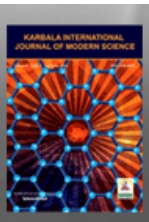
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Chemistry of Metalloguanines: An Overview of Their Synthesis Routes and Their Implementations for the Period 2000-2024

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Abstract

Guanine has a variety of roles in chemistry, from its basic function in the storing and transferring genetic information to its usages in synthetic chemistry and other fields. Because of its distinct structure and biological importance, it is a fundamental component of contemporary study in organic chemistry and molecular biology.

In this review, we focused on covering the synthetic pathways of various derivatives of guanine from the year 2000 until the present. As a result of the guanine molecule containing multiple functional groups, this gives us the ability to prepare several guanines such as O^6-alkylating guanines, O^6-benzylguanines, 8-aza-O^6-benzylguanines, 9-substituted guanines, guanine-azo derivatives, guanine Schiff bases, guanine-oxazepine derivatives and others.

Also, the guanine molecule and some of its derivatives have proven effective as chelating agents, as they coordinate with a variety of transition metal ions by behaving as ambi-, di-, and tridentate depending on the number of donor atoms of the molecules contained that leads to the formation of inorganic guanine derivatives.

A number of these guanines that have been evaluated for various bioactivities have performed well in some assays. They could therefore be used in the pharmaceutical sector to develop novel drugs.

Keywords

Biomolecules. Guanine moiety, Guanines, Organic and inorganic reactions, Purines.

REVIEW ARTICLE

Chemistry of Metalloguanines: An Overview of Their Synthesis Routes and Their Implementations for the Period 2000−2024

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Abstract

Guanine has various roles in chemistry, from its basic function in storing and transferring genetic information to its usage in synthetic chemistry and other fields. Because of its distinct structure and biological importance, it is a fundamental component of contemporary organic chemistry and molecular biology studies.

In this review, we focused on covering the synthetic pathways of various guanine derivatives from the year 2000 until the present. As a result of the guanine molecule containing multiple functional groups, this gives us the ability to prepare several guanines such as O^6-alkylating guanines, O^6-benzylguanines, 8-aza-O^6-benzylguanines, 9-substituted guanines, guanine-azo derivatives, guanine Schiff bases, guanine-oxazepine derivatives, and other guannies.

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Several of these guanines that have been evaluated for various bioactivities have performed well in some assays. Therefore, they could be used in the pharmaceutical sector to develop novel drugs.

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1. Introduction

One important category of chemical substances is biomolecules. Biomolecules can be defined as fundamental organic molecules such as fatty acids, lipids, amino acids, proteins, enzymes, hormones, carbohydrates, purines, and pyrimidines … etc., that enter living systems in all organisms in different maintenance and metabolism processes [1,2].

Biologically, guanine is one of the purines that act as nucleobases (nitrogenous bases), and it is found primarily with DNA and RNA as nucleosides and plays vital roles in organisms' bodies [3,4]. Chemically, guanine is classified as one of the fused heterocyclic organic compounds [5], and as most of these compounds, guanines have biological and pharmacological activity [6,7]. One hundred eighty years ago, German chemist Julius Bodo Unger discovered a guanine molecule in guano for the first time [8,9]. Guanine or 2-amino-1,7-dihydropurin-6-one (the IUPAC name of guanine) [10] is a white solid powder, and due to its structure, it has poor and sparingly solubility in aqueous and ethanolic solutions while can dissolve well in both DMSO and DMF solvents [11,12]. In addition, ionized guanine can be dissolved in alkalis such as NaOH and NH_3 and mineral acids [13].

The guanine molecule contains many tautomers, which are estimated at about 36 structural isomers, which are produced through exchange at the positions of the H-atoms on the molecule. Still, the most abundant tautomer of the guanine crystal is the keto-amino form (keto-N7H and keto-N9H), Fig. 1. The last form (keto-N9H) is most commonly tautomer in the aqueous solution [14−16].

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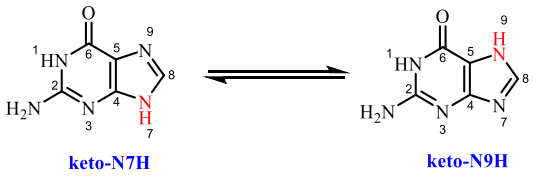


Fig. 1. The difference in the molecular structure of keto-N9H and keto-N7H guanine tautomers.

Guanine can be found in nature as nucleosides, compounds with guanine chemically bound to either deoxyribose (found in deoxyguanosine) or ribose (found in guanosine). They also contain phosphorylated sugar units. Such groups increase the solubility of guanine in its native state [17]. However, unsubstituted anhydrous guanine crystals as β-form can be found and isolated from biogenic systems (like fish, spiders, frogs, nudibranchs, bacteria … etc.) as natural sources [12,18,19].

In this literature review, we focus on guanine biomolecules and other structures based on guanine and investigate several previous and recent studies related to these molecules.

2. Synthesis and applications of organic derivatives of guanine

Guanosine and deoxyguanosine are the most well-known natural compounds of 9-substituted guanine. Due to their important physiological and biological roles [20–23], the researchers have devoted their attention to designing similar compounds of interest by conducting scientific experiments to prepare derivatives of guanine by substituting organic groups at different sites of guanine [24–26], especially after discovering penciclovir and acyclovir, shown in Fig. 2, that behave as antiviral.

Clausen F.*Pd and* Juhl-Christensen J.R [27]. surveyed the synthesis methods of 9-substituted guanines. The review discussed several methods,

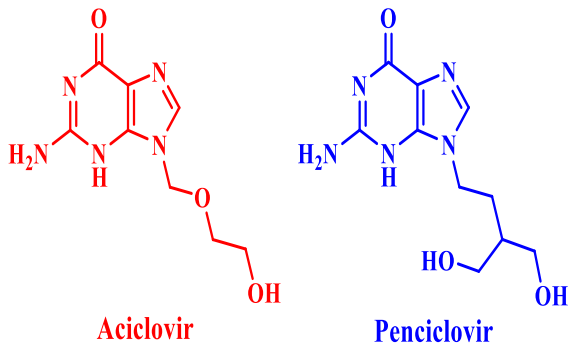


Fig. 2. The structure of penciclovir and acyclovir.

including synthesis from purines, pyrimidines, imidazoles, interconversion of adenines, and enzymatic transformations.

In 2001, Robert C. Moschel *et al*. [28] made some derivatives of 8-substituted O^6-benzyl-guanine, which were examined as tumor inhibitors through their activities in the inhibition of O^6-alkylguanine-DNA alkyl transferase (AGT) which in turn work as human DNA repair protein. Inactivation of (AGT) causes the improvement in tumor cells' response towards chemotherapeutics. This technique involved giving a mammal an effective dose of prepared chemicals with the formula to improve the chemotherapeutic drug of tumor cells by causing cytotoxic lesions at the O^6-position of guanine due to antineoplastic alkylating agent [29,30]. The structure of O^6-benzyl-8-aza-guanine and the other twelve derivatives is shown in Fig. 3, where various analyses and spectroscopic techniques characterize the prepared compounds. The antineoplastic alkylating agent activity of prepared compounds was studied versus three types of cancer cell lines (human colon cancer HT29, prostate cancer DU-145, breast cancer MCF-71) and to increase the toxicity of prepared guanines, bis-chloro-ethyl-nitroso-urea (BCNU) was used and the cancer cells were exposed to BCNU before testing the efficiency of O^6-benzyl-8-aza-guanines. All results were compared with O^6-benzylguanine and 8-aza-O^6-benzylguanine. The study shows that prepared guanines are more effective than O6-benzyl guanine and may be helpful in deactivating mutant alkyl-transferase if the correct intracellular dosage is reached. The activity of these compounds can be attributed to the presence of electron-withdrawing groups at the 8-position.

Some of the azo derivatives of guanine, Fig. 4, were prepared by Yousif H. Khalaf [31] and examined to know their biological effectiveness towards five species of pathogenic bacteria that consist (*Sh. Dysenteriae*, *E. coli*; Ps. Aeruginosa, *Str. Viridans* and *Staphylococcus aureus*). Derivatives were synthesized by a coupling reaction between guanine (as a source of amine) and a variety of diazonium salts [(*p*-chlorobenzene/*p*-bromobenzene/1-naphthalene/*p*-hydroxyphenyl and *o, p*-dihydroxyphenyl) diazonium chloride]. C.H.N. analysis, FT-IR, and electronic spectra made the identification of prepared compounds. The antibacterial study evaluated the sensitivity of selected bacteria vs. prepared compounds and minimum inhibitory concentration (MIC). To calculate MIC, eight concentrations (100, 50, 25, 20, 15, 10, 5, 1) mg/mL were used for each derivative and the results were as follows [(D1 = 50, D2 = 20, D3 = 50, D4 = 25, D5 = 25) mg/mL with *S. aureus*; (D1 = 25,

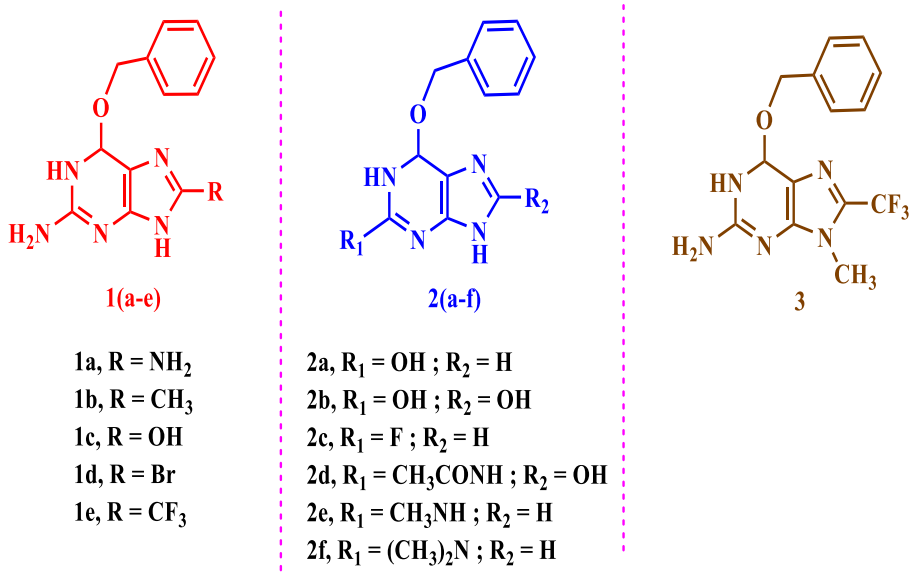


Fig. 3. The structure of prepared 8-substituted O^6-benzylguanines

D2 = 10, D3 = 50, D4 = 20, D5 = 20) mg/mL with *E. coli*; (D1 = 25, D2 = 20, D3 = 20, D4 = 20, D5 = 15) mg/mL with *Pseudomonas aeruginosa*; (D1 = 20, D2 = 10, D3 = 20, D4 = 25, D5 = 15) mg/mL with *Staphylococcus typhi* and (D1 = 20, D2 = 10, D3 = 15, D4 = 20, D5 = 15) mg/mL with *K. pneumoniae*]. The Kirby–Bauer method was applied to determine the inhibition zone, employing six concentrations (100, 50, 25, 10, 1, 0.1) mg/mL for each derivative. The results showed good activity against bacteria in high concentrations, and this is attributed to many reasons, such as the aromaticity of these compounds, which can prevent DNA polymerase III through the hydrophobic interaction, as well as the chelation ability of these compounds to capture the metals present in the bacteria cell by coordination will kill the bacteria.

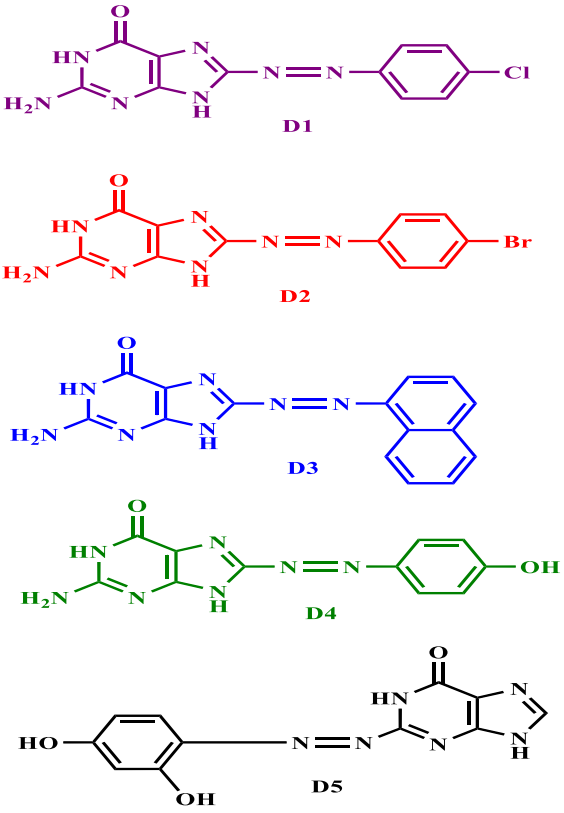


Fig. 4. The structure of some prepared azo-guanines.

In another study conducted by Shireen R. Rasool and her co-workers in 2020 [32], N-substituted heterocyclic derivatives of guanine were prepared by guanine with phthalic anhydride as starting materials and followed by an alkylation reaction to yield N-carboxymethyl substituted derivative which used to form three derivatives by reacting the N-carboxymethyl moiety (2 mol) once with resorcinol and another with ethylene glycol (1 mol), in addition to cyclization reaction to form a ring of thiadiazol. Followed by a series of reactions to create other products, as shown in Scheme 1. All produced derivatives were tested as bioactive compounds vs. selected genera of bacteria (*S. aureus* and *Pseudomonas*). Some synthetic chemicals exhibited resistance to the growth of the selected bacteria, where the results were compared with several known antibiotics. In general, the prepared compounds were more effective against *Pseudomonas* as compared to *S. aureus.*

Schiff bases and oxazepines derived from guanine were prepared by Marwa I. Khalil [33]. The study

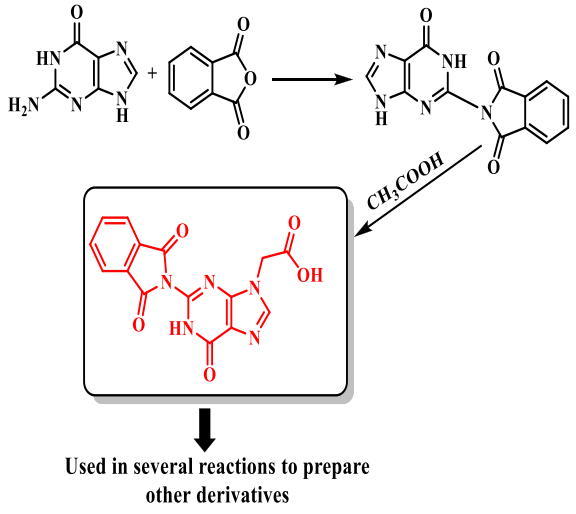
involved the formation of four Schiff bases from the reaction of guanine with diverse carbonyl compounds (4-carboxybenzaldehyde; *p*-chlorobenzaldehyde; *p*-hydroxyl benzaldehyde and isatine) by condensation reaction in an acidic medium. Synthetic imines were mixed with (maleic and phthalic) anhydrides, respectively, in dry benzene and refluxed for 6 h under 70 °C to produce eight oxazepine compounds. All prepared derivatives, Scheme 2, were identified by ^{1}HNMR and FTIR techniques.

Studies are still ongoing to prepare new organic derivatives of guanine, as we will point out in the next part of this review.

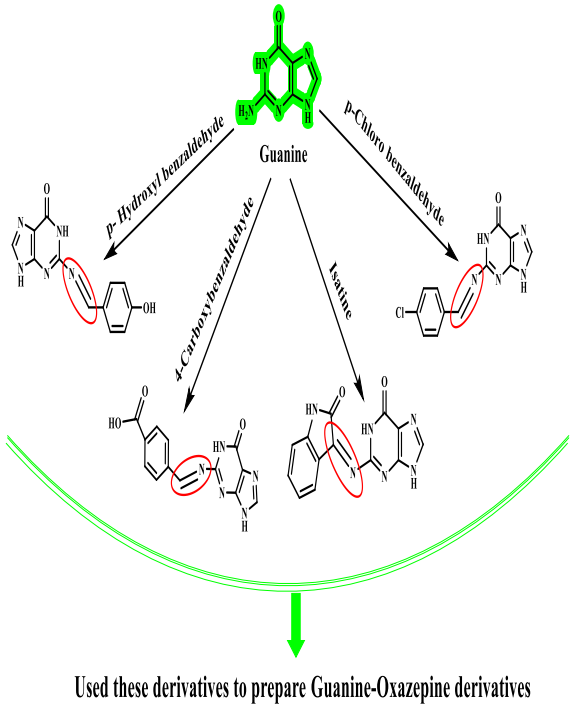
3. Synthesis and applications of metallo-guanines

A few studies were conducted after the mid-nineties, including forming some guanine complexes with different transition metal ions [34–36]. They can be considered among the first articles devoted to studying the possibility of the occurrence of the complexation between guanines and metals and identifying the chelation sites.

A study was conducted in 2002 by Kalyan K. Mukherjea and Ila Bhaduri [37]; the study used anionic guanine to prepare complexes with some metal ions [Fe^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2}, Pd^{+2}, and UO_2^{+2}], in addition, to using neutral guanine to prepare complexes with [Co^{+2} and Mn^{+2}] ions. All prepared complexes were isolated and investigated by (IR & EPR) spectroscopy and (Elemental & T.G.A.) analysis. The analysis data showed that all prepared complexes are octahedral except the Pd and Zn complexes, which are Sq.pl and Td, respectively.



Scheme 1. Preparation of N-substituted heterocyclic derivatives of guanine.



Scheme 2. Preparation of Schiff bases and oxazepines derived from guanine.

Fig. 5 shows the geometry of all complexes. We can note that the atoms of N(3), and N(9) are determined as chelation sites in anionic guanine, so it behaves as bidentate. In contrast, the molecule of neutral guanine behaves as unidentate and may coordinate either through N(9) or N(3).

In 2004, Mamdouh S. Masoud *et al.* [38] used Co^{+2}, Ni^{+2}, and Cu+2 with guanine to prepare complexes in the molar ratio 1M:2L in the complexes of Co+2 and Cu^{+2} and 2M:3L for nickel and the reaction was carried out in alcoholic-ammoniacal solutions for 2 h to yield three different complexes. All prepared complexes had the Oh structure and showed a semiconductor behavior. Fig. 6 shows that the Ni^{+2} complex involves the coordination of one metal with two molecules of guanine in addition to metallic interaction between Ni atoms. The structure of complexes was confirmed by IR, Uv.–Vis, electrical conductivity, ESR, and thermal analysis.

The complex of guanine with hafnocene was prepared, characterized, and applied as an antimicrobial in 2006 by Ekta Malhotra *et al.* [39], the idea of this work involved the formation of chelation ion in the formula $[(\eta^5\text{-}C_5H_5)_2Hf(C_5H_5N_5O)]^+$ which reacted with five different negative ions. The structure and behavior of prepared complexes were studied by ^{13}C,^{1}H NMR, IR, fluorescence, electronic spectra, and electrical and thermal properties. The used spectral techniques showed that the guanine

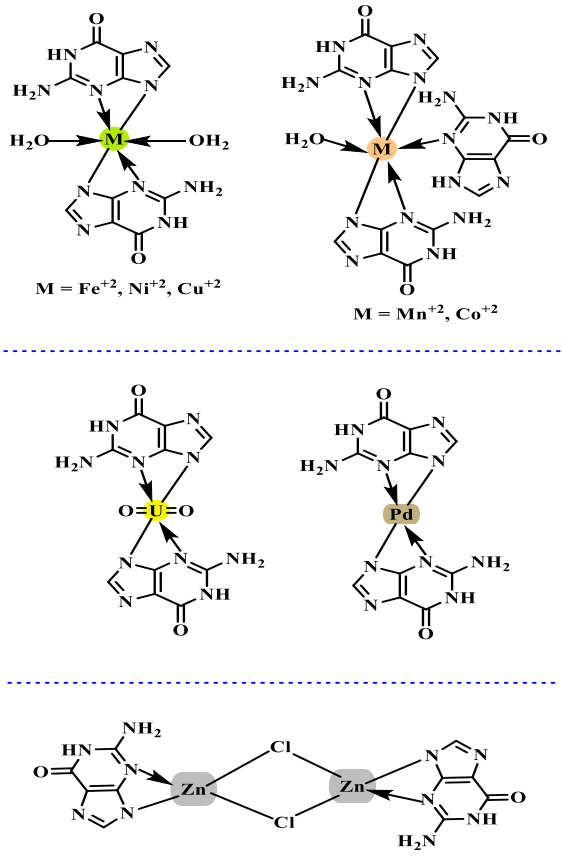


Fig. 5. The structure of some prepared N, N-guanine complexes.

chelated through O(6), deprotonated N(7) atoms, as shown in Fig. 7, and all complexes are soluble in the non-polar solvent (DMSO, DMF, THF) and considered 1:1 electrolytes. Some of the prepared complexes were tested against some bacteria (*Z.mobilis*, *P.aeruginosa*, and *E.coli*) and fungi (*Aspergillus niger* and *A.awamori*) and compared with guanine ligand at two concentrations (25 and 50)μg/mL. The biological testes data exhibited that the examined organohafnium (IV) complexes have more ability to inhibit the growth of microbes than guanine in both lower and higher concentrations.

Masoud M. S. *et al*. [40] prepared a series of complexes by reacting the various metal chlorides consisting (Co, Ni, Cd, Hg, Cu) with guanine. The elemental analysis, magnetic measurements, and spectral studies (Uv–Vis. & IR) were used to determine the geometry of prepared complexes. A different molar ratio was recorded for the prepared complexes between metal and ligand as 1:1 (for Cd and Hg complexes), 1:2 (for Co and Ni complexes), and 1:1:3 (for Co–Cu-guanine, where each atom was chelated with two ligands). All complexes were stable and insoluble in water, and the geometries of complexes were either tetrahedral, square planar, or

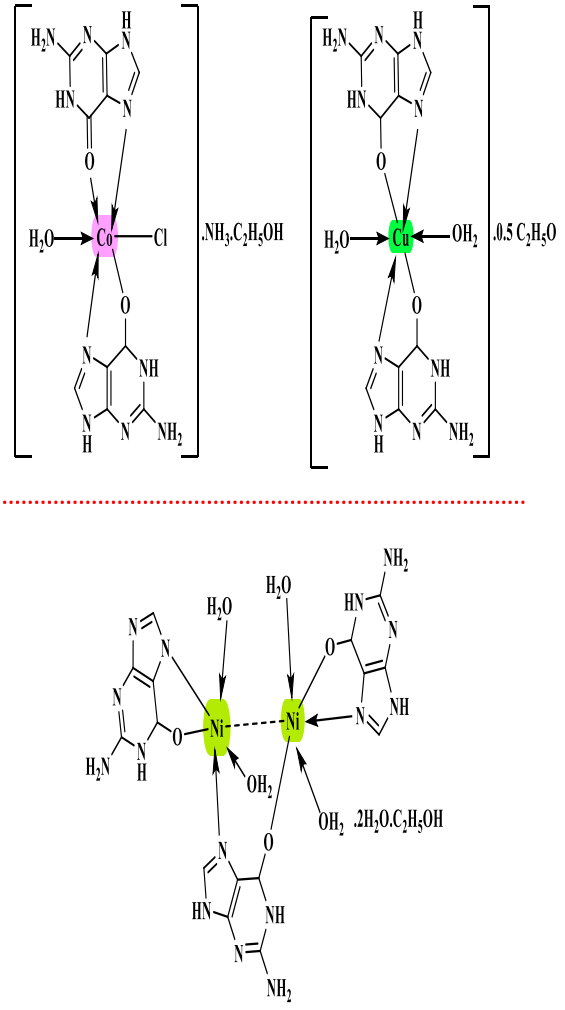


Fig. 6. Structure of some prepared O, N-guanine-complexes.

octahedral, as shown in Fig. 8. The chelating atoms were identified either from O(6) and N(7) in Co, Ni, Cd, and Hg complexes or from N(9) and N(3) in the Co–Cu-guanine complex.

One of the studies used guanine to prepare azo dye as a chelating agent which chelated with Pd(II), Pt(II), and Pt(IV) ions [41]. The work consists of forming 8-[(4-nitrophenyl) azo] guanine and studying the effect of change in the pH value on the complexes formation. This change led to the obtaining of four diverse complexes. One can note from Fig. 9 that the Pd2+ ion gave a square planar complex with a molar ratio of 1Pd2+: 2L in the pH = 8 while giving Oh complex with a molar ratio of 1Pd^{2+}: 3L at pH = 4.5. Likewise, Pt^{2+} gave a sq. pl. complex with the molar ratio 1 Pt^{2+}: 2L at pH = 7.5, and Pt^{4+} gave Oh complex as 1 Pt^{4+}: 3L molar ratio at pH = 6. The prepared ligand and its complexes were confirmed by spectral and physiochemical analysis. Job and Molar ratio methods were used to

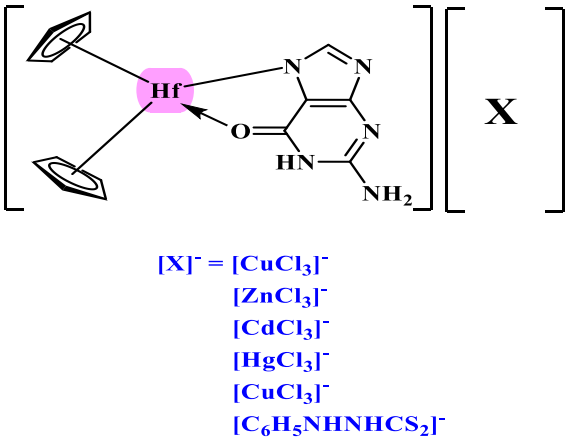


Fig. 7. The structure of some prepared O,N-guanine- hafnocene complexes.

ensure the ratio of metal to the ligand in the prepared complexes, as well as to examine the effect of time on the stability of prepared complexes. The ligand behaved as bidentate, and the coordination sites involved the N atom of the azo group and the N atom of the imine group in the imidazole ring. Tests of the ligand and its complexes' dyeing abilities on acrylic and wool produced fine, bright colors (grey, red, orange, blue-violet, and light-violet). The evaluation of antibacterial activity was performed versus positive and negative grams bacteria (*S. aureus*, *Bacillus*, *P mirabilis*, *E coli*) and was compared with metronidazole as a control. All complexes and their ligand showed greater ability to deactivate bacteria growth than control antibiotics except for *Bacillus*.

Farideh Abbasloo *et al*. [42] used a sonochemical solvothermal method to prepare a bioactive metal–organic framework based on guanine. The synthesized Bio-MOF involved a mixture of cupric cation, guanine, and 4,4`-biphenyl dicarboxylic in the ratio 2:2:3 respectively, and was identified by FE-SEM, FTIR, and XRD techniques, Fig. 10. This framework exhibits good antibacterial activity towards *P. aeruginosa* due to its high stability and surface properties, and it may be used further in medicine.

Anton Petrovich Novikov's coworker recorded a chelation of the Pd(II) ion with the N-atom of the imidazole ring of the guanine molecule in 2021 [43]. In this study, guanine behaved as a bidentate and formed a Sq. planar complex in an acidic medium, as shown in Fig. 11.

Another study was performed in 2021 by Mangesh S. Tihile and Gajanan N. Chaudhari [44]. The study included the formation of Schiff base from guanine and salicylaldehyde in an ethanolic medium

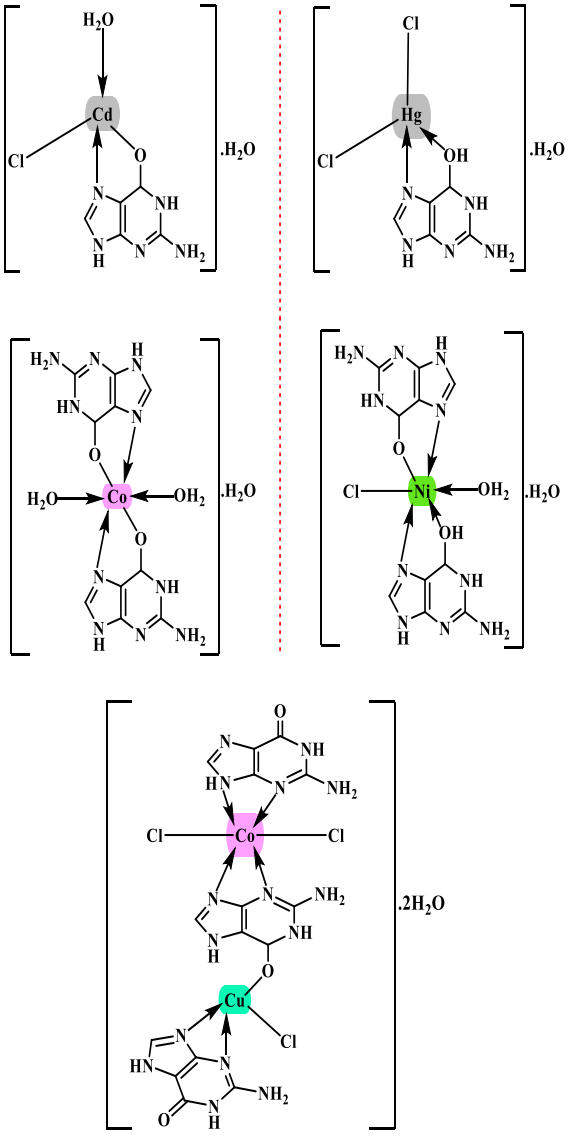


Fig. 8. The structure of prepared (Co, Ni, Cd, Hg, Cu)–guanine complexes.

catalyzed by acid and used to yield Schiff base in complexation reaction with some light metal acetate [Mn(II); Co(II); Ni(II); Cu(II) and Zn(II)] in the molar ratio (2 Schiff base: 1 metal acetate). Several spectroscopic techniques and all complexes characterized the structure of prepared compounds showed four coordination structures as tetrahedral except Cu-complex has square planar geometry, Fig. 12. The coordination atoms were determined through the N-atom of the imine group and the O-atom of the deprotonated hydroxyl group. All complexes were non-electrolytes. The bacterial growth inhibitory were evaluated vs. *S. aureus* (Gm + ve) and [*Salmonella typhi*, *E coli*, *K. Pneumonia*, *P. aeruginosa*] (Gm -ve), according to the antibacterial study the

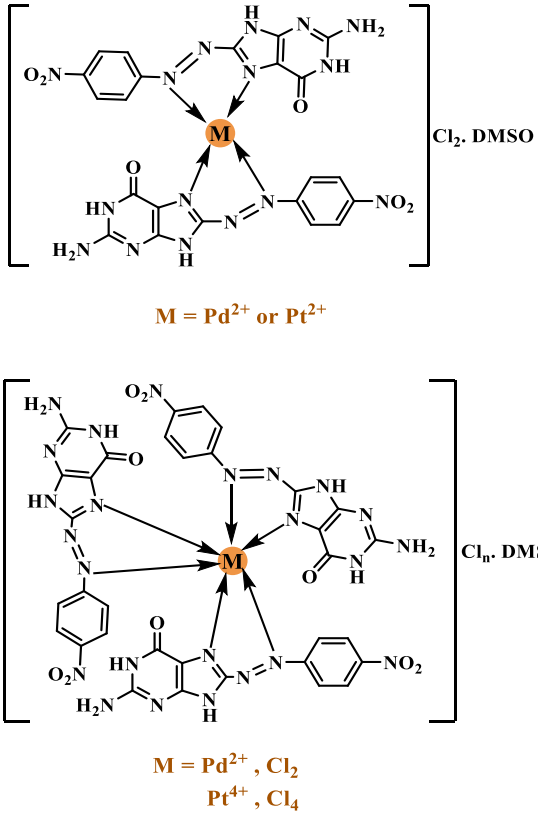


Fig. 9. The structure of prepared complexes of Pd(II), Pt(II) and Pt(IV) with 8-[(4-nitrophenyl)azo]guanine.

metal ion complexes of Ni^{2+}, Cu^{2+}, and Zn^{2+} exhibited the best inhibitory action against all bacterial strains. In contrast, the remaining complexes showed good activity against both gram + ve and gram -ve bacteria.

Also, an azo derivative of (guanine + *p*-hydroxy aniline), its Zn-complex, and ZnO nanoparticles were prepared by Sanbul H. Jerwan and his teamwork [45] in 2021. A chelating reaction between 2 mol of prepared 8-[(4-

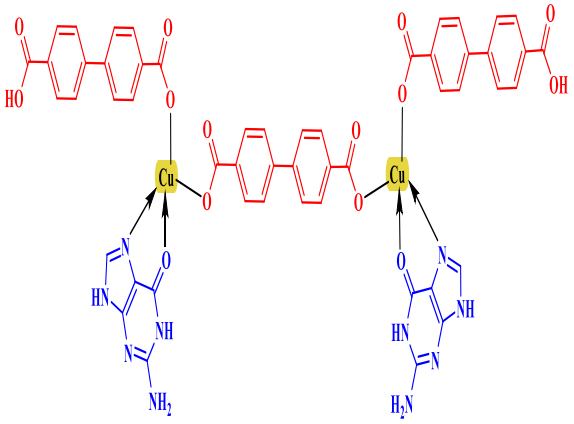


Fig. 10. The structure of prepared Cu(II)-organic framework based on guanine.

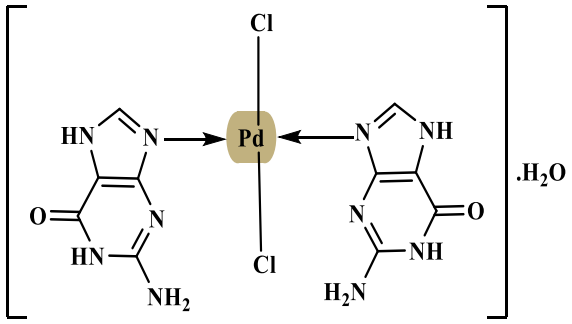


Fig. 11. The structure of prepared bis guanine-Pd(II) complex.

hydroxyphenyl) azo] guanine with 1 mol of $ZnCl_2$ at pH = 8 led to producing Zn-complexes by the coordination of Zn ion with azo-N atom and imine-N atom in imidazole ring, as shown as in Fig. 13. Spectrophotometric identification was carried out on the produced azo ligand and its complex by utilizing infrared, and UV–Visible spectra and micro-elemental analysis. After this, nanoparticles of ZnO were made using a thermal breakdown technique, and by using an XRD, AFM, and SEM, researchers were able to determine the structural properties. The study involved the evaluation of the bioactivity of both prepared Zn(II) compounds against *S. aureus*, *Ps. aeruginosa*, and *E.* coli; when it came to these bacterial genera, we found that the nano-ZnO outperformed Zn-complex.

In 2022, Saif Din K. Alzamili and Mohammed H. Shamran prepared an azo compound derived from guanine and 4-amino antipyrine in an alkaline medium [46]. The prepared compound was used as a ligand to prepare some complexes of Cobalt and Zinc divalent ions. According to different spectrum analyses and physical characteristics, Co2+ and Zn2+ seemed to have an Oh structure, and the azo-guanine appeared at three sites for chelation, as demonstrated in Fig. 14. Complexes were produced in the ratio of 1 metal:2 ligand and had an electrolyte nature. In addition, the prepared compounds

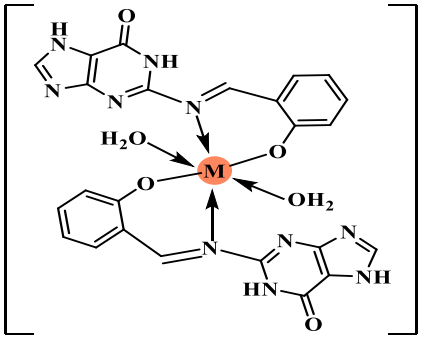


Fig. 12. The structure of some complexes of guanine Schiff base.

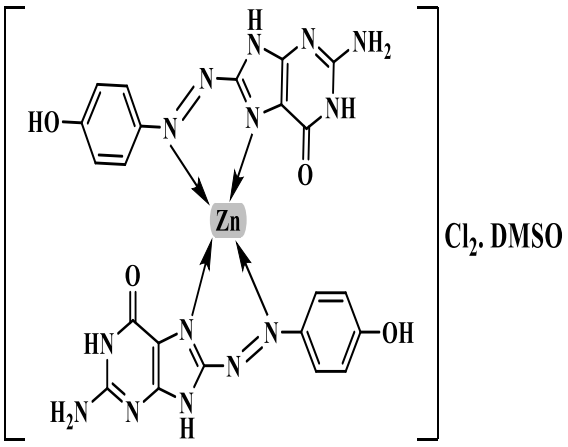


Fig. 13. Show the structure of Zn(II) with 8-[(4-hydroxyphenyl) azo] guanine.

showed crystalline patterns and nano-sized particles. The antibacterial test and MTT-assay assay were applied to all prepared compounds, and the ligand and its complexes were examined against *E. coli* and *S. aureus* when the results revealed that the complexes were more effective than their ligand. The MTT-assay of ligand and Zn-complex results versus HdFn and MCF-7 cell lines showed that both compounds had a low potential for cytotoxicity vs. HdFn cells and a significant capacity for toxicity towards MCF-7 cells. Compared to ligand, the zinc complex had a greater potential for cytotoxicity vs. MCF-7 cells.

A solvent-free reaction was conducted in 2023 by Jamilu Jaafar *et al*. [47]; the reaction involved the formation of tris[guanine]chromium $^{(III)}$ by coordinating the N(imine) in pyrimidine ring and deprotonated N(amine) in imidazole ring and show the octahedral geometry, Fig. 15, in the ratio of 3L:1M and did not conduct any electricity. The sites of chelation and structure were confirmed by FTIR and electronic spectra in addition to other physiochemical measurements. Some *in vitro* biological tests were performed on the ligand and its complex (antioxidant, and antimicrobial), the result of antimicrobial tests on a number of pathogenic organisms including the bacterial strains (*K. pneumoniae*, *S. typhi*, *B. subtilis*, and *Staphylococcus pyogenes*) and the fungal isolates consists (*C. albicans* and *Aspergillus fumigatus*) by using two concentration [500 & 1000] μg/mL of examined compounds, it appeared that the $Cr^{(III)}$-complex was more effective to inhibit the growth of selected microbes than guanine. Both were more effective than controlled drugs. Moreover, the antioxidant test results showed a little bit of action of both guanine and its complex.

Hamad. M. A. Hasan *et al*. prepared additional complexes with guanine [48]. Preparing guanine complexes with metal ions (Pb^{2+}, Mn^{2+}, Fe^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Cr^{3+}, and Fe^{3+}) was the work's main objective. Physical-chemical and spectroscopic methods, including: UV–visible spectra, infrared, metal content, and molar conductivity were used to characterize the complexes. The molar ratio approach yielded a molar ratio (1:2) for the guanine to metal ion conversion. Using spectrophotometry, the dissociation constants of guanine ligands were found. Contrarily, polar solvents were used to investigate the impact of solvents on the electronic spectra of guanine ligands. According to the FTIR spectrum, the coordination was done through the exocyclic NH_2 nitrogen atom.

In vitro tests were conducted to assess the bioefficiency of metal complexes and their guanine ligand towards specific fungi (*A. niger*) and bacterial

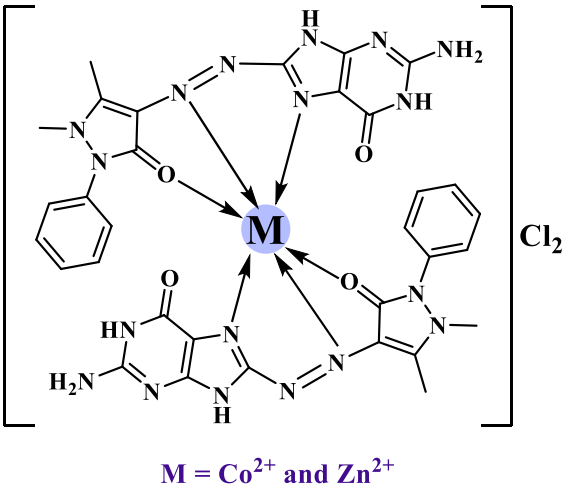


Fig. 14. The structure of complexes of Co^{2+} and Zn^{2+} with 8-(4-(antipyrinyl)azo)-guanine.

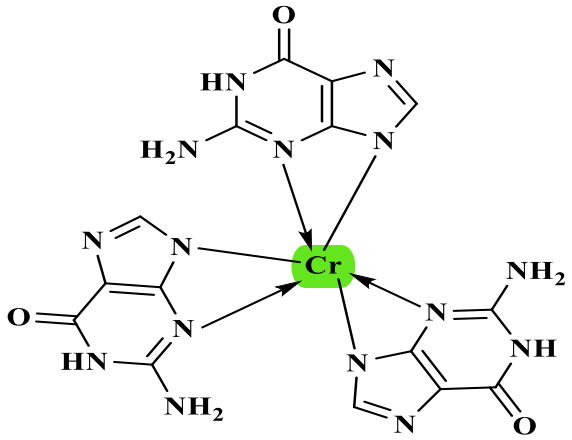


Fig. 15. The structure of tris-guanine chromium (III) complex.

species (*E. coli* and *Streptococcus*). The organisms under test exhibited satisfactory spectra, according to the findings.

Additionally, in the research conducted by Hasan S. Mohammed and Saif D. K. Alzamili, an azo ligand was produced from guanine and 2-methoxyaniline [49]. The prepared azo-ligand (8-[2-methoxyphenyl azo]-guanine) was isolated and identified and then used to complex with chlorides of Cu(II) and Zn(II) in the ratio of 2L:1M by conventional reaction. The complexes also were isolated and recognized through various spectral and analysis methods. The azo-ligand could behave as tridentate, and the complexes have six-coordinate structures characterized by: they were electrically conductive, nanoparticles, and crystalline. In addition, the azo-ligand might be used as a colorimetric sensor where it was tested with some ions (Co(II), Ni(II), Cu(II), and Zn(II)) in an aqueous solution. Fig. 16 shows the structure of azo-ligand and its complexes. Using sabouraud agar and the diffusion method, the compounds' in-vitro antifungal activity was evaluated against *A. niger*. Compared to azo-ligands, all of the produced complexes exhibited greater antifungal activity.

Asmaa E. Fadhil and Alyaa Kh. Abbas prepared two azo dyes derived from guanine with their different metal complexes, and they were published in three separate research papers [50–52]. The first derivative consists of guanine and diazonium salt of 4-amino-2-chlorophenol, this dye is used as a ligand to produce some complexes by reacting with $ZnCl_2$, $AgNO_3$, and $CdCl_2$ in the ratio (1L:1M) and reacting with $CuCl_2.6H_2O$ in the ratio (2L:1M). All prepared compounds were distinguished by spectral methods. The ligand and its complexes showed high thermostability and photostability and can be employed in the industry of dye wool. The ligand acted as neutral N,N-bidentate, and all prepared complexes had Td geometry except Cu-complex, which showed Oh geometry as shown in Fig. 17 [50].

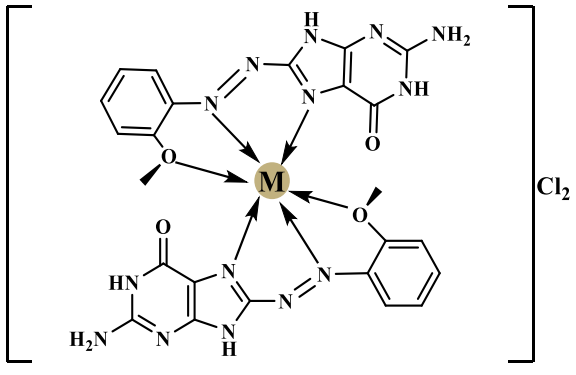


Fig. 16. The structure of Cu(II) & Zn(II) with 8-[2-methoxyphenylazo]-guanine.

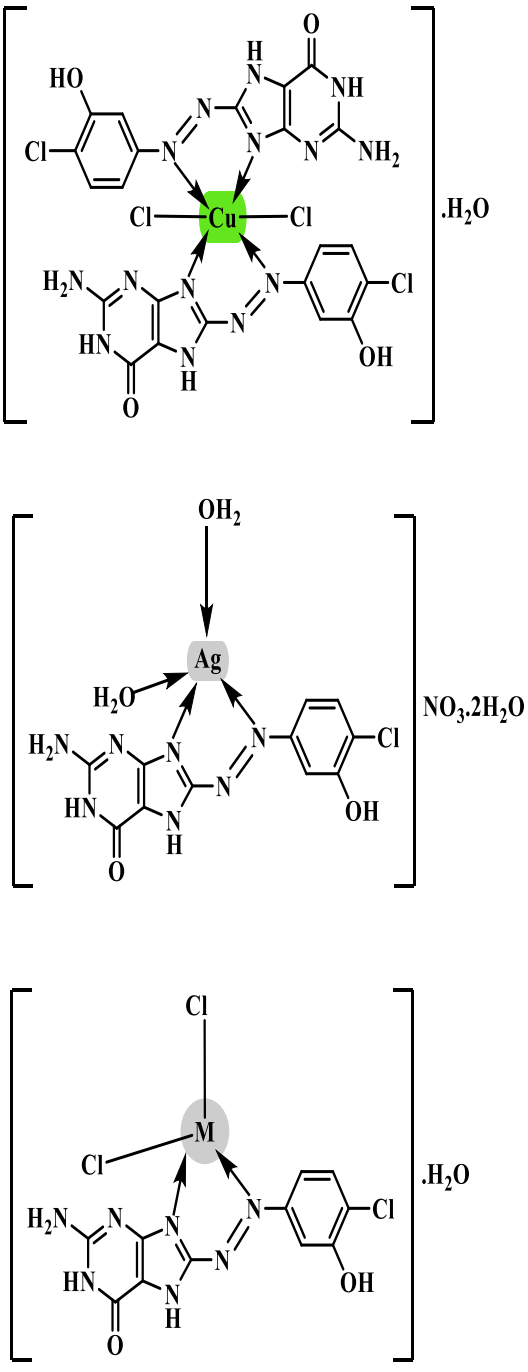


Fig. 17. The structure of some complexes of 8-[(4-chloro-3-hydroxyphenyl)azo]-guanine.

Both copper and silver complexes and their ligand were evaluated as fungicide vs. *Candida*, bactericide in relation to the two kinds of bacteria (*S. aureus*, and *Klebsiella pneumonia*), and antioxidant [51]. This investigation demonstrated the presence of greater biological activity and for all substances (the ligand and its complexes). Where ligand and its complexes showed convergent results in comparison with control. As an antioxidant, the ligand outperformed the Ag-complex.

The second azo ligand was formed by the reaction between diazonium salt of m-aminobenzoic acid and guanine [52]. Zinc (II) and silver (I) ion complexes of this azo-ligand were prepared and investigated by various spectral and analysis ways, the ligand behaved as N,N-bidentate and formed tetrahedral complexes with both metal ions in the ratio [1M:1L], Fig. 18. The ligand and its complexes

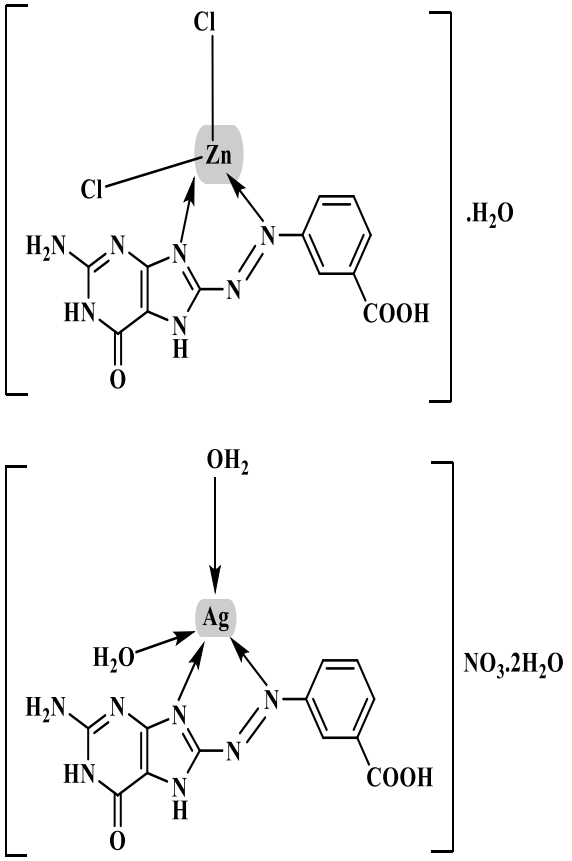
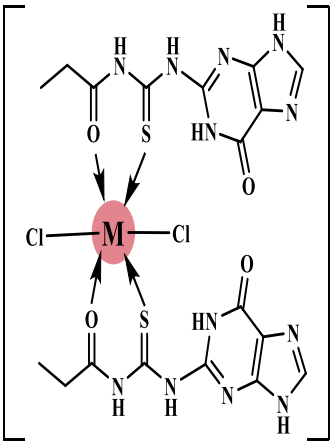


Fig. 18. The structure of Zn(II) & Ag(I) complexes with 8-[1-(3-carboxy) azo]-guanine.



M = Pd(II); Mn(II); Co(II); Ni(II); Cu(II); Zn(II), and Cd(II)

Fig. 19. The structure of some complexes with N-((6-oxo- 6,9-dihydro-1H-purin-2-yl)carbamothioyl)propionamide.

showed high thermal stability, and by applying the dyeing performance test, it was found that they could be used as good dyes for wool fibers. Both prepared azo-ligands in the studies mentioned [50,52] may be utilized as an indicator in acid-base titration methods.

The study was conducted by Abdullah Sh. Abdullah Alani *et al.* [53] involved the preparation of substituted guanine by reacting its amine group with propionyl isothiocyanate to make a novel ligand that is used to coordinate with a series of metal ions including [$Pd^{(II)}$; $Mn^{(II)}$; $Co^{(II)}$; $Ni^{(II)}$; $Cu^{(II)}$; $Zn^{(II)}$, and $Cd^{(II)}$]. The ligand behaved as S, O-bidentate where chelated from the sulfur atom of the thioamide group (C]S) and the neighboring oxygen atom of the amide group (C]O) to produce nonelectrolyte octahedral complexes, which was demonstrated by techniques involving [^{1}H,^{13}C NMR; CHNS.; Uv–Vis.; FTIR; FAA; magnetic susceptibility; melting point; and molar conductivity]. The structure of the ligand and its complexes are shown in Fig. 19. The bioactivities of these guanines are summarized in Table 1.

4. Conclusion

Guanine is an important chemical compound whose structure and function continue to be of great interest in both basic scientific research and applied

Table 1. Summary of bioactivity of studied guanines.

Guanine Derivative	Bio-application	Results	Studied by	Ref.
8-Substituted O^6-benzyl-guanine	Antitumor vs. (human colon cancer HT29, prostate cancer DU-145, breast cancer MCF-71)	O^6-benzyl-8-aza-guanines are more effective than O^6-benzyl-guanine by increasing the inhibition of O6-alkylguanine- DNA alkyl transferase (AGT), leading to increased responses to chemotherapy.	Robert C. Moschel *et al.*	[28]
(D1) 2-Amino-8-((4-chloro phenyl) diazenyl)- 1,9- dihydro -6H-purin-6-one **(D2)** 2-Amino-8-((4-bromophenyl) diazenyl)-1,9-dihydro -6H-purine-6-one **(D3)** 2-Amino-8-(naphthalen-1-yl diazenyl)-1,9-dihydro -6H-purin-6-one **(D4)** 2-Amino-8-((4-hydroxyphenyl) diazenyl)-1,9-dihydro -6H-purin-6-one **(D5)** 2-((2,4-dihydroxyphenyl)diazenyl)-1,9-dihydro-6H-purin-6-one	Antibacterial vs. *S. aureus* *E. coli* *P. aeruginosa* *S. typhi* *K. pneumoniae*	D2 is often the most efficacious compound, with the pattern of ascending inhibition as follows: D2 > D4, D5 > D1, D3 with *S. aureus* D2 > D4, D5 > D1> D3 with *E. coli* D5 > D2, D3, D4 > D1 with *P. aeruginosa* D2 > D5 > D1,D3 > D4 with *S. typhi* D2 > D3,D5 > D1,D4 with *K. pneumoniae*	Yousif H. Khalaf	[31]
N-substituted heterocyclic derivatives of guanine	Antibacterial vs. *S. aureus* *P. aeruginosa*	The prepared compounds were more effective against *Pseudomonas* than *S. aureus*.	Shireen R. Rasool *et al.*	[32]
Organohafnium (IV) complexes $[(\eta^5\text{-}C_5H_5)_2Hf(C_5H_5N_5O)]^+$	Antibacterial vs. *E. coli* *P. aeruginosa* *Z. mobilis* Antifungal vs. *A. niger* *A.awamori*	The prepared O, N-guanine-hafnocene complexes are more effective than guanine at (25 and 50)g/mL in inhibiting the growth of microbes.	Ekta Malhotra *et al.*	[39]
8-[(4-nitrophenyl)azo]guanine (L) complexes of Pd(II), Pt(II) and Pt(IV).	Antibacterial vs. *E. coli* *S. aureus* *Bacillus* *P mirabilis*	All complexes and their ligands showed greater ability to deactivate bacteria growth than the metronidazole standard except for *Bacillus*.	Thanaa J. Al-Hasani and Zainab S. Almaliky	[41]
Cu(II)-organic framework based on guanine	Antibacterial vs. standard and clinical strains *P. aeruginosa*	−MIC of (guanine-Cu(II)-MOF) = 400 μg/mL against standard and clinical strains. −MBC of (guanine-Cu(II)-MOF) = 700 μg/mL for standard strain only. −MBC of (guanine-Cu(II)-MOF) = 800 μg/mL for clinical strains only.	Farideh Abbasloo *et al.*	[42]
Bis ((E)-2-(2-hydroxy benzylideneamino)-1H-purin −6(7H)-one) (L) complexes of Mn(II); Co(II); Ni(II); Cu(II) and Zn(II)	Antibacterial vs. *S. aureus* *E. coli* *P. aeruginosa* *S. typhi* *K. pneumoniae*	The complexes of Ni(II), Cu(II), and Zn(II) showed more bioactivity toward bacterial species than Mn(II) and Co(II) complexes and ligands.	Mangesh S. Tihile and Gajanan N. Chaudhari	[44]
8-[(4-Hydroxyphenyl) azo] guanine Zn(II) complex. Derived ZnO-NPs	Antibacterial vs. *S. aureus* *E. coli* *P. aeruginosa*	ZnO nanoparticles exhibited greater bioactivity against bacterial species compared to the zinc complex.	Sanbul H. Jerwan *et al.*	[45]

(*continued on next page*)

Table 1. (continued)

Guanine Derivative	Bio-application	Results	Studied by	Ref.
8-(4-(antipyrinyl)azo)-guanine complexes of Co(II) and Zn(II)	Antibacterial vs. *S. aureus* *E. coli*	The complexes exhibited more efficacy than their ligands against the examined bacteria.	Saif Din K. Alzamili and Mohammed H. Shamran	[46]
	Antitumor vs. HdFn and MCF-7	The zinc complex had a greater potential for cytotoxicity compared to MCF-7 cells than its ligand, whereas the ligand and Zn-complex had a low potential for cytotoxicity compared to HdFn cells.		
N,N- tris[guanine]-Cr(III) complex	Antibacterial vs. *S. typhi* *K. pneumoniae* *B. subtilis* *S. pyogenes* Antifungal vs. *C. albicans* *A. fumigatus*	The Cr(III)-complex exhibited greater efficacy in inhibiting the development of selected microorganisms compared to guanine at concentrations of [500 & 1000] μg/mL.	Jamilu Jaafar *et al.*	[47]
	Antioxidant	Both guanine and its complex exhibited little antioxidant activity against DPPH radicals.		
Guanine complexes of (Pb^{2+}, Mn^{2+}, Fe^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+}, Cr^{3+}, and Fe^{3+}	Antimicrobial vs. *A. niger* *E. coli* *Streptococcus*	−In general, the complexes exhibited increased sensitivity to Streptococcus compared to *E. coli*, with the products of Cd2+, Fe2+, and Fe3+ demonstrating superior efficacy against *E. coli*. −Mn2+ and Cd2+ complexes have superior efficacy against *A. niger* compared to other complexes.	Hamad. M. A. Hasan *et al.*	[48]
8-[2-methoxyphenylazo]-guanine complexes of Cu(II) & Zn(II)	Antifungal vs. *A. niger*	Cu(II) and Zn(II)-Complexes showed greater activity than their azo-guanine ligand.	Hasan S. Mohammed and Saif D. K. Alzamili	[49]
8-[(4-Chloro-3-hydroxyphenyl) azo]-guanine complexes of Cu^{2+}, Zn^{2+}, Cd^{2+}, and Ag^{+}	Antimicrobial vs. *Candida* *S. aureus* *K. pneumoniae*	The sequence of increasing inhibition of all studied microbes is as follows: Ag^{+}-complex > Cu^{+}-complex > L	Asmaa E. Fadhil and Alyaa Kh. Abbas	[51]
	Antioxidant	The Ag-complex exhibited more efficacy in scavenging DPPH radicals compared to the azo-guanine ligand.		

fields. Several previous review studies presented the importance of guanine, its physiological, physical, and chemical properties, and innovative preparation methods at that time. In this study, we complement what has been achieved on this topic for about 25 years.

However, there is still additional research that must focus on guanine and its derivatives through the conducting of experiments related to the detection of guanine molecules using novel sensors prepared for this purpose, in addition to different preparation methods and performing different applications on the preparation products. So, the formation of guanine, its organic and inorganic derivatives, was found to be an essential subject for investigation in this review.

Guanine molecules have various functional sites [N (1); N (2); N (3); O (6); N (7); N (9), and N (10)], which gives them the tautomeric property. These molecules are also characterized by their low solubility in most solvents. These properties make it difficult to involve guanine directly in reactions, especially alkylation reactions. As a result, protected guanines or other purines are always a favourite to start with preparative methods.

Furthermore, this study displays the metallo -guanines that initiated their preparation by using a guanine molecule, while guanine analogs such as: (guanosine, acyclovir, famciclovir, ganciclovir, … etc.), that may exhibit guanine-like behavior, are not discussed. Most previous works used guanine alone to prepare metal complexes and showed that it behaves as a bidentate ligand and coordinates from O(6) and N(7). While a few studies showed that it coordinates from N(3) and N(9), and as is known the chelate rings with five or six members exhibit greater stability in comparison to those with three, four, seven, or eight members. This is due to the high strain on the members that are larger or smaller than five or six members, and this

supports the coordination from O(6) and N(7) sites. In addition, the resonance stabilization of N(7) makes it more donating than N(3). However, spectral identification remains the basis for determining coordination sites, donor atoms, and the behavior of ligands. The other guanines that may show different donor atoms than the guanine ligand due to the modification of the structure of the guanine molecule and the presence of additional functional groups can coordinate with elements as we observed in azo derivatives for example.

These guanines can be used in diverse applications such as bio-evaluations, industrial, and nanoscience. Also, they may be used as electro-optical sensors due to their magnetic and optical properties.

Ethical information

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Conflict of interest

The authors declare that they have no competing interests.

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References

[1] S.P. Bhutani, Chemistry of biomolecules, 2nd ed., CRC Press-Taylor and France Group, LCC. 2020 https://doi.org/10.1201/9780429266423.
[2] D.P. Lakshmi, Sh Manchineella, Th Govindaraju, Biomolecules-derived biomaterials, Biomaterials 230 (2020) 1–49, https://doi.org/10.1016/j.biomaterials.2019.119633.
[3] P. Vidhi, M.P. Anthony, J.B. Stephen, Human de novo purine biosynthesis, Crit. Rev. Biochem Mol. Biol. 56 (2021) 1–16, https://doi.org/10.1080/10409238.2020.1832438.
[4] J.R. Štoček, M. Dračínský, Tautomerism of guanine analogues, Biomolecules 10 (2020) 1–10, https://doi.org/10.3390/biom10020170.
[5] O. Asmaa, Review article; anticancer activities of some fused heterocyclic moieties containing nitrogen and/or sulfur heteroatoms, AJPS (Asian J Plant Sci) 62 (2020) 39–54, https://doi.org/10.21608/ajps.2020.1183.75.
[6] J. Baranwal, S. Kushwaha, S. Singh, A. Jyoti, A review on the synthesis and pharmacological activity of heterocyclic compounds, Curr Phys. Chem. 13 (2023) 2–19, https://doi.org/10.2174/18779468.13666221021144829.
[7] Sh Vikas, G. Mohit, K. Pradeep, Sh Atu, A comprehensive review on fused heterocyclic as DNA intercalators: promising anticancer agents, Curr. Pharmaceut Des. 27 (1) (2021) 15–42, https://doi.org/10.2174/1381612826666201118113311.
[8] Sh Robert, Chemistry of guanine and its biologically significant derivatives, Prog. Nucleic Acid Res. Mol. Biol. 8 (1968) 73–112, https://doi.org/10.1016/S0079-6603(08)60544-9.
[9] B.K. Sharma, A. Lal, D.K. Singh, Quantum chemical study of hydrogen bonded guanine-water complexes, IJRSI 10 (2023) 28–35. https://ideas.repec.org/a/bjc/journl/v10y2023i1p28-35.html.
[10] J.S. Al-Otaibi, Y. Sh Mary, Y.S. Mary, A.M. Nivedita, A.S. Balachandar, Investigation of the adsorption of a DNA based purine derivative on N/B-doped coronene and coronene by means of DFT and NCI interaction analysis, J Mol Liq 367 (2022) 1–9, https://doi.org/10.1016/j.molliq.2022.120373.
[11] F. Chen, B. Wu, N. Elad, A. Gal, Y. Liu, Y. Ma, et al., Controlled crystallization of anhydrous guanine β nanoplatelets via an amorphous precursor, CrystEngComm 21 (2019) 3586–3591, https://doi.org/10.1039/C9CE00245F.
[12] D. Gur, M. Pierantoni, D.N. Elool, A. Hirsh, Y. Feldman, S. Weiner, L. Qi, Guanine crystallization in aqueous solutions enables control over crystal size and polymorphism, Cryst. Growth Des. 16 (2016) 4975–4980, https://doi.org/10.1021/acs.cgd.6b00566. .
[13] H. Haoxin, R. Xue, F. Chen, Biomineralization and properties of guanine crystals, Molecules 28 (2023) 1–24, https://doi.org/10.3390/molecules.28166138.
[14] L. Wanchun, H. Li, X. Hu, Sh Han, Systematic theoretical investigations on all of the tautomers of guanine: from both dynamics and thermodynamics viewpoint, Chem. Phys. 328 (2006) 93–102, https://doi.org/10.1016/j.chemphys.2006.06.025.
[15] Y. Li-Juan, R. Pang, Sh Tao, Y. Hong-Tao, W. De-Yin, T. Zhong-Qun, Solvent effect and hydrogen bond interaction on tautomerism, vibrational frequencies, and Raman spectra of guanine: a density functional theoretical study, J. Phys. Chem A 117 (2013) 4286–4296, https://doi.org/10.1021/jp401070m.
[16] P.V. Bharatam, O.R. Valanju, A.A. Wani, D.K. Dhaked, Importance of tautomerism in drugs, Drug Discov Today 28 (2023) 1–8, https://doi.org/10.1016/j.drudis.2023.103494.
[17] T.O.P. Paul, Bases, nucleosides and nucleotides, in: P. Ts'o, eds., Basic principles in nucleic acid chemistry. I., Academic Press, New York. 1974, pp. 453–584. https://books.google.iq/books/Bases.
[18] M.E. Pavan, F. Movilla, E.E. Pavan, F.D. Salvo, N.I. López, M. J. Pettinari, Guanine crystal formation by bacteria, BMC Biol 21 (2023) 1–9, https://doi.org/10.1186/s12915-023-01572-8.
[19] N. Pinsk, A. Wagner, L. Cohen, C.J. Smalley, C.E. Hughes, G. Zhang, M.J. Pavan, N. Casati, A. Jantschke, G. Goobes, K. D. Harris, Biogenic guanine crystals are solid solutions of guanine and other purine metabolites, J. Am. Chem. Soc. 144 (2022) 5180–5189, https://doi.org/10.1021/jacs.2c00724.
[20] G.J. Peters, A. Oosterhof, J.H. Veerkamp, Metabolism of guanosine and deoxyguanosine in mammalian lymphocytes and their influence on mitogenic stimulation, in: Purine metabolism in man-IV: Part B: biochemical, immunological, and cancer research, Springer US, Boston, MA. 1984, pp. 119–124, https://doi.org/10.1007/978-1-4757-0390-0_24.
[21] L.E. Bettio, J. Gil-Mohapel, A.L.S. Rodrigues, Guanosine and its role in neuropathologies, Purinergic Signal 12 (2016) 411–426, https://doi.org/10.1007/2Fs11302-016-9509-4.
[22] Y. Li, J. Liu, Sensing guanine and its derivatives: from molecular recognition to applications, Sens. Actuators Rep. 2 (2020) 1–15, https://doi.org/10.1016/j.snr.2020.100020.
[23] A. Camargo, A.L.S. Rodrigues, Guanosine as a promising target for fast-acting antidepressant responses, Pharmacol Biochem Behav 218 (2022) 1–8, https://doi.org/10.1016/j.pbb.2022.173422.
[24] E.D. Clercq, H.J. Field, Antiviral prodrugs–the development of successful prodrug strategies for antiviral chemotherapy, Br. J. Pharmacol 147 (2006) 1–11, https://doi.org/10.1038/2Fsj.bjp.0706446.
[25] S. Krištafor, A. Meščić, M. Cetina, S. Korunda, D. Makuc, J. Plavec, S. Raić-Malić, Synthesis, structural and conformational studies of Z-and E-isomers of fluorinated C-6 isobutenyl N-methyl thymine derivatives, J. Fluor Chem. 132 (2011) 573–578, https://doi.org/10.1016/j.jfluchem.2011.06.002.

[26] D.R. Haines, C.K. Tseng, V.E. Marquez, Synthesis and biological activity of unsaturated carboacyclic purine nucleoside analogs, J. Med. Chem. 30 (1987) 943–947, https://doi.org/10.1021/jm00388a.036.
[27] F.P. Clausen, J.R. Juhl-Christensen, Synthesis of 9-substituted guanines, Review 25 (1993) 373–401, https://doi.org/10.1080/00304949309457.984. OPPI.
[28] R.C. Moschel, A.E. Pegg, M.E. Dolan, M.Y. Chae, Substituted O6-benzyl-8-aza-guanines and 6 (4)-benzyloxypyrimidines, U.S. Patent. 6172070 (2001) 1–20. https://patents.google.com/patent/US6172070.
[29] J. Ferrís, O. Berbel, J. Alonso-López, J. Garcia, J.A. Ortega, Environmental non-occupational risk factors associated with bladder cancer, Actas. Urol. Esp. 37 (2013) 579–586, https://doi.org/10.1016/j.acuroe.2013.02.008.
[30] D. Karati, K.R. Mahadik, P. Trivedi, D. Kumar, Alkylating agents, the road less traversed, changing anticancer therapy, Curr. Med. Chem. Anticancer Agents. 22 (2022) 1478–1495, https://doi.org/10.2174/1871520621666210811105344.
[31] Y.H. Khalaf, Synthesis a number of azo compounds derived from guanine and studying their biological activity on pathogenic bacteria, JUAPS 2 (2008) 38–45, https://doi.org/10.37652/juaps.2008.15646.
[32] S.R. Rasool, N.M. Aljamali, A.J. Al-Zuhairi, Guanine substituted heterocyclic derivatives as bioactive compounds, Biochem Cell Arch 20 (2020) 3651–3655. https://connectjournals.com/03896.20.20.20.3651.
[33] M.I. Khalil, Synthesis and characterization of new oxazepine compounds derived from guanine, Mater, Today Proc. 45 (2021) 4960–4963, https://doi.org/10.1016/j.matpr.2021.01.389.
[34] A.T. Tu, C.G. Friederich, Interaction of copper ion with guanosine and related compounds, Biochemist 7 (1968) 4367–4372, https://doi.org/10.1021/bi00852a032.
[35] J.A. Carrabine, M. Sundaralingam, Stereochemistry of nucleic acids and their constituents. VIII. Metal binding studies. Crystal structure of a guanine-copper chloride complex, a trigonal-bipyramidally coordinated copper, J. Am. Chem. Soc. 92 (1970) 369–371, https://doi.org/10.1021/ja00705a601.
[36] C.M. Mikulski, L. Mattucci, Y. Smith, T.B. Tran, N.M. Karayannis, Guanine complexes with first row transition metal perchlorates, Inorg Chim Acta 80 (1983) 127–133, https://doi.org/10.1016/S0020-1693(00)91273-8.
[37] K.K. Mukherjea, I. Bhaduri, Metallo-guanines and metallo-guanosines, transit, Met. Chem. 27 (2002) 22–26. https://link.springer.com/article/10.1023/a:1013498816933.
[38] M.S. Masoud, A.A. Soayed, A.E. Ali, Complexing properties of nucleic-acid constituents adenine and guanine complexes, Spectrochim. Acta. A. Mol. Biomol. Spectrosc. 60 (2004) 1907–1915, https://doi.org/10.1016/j.saa.2003.09.025.
[39] E. Malhotra, N.K. Kaushik, H.S. Malhotra, Synthesis and studies of ionic chelates of hafnocene with guanine, NIScPR 45 (2006) 370–376. https://nopr.niscpr.res.in/handle/123456789/19972.
[40] M.S. Masoud, A. El-Merghany, M.Y. Abd El-Kaway, Synthesis and physico-chemical properties of biologically active purine complexes, Synth React Inorg Met Org Chem 39 (2009) 537–553, https://doi.org/10.1080/15533170903327844.
[41] T.J. Al-Hasani, Z.S. Almaliky, New Pd and Pt complexes of guanine–azo dye: structural, spectroscopic, dyeing performance and antibacterial activity studies, IJS 56 (2015) 2718–2731. https://ijs.uobaghdad.edu.iq/index.php/eijs/article/view/9449.
[42] F. Abbasloo, S.A. Khosravani, M. Ghaedi, K. Dashtian, E. Hosseini, L. Manzouri, S.S. Khorramrooz, A. Sharifi, R. Jannesar, F. Sadri, Sonochemical-solvothermal synthesis of guanine embedded copper-based metal-organic framework (MOF) and its effect on oprD gene expression in clinical and standard strains of Pseudomonas aeruginosa, Ultrason Sonochem 42 (2018) 237–243, https://doi.org/10.1016/j.ultsonch.2017.11.035.
[43] A.P. Novikov, M.A. Volkov, A.V. Safonov, M.S. Grigoriev, E. V. Abkhalimov, Synthesis and characterization of new guanine complexes of Pt (IV) and Pd (II) by X-Ray diffraction and Hirshfeld surface analysis, Cryst 11 (2021) 1–14, https://doi.org/10.3390/cryst11111417.
[44] S.T. Mangesh, N.Ch Gajanan, Synthesis, characterization, magnetic susceptibility and antibacterial screening of novel transition metal ion complexes of (E)-2-(2-hydroxybenzylideneamino) -1H-purin-6(7H)-one, IJSRST 9 (2021) 676–682. https://ijsrst.com/home/issue/view/article.php?id=IJSRST2196108.
[45] S.H. Jerwan, Y.H. Khalaf, A.M. Mohammed, Synthesis of ZnO nanoparticles from azo complexes and study their biological activity, SRP 12 (2021) 350–358. https://www.sysrevpharm.org/abstract/67642.html.
[46] S.K. Alzamili, M.H. Shamran, Synthesis, characterization and biological activity of azo guanine and its complexes, Res. J. Chem. Environ. 26 (2022) 129–141, https://doi.org/10.25303/2610rjce.1290141.
[47] J. Jamilu, B.Y. Umar, Sh Ishaq, Solvent free synthesis of guanine, Benzoguanamine with chromium (III) Chracterization and antimicrobial activity, Eur Acad Res 10 (2023) 4043–4052. https://euacademic.org/ArticleDetail.aspx?id=5738.
[48] H. Hasan, F. Elmagbari, A. Othman, A.N. Hammouda, Chemical and biological study of some transition metal complexes with guanine as ligand, Int. J. New. Chem. 10 (2023) 172–183, https://doi.org/10.22034/ijnc.2023.1998996.1329.
[49] S.M. Hasan, D.K. Saif, Synthesis, characterization and biological activity of azo dye derived from 2-methoxyaniline and its complexes, Int. J. Drug Deliv. Technol. 13 (2023) 395–400, https://doi.org/10.25258/ijddt.13.1.63.
[50] A.E. Fadhil, A.K. Abbas, Synthesis and structural views on new azo ligand and its metal complexes with some of their application, IJS 64 (2023) 6119–6134. https://ijs.uobaghdad.edu.iq/index.php/eijs/article/view/8499.
[51] A.E. Fadhil, A.K. Abbas, Antioxidant, antimicrobial and spectroscopic discussion of guanine azo ligand with Cu (II) and Ag (I) complexes, IHJPAS. 36 (2023) 207–220, https://doi.org/10.30526/36.4.3134.
[52] A.E. Fadhil, A.K. Abbas, Guanine metal complexes: spectroscopic studies, dying performance and as indicator, IHJPAS 37 (2024) 198–210, https://doi.org/10.30526/37.1.3242.
[53] A.S.A. Alani, B.M. Sarhan, V.D. Tripathi, Synthesis and spectral study of new guanine derivative (N-((6-Oxo-6,9-Dihydro-1H-Purin-2-yl)Carbamo-thioyl) propionamide) and its complexes with some metals ion, IHJPAS. 37 (2024) 283–296. https://jih.uobaghdad.edu.iq/index.php/j/article/view/3313.