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Drug delivery using doping of boron nitride nanosensor towards releasing chloroquine drug in the cells: A promising method for overcoming viral disease

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Summary

Introduction: Chloroquine drug as the SARS-CoV-2's primary protease which can prevent *in vitro* viral duplication of all diverse experiments to now. Chloroquine drug is an anti-viral drug enlarged by Pfizer which can operate as an orally effective 3C-like protease inhibitor. **Materials and Methods:** In this work, chloroquine drug has been evaluated in forbiddance of coronavirus across trapping on the boron nitride nanocage (B_4N_{10}_NC) functionalized with some atoms as the drug delivery procedure owing to the direct electron transfer principle which can be illustrated by quantum mechanics method of density functional theory (DFT). **Results and Discussion:** As a matter of fact, it was performed the theoretical method of the B3LYP/6-311+G (d,p) to account the aptitude of B_4N_{10}_NC for grabbing Chloroquine drug via density of electronic states, nuclear quadrupole resonance, nuclear magnetic resonance, and thermodynamic specifications. Finally, the resulted amounts illustrated that using B_4N_{10}_NC functionalized with aluminum (Al), carbon (C), silicon (Si) for adsorbing Chloroquine drug towards formation of Chloroquine @Al–B_4N_{10}_NC, Chloroquine @C–B_4N_{10}_NC, Chloroquine @Si–B_4N_{10}_NC might provide the reasonable formula in drug delivery technique which is able to be fulfilled by quantum mechanics computations due to physicochemical properties of PDOS, NMR, NQR, and IR spectrum. **Conclusions:** Here, we used network pharmacology, metabolite analysis, and molecular simulation to figure out the biochemical basis of the health-raising influence of Chloroquine drug through

drug delivery with B_4N_{10}_NC. This research article peruses the drug ability, metabolites, and potential interaction of Chloroquine drug with Coronavirus-induced pathogenesis.

Keywords: Chloroquine, Drug delivery, COVID–19, X–B_4N_{10} (X=Al/C/Si)

Resumen

Administración de fármacos mediante dopaje de nanosensor de nitruro de boro para liberar el fármaco cloroquina en las células: un método prometedor para superar la enfermedad viral

Introducción: El fármaco cloroquina es la proteasa primaria del SARS-CoV-2 que puede prevenir la duplicación viral *in vitro* de todos los experimentos diversos hasta ahora. El fármaco cloroquina es un fármaco antiviral ampliado por Pfizer que puede funcionar como un inhibidor de la proteasa similar al 3C eficaz por vía oral. **Materiales y métodos:** en este trabajo, el fármaco cloroquina se ha evaluado para prevenir el coronavirus mediante la captura en la nanojaula de nitruro de boro (B_4N_{10}_NC) funcionalizada con algunos átomos como procedimiento de administración del fármaco debido al principio de transferencia directa de electrones que puede ilustrarse mediante la mecánica cuántica. Método de teoría funcional de la densidad (DFT). **Resultados y Discusión:** De hecho, se realizó el método teórico del B3LYP/6-311+G (d,p) para dar cuenta de la aptitud de B_4N_{10}_NC para capturar la droga cloroquina a través de la densidad de estados electrónicos, resonancia cuadrupolo nuclear, resonancia magnética nuclear y especificaciones termodinámicas. Finalmente, las cantidades resultantes ilustraron que el uso de B_4N_{10}_NC funcionalizado con aluminio (Al), carbono (C), silicio (Si) para adsorber el fármaco cloroquina hacia la formación de cloroquina @Al–B_4N_{10}_NC, cloroquina @C–B_4N_{10}_NC, cloroquina @Si–B_4N_{10}_NC podría proporcionar la fórmula razonable en la técnica de administración de fármacos que puede cumplirse mediante cálculos de mecánica cuántica debido a las propiedades fisicoquímicas de PDOS, NMR, NQR y espectro IR. **Conclusiones:** Aquí utilizamos farmacología de red, análisis de metabolitos y simulación molecular para descubrir la base bioquímica del efecto saludable del medicamento cloroquina a través de la administración de fármacos con B_4N_{10}_NC. Este artículo de investigación examina detenidamente la capacidad del fármaco, los metabolitos y la posible interacción del fármaco cloroquina con la patogénesis inducida por el coronavirus.

Palabras clave: cloroquina, administración de fármacos, COVID–19, X–B_4N_{10} (X=Al/C/Si)

RESUMO

Entrega de medicamentos usando dopagem de nanosensor de nitruro de boro para liberação de cloroquina nas células: um método promissor para superar doenças virais

Introdução: A droga cloroquina como a protease primária do SARS-CoV-2 que pode prevenir a duplicação viral *in vitro* de todos os diversos experimentos até agora. O medicamento cloroquina é um medicamento antiviral ampliado pela Pfizer que pode operar como um inibidor de protease semelhante ao 3C por via oral. **Materiais e Métodos:** Neste trabalho, a droga cloroquina foi avaliada na proibição do coronavírus através do aprisionamento na nanogaiola de nitruro de boro (B_4N_{10}_NC) funcionalizada com alguns átomos como procedimento de entrega da droga devido ao princípio de transferência direta de elétrons que pode ser ilustrado pela mecânica quântica, método da teoria do funcional da densidade (DFT). Resultados e **Discussão:** Na verdade, foi realizado o método teórico do B3LYP/6-311+G (d,p) para contabilizar a aptidão do B_4N_{10}_NC para capturar a droga Cloroquina via densidade de estados eletrônicos, ressonância quadrupolo nuclear, ressonância magnética nuclear e especificações termodinâmicas. Finalmente, os valores resultantes ilustraram que o uso de B_4N_{10}_NC funcionalizado com alumínio (Al), carbono (C), silício (Si) para adsorver o medicamento Cloroquina para a formação de Cloroquina @Al – B_4N_{10}_NC, Cloroquina @ C – B_4N_{10}_NC, Cloroquina @ Si – B_4N_{10}_NC pode fornecer a fórmula razoável na técnica de entrega de medicamentos que pode ser realizada por cálculos de mecânica quântica devido às propriedades físico-químicas do espectro PDOS, RMN, NQR e IR. **Conclusões:** Aqui, usamos farmacologia de rede, análise de metabólitos e simulação molecular para descobrir a base bioquímica da influência do medicamento Cloroquina na melhoria da saúde por meio da entrega de medicamentos com B4N10_NC. Este artigo de pesquisa examina a capacidade do medicamento, os metabólitos e a interação potencial do medicamento Cloroquina com a patogênese induzida pelo Coronavírus.

Palavras-chave: Cloroquina, Drug delivery, COVID–19, X–B_4N_{10} (X=Al/C/Si)

Introduction

The arrival of a recent coronavirus, known as the severe acute respiratory syndrome coronavirus 2 (SARS–CoV–2) has involved a pandemic of Coronavirus Disease of 2019 (COVID–19) [1-9]. After its precedent reported sample in Wuhan, China in

December 2019, recent explored proof by both medical doctors and scientists have supported some ideas on the malady pathogenesis and the nature of the virus itself [10]. The intensity of the COVID-19 pandemic has waned since the beginning of 2022, in parallel with a significantly reduced risk for disease progression and death due to widespread vaccination, hybrid immunity, and the intrinsic low virulence of the Omicron subvariants [11]. The use of early therapies (antiviral monoclonal antibodies and small molecules) has been approved for the prevention of disease progression and hospitalizations among high-risk outpatients with comorbidities [12]. Gottlieb *et al.* have investigated on early treatment of COVID-19 outpatients with oral antivirals or with short daily infusions is considered a treatment strategy that assisted in turning the tides of the pandemic by reducing hospital admissions and mortality [13]. Furthermore, Kim *et al.* have indicated that, while treatment options for patients with severe disease requiring hospitalization are now available, with corticosteroids emerging as the treatment of choice for critically ill patients, interventions that can be administered early during infection to prevent disease progression and longer-term complications are urgently needed [14]. There is not a certain therapy or vaccine receivable to battle versus SARS-CoV-2 [15]. Lately, antibodies have been almost all created in human cells and metamorphosed animal cells which are programs with many tools that are very difficult to run [16, 17]. In addition, SARS-CoV-2 is a current major challenge for researchers, and they are still working on the development of antiviral drugs against SARS-CoV-2 [18-20]. Currently, researchers and scientists are working on the development of a drug against COVID-19 in the following ways such as the prevention of self-assembly (structural proteins), viral replications (Nsps), viral entry, and the blocking of the signaling pathways required for viral infection [21-23].

Chloroquine with formula $C_{18}H_{26}ClN_3$ has antiviral and anti-inflammatory specifications which has been used in MERS-CoV, Zika virus, enterovirus EV–A71, OC43, influenza A H5N1, SARS-CoV, and SARS-CoV-2 infection treatment [24, 25].

Recently, some studies have done to investigate the possibility advantages of chloroquine or the derivative hydroxychloroquine, an economical anti-malaria medication that has been applied for years for COVID-19 therapy [26, 27].

Daolin *et al.* have exhibited that chloroquine with a dual function in antiviral immunity can be critical to remark for introducing the COVID-19 cure [28].

There is a regard to augmenting the bioavailability and interval of operation for a medication to correct remedial outcomes. Drug delivery approach can alter a medication's pharmacokinetics and quality by providing it with diverse components, medication transfers, and medical tools [29-38].

Amongst nanoparticles, boron nitride (BN) nanomaterials have shown excellent physical and chemical properties [39] and a wide usage perspective in drug delivery system [40]. In this work, it was concentrated on Chloroquine drug attached to functionalized B_4N_{10}_NC with Al, C, and Si atoms towards formation of Chloroquine @Al–B_4N_{10}_NC, Chloroquine @C–B_4N_{10}_NC, Chloroquine @Si–B_4N_{10}_NC complexes for decreasing the function of COVID–19 (Figure 1).

Figure 1. Adsorption of Chloroquine by functionalized B_4N_{10}_NC with Al, C, and Si atoms towards formation of Chloroquine @Al–B_4N_{10}_NC, Chloroquine @C–B_4N_{10}_NC, Chloroquine @Si–B_4N_{10}_NC complexes.

Theory, materials and approaches

The theoretical method of density functional theory (DFT) is one of the most utilized approximations of Hohenberg, Kohn and Sham which permits the theoretical investigation of material specifications [41]. DFT approach titrates a beneficial level for estimating the chemical systems [42-48].

In this work, the structures of Chloroquine drug adsorbed on the X–B_4N_{10} (X=Al/C/Si) were minimized at the skeleton of DFT approach accompanying the three-parameter Becke's exchange [49] and Lee–Yang–Parr's correlation non-local functional [50], introduced as B3LYP level of theory and basis set of 6–311+G(d,p). In fact, molecular modeling techniques are used to describe the process of interaction between Chloroquine drug and X–B_4N_{10} (X=Al/C/Si) towards formation of Chloroquine @Al–B_4N_{10}_NC, Chloroquine @C–B_4N_{10}_NC, Chloroquine @Si–B_4N_{10}_NC complexes as the drug delivery system for treatment of Covid-19 disease (Figure 1).

In this research, the Onsager pattern was carried out which was extended by Frisch, Wong and Wiberg by applying spherical cavities [51]. This model conveys a less accurate explanation of the solute/solvent interface, but it can lighten the assessment of energy derivatives in optimizing of geometries and analyzing the frequencies. Furthermore, Cramer and Truhlar developed this pattern at the dipole level [52]. As a matter

of fact, a cavity should have a physical impression like Onsager design, and has a mathematical susceptibility as frequently occurred in other definitions of solvent influences [53-58]. So, the cavity must maintain the solvent and its neighbors as the greatest possibility section of the solute charge diffusion [59, 60].

The compound of CNT is discoursing drug delivery programs that might be enforced with a variety of biomaterials containing DNA, proteins, and antibodies. This gives clearance the own aim for assignment the special cells, tissues, and organs. These substances might lightly interpenetrate cells, releasing medications straightly to the nucleus or cytoplasm. Drug releasing platforms ameliorate the pharmacological and therapeutic profile and influence of the medication and pull down the occurrence of off-targets [61-67].

In fact, a mass of quantum mechanical technics can accomplish discovering certain properties aspect of physicochemical specifications extracted from minimized frame of Chloroquine drug attached to X–B_4N_{10} (X=Al/C/Si) consisting of density of electrical states, electric potential, Bader charge distribution, vibrational computations and nuclear magnetic resonance analysis owing to running a drug delivery model using Gaussian 16 revision C.01 program [68]. In addition, the level of gauge including atomic orbitals (GIAO) has been dedicated to work out the gauge difficulty in the measurement of nuclear magnetic shielding for [Chloroquine @ X–B_4N_{10} (X=Al/C/Si)] complexes using DFT approach.

Results

PDOS study

The electronic structures of Chloroquine drug attached to the X–B_4N_{10} (X=Al/C/Si) nanocage were evaluated to explain the interfacial electronic parameters using quantum methods.

Figure 2a-d introduces the projected density of state (PDOS) of Chloroquine drug, Al–B_4N_{10}, C–B_4N_{10}, Si–B_4N_{10}, respectively. It is obvious from the figure that after adsorption of Chloroquine drug on the X–B_4N_{10} (X=Al/C/Si), there is a significant contribution of *p*-orbitals of Al, C, Si, N and Cl atoms in the unoccupied stage. Population analysis and PDOS indicate that C, N and Cl atoms of Chloroquine remain in the linkage with X–B_4N_{10} (X=Al/C/Si) and it can grab more electrons from other elements. So, the graph of PDOS has discovered that the *p* states of the adsorption of C, N and Cl atoms on the X–B_4N_{10} (X=Al/C/Si) are significant through the conduction band (Figure 2a-d). Furthermore, the existence of covalent features for [Chloroquine

@ X–B_4N_{10} (X=Al/C/Si)] complex has shown the equal energy content and configuration of the PDOS for the *p* orbitals of Al, C, Si, N and Cl atoms (Figure 2a-b).

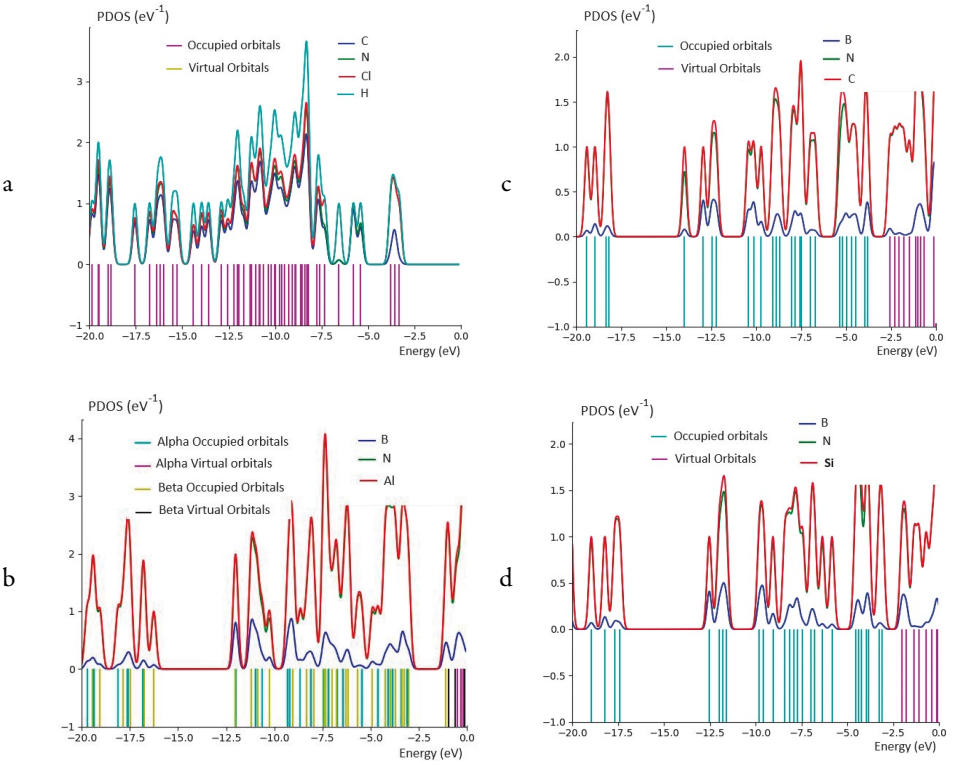

Figure 2. Electronic properties of Partial Density of States (PDOS) for **a)** Chloroquine drug adsorbed on **b)** Al–B_4N_{10} **c)** C–B_4N_{10} and **d)** Si–B_4N_{10}.

Figure 2a-d shows that the Chloroquine drug states adsorbed onto X–B_4N_{10} (X=Al/C/Si) complexes have more contribution at the middle of the conduction band between −5eV to −15eV, while contribution of C, N, Cl states in Chloroquine drug are expanded and close together (Figure 2a), and Al states in Al–B_4N_{10}_NC (Figure 2b), C in C–B_4N_{10}_NC (Figure 2c) and Si in Si–B_4N_{10}_NC (Figure 2d) approximately have the most contributions.

As a matter of fact, the mentioned consequences display that the principal complex and a certain degree of covalent traits can describe ameliorating of the straight conducting band gap of Chloroquine drug absorbing on the X–B_4N_{10} (X=Al/C/Si) complexes.

Spectroscopy of NMR

The nuclear magnetic resonance (NMR) information of shielding tensors (ppm) containing isotropic (σ_{iso}) and anisotropic (σ_{aniso}) for Chloroquine drug linked to X–B_4N_{10} (X=Al/C/Si) complexes were computed (Table 1). The accomplished consequences have demonstrated the "SCF/GIAO" magnetic shielding tensor for Al, C, Si, N and Cl atoms discovering the active zone of Chloroquine material as the medication for viral disease therapy. The measurements were run on "B3LYP/6–311+G (d, p)" level of theory using Gaussian 16 revision C.01 program [68] and were announced in Table 1.

The [Chloroquine @ X–B_4N_{10} (X=Al/C/Si)] complexes have reflected the significance of chemical shielding consisting of σ_{iso} and σ_{aniso} (ppm) for diverse elements of B, Al, C, Si, N and Cl atoms in the active zones of the system owing to the NMR curve (Table 1).

Furthermore, the ^{13}C–NMR considerations on Chloroquine drug have approved the active zones of this compound owing to unraveling the most electron donor elements during Chloroquine drug adsorption onto X–B_4N_{10} (X=Al/C/Si) complexes which expose the major shift in tetramethylsilane (TMS) using quantum methods (Figure 3a-d).

The most alterations were declared for atoms of N11 in Chloroquine drug (Figure 3a), N11, Al13 in Chloroquine @Al–B_4N_{10} (Figure 3b), N11, C13 in Chloroquine @C–B_4N_{10} (Figure 3c), N11, Si13 in Chloroquine @Si–B_4N_{10} (Figure 3d).

The progress of impressive DFT methods including electronic correlation effects has illustrated to be a significant key in the field of shielding computations. By DFT theory, which measures N^2 (N=number of electrons), it is feasible to compute shielding in molecular systems of practical interest consisting of electronic correlation impacts. Furthermore, new DFT approaches with linear scaling are accessible and these will supply further developments in the implementation of these technics to compute magnetic shielding in the large the large groups [69].

This skeleton based on the theory analyses the solvent effects on magnetic shielding. The real computation of these impacts is quite puzzling because any model that seeks to indicate these interactions must estimate both the electromagnetic iterations produced by the solvent molecules as well as their dynamic parameters.

Table 1. Data of nuclear magnetic resonance (NMR) tensors (ppm) for Chloroquine drug attached to Al–B_4N_{10}_NC, C–B_4N_{10}_NC, and Si–B_4N_{10}_NC by quantum methods. SCF GIAO Magnetic shielding tensors (ppm) consisting of isotropic shielding tensor (σ_{iso}) and anisotropic shielding tensor (σ_{aniso}).

Chloroquine			Al–B_4N_{10}			C–B_4N_{10}			Si–B_4N_{10}		
Atom	σ_{iso}	σ_{aniso}	Atom	σ_{iso}	σ_{aniso}	Atom	σ_{iso}	σ_{aniso}	Atom	σ_{iso}	σ_{aniso}
C (1)	132.52	130.65	B1	96.71	82.91	B1	103.95	91.64	B1	69.65	66.87
C (2)	134.71	115.73	N2	259.30	626.11	N2	111.66	621.75	N2	211.97	928.02
C (3)	154.14	132.97	N3	58.49	79.64	N3	1655.31	2921.16	N3	890.97	2652.00
C (4)	133.90	120.89	B4	105.97	72.42	B4	99.38	130.29	B4	93.00	40.07
C (5)	129.01	112.43	B5	94.94	58.17	B5	111.94	44.71	B5	56.79	52.74
C (6)	121.43	90.28	B6	78.48	78.26	B6	111.96	63.24	B6	55.44	76.88
C (7)	135.35	119.43	N7	180.32	573.04	N7	268.02	362.56	N7	147.71	1114.40
C (8)	145.64	85.83	N8	79.95	253.36	N8	557.61	1335.78	N8	1417.29	2153.41
C (9)	124.85	112.78	N9	460.09	832.80	N9	601.87	1305.01	N9	588.36	4046.60
N (10)	76.90	440.22	N10	558.79	717.03	N10	877.08	1752.31	N10	575.52	2937.29
N (11)	236.30	37.80	N11	512.23	941.85	N11	1094.84	1854.46	N11	88.60	3677.85
C (12)	179.56	34.90	N12	283.32	712.10	N12	637.42	1166.30	N12	300.50	2936.03
C (13)	204.91	29.29	Al13	488.58	206.97	C13	99.65	87.81	Si13	670.58	157.49
C (14)	198.50	27.14	N14	28.48	599.67	N14	35.63	1510.04	N14	123.22	1007.9
C (15)	200.92	22.42	N15	21.33	591.87	N15	262.85	1199.51	N15	40.17	1170.06
C (16)	179.88	55.74									
N (17)	274.67	37.68									
C (18)	184.27	51.36									
C (19)	208.57	23.61									
C (20)	186.65	40.51									
C (21)	208.71	17.64									
Cl (22)	920.80	169.33									

Note: Isotropic chemical-shielding (σ_{iso}/ppm) & anisotropic chemical-shielding (σ_{aniso}/ppm) [70]:

$$\sigma_{iso} = (\sigma_{33} + \sigma_{22} + \sigma_{11})/3$$

$$\sigma_{aniso} = \sigma_{33} - (\sigma_{22} + \sigma_{11})/2.$$

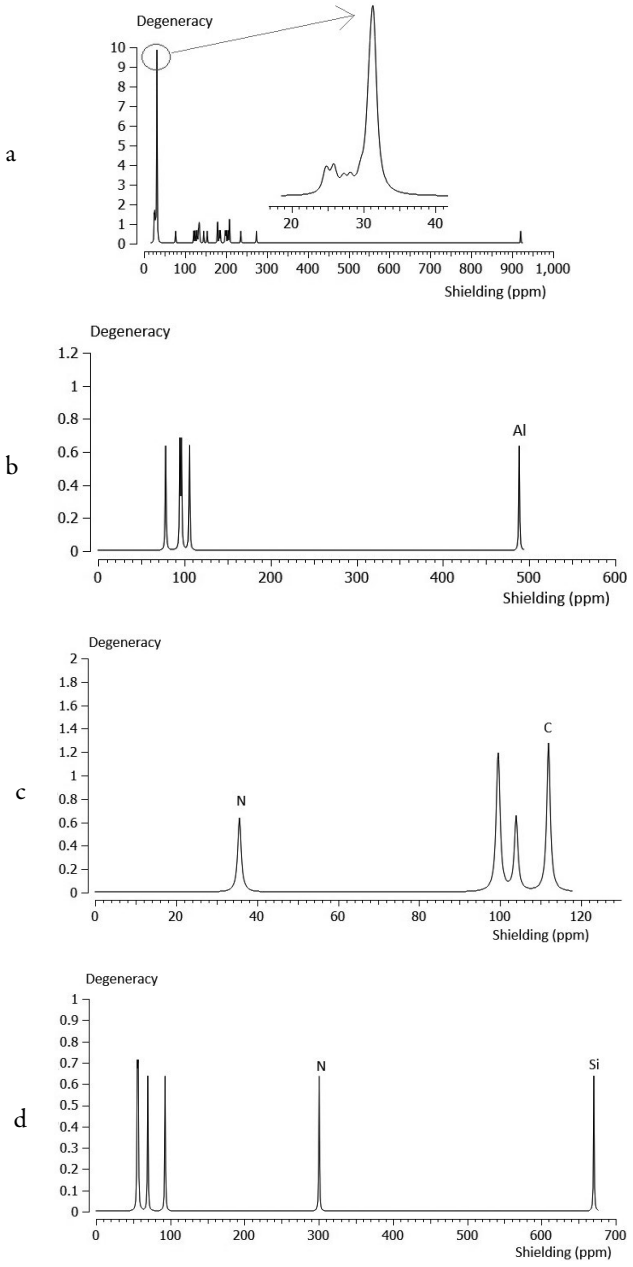

Figure 3. The NMR spectrums for **a)** Chloroquine drug, **b)** Chloroquine @Al–B_4N_{10}_NC, **c)** Chloroquine @C–B_4N_{10}_NC, **d)** Chloroquine @Si–B_4N_{10}_NC.

NQR analysis

The Nuclear Quadrupole Resonance (NQR) spectrums can prepare exact data on the structural and composition properties of active groups in biological reactions. It presents a special probability of identifying the quadrupole coupling constants and impressive charges which lets us knowledge of the electronic structure of the system. In fact, NQR spectrums become visible to propose an intense approach for the inquiry of diverse chemical influences in the solid phase of many nitrogen possessing substances. Analyzing the quadrupole coupling constants of nitrogen atoms permits an assessment of the electron density distribution on the nitrogen nuclei and authorizes the analysis of charge distribution in chemical bonding dealing with nitrogen atom.

So, "nuclear quadrupole resonance" or "NQR" was evaluated for Chloroquine drug trapped by the surface of X–B_4N_{10} (X=Al/C/Si) nanocages towards formation of [Chloroquine @X–B_4N_{10} (X=Al/C/Si)] complexes based on the "nuclear quadrupole moment", and the "electric field gradient" or "EFG" [70].

As the "EFG" at the citation of the nucleus in Chloroquine drug is allocated by the valence electrons twisted in the particular attachment with close nuclei of X–B_4N_{10} (X=Al/C/Si) nanocages, the "NQR" frequency at which transitions occur is particular for of [Chloroquine @(5,5) B_4N_{10} (X=Al/C/Si)] complexes (Table 2).

Furthermore, in Figure 4a-d, it was drawn the electric potential versus Bader charge of nuclear quadrupole resonance for some atoms in the attachment of Chloroquine drug onto X–B_4N_{10} (X=Al/C/Si) nanocages which was measured by theoretical method. In Figure 4a, it was exhibited the fluctuation of the charge distribution for all atoms in the Chloroquine drug towards understanding which atoms have more electron donating tendency in the attachment to the X–B_4N_{10} (X=Al/C/Si) complexes.

On the other hand, the element of N in Chloroquine drug acts like an electron donor which has a high energy orbital with one or more electrons. So, in X–B_4N_{10} (X=Al/C/Si) complexes, the elements of Al, C and Si can be considered as the electron acceptors which have a low energy orbital with one or more vacancies (Figure 4b,c,d).

In fact, it was presented the influence of the linkage between N11 in Chloroquine drug (Figure 4a) and Al13, C13 and Si13 in Al–B_4N_{10}_NC (Figure 4b), C–B_4N_{10}_NC (Figure 4c) and Si–B_4N_{10}_NC (Figure 4d) complexes, respectively during adsorbing Chloroquine owing to achieved data of E_p from NQR spectroscopy. The competence of X–B_4N_{10} (X=Al/C/Si) complexes for sensing of Chloroquine is oscillated by their selectivity and sensitivity which can indicate the yield of these materials as the engaged detectors.

Table 2. The electric potential (E_p/a.u.) and Bader charge (Q/coulomb) through NQR calculation for functionalized elements of Chloroquine drug attached to Al–B_4N_{10}, C–B_4N_{10}, and Si–B_4N_{10} nanocages using CAM-B3LYP/EPR-III,6-311+G(d,p) calculation.

Chloroquine			Al-B_4N_{10}			C-B_4N_{10}			Si-B_4N_{10}		
Atom	Q	E_p	Atom	Q	E_p	Atom	Q	E_p	Atom	Q	E_p
C (1)	0.01	−14.54	B1	−0.42	−11.30	B1	0.29	−11.27	B1	0.33	−11.26
C (2)	0.00	−14.54	N2	0.32	−18.14	N2	−0.15	−18.09	N2	−0.16	−18.11
C (3)	−0.04	−14.53	N3	−1.49	−18.12	N3	−0.13	−18.07	N3	−0.16	−18.10
C (4)	0.09	−14.51	B4	−0.37	−11.30	B4	0.29	−11.26	B4	0.33	−11.27
C (5)	0.04	−14.55	B5	−0.54	−11.30	B5	0.30	−11.28	B5	0.33	−11.26
C (6)	0.00	−14.50	B6	−0.26	−11.28	B6	0.29	−11.27	B6	0.33	−11.26
C (7)	0.10	−14.47	N7	0.58	−18.14	N7	−0.15	−18.09	N7	−0.16	−18.12
C (8)	0.04	−14.57	N8	1.57	−18.13	N8	−0.13	−18.08	N8	−0.15	−18.09
C (9)	0.10	−14.53	N9	0.47	−18.20	N9	−0.10	−18.08	N9	−0.33	−18.18
N (10)	−0.28	−18.14	N10	−0.24	−18.20	N10	−0.10	−18.09	N10	−0.33	−18.17
N (11)	−0.07	−18.01	N11	−0.02	−18.18	N11	−0.09	−18.08	N11	−0.31	−18.16
C (12)	0.12	−14.46	N12	0.20	−18.18	N12	−0.10	−18.07	N12	−0.32	−18.15
C (13)	0.02	−14.52	Al13	−0.00	−43.70	C13	0.11	−14.53	Si13	0.96	−48.39
C (14)	0.02	−14.52	N14	0.73	−18.12	N14	−0.14	−18.08	N14	−0.18	−18.12
C (15)	0.01	−14.52	N15	0.46	−18.13	N15	−0.14	−18.08	N15	−0.18	−18.12
C (16)	0.08	−14.51	Note:								
N (17)	−0.25	−18.10									
C (18)	0.08	−14.51									
C (19)	0.00	−14.55									
C (20)	0.08	−14.51									
C (21)	0.01	−14.54									
Cl (22)	−0.10	−63.31									

Electric potential: E_p/a.u.
Bader charge: Q/coulomb

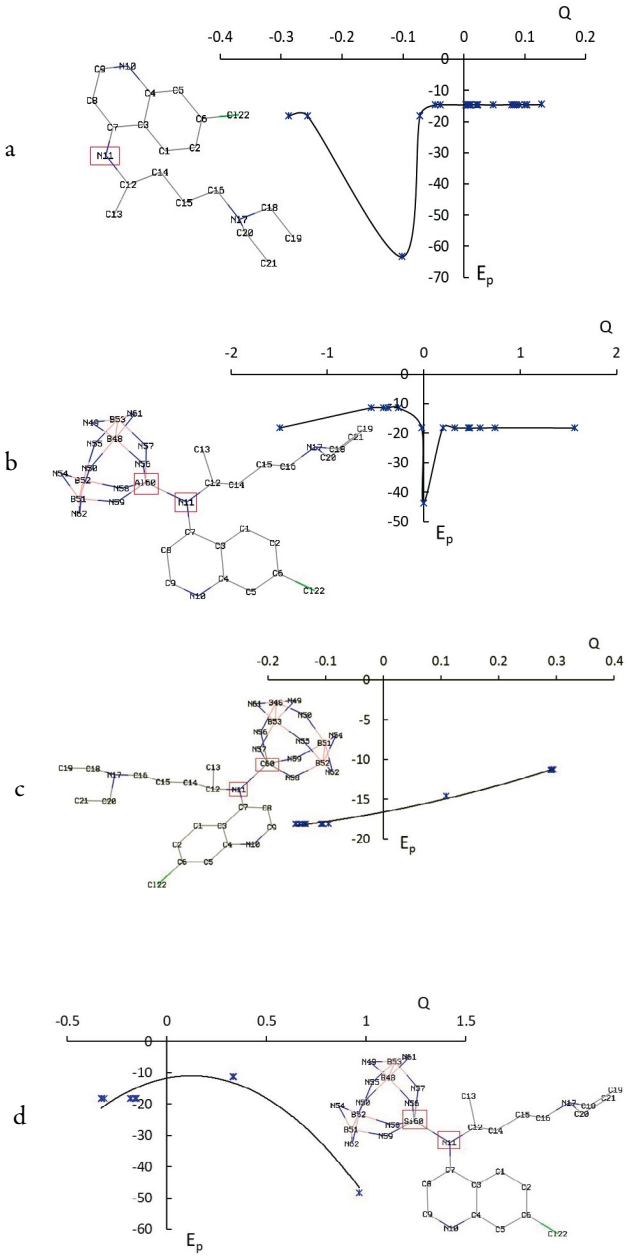

Figure 4. The amounts of electric potential (E_p/a.u.) versus Bader charge (Q/coulomb) through NQR calculation for **a)** Chloroquine drug, **b)** Chloroquine @Al–B_4N_{10}_NC, c) Chloroquine @C–B_4N_{10}_NC, **d)** Chloroquine @Si–B_4N_{10}_NC.

Spectroscopy of IR

The spectroscopy of infrared (IR) through some computations were completed for Chloroquine drug (Figure 5a) attached to X–B_4N_{10} (X=Al/C/Si) complexes by DFT approach to catch a more stable system accompanying thermodynamic attributes. Therefore, it has been simulated the several complexes containing Chloroquine @Al–B_4N_{10}_NC (Figure 5b), Chloroquine @C–B_4N_{10}_NC (Figure 5c), Chloroquine @ Si–B_4N_{10}_NC (Figure5d), respectively.

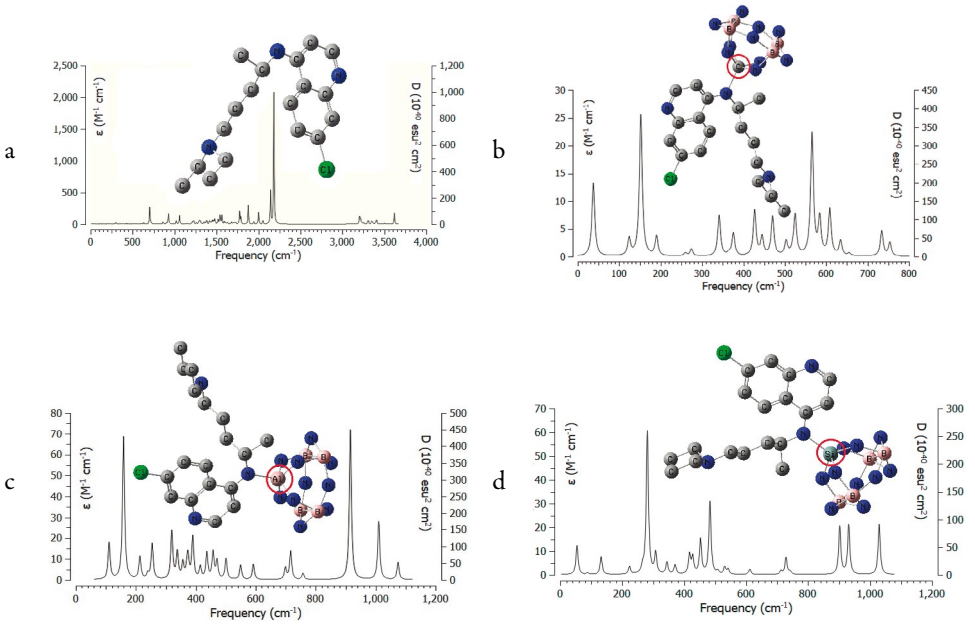

Figure 5. The Frequency (cm^{-1}) amounts of IR spectrums for a) v drug, b) Chloroquine @Al–B_4N_{10}_NC, c) Chloroquine @C–B_4N_{10}_NC, d) Chloroquine @Si–B_4N_{10}_NC.

The curve of Figure 5a was shown in the frequency limitation across 500–3500 cm^{-1} for v drug with a sharp peak around 2183.43 cm^{-1}. Figure 5b has shown the frequency range between 100–1500 cm^{-1} for Chloroquine @Al–B_4N_{10}_NC with two sharp peaks around 158.81 and 915.64 cm^{-1}. Figure 5c has indicated the fluctuation of frequency between 50–750 cm^{-1} for Chloroquine @C–B_4N_{10}_NC with the sharp peaks around 37.34, 152.01 and 565.57 cm^{-1}. Figure 5d has showed the fluctuation of frequency between 100–1100 cm^{-1} for Chloroquine @Si–B_4N_{10}_NC with sharp peaks around 281.19, 483.33, 902.26, 931.18 and 1029.57 cm^{-1}.

The outlook of Figure 5a-d introduces the proof for different frequencies of [Chloroquine @ X–B_4N_{10} (X=Al/C/Si)] complexes which indicate the active sites in the Chloroquine drug and functionalized atoms in X–B_4N_{10} (X=Al/C/Si) that can transfer the charge of electrons in polar Chloroquine into the X–B_4N_{10} (X=Al/C/Si) complexes.

Furthermore, Table 3 through the thermodynamic specifications concluded that X–B_4N_{10} (X=Al/C/Si) due to adsorption of Chloroquine drug might be more efficient sensor for a drug delivery system.

Table 3. The thermodynamic characters thermal energy ($\Delta E°$), thermal enthalpy ($\Delta H°$), Gibbs free energy ($\Delta G°$), entropy ($S°$) and dipole moment of Chloroquine drug, Chloroquine @Al–B_4N_{10}_NC, c) Chloroquine @C–B_4N_{10}_NC, Chloroquine @Si–B_4N_{10}_NC using CAM-B3LYP/6-311+G (d, p), LANL2DZ calculation.

Compound	Dipole moment (Debye)	$\Delta E°\times10^{-4}$ (kcal/mol)	$\Delta H°\times10^{-4}$ (kcal/mol)	$\Delta G°\times10^{-4}$ (kcal/mol)	$S°$ (cal/K.mol)
Chloroquine drug	5.83	–821.87	–821.87	–821.91	129.09
Chloroquin @Al–B_4N_{10}	3.42	–55.03	–55.03	–55.04	98.17
Chloroquine @C–B_4N_{10}	1.41	–42.35	–42.35	–42.35	99.09
Chloroquine @Si–B_4N_{10}	1.29	–57.95	–57.95	–57.95	99.25

It is remarkable that polarization functions into the practical basis set in the enumerations indicate a notable prosperity on the quantum theoretical technics. The outcomes of the mentioned perceptions intensely offer that Chloroquine attached to X–B_4N_{10} (X=Al/C/Si) complex which are persuades by a mutation in the polarization of the ambiance. It can be found that a growth in the dielectric constant augments the endurance and turnover of this medication for curing COVID-19 viral malady.

The adsorption process of Chloroquine drug on the surface of functionalized B_4N_{10}_NC by Al, C, and Si elements is affirmed by $\Delta G°_R$ the quantity:

$$\Delta G°_R = \Delta G°_{\text{Chloroquine@ X–B4N10\_\_NC}} - (\Delta G°_{\text{Chloroquine-adsorbed}} + \Delta G°_{\text{X–B4N10\_\_NC}}); \text{X= Al, C, Si}$$

As seen in Table 3, all accounted amounts of Al–B_4N_{10}_NC, C–B_4N_{10}_NC and Si–B_4N_{10}_NC are close which can demonstrate an appropriate potential of these functionalized nanocages for Chloroquine drug adsorption as a drug delivery technique (Figure 6).

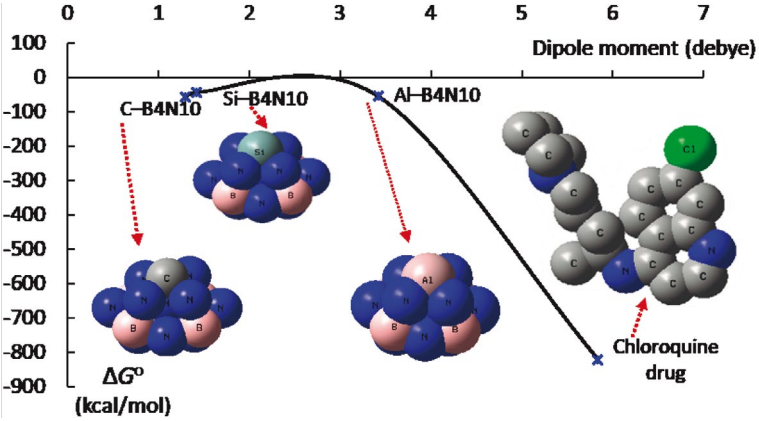

Figure 6. Gibbs free energy (ΔG°_{R}) versus dipole moment (Debye) for Chloroquine drug, Al–B_4N_{10}_NC, C–B_4N_{10}_NC, Si–B_4N_{10}_NC complexes using CAM-B3LYP/6-311+G (d,p), LANL2DZ.

Figure 6 has shown the fluctuation of ΔG° versus dipole moment for different functionalized nanocages of Al–B_4N_{10}_NC, C–B_4N_{10}_NC and Si–B_4N_{10}_NC as electron acceptors (adsorbents) for trapping Chloroquine drug as an electron donor (adsorbate) during interaction process as a promising drug delivery system.

Conclusions

In this work, the effect of Chloroquine drug on the COVID-19 treating has been studied owing to attaching to the X–B_4N_{10} (X=Al/C/Si) complex surrounds by periodic box of H_2O as the drug delivery technics. Chloroquine drug has motivated the scientists for investigation on the clinical therapy of viral coronavirus malady (COVID-19) using linkage to the B_4N_{10}_NC which can engage an impressive drug delivery approach due to computational analysis on the optimized structure extracted from DFT measurements. The progress of impressive DFT methods including electronic correlation effects has illustrated to be a significant key in the field of shielding computations. On the other hand, the element of N in Chloroquine drug acts like an electron donor which has a high energy orbital with one or more electrons. So, in X–B_4N_{10} (X=Al/C/Si) complexes, the elements of Al, C and Si can be considered as the electron acceptors which have a low energy orbital with one or more vacancies. In addition, thermodynamic properties have exhibited that functionalized nanocages of Al–B_4N_{10}_NC, C–B_4N_{10}_NC and Si–B_4N_{10}_NC as electron acceptors (adsorbents) for trapping Chloroquine drug as an electron donor (adsorbate) during interaction process can b promising drug delivery system. Concerning boron-based drug delivery

systems applied as a specific drug transport, as well as other essential drug delivery system design necessities, the authors have purposed to give readers a detailed conception of these systems.

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Conflicts of interest

Authors declare that they have no conflicts of interest

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