyl complexes of isatin derivatives (Complexes 2 and 3). Although the aniline containing Complex 2 has a better capacity to scavenge hydrogen peroxide, the sulphanilamide containing Complex 3 has better reducing power than it. The possible explanation for this behavior would be that a strong deactivating effect of the SO_2 group, an electron-withdrawing specie, from the sulphonamide (SO_2NH_2 molecule) is being experienced by complex 3.²³ Therefore, the sulphonamide group would attract the delocalized electrons within the ring system towards itself, thereby producing a less reducing power effect than Complex 2. Contrary to this deactivating effect of the SO_2 group, the NH_2 group present on the same molecule of sulfonamide produces a stronger activating effect which must have annulled its effect. The NH_2 group is an electron donating specie that activates ring systems.

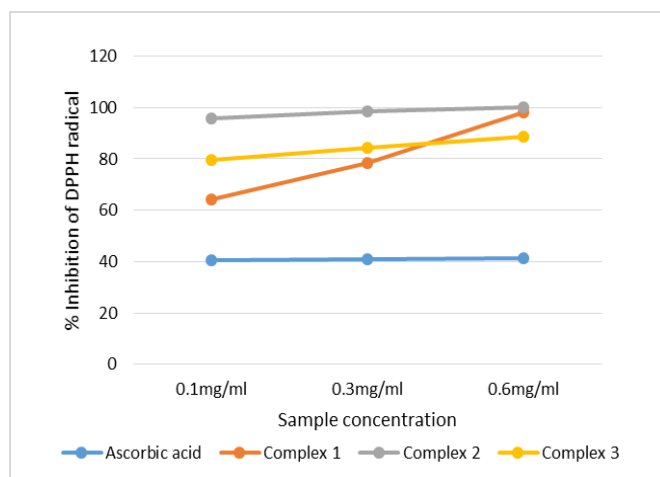


Figure 1: Percentage DPPH radical scavenging activity of Re(I) complexes. Complex 1 = $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Cl}]$; Complex 2 = $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Br}]$; Complex 3 = $[\text{Re}(\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S})(\text{CO})_3\text{Br}]$

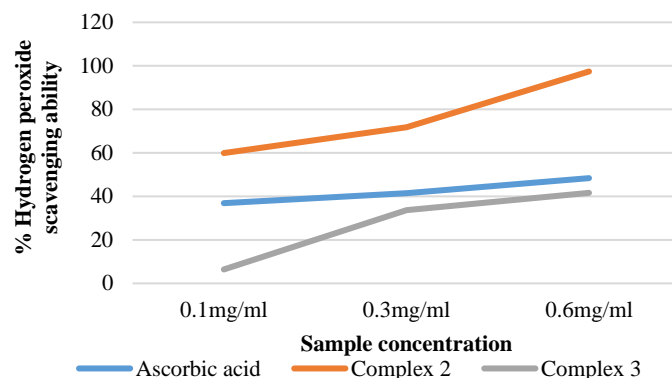


Figure 2: Percentage H_2O_2 radical scavenging activity of Re(I) complexes

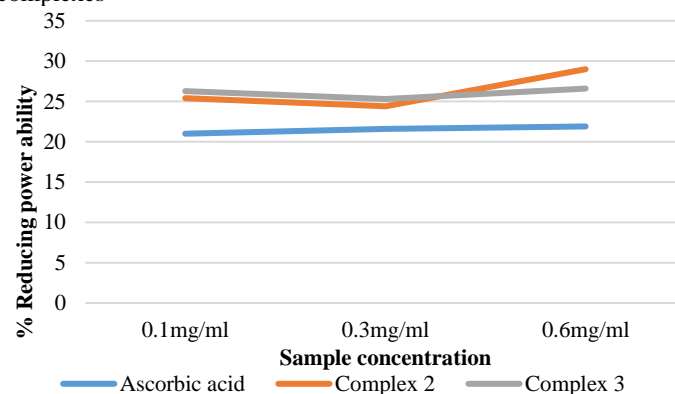


Figure 3: Reducing power of Re(I) complexes

Table 1: inhibitory concentration of the Re(I) complexes at 50 %, and their ascorbic acid equivalent DPPH radical scavenging activities

Compound	IC50 (mg/mL)	Ratio of % DPPH Radical Scavenging activity compared to Ascorbic acid
Ascorbic acid	3.01	
$[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Cl}]$	0.23	Complex 1 is 13 times as effective as ascorbic acid
$[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Br}]$	0.07	Complex 2 is 43 times as effective as ascorbic acid
$[\text{Re}(\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S})(\text{CO})_3\text{Br}]$	0.11	Complex 3 is 27 times as effective as ascorbic acid

Conclusion

This study involved the antioxidant property investigations of three Re(I) tricarbonyl complexes of isatin origin. Complex 1 was $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Cl}]$, Complex 2 was $[\text{Re}(\text{C}_{14}\text{H}_{10}\text{N}_2\text{O})(\text{CO})_3\text{Br}]$ and complex 3 was $[\text{Re}(\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S})(\text{CO})_3\text{Br}]$. The ability of Complexes 2 and 3 to scavenge singlet radicals was enhanced in the presence of bromine as compared to chlorine-containing complex 1. Although Complex 2 with aniline had a greater ability to scavenge hydrogen peroxide, Complex 3 with sulphanilamide exhibited a greater ability to reduce. This anomalous behavior may pave the way for additional, intriguing research on the structure-to-function relationships in complexes containing aniline and sulphanilamide.

Table 2: Inhibitory concentration of the Re(I) complexes at 50 %, and their ascorbic acid equivalent H_2O_2 / sensing scavenging activities

Compound	IC50 (mg/mL)	Ratio of % H ₂ O ₂ Radical Scavenging activity compared to Ascorbic acid
Ascorbic acid	3.35	
[Re(C ₁₄ H ₁₀ N ₂ O)(CO) ₃ Br]	0.59	Complex 2 is 6 times more effective as ascorbic acid
[Re(C ₁₄ H ₁₁ N ₃ O ₃ S)(CO) ₃ Br]	3.29	Complex 3 is almost as effective as ascorbic acid,

Table 3: Reducing power of the Re(I) complexes in comparison with ascorbic acid

Compound	IC50 (mg/mL)	Ascorbic acid equivalent reducing power
Ascorbic acid	5.3	
[Re(C ₁₄ H ₁₀ N ₂ O)(CO) ₃ Br]	0.39	14 times as effective as ascorbic acid
[Re(C ₁₄ H ₁₁ N ₃ O ₃ S)(CO) ₃ Br]	0.1	53 times as effective as ascorbic acid

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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References

- Seifriz I, Konzen M, Paula MMS, Norberto S, Goncalves A, Sponganickz B, Tania B, Creczynski-Pasa B, Vilson R, Bonnetti B, Beirith A, Joao B, Calixto C, Franco CV. Synthesis, potentiometric titration, electrochemical investigation and biological properties of *trans*-[RuCl₂(dinic)₄](dinic = 3,5-pyridinecarboxylic acid). *J Inorg Biochem.* 1999; 76:153–163.
- Beirith A, Creczynski-Pasa TB, Bonetti VR, Konzen M, Seifriz I, Paula MS, Franco CV, Calixto JB. Antinociceptive properties and nitric oxide synthase inhibitory action of new ruthenium complexes. *Eur J Pharmacol.* 1999; 369:289-297.
- Creczynski-Pasa TB, Bonetti VR, Beirith A, Ckless K, Konzen M, Seifriz I, Paula MS, Franco CV, Filho DW, Calixto JB. Complexes *trans*-[RuCl₂(nic)₄] and *trans*-[RuCl₂(i-nic)₄] as free radical scavengers. *J. Inorg. Biochem.* 2001; 86:587-594.
- Domenichini A, Casari I, Simpson PV, Desai NM, Chen L, Dustin C, Edmands JS, Vliet AV, Mohammadi M, Massi M, Falasca M. Ruthenium N-heterocyclic carbene complexes block growth of aggressive cancers by inhibiting FGFR- and SRC-mediated signalling. *J Exp Clin Cancer Res.* 2020; 39:276.
- Sridhar SK, Pandeya SN, Stables JP, Ramesh A. Anticonvulsant activity of hydrazones, Schiff and Mannich bases of isatin derivatives. *Eur J Pharm Sci.* 2002; 16:129-132.
- Ikotun AA, Adelani PO, Egharevba GO. 1-Benzyl-3 [(4methylphenyl)imino]-indolin-2-one. *Acta Cryst.* 2012; E68:o2098.

- Visagaperumal S, Ezekwem JE, Munji H, Chandy V. Isatin Schiff base – an overview. *Pharma Tutor.* 2018; 6(5):38-47.
- Matesic L, Locke JM, Bremner JB, Pyne SG, Skropeta D, Ranson M, Vine KL. *N*-Phenethyl and *N*-naphthylmethyl isatins and analogs as *in vitro* cytotoxic agents. *Bioorg Med Chem.* 2008; 16(6):3118-3124.
- Pradeep SD, Sebastian D, Gopalakrishnan AK, Mohan PV. A novel and cost effective isatin based Schiff base fluorophore: a highly efficient 'turn-off' fluorescence sensor for the selective detection of cysteine in an aqueous medium. *New J Chem.* 2021; 45:16306-16312.
- Schindler K and Zobi F. Anticancer and Antibiotic Ruthenium Tri- and Dicarbonyl Complexes: Current Research and Future Perspectives. *Molecules.* 2022; 27(2):539.
- Coogan MP, Fernandez-Moreira V, Kariuki BM, Pope SJA, Thorp - Greenwood FL. A ruthenium fac-tricarbonyl 4'-oxo-terpy trimer as a luminescent molecular vessel with a removable silver stopper. *Angew. Chem Int Ed Engl.* 2009; 48:4965-8.
- Ikotun AA, Owoseni AA, Egharevba GO. Synthesis, physicochemical and antimicrobial properties of ruthenium (II) tricarbonyl complexes of isatin Schiff bases. *Afr J Biotec.* 2021; 20(5):175-185.
- Ikotun AA, Coogan MP, Owoseni AA, Egharevba GO. Design, Synthesis, Physicochemical and Antimicrobial Properties of Ruthenium (I) tricarbonyl complexes of 3-(phenylimino)indole-2-one. *J Chem Soc Nig.* 2019; 44(5):948-958.
- Ikotun AA and Omolekan TO. Microwave-assisted Synthesis, Characterization, Indolin-2-One and Its Co(II) Complex. *Chem Sc Int J.* 2019; 28(1):1-12.
- Gyamfi MA, Yonamine M, Aniya Y. Free radical scavenging activity of medicinal herb of Ghana: *Thonningia sanguinea* on experimentally induced liver injuries. *Gen Pharmacol.* 1999; 32:661–667.
- Yupparach P and Konsue A. Phytochemical Screening and Antioxidant Activities of *Cornuacaempferia chayanii* Extracts and *in vitro* Inhibitory Effects on Digestive Enzymes. *Trop J Nat Prod Res.* 2022; 6(5):705-708.
- Awote OK, Adeyemo AG, Igbalaye JO, Awosemo RB, Ibrahim AB, Omolaja BE, Abdulrafii F, Fajobi T. *In Vitro* Alpha-Amylase Inhibitory Activity, Antioxidant Activity and HPLC Analysis of *Eichhornia crassipes* (water hyacinth) Methanol Extracts. *Trop J Nat Prod Res.* 2021; 5(12):2174-2181.
- Omolekan TO, Esan AM, Olaiya CO, Anjorin AJ, Aremu KA, Adeyemi HR. Comparative effects of postharvest ultraviolet light treatments on antioxidants properties, nutritional and vitamin D contents of some indigenous green leafy vegetables. *ALST.* 2021; 88:33-42
- Olaleye OO, Sofidiya MO, Ogba JO, Lasore W. Antioxidant activities of *Daniellia oliveri* (Rolfe) Hutch. & Dalziel and *Daniellia ogea* (Harms) Rolfe ex Holland (Caesalpinaceae). *Trop J Nat Prod Res.* 2020; 4(5):210-215.
- Meida NS, Purwanto B, Wasita B, Senyum Indrakila S, Soetrisno, S, Poncorini E, Cilmiaty R, Pratiwi WR, Setyandriana Y, Almahira S. Effect of Propolis Extract on Oxidative Stress Biomarker in Diabetic Wistar Rat (*Rattus norvegicus*). *Trop J Nat Prod Res.* 2022; 6(8):1193-1196.
- Török B, Sood A, Bag S, Tulsan R, Ghosh S, Borkin D, Kennedy AR, Melanson M, Madden R, Zhou W, Levine H, Torok M. Diaryl hydrazones as multifunctional inhibitors of amyloid self-assembly. *Biochem.* 2013; 52:1137–1148.
- Zain MH, Al-Ismaeel WNH, Al-Jaber GT. Cytotoxic and Antioxidant Activities of Clary Sage (*Salvia sclarea* L.) Essential Oil against AMJ-13 Cancer Cell Line. *Trop J Nat Prod Res.* 2022; 6(5):732-735.
- Ikotun AA, Egharevba GO, Obafemi CA, Owoseni OO. Ring deactivating effect on antimicrobial activities of metal complexes of the Schiff base of p-nitroaniline and isatin. *J Chem Pharm Res.* 2012; 4(1):416-422