ISSN 1068-1620, Russian Journal of Bioorganic Chemistry, 2023. © Pleiades Publishing, Ltd., 2023.

G4 Ligands and Their Interaction Diversity with G-Quadruplex

V. K. Vashistha[a, 1], A. Mittal[a], P. K. Upadhyay[a], H. Nagar[b], R. Kumar[c], H. Gupta[d], R. Bala[e], and D. K. Das[a]

[a] *Department of Chemistry, GLA University, Mathura, Uttar Pradesh-281406, India*

[b] *Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh-281406, India; Department of Applied and Bio-Sciences, Suresh Gyan Vihar University, Jaipur (Rajasthan), 302025 India*

[c] *Department of Chemistry and Chemical Sciences, Central University of Himachal Pradesh, Kangra, Himachal Pradesh, India*

[d] *School of Sciences, IFTM University, Moradabad, Uttar Pradesh, India*

[e] *Department of Chemistry, Kalindi College, University of Delhi, Delhi, India*

Received October 26, 2022; revised November 12, 2022; accepted November 20, 2022

Abstract—Cisplatin-based metallodrugs are traditionally utilized as anticancer agents. Nonetheless, these drugs have adverse effects on normal tissues since cisplatin eliminates the body amid cancerous growth cells by destroying the sequence of genomic DNA. As a result, the metallodrug structure demonstrated numerous antagonistic behaviours to the malignant tumour development system associated with nucleic acid G-quadruplex. This paper systematically explored the development of successful procedures and competent anticancer drugs that expressly collaborate, resolve, or divide G4 structures. In the therapeutic domain, we highlighted the cutting-edge G4-metallo-structures, their interface mechanisms, and the potential for use as anticancer medicines. Furthermore, this paper also describes the methodologies utilized to discriminate the binding capacity between G-quadruplex and metallo-structures. This review will help to create metallodrugs from the most significant electrical supplementary design specification to a progressively logical bio-science level.

Keywords: cisplatin, macrocycles, anticancer drugs, G-quadruplex, DNA, RNA

DOI: 10.1134/S1068162023030238

1. INTRODUCTION

G-Quadruplex is a structurally unique architecture of DNA and RNA created by the deformation of tandem repetitions of guanine sequences [1]. The G-tetrad, the architectural subunit of G-quadruplexes, is developed by joining four guanines together by eight H-bonds to generate a square planar geometry. The guanine nucleotide in the G-tetrad possess H-bonds that couple together neighbouring guanines in positions N(1), N(7), O(6), and N(2) (Fig. 1a) [2–4]. These G-tetrads are joined by four G-tracts, which represent four different lines of three nucleotide bases. In comparison to the quadrimolecular G-quadruplex, the intermediate sequences connecting two neighbouring G-tracts are extended out to form a single-stranded loop (Fig. 1b) [3]. G-Quadruplex is built when two or more parallel G-tetrads are piled over one another. Due to the presence of hydroxyl group in the pentose phosphate framework, the G-quadruplexes of RNA are thermally more stable than the G-quadruplexes of DNA in a variety of conditions [5–8]. Nonetheless, several factors including number of nucleotide strands, the polarity of the primary strands of G-quadruplexes, and the type of twists influence the conformation of DNA G-quadruplexes [9, 10]. Moreover, the type of cations and G-quadruplex binding proteins have a significant impact on G-quadruplex orientation [11–13]. The human genome has around 376000 possible G-quadruplex sequences which are found in

[1] Corresponding author: email: vinod.vashistha@gla.ac.in.

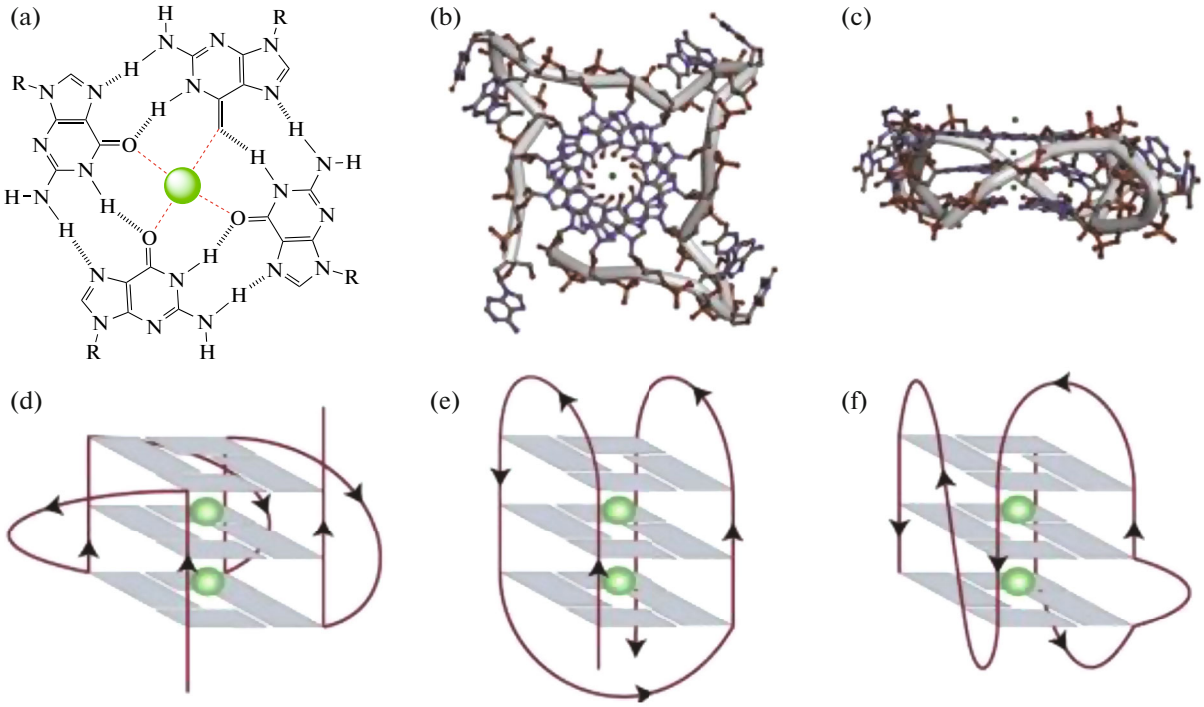

Fig. 1. Structure of G-quartet (a) consist of the central cation (shown in green) joined to O atoms and the Hoogsteen H-bonded guanines. 3D structure of human telomeric G4s structure, shown in (b) top and (c) side views; the backbone is shown as a grey tube, and the structures are color-coded by atoms. Unimolecular G4s structures are shown schematically as (d) parallel, (e) anti-parallel, and (f) hybrid structures with a bulge. Adapted from reference by Spiegel et al. [24].

numerous key gene areas like telomeres, gene promoter regions, and replicating sites [14–17].

These G-quadruplexes possess significant biological activities like inhibition of telomerase activity and regulating transcription, translation, and replication of DNA [18, 19]. The G-quadruplex has been considered as a significant cancer therapeutic agent because of their important chromosomal position as well as the presence of multiple quadruplex-driven genes [20]. Various evidence have emerged over the past two decades demonstrating the therapeutic importance of G4 nucleic acids, notably in the development of anticancer drugs. Several chemically generated G-quadruplex combinations have shown good bioactivity, for instance, a synthesized G-quadruplex, AS1411, is used as an external therapeutic agent to prevent the growth of cancerous tumors without any negative effects on healthy cells [21, 22]. Researches on AS1411 has progressively expanded in recent years, with majority of them concentrating on its usage as a nanoparticle delivery device or for tailored cancer treatment [23]. It has been reported that conformational changes in G-quadruplexes affect their stability and performance, thus, it is critical to understand which variables greatly affect G-quadruplex architectures [24] (Fig. 1).

Current breakthroughs in the investigations of physiologically significant G-quadruplexes produced in human telomeres and promoter sections of human oncogenes, and significant advancements in the creation of G-quadruplex-interactive medicines supports the G-quadruplexes as potential anticancer agents. DNA G-quadruplexes are globularly foldable nucleic acid nanostructures that could rapidly assemble in solution under physiological circumstances. The molecular architectures of intramolecular G-quadruplexes seem to vary and could thus be variously controlled and addressed by various proteins and medicines.

The use of platinum-based complexes and their analogues are gaining long-term interest as therapeutic agents in the treatment of tumour cells [25, 26]. However, nephrotoxicity, ototoxicity, and other side effects associated with such models limits their use as potential therapeutic agents. Primarily, these agents have a high potential to interact with genetic DNA structure, and thus the failure of certain internal processes, such as transcriptions and translations, eventually causing tumour cell terminations. However, it has been seen that this type of interaction between metal-drug and receptor cannot identify ordinary and unusual cells, resulting in some genuine detrimental effects in terms of response to normal cell tissues [27, 28]. Consequently, there is a need for the development of unique future models with different mechanism, and to make an assessment of the sequential cutting-edge innovation that would make a significant contri-

bution to the advances. Due to tandem repetitions of guanine sequences in DNA or RNA, G-quadruplexes wrap into certain shapes [28–30].

Furthermore, metallodrugs can be regarded as an impressive agent for developing metallodrugs to examine the newly developed potential natural targets as opposed to genomic DNA [25]. As a result, it is possible to relate the activities of metallodrugs to the organic nucleic acid G-quadruplex. Typically, the guanine-rich nucleic acid self-assembled framework of G-quadruplex reveal incredible organic framework in contrast to controlling the translation efficiently. Nevertheless, the duplex DNA translation quickly stiffens away to detach the G-rich single helix derived from the necessary C-rich helix [31].

G-quadruplex RNA is more stable than comparable G-quadruplex DNA sequences, particularly its parallel macroscopic collapse, and similar circulation throughout the cells like cytoplasm makes it relaxed to concentrate than DNA [32–35]. These auxiliary outlines are not really precisely the same as DNA duplex. Further, due to the 2°-hydroxyl groups, a number of RNA frameworks may assemble into G-quadruplex architecture in vitro [36]. Owing to these functional aspects, G-quadruplex RNA is often regarded as a possible point of focus for anticancer drugs. RNA-coordinated metallodrugs showed high selectivity against target G-quadruplex RNA [37]. Previously, the production of G-quadruplex associated with human cancer (e.g., HIV, and diabetes) [38] has been established, and the subgroups of these structures are generally considered as therapeutic targets [39].

The G4-ligands could thus only communicate clearly with G-quadruplexes, preventing the side relation with duplex DNA [40, 41]. G-quadruplex has drawn researcher's attention for their use as a centerpiece for anticancer drugs, based on designing new effective ligand-based metal drugs and understanding the effective interaction process. Metal complexes may construct the oxygenated guanine nucleic acid by encapsulating ribosyl hydrogen for oxidative DNA releases. However, tetraaza-macrocycles are shown to be reliable in assuming the actual career in DNA interaction and noticed that this interaction depends on the macrocyclic substituent mechanism [42–44].

In this review, we have highlighted the discussion of different G-quadruplexes of DNA/RNA and a summary of the G-quadruplex–ligand cooperative binding. This article will offer a significant guidance to the drug architecture and identification that reflects on G-quadruplexes and the description of G-quadruplex functions. We also summarized the identical and brief discussion about the ongoing modulations of G4 focusing on macrocycles and their coupling modes with G-quadruplexes. In addition, the overall rigidity of macrocyclic frameworks with prominent transcriptional and translational practices and their capacity as chemotherapeutic agents is regarded as the primary research focus. We have also addressed the conceptual underpinnings of G-quadruplex alteration based on macrocycles, followed by various restraint mechanisms, and G-quadruplex DNA cleavage to produce conventional anti-cancer effect.

2. THE IMPLICATIONS OF G4 AND G4-LIGANDS

G-Quadruplex play a significant role in various crucial organic processes such as DNA replication, transcription regulation, and genome stability [45–48]. Generally speaking, the creation of small molecular structures that exhibits extremely meticulous attraction and uniqueness toward the G-quadruplex over most duplex nucleic acids is highly desired. G4-ligands has been versatile and potential agents in the area of anticancer drug design [50, 51]. For example, the medication CX3543 (known as Quarfloxin) was the first-in-class in vivo G4-ligands and has been identified as stage II as diagnostic prefaces with the ultimate goal of treating neuroendocrine and carcinoid tumours. In addition, tetraaza-macrocycles and metal complexes could be fascinated as G4-ligands possessing great sensitivity and selectivity for quadruplex nucleic acids [51, 52]. The unique fundamental features such as the formal charge on metal ions, and the appealing features of tetraaza-macrocycles are the advanced functions which make them a suitable candidate for G4-ligand development. In addition, their planar, octahedral, tetragonal pyramidal, and so on geometries may provide several modes of behaviour, e.g., a planar macrocycle supports the packing approach of interaction with G-4, followed by end-stacking or intercalations.

3. G-QUADRUPLEX TARGETING METAL COMPLEXES

3.1. Cisplatin Derivatives—Platinization of G-Quadruplex

Cisplatin and its analogues are commonly connected with the best anticancer drug in clinical usage, but due to a few disadvantages, their further use is limited. In this way, it obvious to builds up another class of systematically organized cisplatin derivatives that draws much concern for the investigators. For cooperative configuration as a single site trial, cisplatin derivatives, incorporating chlorine and water ligands, have higher probability of binding to G4 DNA nucleobases. The subsidiaries of planar aromatic ligands are essentially suitable for binding with G-quadruplex stacking up to non-covalent limiting approach [53].

Bertrand and co-workers designed novel Pt(II)-based structures (Fig. 2) and observed that these structures could possess a covalent or non-covalent binding interaction without an extending interface with both the biological telomeric G-quadruplex-DNA followed by specific restrictive modes [54]. They

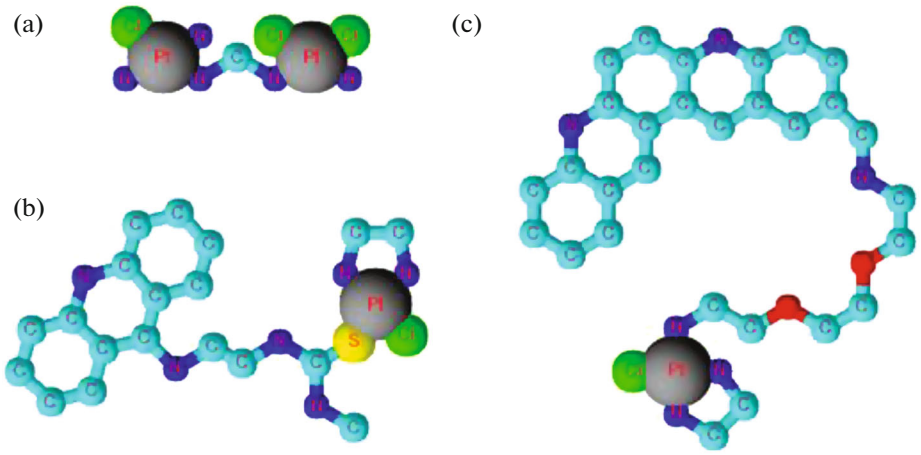

Fig. 2. Chemical structures of cisplatin (a) and their analogues as G4 ligands (b, c).

synthesised platinum-based complexes with tridentate nitrogen-containing ligands *viz.* terpyridine (2,2:6,2-terpyridine, tpy) and tolyl-terpyridine (4-(4-methylphenyl)-2,2:6,2-terpyridine, ttpy). The terpyridine-platinum based structures, referred to 'Pt-tpy' were observed to interact covalently with quadruplex-DNA by means of platinization of adenine [55]. Another arrangement, Pt-quinacridine, known as "Pt-mpq," uses quadruplex–DNA in a dual non-covalent/covalent limiting mode, concentrating on specifically the guanines that make up the outer G-groups of four.

Qin and co-workers developed a Pt(II)-phenanthroline complex (Fig. 3). This complex was reported to exhibit tumour cell-specific cytotoxicity which can be explained by hindering "telomerase movement" by the connection of "c-mycquadruplex and initiation of caspase" [56]. Further, another family of anticancer medications includes planar, non-macrocyclic polydentate metal clusters, such as square-planar Pt(II)-phenanthroline complexes. The phenanthroline moiety in these complexes might be replaced with bipyridine, phenyl pyridine, and dipyridophenazine for further modification. Pt(II) metal with positive charge play a crucial role in DNA limiting functions, despite the fact that their square-planar geometry advances the π–π stacking with G-quartets. Notwithstanding, a near report showed that the ligands groups covering the surface support the G4 bindings, for example, the Pt(II) complexes of bis-phenanthroline and phenanthroline–ethylenediamine ligands were observed to balance out the G-quadruplex configurations, seeming solid communication proclivity than the bis-bipyridine and bipyridine–ethylenediamine derivatives. In this way, the substitution of the phenanthroline by a phenanthroimidazole moiety, encompassing π-delocalization via aromatic moiety, demonstrated the improvement in the affinity and selectivity for the G4 binding [57–63]. Some detailed Pt(II) buildings with bis-phenanthroline or phenanthroline–ethylenediamine are presented in Fig. 3.

3.2. Tetraaza-Macrocycles and Derivatives

Tetraaza-macrocycles like phthalocyanines and porphyrins are normal biological macrocycles, having expanded aromatic moiety capable of promoting end-stacking cooperation with terminal G-quartets. Membrino and co-workers combined guanidino-altered phthalocyanines (GPcs) frameworks (Fig. 4) and used them as G4-DNA ligands and modulators of quality parameters [64]. GPcs displayed great cell take-up into active cells and smothered luciferase articulation. Such outcomes are reliable with G-quadruplex-supported inhibition and give the inspiration to investigate the anticancer capability of GPcs.

Ren and co-workers introduced octacationic zinc phthalocyanine (ZnPc), which was discovered to be an excellent G-quadruplex DNA stabilizer (Fig. 5). Mn based 5,10,15,20-tetra(*N*-methyl-4-pyridyl) porphyrin ($Mn^{III}TMPyP4$) macrocyclic complex was reported as G4-ligands [65]. The findings given herein demonstrate the effectiveness of ZnPc as a strong telomerase inhibitor (IC_{50} = 0.23–0.05 mm) and as a highly effective stabilizer of G-quadruplex DNA, capable of raising the Tm level of G quadruplexes by 4-258C. Through stabilization of the G-quadruplex structure generated in a low K^+ concentration buffer, it may enhance polymerase stopping in the experimentation. Surface plasmon resonance spectroscopy revealed that ZnPc could be attached to G quadruplexes preferentially. More crucially, it might cause an intramolecular G-quadruplex structural change from antiparallel to parallel, as well as parallel structure development in a cation-deficient environment. The structure formed by ZnPc in the absence of salt was slightly less stable than that generated in the Na^+ buffer.

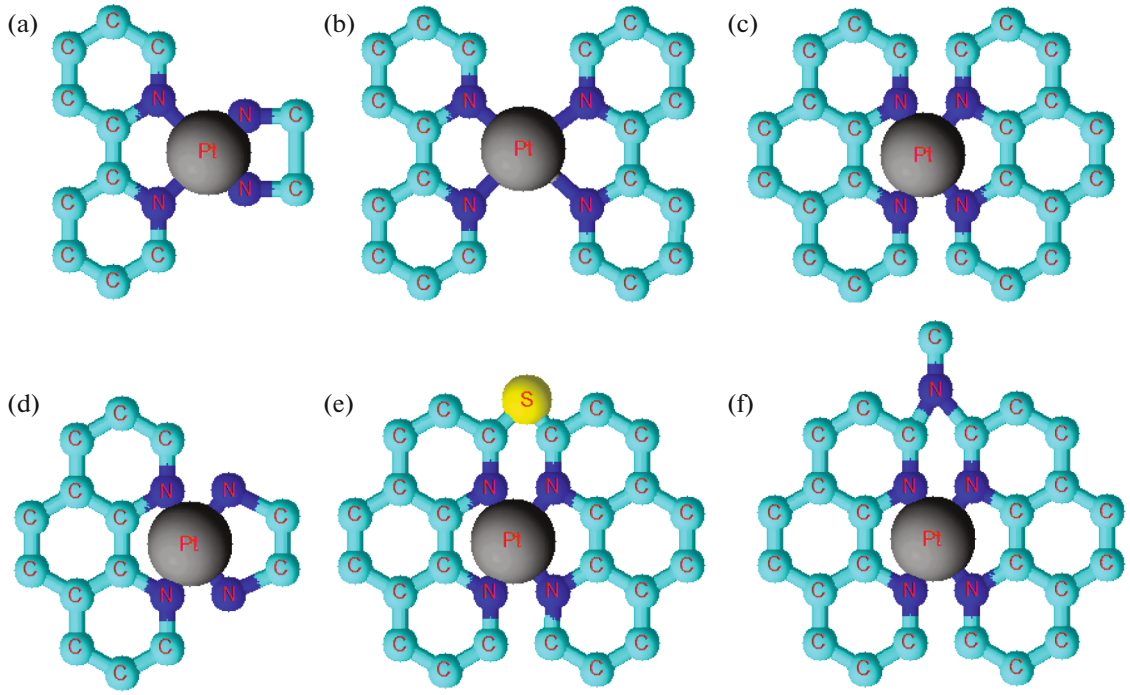

Fig. 3. (a–f) Structures of Pt complexes and derivatives as G4-ligands; these ligands involve the bidentate ligands such as ethylenediamine, bipyridine, phenanthroline, and phenanthroimidazole.

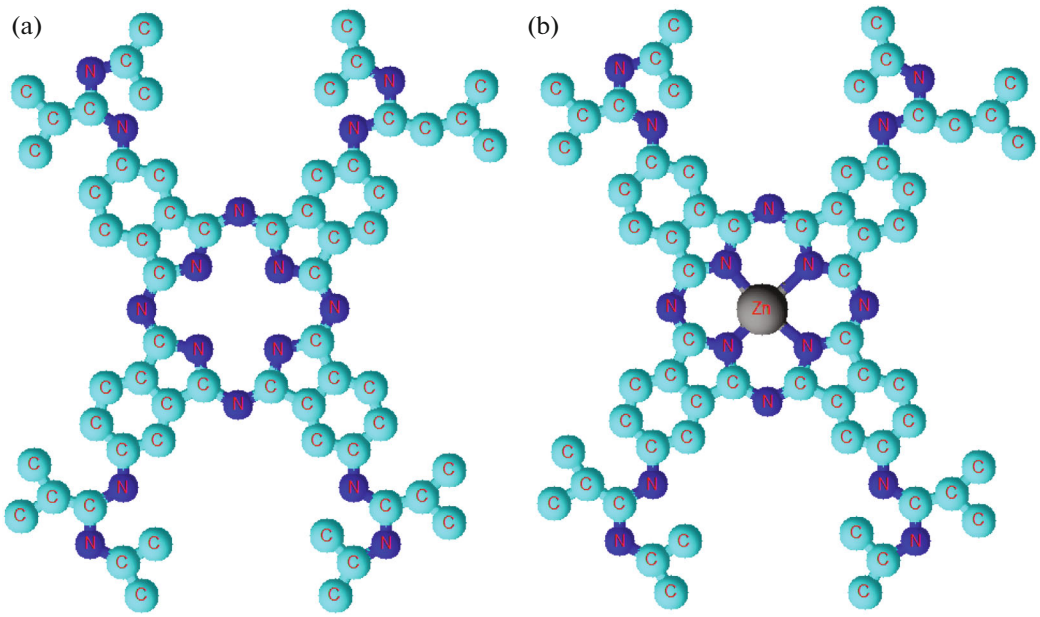

Fig. 4. Chemical structures of (a) guanidino-altered phthalocyanine ligand and (b) guanidino-altered zinc phthalocyanine, as G4-ligands.

Further, the Ni^{II}TMPyP4, in contrast to duplex DNAs, the macrocyclic complex, was shown to be a strong telomerase inhibitor and possess restricted specificity for G4 DNA. Similar to the free TMPyP4 macrocyclic framework, the Mn^{III}TMPyP4 macrocyclic complexes displayed comparable telomerase hindering capability; nevertheless, the Mn^{III}TMPyP4 macrocyclic complex exhibited 10-fold greater specificity for quadruplex versus duplex DNA [66, 67]. Furthermore, the replacement of Mn^{III} with Zn^{II} metal

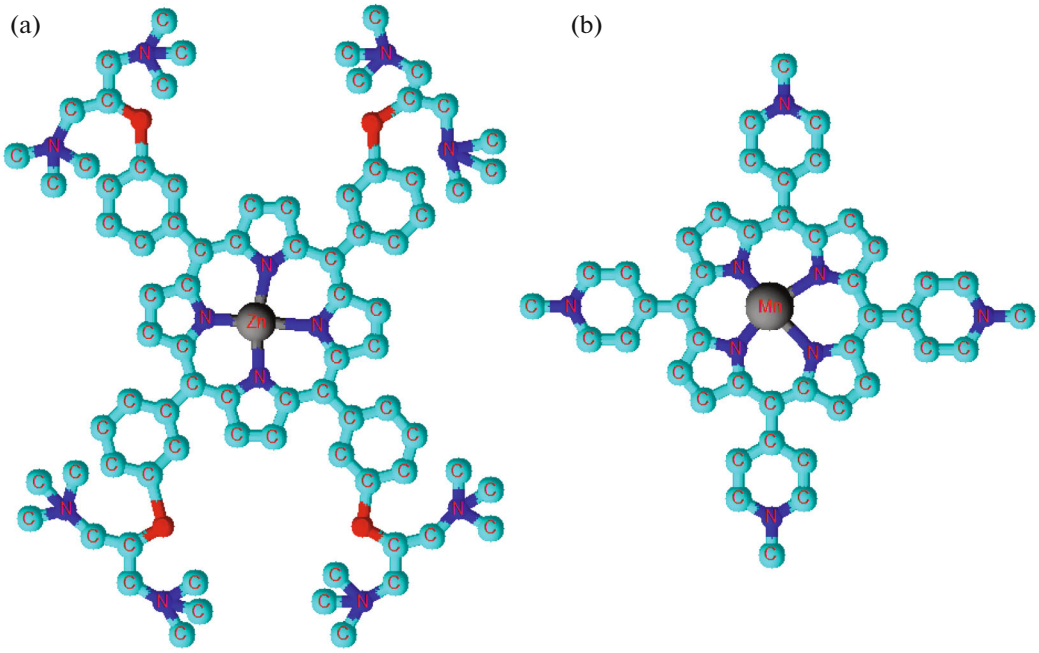

Fig. 5. Chemical structures of (a) octacationic zinc phthalocyanine (ZnPc) and (b) Mn^{III}TMPyP4.

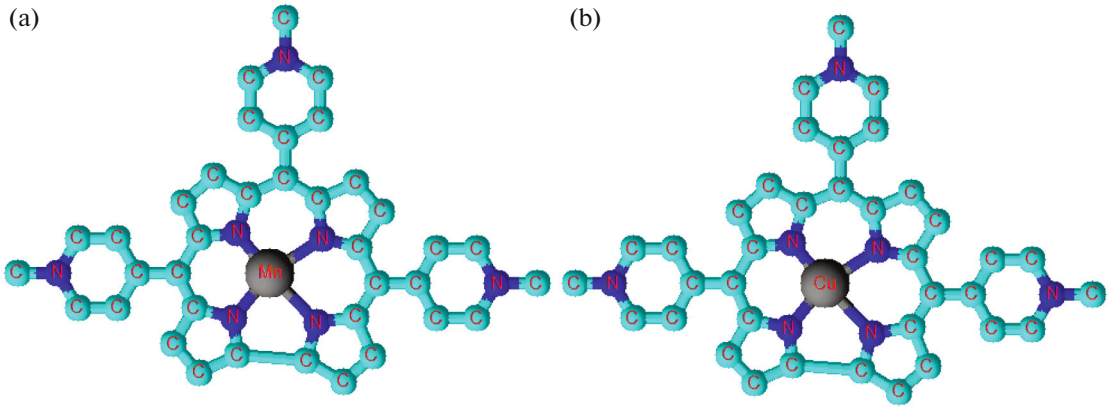

Fig. 6. Chemical structures of (a) Mn corrole and (b) Cu corrole, with cationic arms, as G4-ligands.

limits quadruplex specificity and potency, much as telomerase does [68].

Such studies revealed that the planar macrocyclic moieties and the fundamentally strong charged side arms, as well as the telomerase interference ability, which contributes to the excellent affinity for G-quadruplex. Corrole is another adaptable class of porphyrin subordinate, because of their topologies and electronic structure, the efficient adjustment of changing metal ions in the higher oxidation states. In this way, a progression of Cu^{II} and Mn^{III} corroles (Fig. 6) was accounted for as effective G4-ligands and these buildings were observed to be good telomerase inhibitors [69–71]. Strikingly, these macrocycles have normally saddle-type geometry contradicted to the planar metalloporphyrins.

Meso-methyl pyridinium-substituted Mn^{III} corrole macrocycle is another class of water-solvent and seat-formed frameworks [72, 73]. Because of their particular geometry and high e-inadequacy, these macrocycles display selectivity for G4 over duplex DNA. As indicated by the PCR-stop examination, these edifices effectively initiate and balance out the Tel and c-myc G-quadruplex DNA. Further, meso-substituted Cu^{II} corrole macrocycles, furnished pyridinium or quaternary ammonium moieties by using different types of linkers at the corrole framework, and

were additionally examined as the G4-ligands [74–76]. Such type of substituents increases the density of positive charge on corrole framework which advances the electrostatic interaction of negatively charged DNA backbone.

The formation of G-quadruplexes by certain DNA and RNA sequences has the potential to influence genetic instabilities, promoter activity, RNA splicing, RNA stability, and neurite mRNA localization. TMPyP4 has the ability to destabilise and unwind RNA G-quadruplexes, including the one seen in the MT3-MMP mRNA [77]. TMPyP4 also destabilised the G-quadruplex of DNA and RNA (CGG)n repeats of FMR1, which have been linked to premutation expansions of fragile X syndrome, fragile X-associated tremor ataxia, and fragile X preterm reproductive deficiency. [78–80] Destruction of RNA G-quadruplexes by TMPyP4 resulted into increased levels of translation in experimental models [77, 79]. Zamiri and coworkers reported the binding of TMPyP4 to the ALS-FTD r(GGGGCC)8 replication employing gel mobility shift assays, CD spectroscopy, and UV spectroscopy [81]. It was observed that TMPyP4 destabilises the binding of ASF/SF2 and hnRNPA1 to the ALS-FTD-associated r(GGGGCC)8 repeat. The significance of RAN translation remains unclear; the function of G-quadruplex with TMPyP4 may possibly influence translation. Nevertheless, there are no cellular experiments available to examine TMPyP4 impact on RAN translation.

4. THE INTERACTION MODEL OF MACROCYCLES BASED G4-LIGAND WITH G-QUADRUPLEX

Recent discoveries in G-quadruplexes have demonstrated that they could function in DNA replication, transcriptional regulation, genome stability, and cancer cells [24, 82, 83]. As a result, G-quadruplexes were discovered to be a promising anticancer agent and thus the researchers have concentrated on the construction of a tiny molecular inducer and G-quadruplex stabilizers [84]. To fulfil this, it is critical to understand how to limit the design of G-quadruplexes using G4-ligands? Till now, research on computational and physiochemical breakthroughs demonstrated mainly three types of competent limiting methodologies of G-quadruplexes with G4-ligands: (i) stacking with terminal G-quadruplicates of G-quadruplexes, (ii) interaction among G-quadruplicates of G-quadruplexes, and (iii) interaction with the grooves/loops/spine of G-quadruplexes.

4.1. Stacking with Terminal G-Quadruplicates of G-Quadruplexes

The macrocycles with aromatic moieties, and electron inadequate frameworks can result in more grounded π–π cooperations on terminal G-quadruplicates [85]. Further, the positive charge on metal ions in the macrocycle is arranged in the mid of terminal G-quadruplicates and upgrades the electrostatic adjustment. In this way, the development of macrocycles dependent on G4-ligand is a proficient methodology for the layering of end G-quadruplicates of G-quadruplexes. Thus, the official methods of macrocycles dependent on G4-ligand with G-quadruplexes were set up through π–π cooperations, which are essentially reliant on hydrophobic, electrostatic attraction, and physical associations. The large aromatic groups demonstrated great descriptiveness for G4-DNA over the duplex DNA [81–86]. TMPyP4 is a typical example of a macrocycle-based G4-ligand, that often served as folios for G-quadruplexes and the aromatic ring. Additionally, the four *N*-methylated groups of the TMPyP4 skeleton contributed to the enhancement of water solubility and π–π stacking potential [87].

Supplementary studies established that the TMPyP4 macrocyclic framework interacted on one terminal G-quadruplicate of the G-quadruplexes and have more prominent reactivity and inadequate G-quadruplex selectivity over DNA duplex [88, 89]. Going through these motivations, researchers planned Mn(III) porphyrin analogs for the favorable stacking on terminal G-quadruplicates and intercalation through its four flexible limbs with grooves. Mn(III) porphyrin complexes were required to have good sensitivity and specificity towards the G-quadruplexes [90]. Haudecoeur and collaborators structured a "keen" G4 ligand, showing the high ability to adjust their structure after intercalation with the G-quadruplexes [91]. It was demonstrated that the cationic porphyrin (i.e. TMPyP4) could attach and deform the G-quadruplex created by r(GGGGCC)8, thus, ablates the binding of either hnRNPA1 or ASF/SF. Such results demonstrated that nucleic acid interacting small molecules, like TMPyP4, can modify the conformations of the C9 or f72 repetition, thereby disrupting protein associations and preventing protein sequester and/or RAN translating into potentially hazardous dipeptides. Disrupting the secondary structure development of C9orf72 RNA repeats might be a promising curative approach, and a way to evaluate the function of RNA structure in RAN translation.

Further, it was also stated that the designed G4 ligand can interact with "G-quadruplexes" by the union of two G-quadruplexes and the grip of cooperation. In this manner, a symmetrical helical with a folio demonstrated enantio-specific for the parted pocket located between the telomeric G-quadruplexes. This chiral helix displayed a strong inhibitory movement against the telomerase of G-quadruplexes, and the outcomes gave the confirmation of the sensitivity to small particle telomerase inhibitors [92].

4.2. Intercalation between G-Quadruplicates

The observed bathochromic and hypochromic shift in the electronic absorption spectra suggested that macrocyclic complexes can easily interact with the DNA base pairs through the intercalation binding mode [93]. Interactions involving DNA and pharmaceuticals can result in chemical and structural changes, which leads to alterations in the electromechanical characteristics of nitrogenous bases.

Lubitz et al. demonstrated that without K^+, TMPyP4 macrocyclic complex showed the intercalation behaviour with the neighbouring G-quadruplicates of G4-wires, followed by 1 : 2 stoichiometry association through the π–π assembling. Though, in the presence of K^+, it collaborated with the G-wires via end layering rather than intercalation modality, indicating the great concurrence under the consequences of different gatherings [94].

This could be on the grounds that the K^+ ions, found at the focal point of every G-quadruplicate, can block the way for the TMPyP4 macrocycle to enter into the G-quadruplicate layers. Though, within the sight of K^+, TMPyP4 macrocycles connected with the "G-quadruplexes" of d(G2T2G2TGTG2T2G2), d[AG3(T2AG3)3], and d(T4G4)4 via interaction in a 1:1, 2:1, and 3:1 stoichiometry coupling modality, correspondingly [94]. It is conceivable that the coupling stoichiometry of G-quadruplicate layers and the TMPyP4 macrocycles is very steady and can integrate into each G-quadruplex layer without creating a repulsive environment with the neighbouring sites. The results suggested that the aggressive modes, for example, modalities of end stacking and groove binding were not recognized in this process. Furthermore, the investigations also suggested that the TMPyP4 macrocycle can also intercalate between G-quadruplicates of d(T4G4) at a lower [TMPyP4 macrocycle]/[G-DNA] concentration ratios [95]. However, assuming there are more referred articles, none provided NMR spectroscopic measurements and valuable crystal architectures of the macrocyclic complexes. Thus, it is still in the debate to prove the emphatically bolstered intercalation binding mode of ligands with G-quadruplexes.

4.3. Binding of G-Quadruplexes with the Grooves/Loops/Spine

The size and geometrical improvements of "G-quadruplexes" and duplex DNA are often accomplished in the unique interaction of G4 ligand. The epic "G-quadruplexes" ligands or macrocycles with non-planar aromatic structures were discovered to be messengers and shown the strong preference and selectivity for G-quadruplexes over DNA duplexes [96]. Further, the investigation of electrostatic communications of alkaloid drugs under the 2 : 1 stoichiometric binding mode showed that the nonplanar stereochemistry may speak to another versatile category of G4 systems. In this regard, more critically, the planar aromatic frameworks could not be recognized as the basic gatherings for G-quadruplexes. Most shockingly, Martino et al. suggested that the dist-A will be a regular and examined folio in the B-DNA system, and a 3D image of its association in terms of intercalation between the parallel G-quadruplexes was also established [97].

These findings demonstrated that the antiparallel dist-A dimer forms can interact with two inverse furrows of G-quadruplexes followed by 4 : 1 stoichiometry via four hydrogen atoms securities. Then, it was observed that the charged amidinium gathering of G4 ligand can interact through electrostatic communication with the oppositely charged spine of G-quadruplexes.

Further, the gene structure of a targeted ligand species among an acridine subsidiary and G-quadruplexes was also reported [98] and the results showed favourable communication between the acridine subsidiary and G-quadruplexes under the 1 : 1 stoichiometry. In this way, the acridine moiety is stacked with the nearest terminal G-quadruplicate of G-quadruplexes, connecting through the T4 circle via intermolecular hydrogen bonding. In addition, tetrasubstituted naphthalene diimide interacts from the outside of TTA circle base pairs of G-quadruplexes, internally [99].

5. CONCLUSIONS

In summary, G4-ligands are the metal chelates and macrocycles are observed to be very explicit and particular toward the interaction with G-quadruplex. These G4-ligands appeared to have a high capacity, (i) to settle G-quadruplex telomerase inhibitors, (ii) to manage the interpretation and related procedure, and (iii) to the cleavage of DNA. Subsequently, these motivations open numerous new chances to configure further intense anti-cancer medications.

This survey reiterates an assortment of classes of G4 ligands that have G4-DNA focusing on highlights as far as anticancer intensity by means of settling or breaking the G-quadruplex over the DNA duplex. Metal complexes having distinctive geometrical highlights, for example, square-planar, square pyramidal, and octahedral structure demonstrated a decent variety towards the "G4 authoritative." The electronic correspondence between metal chelates/macrocycles and G-quadruplex has been portrayed by utilizing several biophysical and spectroscopic techniques. The outcomes uncovered that the G4 ligands pursued three noteworthy activity locales, in particular, G-groups of four, scores, and circles of the G-quadruplex.

Further, it was recommended that the G4 ligands favour the end-stacking mode with terminal G-groups of four. Normally, for this interaction mode, the macrocycles should be the highly aromatic or expanded

delocalized framework that disgraces the likelihood of their intercalation. Also, cationic or protonatable substituents on the macrocyclic system disfavour the electrostatic cooperation with the anionic DNA phosphate backbone, improving the fitting of the macrocycles into the depressions. In this manner, the observations regarding electronic and geometrical highlights are advantageous for the high selectivity of macrocycles for G4 over the DNA duplex.

Further, the enormous test is identified by consolidating the notches/circles with the focusing on G-groups of four which are still in discussion. In any case, the different restricting modes could be perceived all the while, however, the furrow/circle restricting association was considered as the optional connection mode. As a result, this review provides a new route for researchers in this field to design the next generation of G4-ligands with a specific notch/circle acknowledgement.

In this manner, these logical inspirations may open new roads for the further structure of metal chelates or macrocyclic G4-ligands connected in appealing reactant biosensing and against the malignant growth medications field. In spite of the fact that, in this field, some obvious advancement has been perceived, most G4-ligands currently lack in vivo applications and structures that are equivalent to those found in commercial medications. In light of this, it becomes sense that future developments in this field would focus on improving restorative research. In the next years, we could also be interested in learning how new generations of G4-ligands that include metals have an impact on medical issues.

ACKNOWLEDGMENTS

The author is grateful to Department of Chemistry, GLA University, Mathura, India for all kind of support in this study.

COMPLIANCE WITH EHICAL STANDARDS

The authors declare that they have no conflicts of interest.

This article does not contain any studies involving human participants performed by any authors and does not contain any studies involving animals performed by any of these authors.

REFERENCES

1. Sundquist, W.I. and Heaphy, S., *Proc. Natl. Acad. Sci. U. S. A.*, 1993, vol. 90, pp. 3393–3397. https://doi.org/10.1073/pnas.90.8.3393
2. Murat, P. and Balasubramanian, S., *Curr. Opin. Genet. Dev.*, 2014, vol. 25, pp. 22–29. https://doi.org/10.1016/j.gde.2013.10.012
3. Bochman, M.L., Paeschke, K., and Zakian, V.A., *Nat. Rev. Genet.*, 2012, vol. 13, pp. 770–780. https://doi.org/10.1038/nrg3296
4. Keniry, M.A., *Biopolymers,* 2001, vol. 56, 123–146. https://doi.org/10.1002/1097-0282(2000/2001)56:3%3C123::AID-BIP10010%3E3.0.CO;2-3
5. Burge, S., Parkinson, G.N., Hazel, P., Todd, A.K., and Neidle, S., *Nucleic Acids Res.*, 2006, vol. 34, pp. 5402–5415. https://doi.org/10.1093/nar/gkl655
6. Collie, G.W., Haider, S.M., Neidle, S., and Parkinson, G.N., *Nucleic Acids Res.*, 2010, vol. 38, pp. 5569–5580. https://doi.org/10.1093/nar/gkq259
7. Collie, G.W., Sparapani, S., Parkinson, G.N., and Neidle, S., *J. Am. Chem. Soc.*, 2011, vol. 133, pp. 2721–2728. https://doi.org/10.1021/ja109767y
8. Patel, D.J., Phan, A.T., and Kuryavyi, V., *Nucleic Acids Res.*, 2007, vol. 35, pp. 7429–7455. https://doi.org/10.1093/nar/gkm711
9. Mukundan, V.T. and Phan, A.T., *J. Am. Chem. Soc.*, 2013, vol. 135, pp. 5017–5028. https://doi.org/10.1021/ja310251r
10. Beaudoin, J.D., Jodoin, R., and Perreault, J.P., *Nucleic Acids Res.*, 2014, vol. 42, pp. 1209–1223. https://doi.org/10.1093/nar/gkt904
11. Azzalin C.M., Reichenbach, P., Khoriauli, L., Giulotto, E., and Lingner, J., *Science*, 2007, vol. 318, pp. 798–801. https://doi.org/10.1126/science.1147182
12. Xu, Y., Suzuki, Y., Ito, K., and Komiyama, M., *Proc. Natl. Acad. Sci. U. S. A.*, 2010, vol. 107, pp. 14579–14584. https://doi.org/10.1073/pnas.1001177107
13. Phillips, K., Dauter Z., Murchie A.I., Lilley, D.M., and Luisi, B., *J. Mol. Biol.*, 1997, vol. 273, pp. 171–182. https://doi.org/10.1006/jmbi.1997.1292
14. Huppert, J.L., *Nucleic Acids Res.*, 2005, vol. 33, pp. 2908–2916. https://doi.org/10.1093/nar/gki609
15. Todd, A.K., Johnston, M., and Neidle, S., *Nucleic Acids Res.*, 2005, vol. 33, pp. 2901–2907. https://doi.org/10.1093/nar/gki553
16. Rhodes, D., *Nucleic Acids Res.*, 2015, vol. 43, pp. 8627–8637. https://doi.org/10.1093/nar/gkv862
17. Qin, Y. and Hurley, L.H., *Biochimie*, 2008, vol. 90, pp. 1149–1171. https://doi.org/10.1016/j.biochi.2008.02.020
18. Healy, K.C., *Oncol. Res.*, 1995, vol. 7, pp. 121–130.
19. Lopes, J., Piazza, A., Bermejo, R., Kriegsman, B., Colosio, A., Teulade-Fichou, M.P., Foiani, M., and Nicolas, A., *EMBO J.*, 2011, vol. 30, pp. 4033–4046. https://doi.org/10.1038/emboj.2011.316
20. Balasubramanian, S., Hurley, L.H., and Neidle, S., *Nat. Rev. Drug Discov.*, 2011, vol. 10, pp. 261–275. https://doi.org/10.1038/nrd3428
21. Bates, P.J., Laber, D.A., Miller, D.M., Thomas, S.D., and Trent, J.O., *Exp. Mol. Pathol.*, 2009, vol. 86, pp. 151–164. https://doi.org/10.1016/j.yexmp.2009.01.004

22. Reyes-Reyes, E.M., Teng, Y., and Bates, P.J., *Cancer Res.*, 2010, vol. 70, pp. 8617–8629. https://doi.org/10.1158/0008-5472.CAN-10-0920
23. Shi, H., Huang, Y., Zhou, H., Song, X., Yuan, S., Fu, Y., and Luo, Y., *Blood*, 2007, vol. 110, pp. 2899–2906. https://doi.org/10.1182/blood-2007-01-064428
24. Spiegel, J., Adhikari, S., and Balasubramanian, S., *Trends Chem.*, 2020, vol. 2, pp. 123–136. https://doi.org/10.1016/j.trechm.2019.07.002
25. Lucaciu, R.L., Hangan, A.C., Sevastre, B., and Oprean, L.S., *Molecules*, 2022, vol. 27, p. 6485. https://doi.org/10.3390/molecules27196485
26. Miglietta, G., Marinello, J., Russo, M., and Capranico, G., *Mol. Cancer*, 2022, vol. 21, pp. 1–15. https://doi.org/10.1186/s12943-022-01649-y
27. Babar, Q., Saeed, A., Tabish, T.A., Pricl, S., Townley, H., and Thorat, N., *Biochim. Biophys. Acta Mol. Basis Dis.*, 2022, vol. 1868, p. 166552. https://doi.org/10.1016/j.bbadis.2022.166552
28. Ilaria, F., Valentina, P., Sara, N.R., and Filippo, D., *Int. J. Biol. Macromol.*, 2022, vol. 204, pp. 89–102. https://doi.org/10.1016/j.ijbiomac.2022.01.197
29. Shu, H., Zhang, R., Xiao, K., Yang, J., and Sun, X., *Biomolecules*, 2022, vol. 12, p. 648. https://doi.org/10.3390/biom12050648
30. Zhai, L.Y., Liu, J.F., Zhao, J.J., Su, A.M., Xi, X.G., and Hou, X.M., *J. Med. Chem.*, 2022, vol. 65, pp. 10161–10182. https://doi.org/10.1021/acs.jmedchem.2c00649
31. Miglietta, G., Marinello, J., Russo, M., and Capranico, G., *Mol. Cancer*, 2022, vol. 21, pp. 1–15. https://doi.org/10.1186/s12943-022-01649-y
32. Fernando, H., Reszka, A.P., Huppert, J., Ladame, S., Rankin, S., Venkitaraman, A.R., Neidle, S., and Balasubramanian, S., *Biochemistry*, 2006, vol. 45, pp. 7854–7860. https://doi.org/10.1021/bi0601510
33. Rankin, S., Reszka, A.P., Huppert, J., Zloh, M., Parkinson, G.N., Todd, A.K., Ladame, S., Balasubramanian, S., and Neidle, S., *J. Am. Chem. Soc.*, 2005, vol. 127, pp. 10584–10589. https://doi.org/10.1021/ja050823u
34. Siddiqui-Jain, A., Grand, C.L., Bearss, D.J., and Hurley, L.H., *Proc. Natl. Acad. Sci. U. S. A.*, 2002, vol. 99, pp. 11593–11598. https://doi.org/10.1073/pnas.182256799
35. Rangan, A. Fedoroffand, O.Y., and Hurley, L.H., *J. Biol. Chem.*, 2001, vol. 276, pp. 4640–4646. https://doi.org/10.1074/jbc.M005962200
36. Biffi, G. Di Antonio, M., Tannahill, D., and Balasubramanian, S., *Nat. Chem.*, 2014, vol. 6, pp. 75–80. https://doi.org/10.1038/nchem.1805
37. Parkinson, G.N., Lee, M.P., and Neidle, S., *Nature*, 2002, vol. 417, pp. 876 – 880. https://doi.org/10.1038/nature755
38. Simonsson, T., *Biol. Chem.*, 2001, vol. 382, pp. 621–628. https://doi.org/10.1515/BC.2001.073
39. Mergny, J.L., Cian, A.D., Amrane, S., and Silva, M.W., *Nucleic Acids Res.*, 2006, vol. 34, pp. 2386–2397. https://doi.org/10.1093/nar/gkl098
40. Kato, Y. Ohyama, T. Mita, H., and Yamamoto, Y., *J. Am. Chem. Soc.*, 2005, vol. 127, pp. 9980–9981. https://doi.org/10.1021/ja050191b
41. Arora, A. and Maiti, S., *J. Phys. Chem. B*, 2009, vol. 113, pp. 10515–10520. https://doi.org/10.1021/jp810638n
42. Agarwal, T., Jayaraj, G., Pandey, S.P., Agarwala, P., and Maiti, S., *Curr. Pharm. Des.*, 2012, vol. 18, pp. 2102–2111. https://doi.org/10.2174/138161212799958468
43. Xu, Y. and Komiyama, M., *Methods*, 2012, vol. 57, pp. 100–105. https://doi.org/10.1016/j.ymeth.2012.02.015
44. Tang, C.F. and Shafer, R.H., *J. Am. Chem. Soc.*, 2006, vol. 128, pp. 5966–5973. https://doi.org/10.1021/ja0603958
45. Bruijnincx, P.C.A. and Sadler, P.J., *Curr. Opin. Chem. Biol.*, 2008, vol. 12, pp. 197–206. https://doi.org/10.1016/j.cbpa.2007.11.013
46. Gellert, M., Lipsett, M.N., and Davies, D.R., *Proc. Natl. Acad. Sci. U. S. A.*, 1962, vol. 48, pp. 2013–2018. https://doi.org/10.1073/pnas.48.12.2013
47. Patel, D.J., Phan, A.T., and Kuryavyi, V., *Nucleic Acids Res.*, 2007, vol. 35, pp. 7429–7455. https://doi.org/10.1093/nar/gkm711
48. Burge, S., Parkinson, G.N., Hazel, P., Todd, A.K., and Neidle, S., *Nucleic Acids Res.*, 2006, vol. 34, pp. 5402–5415. https://doi.org/10.1093/nar/gkl655
49. Georgiades, S.N., Abd Karim, N.H., Suntharalingam, K., and Vilar, R., *Angew. Chem., Int. Ed.*, 2010, vol. 49, pp. 4020–4034. https://doi.org/10.1002/anie.200906363
50. Campbell, N., Collie, G.W., and Neidle, S., *Current Protocols in Nucleic Acid Chemistry*, Wiley, 2012. https://doi.org/10.1002/0471142700.nc1706s50
51. Huppert, J.L., *Chem. Soc. Rev.*, 2008, vol. 37, pp. 1375–1384. https://doi.org/10.1039/B702491F
52. Zhang, J., Zhang, F., Li, H., Liu, C., Xia, J., Ma, L., Chu, W., Zhang, Z., Chen, C., Li, S., and Wang, S., *Curr. Med. Chem.*, 2012, vol. 19, pp. 2957–2975. https://doi.org/10.2174/092986712800672067
53. Bertrand, H., Monchaud, D. De Cian, A., Guillot, R., Mergny J.-L., and Teulade-Fichou, M.-P., *Org. Biomol. Chem.*, 2007, vol. 5, pp. 2555–2559. https://doi.org/10.1039/B708635K
54. Bertrand, H., Bombard, S., Monchaud, D., and Teulade-Fichou, M.-P., *J. Biol. Inorg. Chem.*, 2007, vol. 12, pp. 1003–1014. https://doi.org/10.1007/s00775-007-0273-3
55. Qin, Y. and Hurley, L.H., *Biochimie*, 2008, vol. 90, pp. 1149–1171. https://doi.org/10.1016/j.biochi.2008.02.020
56. Qin, Q.P., Chen, Z.F., Shen, W.Y., Jiang, Y.H., Cao, D., Li, Y.L., Xu, Q.M., Liu, Y.C., Huang, K.B., and Liang, H., *Eur. J. Med. Chem.*, 2015, vol. 89, pp. 77–87. https://doi.org/10.1016/j.ejmech.2014.10.019
57. Kieltyka, R., Fakhoury, J., Moitessier, N., and Sleiman, H.F., *Chem. Eur. J.*, 2008, vol. 14, pp. 1145–1154. https://doi.org/10.1002/chem.200700783

58. Davis, K.J., Richardson, C., Beck, J.L., Knowles, B.M., Guédin, A., Mergny, J.L., Willis, A.C., and Ralph, S.F., *Dalton Trans.*, 2015, 44, pp. 3136–3150. https://doi.org/10.1039/C4DT02926G
59. Yu, C., Chan, K.H.Y., Wong, K.M.C., and Yam, V.W.W., *Chem. Commun.*, 2009, vol. 25, pp. 3756–3758. http://dx.doi.org/10.1039%2Fb903080h
60. Barry, N.P., Abd Karim, N.H., Vilar, R., and Therrien, B., *Dalton Trans.*, 2009, vol. 48, pp. 10717–10719. https://doi.org/10.1039/B913642H
61. Li, Q., Zhang, J., Yang, L., Yu, Q., Chen, Q., Qin, X., Le, F., Zhang, Q., and Liu, J., *J. Inorg. Chem.*, 2014, vol. 130, pp. 122–129. https://doi.org/10.1016/j.jinorgbio.2013.10.006
62. Xia, Y., Chen, Q., Qin, X., Sun, D., Zhang, J., and Liu, J., *New J. Chem.*, 2013, vol. 37, pp. 3706–3715. https://doi.org/10.1039/C3NJ00542A
63. Chen, X., Wu, J.H., Lai, Y.W., Zhao, R., Chao, H., and Ji, L.N., *Dalton Trans.*, 2013, vol. 42, pp. 4386–4397. https://doi.org/10.1039/C3DT32921F
64. Membrino, A., Paramasivam, M., Cogoi, S., Alzeer, J., Luedtke, N.W., and Xodo, L.E., *Chem. Commun.*, 2010, vol. 46, pp. 625–627. https://doi.org/10.1039/B918964E
65. Ren, L., Zhang, A., Huang, J., Wang, P., Weng, X., Zhang, L., Liang, F., Tan, Z., and Zhou, X., *ChemBioChem*, 2007, vol. 8, pp. 775–780. https://doi.org/10.1002/cbic.200600554
66. Dixon, I.M., Lopez, F., Estève, J.P., Tejera, A.M., Blasco, M.A., Pratviel, G., and Meunier, B., *ChemBioChem*, 2005, vol. 6, pp. 123–132. https://doi.org/10.1002/cbic.200400113
67. Romera, C., Sabater, L., Garofalo, A., M. Dixon, I., and Pratviel, G., *Inorg. Chem.*, 2010, vol. 49, pp. 8558–8567. https://doi.org/10.1021/ic101178n
68. Fu, B., Zhang, D., Weng, X., Zhang, M., Ma, H., Ma, Y., and Zhou, X., *Chem. Eur. J.*, 2008, vol. 14, pp. 9431–9441. https://doi.org/10.1002/chem.200800835
69. Gershman, Z., Goldberg, I., and Gross, Z., *Angew. Chem., Int. Ed.*, 2007, vol. 46, pp. 4320–4324. https://doi.org/10.1002/anie.200700757
70. Wasbotten, I.H., Wondimagegn, T., and Ghosh, A., *J. Am. Chem. Soc.*, 2002, vol. 124, pp. 8104–8116. https://doi.org/10.1021/ja0113697
71. Romera, C., Bombarde, O., Bonnet, R., Gomez, D., Dumy, P., Calsou, P., Gwan, J.F., Lin, J.H., Defrancq, E., and Pratviel, G., *Biochimie*, 2011, vol. 93, pp. 1310–1317. https://doi.org/10.1016/j.biochi.2011.06.008
72. Bendix, J., Gray, H.B., Golubkov, G., and Gross, Z., *Chem. Commun.*, 2000, vol. 19, pp. 1957–1958. https://doi.org/10.1039/B006299P
73. Maraval, A., Franco, S., Vialas, C., Pratviel, G., Blasco, M.A., and Meunier, B., *Org. Biomol. Chem.*, 2003, vol. 1, pp. 921–927. https://doi.org/10.1039/B211634K
74. Bhattacharjee, A.J., Ahluwalia, K., Taylor, S., Jin, O., Nicoludis, J.M., Buscaglia, R., Chaires, J.B., Kornfilt, D.J., Marquardt, D.G., and Yatsunyk, L.A., *Biochimie*, 2011, vol. 93, pp. 1297–1309. https://doi.org/10.1016/j.biochi.2011.05.038
75. Evans, S.E., Mendez, M.A., Turner, K.B., Keating, L.R., Grimes, R.T., Melchoir, S., and Szalai, V.A., *J. Biol. Inorg. Chem.*, 2007, vol. 12, pp. 1235–1249. https://doi.org/10.1007/s00775-007-0292-0
76. Keating, L.R. and Szalai, V.A., *Biochemistry*, 2004, vol. 43, pp. 15891–15900. https://doi.org/10.1021/bi0483209
77. Morris M.J., Wingate K.L., Silwal J., Leeper T.C., and Basu S., *Nucleic Acids Res.*, 2012, vol. 40, pp. 4137–4145. https://doi.org/10.1093/nar/gkr1308
78. Weisman-Shomer P., Cohen E., Hershco I., Khateb S., Wolfovitz-Barchad O., Hurley L. H., and Fry M., *Nucleic Acids Res.*, 2003, vol. 31, pp. 3963–3970. https://doi.org/10.1093/nar/gkg453
79. Ofer N., Weisman-Shomer P., Shklover J., and Fry M., *Nucleic Acids Res.*, 2009, vol. 37, pp. 2712–2722. https://doi.org/10.1093/nar/gkp130
80. Oostra B. A. and Willemsen R., *Biochim. Biophys. Acta*, 2009, vol. 1790, pp. 467–477. https://doi.org/10.1016/j.bbagen.2009.02.007
81. Zamiri, B., Reddy, K., Macgregor, R.B., and Pearson, C.E., *J. Biol. Chem.*, 2014, vol. 289, pp. 4653–4659. https://doi.org/10.1074/jbc.C113.502336
82. Bryan, T.M., *Molecules*, 2019, vol. 24, p. 3439. https://doi.org/10.3390/molecules24193439
83. Valton, A.L. and Prioleau, M.N., *Trends Genet.*, 2016, vol. 32, pp. 697–706. https://doi.org/10.1016/j.tig.2016.09.004
84. Awadasseid, A., Ma, X., Wu, Y., and Zhang, W., *Biomed. Pharmacother.*, 2021, vol. 139, p. 111550. https://doi.org/10.1016/j.biopha.2021.111550
85. Jirásek, M., Rickhaus, M., Tejerina, L., and Anderson, H.L., *J. Am. Chem. Soc.*, 2021, vol. 143, pp. 2403–2412. https://doi.org/10.1021/jacs.0c12845
86. Routh, E.D., Creacy, S.D., Beerbower, P.E., Akman, S.A., Vaughn, J.P., and Smaldino, P.J., *J. Vis. Exp.*, 2017, vol. 121, p. e55496. https://doi.org/10.3791/55496
87. Santos, T., Salgado, G.F., Cabrita, E.J., and Cruz, C., *Pharmaceuticals*, 2021, vol. 14, p. 769. https://doi.org/10.3390/ph14080769
88. Zamiri, B., Reddy, K., Macgregor, R.B., and Pearson, C.E., *J. Biol. Chem.*, 2014, vol. 289, pp. 4653–4659. https://doi.org/10.1074/jbc.C113.502336
89. Morris, M.J., Wingate, K.L., Silwal, J., Leeper, T.C., and Basu, S., *Nucleic Acids Res.*, 2012, vol. 40, pp. 4137–4145. https://doi.org/10.1093/nar/gkr1308
90. Chizhova, N.V.E., Maltceva, O.V., Zvezdina, S.V., Mamardashvili, N.Z., and Koifman, O.I., *J. Coord. Chem.*, 2018, vol. 71, pp. 3222–3232. https://doi.org/10.1080/00958972.2018.1519186
91. Haudecoeur, R., Stefan, L., Denat, F., and Monchaud, D., *J. Am. Chem. Soc.,* 2013, vol. 135, pp. 550–553. https://doi.org/10.1021/ja310056y
92. Shinohara, K.I., Sannohe, Y., Kaieda, S., Tanaka, K.I., Osuga, H., Tahara, H., Xu, Y., Kawase, T., Bando, T.,

and Sugiyama, H., *J. Am. Chem. Soc.*, 2010, vol. 132, pp. 3778–3782. https://doi.org/10.1021/ja908897j

93. Sirajuddin, M., Ali, S., and Badshah, A., *J. Photochem. Photobiol. B, Biol.*, 2013. vol. 124, pp. 1–19. https://doi.org/10.1016/j.jphotobiol.2013.03.013

94. Lubitz, I., Borovok, N., and Kotlyar, A., *Biochemistry*, 2007, vol. 46, pp. 12925–12929. https://doi.org/10.1021/bi701301u

95. Lombardo, C.M., Welsh, S.J., Strauss, S.J., Dale, A.G., Todd, A.K., Nanjunda, R., Wilson, W.D., and Neidle, S., *Bioorg. Med. Chem. Lett.*, 2012, vol. 22, pp. 5984–5988. https://doi.org/10.1016/j.bmcl.2012.07.009

96. Ou, T.M., Lu, Y.J., Tan, J.H., Huang, Z.S., Wong, K.Y., and Gu, L.Q. *ChemMedChem*, 2008, vol. 3, pp. 690–713. https://doi.org/10.1002/cmdc.200700300

97. Martino, A., Virno, B., Pagano, A., Virgilio, S.D., Micco, A., Galeone, C., Giancola, G., Bifulco, L., Mayol, A., and Randazzo, *J. Am. Chem. Soc.*, 2007, vol. 129, pp. 16048–16056. https://doi.org/10.1021/ja075710k

98. Bohunicky, B. and Mousa, S.A., *Nanotechnol. Sci. Appl.*, 2010, vol. 4, pp. 1–10. https://doi.org/10.2147%2FNSA.S13465

99. Rodriguez, R., Pantos, G.D., GonÅalves, D.P., Sanders, J.K., and Balasubramanian, S., *Angew. Chem.*, 2007, vol. 119, pp. 5501–5503. https://doi.org/10.1002/anie.200605075