

Article

Molecular-Level Assessment of Adsorptive Interaction and Corrosion Inhibition Potential of Some Green Compounds with Caffeine Scaffold on Fe(110) Surface

Ekemini Ituen ^{1,2,3,*}, Ivy Edeke ¹, Muhammad Oshafu ⁴, Victor Gentle ^{4,5},
Ifeanyichukwu Aduanya ⁶, Chibueze Olelewe ⁷ and Iniubong Okon ^{1,2}

¹ Computational Materials Science Group, TETFund Centre of Excellence in Computational Intelligence, University of Uyo, Uyo 52003, Nigeria; ivyedeke19@gmail.com (I.E.); okoniniubongg@gmail.com (I.O.)

² Department of Chemistry, Faculty of Physical Sciences, University of Uyo, Uyo 52003, Nigeria

³ Shimmer Center, Tianfu Jiangxi Laboratory, Chengdu 647419, China

⁴ Department of Physics, Federal University of Lafia, Lafia 950101, Nigeria; oshafudeen@gmail.com (M.O.); victorugentle@gmail.com (V.G.)

⁵ Department of Mechanical Engineering, Akwa Ibom State University, Mkpatt Enin 520221, Nigeria

⁶ Department of Mechanical Engineering, Michael Okpara University of Agriculture, Umudike 440101, Nigeria; aduanyiafy@gmail.com (I.A.)

⁷ Department of Mechanical Engineering, University of Nigeria, Enugu 410101, Nigeria; chibuezeolewelep76979@unn.edu.ng (C.O.)

* Corresponding author. E-mail: ekeminiituen@uniuyo.edu.ng (E.I.)

Received: 12 July 2026; Revised: 6 August 2026; Accepted: 14 September 2026; Available online: 16 October 2026

ABSTRACT: Five compounds, namely, caffeine, theobromine, theophylline, paraxanthine, and xanthine, that exhibit the caffeine-based scaffolds, were assessed using density functional theory (DFT) and molecular dynamics (MD) simulations to elucidate their adsorption behaviour on Fe(110) surface. The potential adsorption sites in the compounds were probed in terms of quantum chemical descriptors, frontier molecular orbitals, Fukui functions, and Mulliken charges, while MD simulations provided insight into adsorption energies, binding, and deformation configurations. Results reveal that theobromine exhibited the highest reactivity and strongest adsorption as a result of favourable electronic properties and potential of interaction with the metal surface through two active sites. Caffeine followed closely, but exhibited slight steric limitations. Paraxanthine and theophylline exhibited moderate behaviour, while xanthine displayed the weakest surface interaction as a result of relatively poor donor-acceptor potential. The results also demonstrate the essential role of N-methyl substitution and electronic softness in optimizing caffeine-derived molecules for application as corrosion inhibitors for steel. The findings from this study offer insights into sustainable adsorption corrosion inhibitors derived from naturally occurring scaffolds before engaging in rigorous experiments on trial and error basis, which often consumes time, energy, and resources.

Keywords: Caffeine scaffolds; Corrosion inhibition; DFT; Fe(110) surface; Molecular dynamics simulations; Quantum chemical descriptors



1. Introduction

Corrosion has remained a persistent and economically damaging problem in many industries that rely on ferrous materials such as steel. Being the electrochemical degradation of steel in aggressive environments (which may be acidic, saline, or oxidative), corrosion undermines mechanical performance and shortens equipment lifespan. It also causes industries to incur significant repair and replacement costs. Corrosion typically involves anodic metal dissolution as well as cathodic reactions and is influenced by fluid properties such as pH, temperature, and the presence of aggressive ions. To enhance materials' durability and reduce the cost of maintenance, effective corrosion control strategies are usually deployed.

Among the effective strategies for the mitigation of corrosion, the use of corrosion inhibitors, especially organic compounds, is considered simple and practical. The organic compound often adsorbs onto the steel surface, forming a protective film that hinders further corrosion [1]. It has been established that the presence of some functionalities, such as O, N, S, and P atoms, multiple bonds, and aromatic rings enhances the adsorption and corrosion inhibition performance of organic molecules [2]. A class of compounds that has garnered attention for such applications is the family of purine-derived heterocycles [2–4]. Within this class, caffeine and its naturally occurring analogues, namely, paraxanthine, theobromine, theophylline, and xanthine, stand out due to their aromaticity and abundance of electron-rich nitrogen and oxygen sites in their molecular structure. These features have been established to be responsible for enabling the molecules to interact strongly with metal surfaces through physisorption and/or chemisorption mechanisms [5]. Furthermore, their green chemistry profile, biodegradability, low toxicity, and widespread natural occurrence, make them attractive for deployment as environmentally sustainable corrosion control chemicals.

Several caffeine- and purine-related compounds, as well as the parent xanthine derivatives, have been investigated as corrosion inhibitors for different metallic systems in various media [6]. Adenine and guanine have been demonstrated to effectively inhibit mild steel corrosion facilitated by their multiple nitrogen coordination sites and strong adsorption tendencies [7]. Purines have been functionalized into Schiff bases, imidazoline and pyrimidine derivatives, and also assessed as corrosion inhibitors [8–10]. Also, caffeine-modified polymeric compounds and plant extracts that contain the caffeine and purine alkaloids have been reported to exhibit substantial adsorption and film-forming anti-corrosion properties on metal surfaces. In addition, some studies have separately reported theobromine, theophylline, and xanthine as well as their substituted derivatives as exhibiting corrosion inhibition performance from purely experimental results.

The experimental approach for assessing corrosion inhibition often requires extensive instrumentation, controlled exposure studies, and post-treatment characterization [11]. Although the results are usually informative, the processes are time-consuming and resource intensive. At the end, the results may yield very low efficiency, therefore making a proper selection of molecules for application as corrosion inhibitors to rely on trial and error. However, computational methods such as density functional theory (DFT) and molecular dynamics (MD) simulations offer a fast, cost-effective, and predictive alternative for pre-screening candidate inhibitors. These methods also provide more quantitative insight into the reactivity of a molecule, charge distribution, adsorption energetics, and interaction mechanisms at the atomic level, which can rarely be determined experimentally [7,12,13].

In previous works, researchers have established that organic corrosion inhibitors with multiple nitrogen and oxygen heteroatoms tend to bind effectively to Fe surfaces, because of their delocalized π -systems and flexible geometries [14,15]. Caffeine-based molecules, having an xanthine backbone and diverse substitution patterns, present a rich framework in which such interactions can be explored. Yet, despite their well-documented surface activity in pharmacological and materials research, their corrosion-inhibitory potential on iron, especially from a theoretical perspective, remains underexplored.

This study was designed to fill the gap. The objectives of this study include the investigation of the adsorption behaviour of some caffeine-derived compounds, namely, caffeine, paraxanthine, theobromine,

theophylline, and xanthine, while the DFT and MD simulation methods were deployed to establish structure-activity relationships based on substitution and electronic properties. The molecular structures of the studied molecules are presented in Figure 1. Through analysis of their quantum descriptors, frontier molecular orbitals, Fukui indices, and adsorption energies, we aim to elucidate the structure-activity relationships governing their surface interactions.

The contribution of this work is a like-for-like comparison of five molecules with a caffeine scaffold, treated at the same level of theory on the same Fe(110) model, so that the influence of N-methyl substitution on the computed electronic descriptors and adsorption energies can be isolated. A qualitative correspondence between electronic softness and adsorption strengths is examined, and a recurring N,O-oriented adsorption geometry is identified. These observations provide a structure-activity trend that can guide the selection of related scaffolds for later experimental testing.

Previous experimental and theoretical studies have shown that individual xanthine derivatives, including caffeine and theobromine, can adsorb on metals and, in some media, inhibit corrosion [6,16,17]. Those reports treat one molecule, or a substituted analogue, at a time, so the influence of N-methyl number and position on the same xanthine core is not resolved. The present work addresses this gap by comparing the demethylation series of caffeine, with 1,3,7-trimethyl (caffeine), 3,7-dimethyl (theobromine), 1,3-dimethyl (theophylline), 1,7-dimethyl (paraxanthine), ranking them with the unsubstituted xanthine, on one Fe(110) surface under the same computational conditions. This design emphasizes the influence of the substitution pattern as a structural variable to reveal how it tracks the HOMO-LUMO gap, electronic softness, and other electronic descriptors.

The adsorption model consists of the neutral (unprotonated) molecules on a clean Fe(110) surface under vacuum conditions, water, aggressive ions, protonated forms, tautomers, competitive adsorption and oxide or hydroxide films were not included in the modelling. Therefore, the results are a relative ranking of the intrinsic inhibitor-metal affinity of the five molecules, not a prediction of absolute corrosion inhibition performance in a named acidic or saline medium. Extension of the model to aqueous/acidic electrolytes, protonated species, and oxidized iron surfaces could be a next future study.

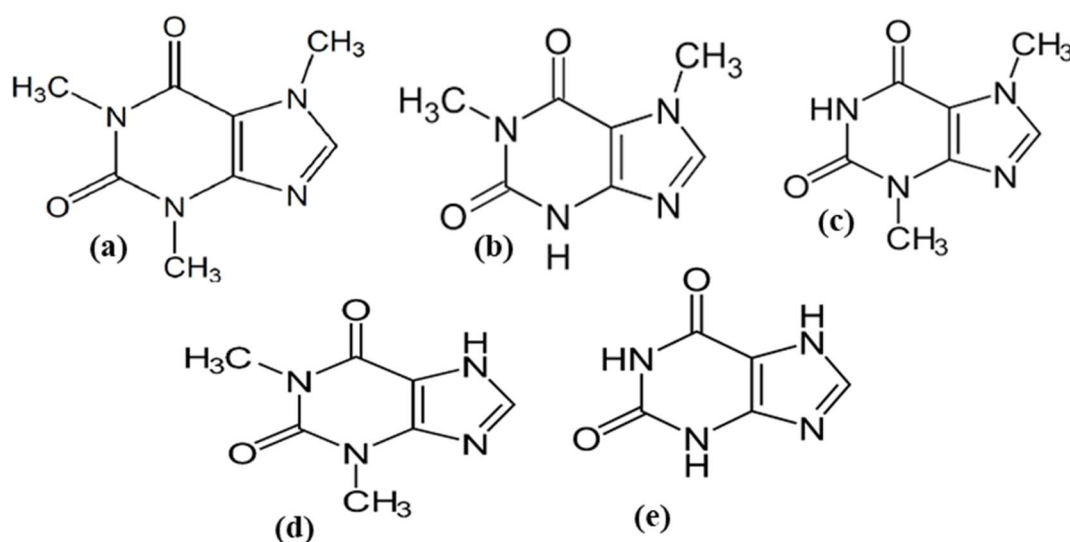


Figure 1. Molecular structure of (a) caffeine (1,3,7-trimethylxanthine), (b) paraxanthine 1,7-dimethylxanthine, (c) theobromine (3,7-dimethylxanthine), (d) theophylline 1,3-dimethylxanthine, and (e) xanthine. The ring numbering follows the International Union of Pure and Applied Chemistry (IUPAC) purine convention (N1, C2, N3, C4, C5, C6, N7, C8, C9; the carbonyl oxygens are O2 and O6).

2. Computational Methodology

2.1. Geometry Optimization

The initial molecular structures (Figure 1) of the five compounds were constructed using the Atomistic Builder in BIOVIA Material Studio 2017. Geometry optimizations were carried out using the Forcite module under the COMPASS force field. Each structure was energy-minimized with fine convergence criteria to ensure thermodynamically stable configurations suitable for quantum chemical analysis [18]. The fully relaxed forcefield geometries obtained in this step were used as input for the single point quantum chemical calculations described in Section 2.2, with no further geometry re-optimization at the DFT level.

2.2. Quantum Chemical Calculations

Quantum mechanical single point electronic-structure calculations were performed using the DMol³ module, on the COMPASS-optimized geometries, employing the hybrid Becke's three-parameter exchange functional with the Lee–Yang–Parr correlation functional (B3LYP) and the double-numeric plus polarization (DNP) basis set. The single-point level of theory is appropriate here because the frontier orbitals, Fukui functions and global descriptors depend on the relaxed molecular geometry, already obtained at the force field level. The B3LYP functional and DNP basis set were selected owing to their proven reliability when electronic properties elucidation of organic molecules is concerned, especially for charge distribution and frontier orbitals. Specifically, DNP affords more accurate treatment of heteroatoms involved in the adsorption. When combined with MDS, the approach ensures that the description of the interaction between the molecule and the surface is reliable.

These calculations yielded key electronic properties, namely, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) energies, the energy gaps (ΔE), ionization energy (IE), electron affinity (EA), electronegativity (χ), global hardness (η), and global softness (σ). These descriptors were calculated using the following relationships [19]:

$$\Delta E = E_{LUMO} - E_{HOMO} \quad (1)$$

$$IE = -E_{HOMO} \quad (2)$$

$$EA = -E_{LUMO} \quad (3)$$

$$\chi = \frac{1}{2}(IE + EA) \quad (4)$$

$$\eta = \frac{1}{2}(IE - EA) \quad (5)$$

$$\sigma = \frac{1}{\eta} \quad (6)$$

where E_{LUMO} is the energy of the LUMO and E_{HOMO} is the energy of the HOMO.

These reactivity descriptors were used for predictive evaluation of surface interaction potential based on electron donation/acceptance tendencies and overall chemical softness.

2.3. Fukui Functions and Mulliken Charge Analysis

The relaxed geometries were subsequently used for the DMol³ single point electronic structure calculations (B3LYP/DNP). Condensed fukui functions were computed with finite-difference approximation [13], and the conventional definitions are used: The $f^+ = q(N) + (1 - q(N))$ measures the response of an atom to nucleophilic attack and therefore flags electron-accepting (electrophilic) sites of the

inhibitor, whereas $f^- = q(N) - q(N - 1)$ measures the response to electrophilic attack and flags electron-donating sites of the inhibitor. Mulliken atomic charges were also obtained on the same geometry and used to identify electron-rich atoms that may donate density to the metal. Atoms that combine a negative charge with a large f^- are treated as the most probable electron-donor towards Fe, and *vice versa* [14].

2.4. Molecular Dynamics Simulations on Fe(110) Surface

Dynamic simulations of interactions between the molecules and the Fe(110) surface were performed, selected for its thermodynamic stability and common occurrence in steel corrosion studies [18]. A slab of Fe(110) was cleaved and expanded into a 5×5 supercell with periodic boundary conditions, and a 15 Å vacuum gap was introduced along the z-axis to eliminate image interference [16]. Each optimized molecule was placed approximately 5 Å above the iron surface, and MD simulations were performed using the Adsorption Locator and Forcite modules in Material Studio under the COMPASS forcefield, applying simulated annealing to capture stable adsorption configurations.

Simulations were performed in a vacuum. The Fe(110) slab was treated as a clean, oxide-free surface, and the inhibitors were modelled only in their neutral (unprotonated) forms. Explicit water, hydronium or halide ions, and iron oxide/hydroxide layers were not introduced. The protocol therefore ranks the intrinsic molecule-Fe(110) affinity of the five scaffolds under identical, highly idealized conditions; it does not reproduce the aqueous acidic or saline environments in which corrosion typically operate.

Forcite MD simulations was run in the canonical (NVT) ensemble at 298 K using the Nose thermostat, a time step of 1.0 fs, 50 ps equilibration followed by 500 ps. The adsorption locator search used Monte Carlo simulated annealing with 5 annealing cycles and 10 lowest energy frames retained per candidate adsorption configurations. Outputs such as adsorption total energy (E_{ads}), deformation energy (E_{def}), and molecule-surface distance were extracted to evaluate adsorption strength and orientation. The adsorption energy (E_{ads}) was computed from the output as the difference between the energy of the combined system and the energies of the isolated components, using Equation (7).

$$E_{ads} = E_{tot} - (E_{surf} + E_{inh}) \quad (7)$$

where E_{tot} is the total energy of the Fe(110)-inhibitor system, E_{surf} is the energy of the isolated Fe(110) surface, and E_{inh} is the energy of the isolated molecule. The total adsorption energy (E_{ads}) is further expressed as the sum of the rigid adsorption energy (E_{rig}) and the deformation energy (E_{def}) according to Equation (8).

$$E_{ads} = E_{rig} + E_{def} \quad (8)$$

where E_{rig} is the energy of adsorption of the unrelaxed (rigid) molecule at its optimized adsorption position on the surface, and E_{def} is the energy change associated with the subsequent relaxation of the adsorbed molecule in the presence of the surface.

3. Results and Discussion

3.1. Geometry Optimisation

During the DFT-based geometry optimization using the B3LYP functional and DNP basis set, all five compounds successfully converged to their stable, minimum-energy configurations as depicted in Figure 2. By inspecting the optimized geometries shown in Figure 3 visually, it can be observed that the molecules retained predominantly planar structure, with minimal torsional strain or steric distortion. This planar configuration is very significant to adsorption because it enables broad π - π and van der Waals interactions with the flat Fe(110) surface, thereby facilitating better surface coverage and electronic coupling [20].

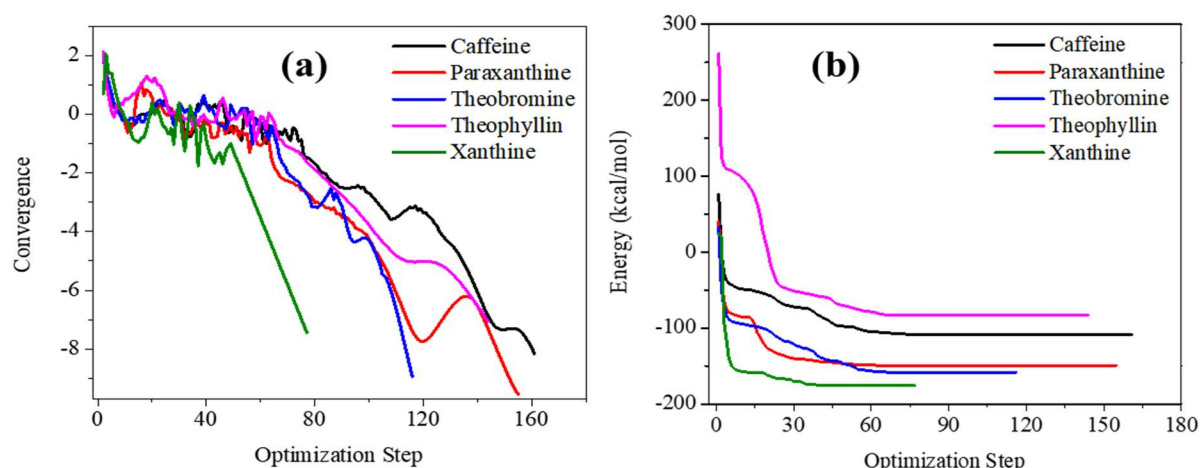


Figure 2. (a) Convergence and (b) Energy obtained from optimization step.

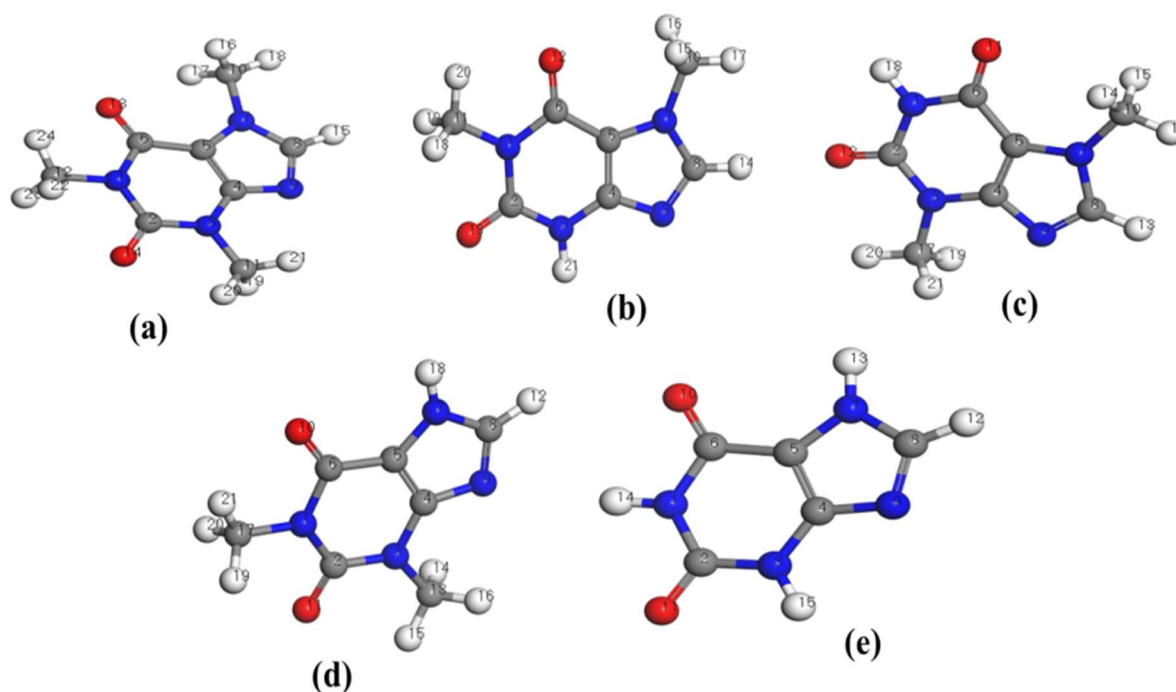


Figure 3. Optimized Structure of (a) Caffeine (b) Paraxanthine (c) Theobromine (d) Theophylline (e) Xanthine [C = grey; H = white; N = blue; O = red].

Although the data for bond lengths were not explicitly included in the results presented, standard bond distances were inferred from the visualization environment within the DMol³ module. The values can be considered to be consistent with well-established values in related nitrogen-containing heterocyclic systems [19]. In particular, the carbon-nitrogen (C–N) and carbon-carbon (C–C) bonds within the conjugated ring system were around 1.33 Å and 1.37 Å, whereas the carbonyl (C=O) bonds at positions C2 and C6 were in the range of 1.21 Å to 1.23 Å. These distances are in agreement with values reported in literature for xanthine derivatives optimized within comparable levels of theory [21], thus indicating proper delocalization and resonance stabilization across the molecular backbone.

Minor deviations were observed only with xanthine, which lacks the steric balance provided by N-methyl substituents but exhibited slight out-of-plane puckering (about 3°). However, the magnitude of this distortion was small and so may not significantly disrupt its ability to adsorb onto the metal surface. The structural features, such as planarity, conjugation, and compactness, could collectively promote effective

surface interaction and also set a favourable foundation for the subsequent adsorption energy and electronic reactivity assessments.

3.2. HOMO–LUMO Energetics

The electronic properties of the HOMO and LUMO can offer important insight into how a molecule may interact with a metal surface. Specifically, the HOMO energy reflects the ability of the molecule to donate electrons to empty d-orbitals on the Fe surface, while the LUMO energy relates to its ability to accept back-donated electron density from the metal [19]. Molecules that possess high-lying HOMO levels and low-lying LUMO levels are generally considered to be more reactive and better suited to form stable coordination interactions with metal atoms [22].

As shown in Table 1, theobromine displayed the highest HOMO energy (approximately -0.19 Ha), hence has the strongest tendency to donate electrons to the Fe(110) surface. This can be attributed to the presence of two N-methyl substituents, which increase electron density within the ring system and raise the HOMO level. Caffeine, with three N-methyl groups, followed closely. Although caffeine has one additional methyl group compared to theobromine, this group is located at N1, a position that may lead to a more diffuse distribution of electron density and slightly reduce the efficiency of orbital overlap with the metal surface.

Paraxanthine and theophylline, which contain only two methyl groups positioned differently, exhibited intermediate HOMO energies. Their electron-donating potentials may be lower than that of theobromine or caffeine, perhaps due to less favourable methylation patterns. However, xanthine, with no N-methyl groups entirely, exhibited the lowest HOMO energy (about -0.25 Ha), and this reflects a relatively poor electron-donating ability due to the absence of alkyl-driven electron release into the conjugated system.

The trend in LUMO energies complements the above observations. Effective corrosion inhibitors should also possess low-lying LUMOs that can accept electron density via back-donation from the metal surface [20]. Thus, caffeine and theobromine again stood out, having LUMO levels around -0.081 Ha and 0.083 , respectively. This indicates a strong electron-accepting potential centred largely on the carbonyl groups. All the molecules possess conjugated systems, which allow for stabilization of π^* orbitals and promote efficient back-bonding. Paraxanthine and theophylline followed with slightly higher LUMO energies, while xanthine afforded the least favourable LUMO (about -0.052 Ha), which portrays weak interaction capability with surface electrons.

Taken together, these HOMO-LUMO characteristics directly influence how strongly each molecule is expected to adsorb on the Fe(110) surface. Theobromine, with its favourable balance of high electron-donating ability and strong back-acceptance potential, may be predicted to exhibit the strongest interaction with Fe(110). Caffeine performs similarly, though slightly less optimally. Paraxanthine and theophylline are moderately reactive, while xanthine, by virtue of its low HOMO and relatively high LUMO, is likely to show the weakest surface adsorption among the five compounds. This ordering is an electronic ranking of adsorption tendency and may not be a measure of experimental corrosion inhibition efficiency.

Table 1. Some quantum chemical parameters were calculated for the studied molecules.

Parameters	Caffeine	Paraxanthine	Theobromine	Theophylline	Xanthine
E_{HOMO} (Ha)	−0.20347	−0.21192	−0.19284	−0.22136	−0.24875
E_{LUMO} (Ha)	−0.08126	−0.07241	−0.08317	−0.07188	−0.05263
ΔE (Ha)	0.12221	0.13951	0.10967	0.14948	0.19612
IE	0.20347	0.21192	0.19284	0.22136	0.24875
EA (Ha)	0.08126	0.07241	0.08317	0.07188	0.05263
χ (Ha)	0.14236	0.14217	0.13801	0.14662	0.15069
η (Ha)	0.06111	0.06976	0.05484	0.07474	0.09806
σ (Ha ^{−1})	16.36284	14.33429	18.2366	13.37951	10.19612

3.3. Energy Gap, Hardness, and Softness

The difference in energy value between the LUMO and HOMO levels is commonly called the energy gap (ΔE), and it serves as an important predictor of chemical reactivity. Molecules with smaller ΔE values can more easily undergo electron excitation or re-distribution, making them more chemically soft and responsive in intermolecular interactions. In the context of corrosion inhibition, a smaller ΔE is usually associated with greater ease of charge transfer that occurs between the inhibitor and the surface of the substrate (metal), enhancing adsorption strength.

Among the five molecules, the smallest HOMO-LUMO gap (approximately 0.11 Ha) was obtained for theobromine, which corresponds to the highest global softness. This signifies that theobromine could be the most polarizable and electronically adaptable compound, ideal for interacting dynamically with Fe(110) surface atoms. Its high softness (about 18.24 Ha⁻¹) and low hardness (about 0.055 Ha) will enable both rapid electron donation and efficient acceptance of back-donated charge. These characteristics point to strong potential for chemisorption and high corrosion inhibition. Caffeine followed closely, with a slightly larger energy gap, still corresponding to good softness (16.36 Ha⁻¹) and reactivity. Though with slightly dispersed electron density, the third methyl group in caffeine could contribute to a favourable delocalization of frontier orbitals, and support strong surface interactions.

Both paraxanthine and theophylline showed moderate ΔE values, which reflect balanced but less pronounced softness and chemical responsiveness. Both molecules have a lower number of methyl groups, or less optimal positioning, which may cause weaker modulation of electron flow across the molecule. This could, in turn, reduce their ability to adapt to the electronic landscape of the Fe(110) surface. Xanthine stood out with the widest HOMO-LUMO gap (approximately 0.20 Ha), the highest hardness, and the lowest softness (about 10 Ha⁻¹). These properties demonstrate limited flexibility in electronic redistribution and a poor capacity to interact effectively with the fluctuating charge fields of Fe atoms. As a result, the adsorption behaviour of xanthine is expected to rely more on weak physical interactions (physisorption) rather than the stronger charge-transfer-driven chemisorption that typifies high-performance corrosion inhibitors.

The observed trends in ΔE , hardness, and softness closely mirror the structural influence of N-methyl substitution. Each methyl group contributes electron density that helps to narrow the energy gap and soften the molecule. Theobromine, with its optimal balance of donor substituents and π -conjugation, is likely to be the most chemically adaptive species in the group, whereas xanthine, lacking such features, is the most rigid and electronically inert.

On further careful observation, a qualitative correlation can be crafted between the quantum chemical descriptors and adsorption energies. Molecules with lower ΔE and higher softness values exhibited stronger adsorption. This is consistent with their reactivity and charge transfer tendency. Similarly, lower electronegativity was found to be associated with stronger interactions with the surface. This trend is consistent with the computed adsorption energies and indicates that the global descriptors can be used to predict adsorption strength with reasonable reliability in the studied compounds.

3.4. Electronegativity and Molecular Charge Transfer Tendency

Theobromine and caffeine each exhibited relatively low electronegativity values (around 0.14), which could make them excellent candidates for spontaneous charge donation to Fe. Their strong potential for electron transfer enhances the likelihood of forming strong molecule-metal bonds, most likely through their electron-rich (nitrogen and carbonyl) sites [23]. Paraxanthine and theophylline afforded slightly higher electronegativity values, which portrays a somewhat weaker tendency to engage in charge transfer with the Fe surface. While they may still favour adsorption, the overall thermodynamic driving force is reduced in comparison to theobromine and caffeine.

As may be expected, xanthine displayed the highest electronegativity of the group (about 0.17), which narrows the potential difference between itself and the Fe surface. This reduced difference dampens electron flow from the molecule to the metal and may limit its adsorption strength and, by extension, its corrosion-inhibition potential. The trend here again highlights the influence of methyl substitution. The more N-methyl groups a molecule possesses, the lower its overall electronegativity tends to be, likely due to the electron-donating inductive effect of the methyl groups. This reduction in electronegativity may enhance the ability a molecule to donate charge, thereby supporting earlier observations from the HOMO-LUMO and reactivity analysis.

The electronegativity values were also converted to eV units ($1 \text{ Hartree} = 27.211 \text{ eV}$), and the results obtained were: theobromine (3.76 eV), caffeine (3.87 eV), paraxanthine (3.87 eV), theophylline (3.99 eV) and 4.10 eV for xanthine. Compared to the work function of Fe ($\approx 4.5 \text{ eV}$), all five molecules χ exhibit values below the work function of Fe, which implies a thermodynamic driving force for initial electron transfer from molecule to the surface, and the magnitude of the driving force decreases in the order theobromine > caffeine > paraxanthine > theophylline > xanthine.

A closer observation of the adsorption energies reveal more negative values than -100 kJ/mol . These values are typically associated with chemisorption mechanisms, whereas lower values indicate physisorption [24]. From the results, strong adsorption behaviour was observed for theobromine and caffeine, supported by significant charge transfer and donor-acceptor interactions. This suggests that the adsorption mechanism was predominantly chemisorption. However, in contrast, the weaker interaction profile of xanthine could indicate a tendency towards physisorption.

3.5. Correlation Between Structure and Activity

The electronic behaviour and adsorption potential of the studied compounds are expected to be dependent on their structural features, mainly the number, type, and position of substituents on the xanthine core. Slight changes in methylation may influence orbital energies, electron distribution, and reactivity, which in turn may determine how effectively each molecule can interact with the Fe(110) surface. For all the molecules, a fused imidazole-pyrimidinone ring system that bears two carbonyl groups (C2=O and C6=O) forms the core moiety. These carbonyl moieties would serve as the primary acceptor sites for back-donation of electron density from the metal surface. Molecules that facilitate strong conjugation between these carbonyl groups and nearby electron-donating substituents can stabilize their LUMOs and improve surface interaction through enhanced $\text{Fe} \rightarrow \pi^*$ back-bonding [25].

The five compounds differ mainly in the number and positions of the N-methyl groups on the common xanthine scaffold. Xanthine has no methyl group, theophylline has methyl groups at N1 and N3, theobromine has two methyl groups, but at N3 and N7, paraxanthine also has two methyl groups, but at N1 and N7, and caffeine has three methyl groups at N1, N3, and N7. Theobromine is a good example of this favourable configuration. It has two N-methyl groups, one at N3 (pyrimidine ring) and the other at N7 (imidazole ring). The methyl groups are positioned in such a way that their inductive effects resonate through the ring and enhance conjugation with the carbonyls. It appears that a kind of electronic “push-pull” effect could be responsible for lowering the HOMO-LUMO gap, thereby increasing softness, which supports both electron donation and acceptance at chemically relevant sites [24]. Structurally, theobromine was appeared planar and compact, which further promotes favourable orientation and stable adsorption on the Fe surface.

For caffeine, although it also contains three N-methyl groups, the reactivity was already observed to be lower than theobromine. The additional methyl group at N1 seems to introduce a more symmetrical electron distribution. This slightly reduces the directional orbital overlap needed for optimal Fe coordination. However, the molecule still retained high softness and strong donor-acceptor characteristics, which make it a potential highly effective corrosion inhibitor candidate. In paraxanthine and theophylline,

methylation is limited to only two nitrogen sites, and their positioning varies. In paraxanthine, the methyl groups occupy N1 and N7, while in theophylline, they are found at N1 and N3. These configurations disrupt the optimal conjugation pathways seen in theobromine and caffeine, possibly leading to less effective orbital overlap with the carbonyl groups and moderate reactivity. Consequently, these molecules would show diminished but still meaningful potential for adsorption and corrosion inhibition.

Xanthine has no methyl substitution, hence exhibits the least electronically favourable structure. Without the electron-donating influence of N-methyl groups, the xanthine ring remains relatively hard and less polarizable (Figure 4). As can be observed in Figure 5, its HOMO is deeply buried (low electron-donating ability), and its LUMO is poorly stabilized (high energy, weak electron-accepting ability). Moreover, the absence of alkyl groups reduces conjugation with the carbonyls, weakening any possible “push-pull” electronic effects. Though it maintains planarity, xanthine may therefore be electronically and functionally the least well-suited for adsorption and may therefore show the weakest adsorption and lowest predicted inhibition potential.

For all the studied compounds, the structural modifications conferred by N-methylation directly affect the electron distribution, orbital alignment, and chemical softness. These changes, in turn, may control how effectively the molecules can interact with the Fe surface. Theobromine, therefore, seems a more structurally and electronically optimal, while xanthine represents a baseline for poor inhibitor design among the five compounds. The observed hierarchy of performance can be seen as mirroring the underlying structural logic encoded in the substitution pattern.

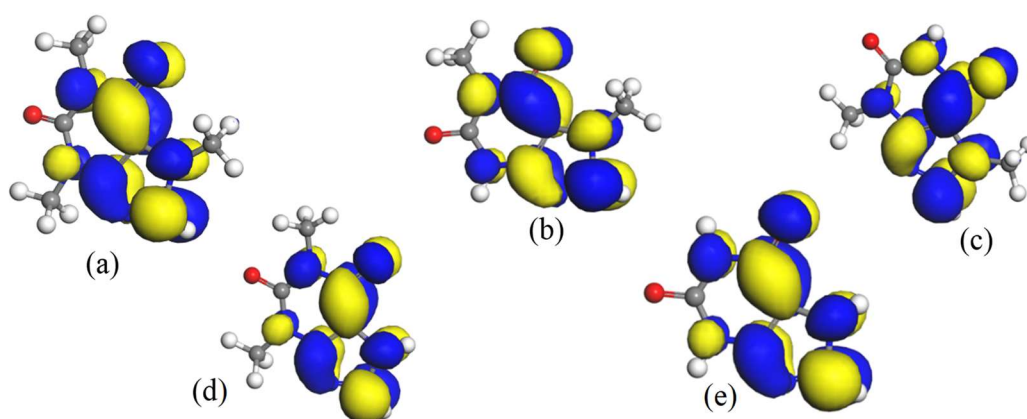


Figure 4. LUMO diagrams of (a) Caffeine, (b) Paraxanthine, (c) Theobromine, (d) Theophylline, and (e) Xanthine.

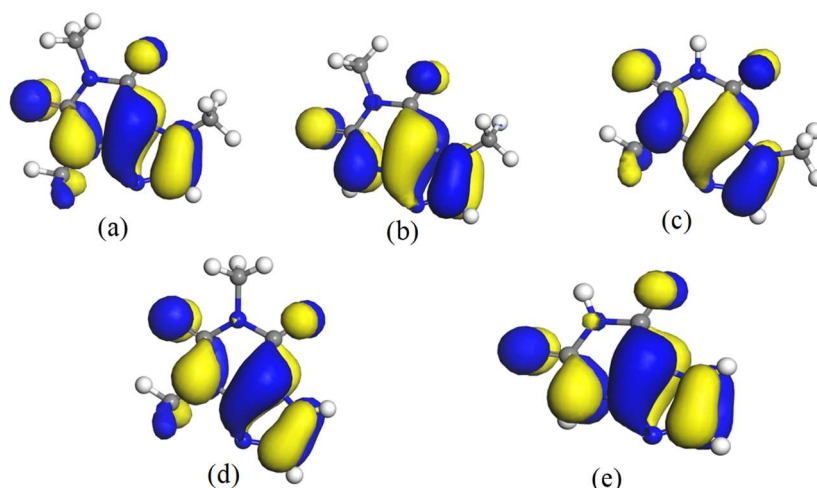


Figure 5. HOMO diagrams of (a) Caffeine, (b) Paraxanthine, (c) Theobromine, (d) Theophylline, and (e) Xanthine.

3.6. Fukui Functions and Mulliken Charge Distribution

Local reactivity was examined using condensed Fukui functions and Mulliken charges (Tables 2–4). The sites for f^+ nucleophilic attack on the inhibitor or electron-accepting sites are listed in Table 2, electrophilic attack or electron-donating sites are listed in Table 3, while Mulliken charges are listed in Table 4. Atom labels in the Table are the Material Studio serial numbers, and their mapping onto the IUPAC xanthine numbering of Figure 1 is shown in the table footnotes.

On the conventional reading of f^+ , the largest electron-accepting sites in the inhibitor molecule lie on the conjugated carbon C8 and C6 and on the carbonyl oxygen atoms. These centers are the most probable locations for metal-to-ligand back donation into the π^* framework. Conversely, based on the f^- , convention, the principal electron-donating sites are the carbonyl oxygen atoms and C5. The ring nitrogens N7 and N9 have only modest f^- values, and may be potential donor sites based on their negative Mulliken charges or on their MD geometries.

With Mulliken charges of -0.50 to -0.54 , the carbonyl oxygen atoms are electron rich and carry f^- large values, hence they can be considered as possible nucleophilic centers. However, since the same atoms also carry appreciable f^+ , they may also be seen as amphiphilic reactive centers, whereby they can donate lone-pair density and can also accept back-donated charge into the $C=O \pi^*$ orbital.

The donor and acceptor maps suggest an N,O-oriented interaction as a working hypothesis for the stringer adsorbates, especially theobromine and caffeine. Which carbonyl oxygen and a ring nitrogen can face the surface simultaneously.

Table 2. Fukui indices for nucleophilic attack.

Caffeine	Paraxanthine	Theobromine	Theophylline	Xanthine
N(1) 0.007	N(1) 0.007	N(1) 0.021	N(1) 0.007	N(1) 0.023
C(2) 0.014	C(2) 0.012	C(2) 0.013	C(2) 0.015	C(2) 0.011
N(3) 0.006	N(3) 0.021	N(3) 0.006	N(3) 0.007	N(3) 0.021
C(4) 0.084	C(4) 0.080	C(4) 0.087	C(4) 0.084	C(4) 0.085
C(5) 0.029	C(5) 0.028	C(5) 0.031	C(5) 0.029	C(5) 0.029
C(6) 0.120	C(6) 0.124	C(6) 0.120	C(6) 0.119	C(6) 0.123
N(7) 0.023	N(7) 0.022	N(7) 0.023	N(7) 0.045	N(7) 0.047
C(8) 0.129	C(8) 0.133	C(8) 0.131	C(8) 0.133	C(8) 0.138
N(9) 0.046	N(9) 0.053	N(9) 0.047	N(9) 0.050	N(9) 0.058
C(10) -0.031	C(10) -0.032	C(10) -0.032	O(10) 0.128	O(10) 0.142
C(11) -0.028	C(11) -0.031	O(11) 0.130	O(11) 0.072	O(11) 0.086
C(12) -0.030	O(12) 0.124	O(12) 0.076	H(12) 0.086	H(12) 0.090
O(13) 0.121	O(13) 0.077	H(13) 0.083	C(13) -0.029	H(13) 0.052
O(14) 0.070	H(14) 0.083	H(14) 0.042	H(14) 0.037	H(14) 0.050
H(15) 0.081	H(15) 0.042	H(15) 0.043	H(15) 0.042	H(15) 0.045
H(16) 0.041	H(16) 0.042	H(16) 0.049	H(16) 0.032	
H(17) 0.041	H(17) 0.049			
H(18) 0.048	H(18) 0.047			
H(19) 0.036	H(19) 0.047			
H(20) 0.040	H(20) 0.029			
H(21) 0.031	H(21) 0.043			
H(22) 0.044				
H(23) 0.047				
H(24) 0.029				

Footnotes: Atom numbers are the Material Studio serial numbers. Ring serials 1–9 map onto the IUPAC numbering as follows N(1) → N1, C(2) → C2, N(3) → N3, C(4) → C4, C(5) → C5, C(6) → C6, N(7) → N7, C(8) → C8 and N(9) → N9. The two

carbonyl oxygens are O2(on C2) and O6 (on C6); their serials are O(13)/(O14) in caffeine, O(12)/O(13) in paraxanthine, O(11)/O(12) in theobromine, O(10)/O(11) in theophylline, and O(10)/O(11) in xanthine.

Table 3. Fukui indices for electrophilic attack.

Caffeine	Paraxanthine	Theobromine	Theophylline	Xanthine
N(1) 0.003	N(1) 0.005	N(1) 0.012	N(1) 0.003	N(1) 0.015
C(2) 0.022	C(2) 0.019	C(2) 0.022	C(2) 0.023	C(2) 0.020
N(3) 0.068	N(3) 0.081	N(3) 0.068	N(3) 0.071	N(3) 0.087
C(4) 0.050	C(4) 0.055	C(4) 0.051	C(4) 0.049	C(4) 0.055
C(5) 0.110	C(5) 0.117	C(5) 0.110	C(5) 0.116	C(5) 0.125
C(6) 0.022	C(6) 0.023	C(6) 0.022	C(6) 0.022	C(6) 0.023
N(7) 0.017	N(7) 0.020	N(7) 0.017	N(7) 0.032	N(7) 0.037
C(8) 0.067	C(8) 0.071	C(8) 0.069	C(8) 0.068	C(8) 0.073
N(9) 0.053	N(9) 0.063	N(9) 0.054	N(9) 0.053	N(9) 0.065
C(10) −0.026	C(10) −0.027	C(10) −0.027	O(10) 0.103	O(10) 0.115
C(11) −0.034	C(11) −0.026	O(11) 0.104	O(11) 0.131	O(11) 0.146
C(12) −0.025	O(12) 0.097	O(12) 0.133	H(12) 0.076	H(12) 0.057
O(13) 0.096	O(13) 0.132	H(13) 0.074	O(12) 0.103	H(13) 0.048
O(14) 0.125	H(14) 0.078	H(14) 0.039	O(13) 0.131	H(14) 0.052
H(15) 0.073	H(15) 0.078	H(15) 0.074	H(15) 0.076	H(15) 0.082
H(16) 0.034	H(16) 0.041	H(16) 0.039	H(16) 0.051	
H(17) 0.037	H(17) 0.048	H(17) 0.046	H(17) 0.058	
H(18) 0.033	H(18) 0.041	H(18) 0.039	H(18) 0.049	
H(19) 0.049	H(19) 0.038	H(19) 0.050	H(19) 0.034	
H(20) 0.056	H(20) 0.037	H(20) 0.057	H(20) 0.038	
H(21) 0.048	H(21) 0.034	H(21) 0.049	H(21) 0.034	
H(22) 0.038				
H(23) 0.046				
H(24) 0.038				

Footnotes: Identical values arise from similar local electronic environments and/or rounding to three decimal places and do not necessarily imply identical reactivity.

Table 4. Mulliken atomic charges.

Caffeine	Paraxanthine	Theobromine	Theophylline	Xanthine
N(1) −0.571	N(1) −0.576	N(1) −0.432	N(1) −0.570	N(1) −0.437
C(2) 0.722	C(2) 0.689	C(2) 0.683	C(2) 0.722	C(2) 0.653
N(3) −0.522	N(3) −0.401	N(3) −0.531	N(3) −0.524	N(3) −0.412
C(4) 0.415	C(4) 0.385	C(4) 0.419	C(4) 0.417	C(4) 0.385
C(5) 0.141	C(5) 0.128	C(5) 0.127	C(5) 0.110	C(5) 0.090
C(6) 0.506	C(6) 0.508	C(6) 0.468	C(6) 0.515	C(6) 0.479
N(7) −0.456	N(7) −0.457	N(7) −0.455	N(7) −0.354	N(7) −0.357
C(8) 0.225	C(8) 0.228	C(8) 0.228	C(8) 0.209	C(8) 0.212
N(9) −0.429	N(9) −0.426	N(9) −0.426	N(9) −0.425	N(9) −0.417
C(10) 0.008	C(10) 0.009	C(10) 0.007	O(10) −0.515	O(10) −0.503
C(11) −0.012	C(11) −0.001	O(11) −0.513	O(11) −0.533	O(11) −0.517
C(12) 0.005	O(12) −0.516	O(12) −0.528	H(12) 0.075	H(12) 0.078
O(13) −0.520	O(13) −0.527	H(13) 0.066	C(13) −0.012	H(13) 0.202
O(14) −0.535	H(14) 0.066	H(14) 0.106	H(14) 0.081	H(14) 0.225
H(15) 0.065	H(15) 0.104	H(15) 0.105	H(15) 0.112	H(15) 0.217
H(16) 0.104	H(16) 0.104	H(16) 0.076	H(16) 0.097	
H(17) 0.103	H(17) 0.076	C(17) −0.012	C(17) 0.003	

H(18) 0.074	H(18) 0.088	H(18) 0.222	H(18) 0.200
H(19) 0.080	H(19) 0.086	H(19) 0.082	H(19) 0.092
H(20) 0.111	H(20) 0.121	H(20) 0.112	H(20) 0.081
H(21) 0.098	H(21) 0.215	H(21) 0.097	H(21) 0.119
H(22) 0.091			
H(23) 0.080			
H(24) 0.117			

Footnotes: See footnotes on Table 3.

3.7. Molecular Dynamics Simulation and Adsorption on Fe(110)

To better understand how the electronic properties of each molecule translate into real adsorption behaviour, molecular dynamics (MD) simulations were performed. The simulations provided key output parameters such as total adsorption energy (E_{ads}), rigid adsorption energy (E_{rid}), and deformation energy (E_{def}), along with geometric data such as average molecule-surface distance and adsorption configuration (Figure 6). These values are displayed in Table 5 and were used to predict how strongly, and in what manner, each molecule binds to the Fe(110) surface.

Among the five compounds, theobromine displayed the most favourable overall interaction with the Fe surface. Its total adsorption energy was the most negative, at approximately $-45.1 \text{ kcal mol}^{-1}$, indicating strong and spontaneous adsorption [26,27]. The rigid adsorption energy (the energy change without structural relaxation of the molecule) was also significantly negative (about $-38.4 \text{ kcal mol}^{-1}$), which indicates that even the unrelaxed molecule is intrinsically well-suited for surface binding. On relaxation, the molecule experienced a modest deformation energy (about $-6.7 \text{ kcal mol}^{-1}$), which shows that only a small structural adjustment was required to maximize contact with the surface. The final configuration was nearly coplanar, with N7 and the C6=O carbonyl both lying within about $2.05 \text{ \AA}$ of the Fe atoms, confirming the expected bidentate binding mode. Additional stabilization may have been provided by π - π overlap between the aromatic ring system and the Fe(110) terrace.

Caffeine followed closely, with a total adsorption energy of around $-41.2 \text{ kcal mol}^{-1}$, E_{rig} of about $-35.1 \text{ kcal mol}^{-1}$, and E_{def} of about $-6.1 \text{ kcal mol}^{-1}$. The molecule adopted a slightly tilted adsorption geometry due to steric repulsion from its third methyl group at N1. The key interacting sites, mainly N7 and O6, remained oriented favourably toward the surface as shown in Figure 7a. This may not substantially weaken adsorption but may reduce contact efficiency relative to theobromine. This small trade-off between methyl-induced steric hindrance and electron donation capacity explains why caffeine may perform nearly as well as theobromine, but may not perform better.

For paraxanthine and theophylline, the obtained total adsorption energies were moderate (-36.4 to $-35.9 \text{ kcal mol}^{-1}$, respectively), with rigid adsorption energies of 31.2 and $30.7 \text{ kcal mol}^{-1}$ and deformation energies of $-5.2 \text{ kcal mol}^{-1}$ in both cases (Table 5), indicating that these molecules may not be inherently pre-organized for surface interaction. In both cases, the molecules are most likely to be adsorbed in monodentate fashion, primarily via the N7 atom, with secondary stabilization provided by the ring π -system. The observed intermediate binding strength (for both molecules) implies that they may potentially serve as functional corrosion inhibitors, but perhaps with lower film stability and possibly higher desorption rates under harsh conditions.

Lastly, the least favourable adsorption profile was observed with xanthine, and this is consistent with its electronic and structural limitations. Its total adsorption energy was the weakest (around $-28 \text{ kcal mol}^{-1}$), with a rigid adsorption energy of just around $-20 \text{ kcal mol}^{-1}$ and a deformation energy of about 8 kcal mol^{-1} . From these values, it can be implied that not only is xanthine poorly suited for surface binding in its native conformation, but also that it gains relatively little stability from structural relaxation [28]. The molecule adopted a somewhat non-planar, tilted geometry and formed weak, non-directional contacts with the surface.

The comparatively weak interaction of xanthine may be attributed to its less favourable global electronic descriptors and to this less intimate contact with Fe(110) slab. Within the present force field model, the xanthine-Fe(110) contact is the weakest of the five and may be best described as a physisorption-like interaction. However, a firm assignment of physisorption or chemisorption would require periodic electronic structure calculations, which were not performed within the scope of the present study.

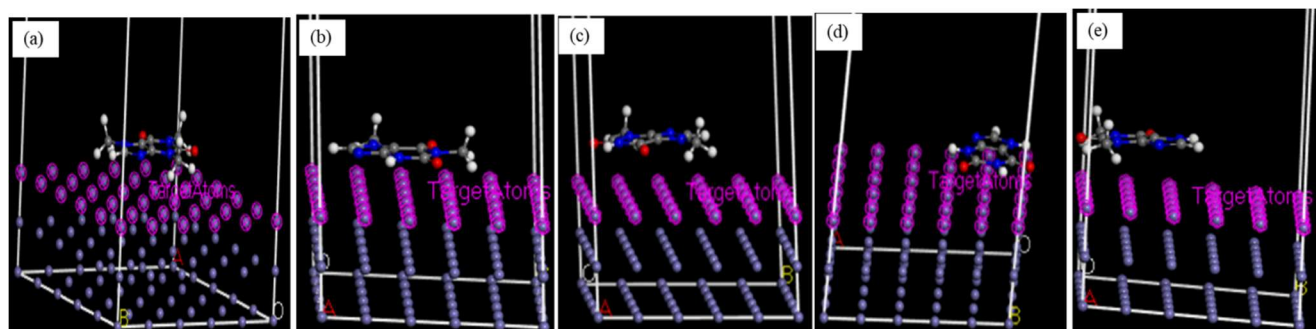


Figure 6. Side view of the adsorption of (a) Caffeine, (b) Paraxanthine, (c) Theobromine, (d) Theophylline, and (e) Xanthine on the Fe(110) surface obtained by MD simulation.

The negative values of E_{def} indicate that relaxation of the adsorbate on the surface provides additional stabilization to the rigid molecule configuration. The adsorption performance of the caffeine-based compounds correlates strongly with their electronic softness, functional group positioning, and structural pre-organization. Theobromine, with its ideal electron-donating and accepting sites and low deformation energy, appears to be the most chemically efficient and surface-compatible molecule in the series. Caffeine offers nearly comparable performance, slightly offset by its more crowded substituent arrangement. The remaining compounds, namely, paraxanthine, theophylline, and especially xanthine, exhibit diminishing adsorption strength and structural suitability, buttressing the point that optimal corrosion inhibition arises from a precise balance of molecular flexibility, planarity, and electronic reactivity. The stability of the various adsorption configurations, as well as the consistency in the adsorption energies portray that the simulation conditions were adequate for reliable evaluation of the molecule-Fe(110) surface interactions.

It must be emphasized that the COMPASS forcefield employed in this work is non-relative, hence it can not explicitly describe covalent/coordinate bond formation, orbital hybridization, or metal-to-ligand back donation at the electronic structure level. A short molecule surface distance together with a strongly negative forcefield adsorption energy does not by itself prove chemisorption. The N,O coordination pictured present in this section is therefore a mechanistic hypothesis inferred from (i) the near-planar adsorption geometries and the short N7/O6-Fe distances obtained in MD simulations, (ii) the Fukui function and Mulliken charge analysis of the donor sites, and (iii) the strong, negative adsorption energies. To confirm the binding structure, direct electronic structure evidence such as optimized adsorption geometries, charge density differences, projected density states, bond analysis, and quantitative (Bader) charge transfer on a periodic slab, may be required, as outlined in suggestions future work.

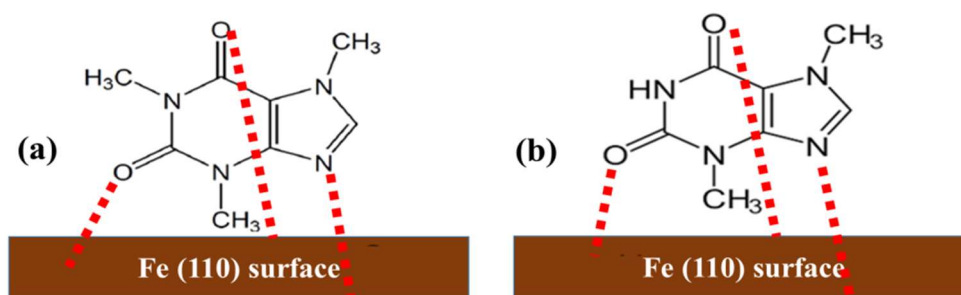
The ranking obtained here, although using a vacuum adsorption energy, appears consistent with available experimental reports. Theobromine has been shown through electrochemical tests to inhibit mild steel in hydrochloric acid [25], caffeine and related xanthines have been reported as adsorbing inhibitors on ferrous and non-ferrous metals [6], and functionalized xanthine derivatives have afforded high experimental inhibition efficiencies on API-L5 steel in acid [28]. However, a targeted five-compound electrochemical series on steel in one medium is still needed to test the order established in this study.

Table 5. Adsorption related energies obtained from MD simulations.

Parameters (kcal/mol)	Caffeine	Paraxanthine	Theobromine	Theophylline	Xanthine
Total Adsorption Energy	−41.2	−36.4	−45.1	−35.9	−28.4
Deformation Energy	−6.1	−5.2	−6.7	−5.2	−8.3
Rigid Adsorption Energy	−35.1	−31.2	−38.4	−30.7	−20.1

3.8. Possible Mode of Interaction

The adsorption of the different molecules on Fe(110) surface is illustrated using caffeine and theobromine as depicted in Figure 7. The adsorptions would involve a combination of donor-acceptor interactions and π -electron interactions. The electron rich hetero N atoms would act as active centers that could form coordinate covalent bonds with vacant d-orbitals of Fe(110) through donation of their lone pairs of electrons, whereas the conjugated ring system would enable additional π -metal interactions. Depending on the substitution pattern and planarity as previously described, this interaction would lead to the adsorption of the molecules on the Fe(110) surface. Since the structural backbone of the different molecules is similar, caffeine and theobromine are used in Figure 7 to depict the contact that could likely occur for the other molecules. However, whether the adsorption results in the formation of a protective film, the blocking of active sites, or the reduction of metal dissolution is a likely occurrence in the experimental scenario. However, these cannot be established from adsorption energy alone and would require electrochemical or surface experimental measurements.

**Figure 7.** Schematic representation of possible interactions between (a) caffeine and (b) theobromine with Fe(110) surface.

3.9. Limitations and Future Direction

This study is a vacuum screening of five neutral caffeine-scaffold molecules on a clean Fe(110) slab and has some limitations from the choice of model, which should be kept in view when results are used. First, corrosion inhibitors operate in aqueous or saline electrolytes where water, hydronium, chloride, or sulphate ions, and competitive adsorption with solvent can modify the speciation of the inhibitor and the structure of the interface. These factors were not modelled in the simulation cell. Second, in acid media, the imidazole nitrogen of xanthine is most likely to be protonated, and keto-enol tautomerism is possible. Only the neutral forms were treated, hence the ranking here may change once the protonated and tautomeric species are included.

Third, industrial steel surfaces carry thin oxide or hydroxide films, the present Fe(110) terrace is a convenient, thermodynamically stable model of metallic iron, different from Fe₃O₄, Fe₂O₃, or FeOOH termination. Adsorption on oxidized interface is a separate problem that could be addressed in future studies. Fourth, the adsorption energies come from a non-reactive classical force field (COMPASS). They rank the five molecules relative to one another under identical conditions, they do not, by themselves, establish chemisorption. Coordinate Fe–N or Fe–O bonds, protective film stability, or numerical inhibition efficiency.

Future work could repeat the ranking for the protonated forms in explicit solvents, compare Fe(110) with a thin iron-oxide/Fe interface, obtain periodic DFT adsorption geometries, charge-density differences,

and projected densities of states, and measure electrochemical inhibition efficiencies for the same compounds on steel in a defined medium, so that the vacuum ranking can be compared against the environment.

4. Conclusions

In this study, DFT and MD simulations were deployed to evaluate the adsorption behaviour and corrosion inhibition potential of five caffeine-based compounds on Fe(110). The results revealed that N-methyl substitution significantly enhances electronic softness, donor-acceptor reactivity, and adsorption strength. Theobromine ranked first in adsorption strength on Fe(110), combining strong bidentate binding, low deformation energy, and favourable orbital alignment. The performance of caffeine was similar but may have been slightly limited by steric effects. However, adsorption by xanthine was weak owing to low reactivity and poor electron-transfer characteristics, whereas paraxanthine and theophylline showed moderate behaviours. The findings demonstrate that the presence of a methyl group in the molecular structure and electronic adaptability are factors that are crucial to designing efficient, eco-friendly inhibitors based on caffeine scaffolds.

Statement of the Use of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used ChatGPT-6, Open AI in order to craft the idea of Figure 7, check spellings and typographical errors. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Acknowledgements

The authors appreciate the support of the Tertiary Education Trust Fund (TETFund) of the Federal Republic of Nigeria, through the TETFund Centre of Excellence in Computational Intelligence Research, as well as the Management of the University of Uyo, Uyo, Nigeria.

Author Contributions

Conceptualization, E.I. and I.E.; Methodology, E.I. and I.O.; Software, E.I., I.E. and I.O.; Validation, E.I., I.E., M.O., V.G., I.A., C.O. and I.O.; Formal Analysis, I.E. and I.O.; Investigation, E.I., I.E., M.O., V.G., I.A., C.O. and I.O.; Resources, E.I. and I.E.; Data Curation, I.E. and I.O.; Writing—Original Draft Preparation, E.I.; Writing—Review & Editing, E.I., I.E., M.O., V.G., I.A., C.O. and I.O.; Visualization, E.I., I.E., M.O., V.G., I.A., C.O. and I.O.; Supervision, E.I.; Project Administration, E.I.; Funding Acquisition, E.I., I.E. and I.O.

Ethics Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Further data can be obtained from the corresponding author on reasonable request.

Funding

This work received no funding.

Declaration of Competing Interests

The authors declare that there are no conflicting interests.

References

1. Shwetha KM, Praveen BM, Devendra BK. A review on corrosion inhibitors: Types, mechanisms, electrochemical analysis, corrosion rate and efficiency of corrosion inhibitors on mild steel in an acidic environment. *Results Surf. Interfaces* **2024**, *16*, 100258. DOI:10.1016/j.rsurfi.2024.100258
2. Ouakki M, Dahmani K, Aribou Z, Ech-chihbi E, Galai M, AlZeqri N, et al. Adsorption of novel heterocyclic compounds of the purine derivatives as corrosion inhibitors over mild steel surface in acidic medium: Electrochemical, surface characterization and theoretical investigations. *Inorg. Chem. Commun.* **2023**, *157*, 111342. DOI:10.1016/j.inoche.2023.111342
3. Jiang Z, Li Y, Zhang Q, Hou B, Xiong W, Liu H, et al. Purine derivatives as high efficient eco-friendly inhibitors for the corrosion of mild steel in acidic medium: Experimental and theoretical calculations. *J. Mol. Liq.* **2021**, *323*, 114809. DOI:10.1016/j.molliq.2020.114809
4. Tan L, Li J, Zeng X. Revealing the Correlation between Molecular Structure and Corrosion Inhibition Characteristics of N-Heterocycles in Terms of Substituent Groups. *Materials* **2023**, *16*, 2148. DOI:10.3390/ma16062148
5. Verma C, Dubey S, Qiang Y, Ebenso EE, Barsoum I, Rhee KY, et al. Heteroatomic multiple bonded corrosion inhibitors: Coordination chemistry, bonding and synergistic behavior of σ -donors and π -acceptors. *Coord. Chem. Rev.* **2025**, *537*, 216683. DOI:10.1016/j.ccr.2025.216683
6. Espinoza Vázquez A, Figueroa IA, Sánchez Molina D, Rodríguez-Gómez FJ, Angeles Beltrán D. Effects of corrosion inhibition with xanthines in gray cast iron protection with Paraloid B-72 in a saline medium. *Prog. Org. Coat.* **2021**, *154*, 106200. DOI:10.1016/j.porgcoat.2021.106200
7. Cruz-Gonzalez DY, Negrón-Silva G, Angeles-Beltrán D, Palomar-Pardavé M, Romero-Romo M, Herrera-Hernández H. Adenine and Guanine Derivative Bases of Purines and Their Corresponding Nucleosides as Corrosion Inhibitors in 1M Hydrochloric Acid. *ECS Trans.* **2011**, *36*, 179–185. DOI:10.1149/1.3660611
8. Cao K, Huang W, Huang X, Pan J. Imidazo [1,2-a] Pyrimidine Derivatives as Effective Inhibitor of Mild Steel Corrosion in HCl Solution: Experimental and Theoretical Studies. *Front. Mater.* **2022**, *9*, 843522. DOI:10.3389/fmats.2022.843522
9. Sajai N, Er-rahmany N, Saber I, Ouabane H, Yaqouti S, Nounah M, et al. Performance of two new imidazoline derivatives as potential corrosion inhibitors for mild steel in 1.0 M HCl medium: Combining experimental and computational approaches. *J. Mol. Struct.* **2025**, *1331*, 141292. DOI:10.1016/j.molstruc.2024.141292
10. Hussein AHM, Ashmawy AM, Rady MA, Gad-Elkareem MAM, Mostafa MA. Synthesis and quantum chemical studies of polyfunctionally substituted pyridines incorporating pyrimidine moiety for corrosion Inhibition. *Sci. Rep.* **2026**, *16*, 14637. DOI:10.1038/s41598-026-39989-0
11. Rizvi M, Gerengi H, Gupta P. Experimental Methods of Corrosion Inhibition Assessment. *ACS Symp. Ser.* **2021**, *1403*, 49–60. DOI:10.1021/bk-2021-1403.ch004
12. Samuel HS, Nweke-Maraizu U, Johnson G, Etim EE. A review of theoretical techniques in corrosion inhibition studies. *Commun. Phys. Sci.* **2023**, *9*, 394–403. DOI:10.4314/cps.v9i4
13. Ituen E, Ituen GC, Essien U, Daniel B, Micheal P, Oyeniran A, et al. Adsorption of Some Pteridine-Based Compounds on Fe(110) Surface and Potential for Corrosion Inhibition: Quantum Computations Molecular Dynamics Simulations. *Commun. Comput. Chem.* **2026**, *7*, 361–371. DOI:10.4208/cicc.2025.192.01
14. Castillo-Robles JM, de Freitas Martins E, Ordejón P, Cole I. Molecular modeling applied to corrosion inhibition: A critical review. *Mater. Degrad.* **2024**, *8*, 72. DOI:10.1038/s41529-024-00478-2
15. Kathim SH, Arkawazi HD, Bouazizd M, Loukil M. Substituted Schiff Bases for Mild Steel Protection: Corrosion Inhibition Performance, Antibacterial Activity, and Quantum Chemical Analysis. *ChemistrySelect* **2025**, *10*, e04378. DOI:10.1002/slct.202504378
16. Elmsellem H, Elyoussfi A, Steli H, Sebbar NK, Essassi EM, Dahmani M, et al. The Theobromine (Chocolate) as Green Inhibitor of Mild Steel Corrosion in Hydrochloric Acid: Electrochemical and Theoretical Quantum Studies. *Der Pharma Chem.* **2016**, *8*, 248–256. Available online: <https://www.derpharmachemica.com/abstract/the-theobromine-chocolate-as-green-inhibitor-of-mild-steel-corrosion-in-rnhydrochloric-acid-electrochemical-and-theoretic-4746.html> (accessed on 10 June 2026).
17. Kamarul Baharin NAN, Sheikh Mohd Ghazali SAI, Sirat SS, Mohd Tajuddin A, Pungot NH, Normaya E, et al. In-depth investigation of corrosion inhibition mechanism: Computational, electrochemical, and theoretical studies of vanillin meldrum's acid on mild steel surface in 1 M HCl. *J. Mol. Liq.* **2024**, *416*, 126390. DOI:10.1016/j.molliq.2024.126390

18. Anadebe VC, Lgaz H, Aldalbahi A, Lee H, Mathias GE, Badeji AA, et al. Interfacial Inhibition of Mild Steel Corrosion by Abemaciclib and Abrocitinib in Acidic Media: Insights from Density Functional Theory and Molecular Dynamics Simulations. *ChemistrySelect* **2025**, *10*, e03502. DOI:10.1002/slct.202503502
19. El-Aziz S, Fouda A, Al-bonayan AM, Eissa M, Eid DM. Electrochemical and quantum chemical studies on the corrosion inhibition of 1037 carbon steel by different types of surfactants. *RSC Adv.* **2022**, *12*, 3253–3273. DOI:10.1039/D1RA07983B
20. Hamidi H, Shojaei F, Pourfath M, Vaez-Zadeh M. Adsorption behavior of some green corrosion inhibitors on Fe(110) surface: The critical role of d- π interactions in binding strength. *Appl. Surf. Sci.* **2024**, *655*, 159425. DOI:10.1016/j.apsusc.2024.159425
21. Abozeed AA, Younis O, Al-Hossainy AF, El-Mawla NA, Sayed M, El-dean MK, et al. Combined experimental and TD-DFT/DMO³ investigations, optical properties, and photoluminescence behavior of a thiazolopyrimidine derivative. *Sci. Rep.* **2022**, *12*, 15674. DOI:10.1038/s41598-022-19840-y
22. Alqahtani H, El Tohamy A, Aboelmagd A, Rashwan S, Fouda AA, Kamel M. The Corrosion Inhibition Effect of Salpn Schiff Base on Low-Carbon Steel in a Hydrochloric Acid Environment: An Integrated Study Combining Laboratory Experiments and Computational Modeling. *Corros. Mater. Degrad.* **2026**, *7*, 16. DOI:10.3390/cmd7010016
23. Boughazi H, Boudinar Y, Tlili S, Djedouani A, Naili N. Electrochemical, surface, DFT, and ADMET insights into (*E*)-2-(2-hydroxybenzylidene)hydrazine-1-carboxamide as a corrosion inhibitor. *RSC Adv.* **2025**, *15*, 38946–38968. DOI:10.1039/D5RA05876G
24. Lazrak J, Ech-chihbi E, Salim R, Saffaj T, Rais Z, Taleb M. Insight into the corrosion inhibition mechanism and adsorption behavior of aldehyde derivatives for mild steel in 1.0 M HCl and 0.5 M H₂SO₄. *Colloids Surf. A Physicochem. Eng. Asp.* **2023**, *664*, 131148. DOI:10.1016/j.colsurfa.2023.131148
25. Verma C, Dubey S, Ebenso EE, Rhee KY, Alfantazi A. Polypyridyl-based bridging corrosion inhibitors: A critical review on interface and ligands properties. *Adv. Colloid Interface Sci.* **2025**, *342*, 103534. DOI:10.1016/j.cis.2025.103534
26. Awad MK, Halim WSA, Atlam FM, Fawzy MM. A multiscale computational investigation for protection of carbon steel surface by pyrazolo-pyrimidine derivatives. *Sci. Rep.* **2025**, *15*, 32576. DOI:10.1038/s41598-025-19022-6
27. Chahid A, Mouloudi M, Meftah S, Essahli M, Chafi M, Ech-chahad A. A multi-scale investigation of the anti-corrosion and diffusion properties of a natural dye extract on aluminum in NaCl solution using DFT, RDF, FFV, and MC/MD simulations. *Sci. Afr.* **2025**, *30*, e03063. DOI:10.1016/j.sciaf.2025.e03063
28. Sánchez-Eleuterio A, Mendoza-Merlos C, Corona Sánchez R, Navarrete-López AM, Martínez Jiménez A, Ramírez-Domínguez E, et al. Experimental and Theoretical Studies on Acid Corrosion Inhibition of API 5L X70 Steel with Novel 1-N- α -d-Glucopyranosyl-1H-1,2,3-Triazole Xanthines. *Molecules* **2023**, *28*, 460. DOI:10.3390/molecules28010460