

CHEMICAL COMPOSITION, DFT ANALYSIS, MOLECULAR DOCKING, AND ANTIBACTERIAL ACTIVITY OF SELECTED MEDICINAL PLANT EXTRACTS

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ABSTRACT

Curcumin is a principal polyphenolic compound found in *Curcuma longa* which has gained some interest due to reported antibacterial activity along with several molecular properties. The present study explored the structural, electronic and molecular interaction features of curcumin by means of density functional theory (DFT), molecular electrostatic potential (MEP), global molecular descriptors and molecular docking with the bacterial FtsZ protein. Special focus was given to the keto-enol tautomerism and its effect on molecular stability and electronic properties. The selected enol form was determined to have a lower electronic energy than the diketo form by about 2.01 kcal mol⁻¹, the electronic energies of the enol and diketo forms being **-1264.008247** and **-1264.004354 Hartree**, respectively. For the chosen enol model, the **HOMO and LUMO energies** of the π -electrons are **-5.6869** and **-2.7154 eV**, respectively, and **the gap between the HOMO and LUMO is 2.9715 eV**. The ESP values were **4.2012, -4.2012, 1.4857, 0.3365** and **5.9397 eV** for the corresponding electronegativity, chemical potential, hardness, softness and electrophilicity values respectively. MEP analysis showed that the electron-rich areas are mainly located around the oxygen-containing functional groups, suggesting that these groups might form electrostatic and hydrogen-bonding interactions. Molecular docking was carried out against *Staphylococcus aureus* FtsZ (4DXD) with the crystallographic ligand 9PC for validating docking protocol before drawing conclusions about the poses obtained by curcumin. The obtained docking analysis was taken into account along with previous FtsZ docking evidence such as a previously reported Glide score of -5.273 kcal mol⁻¹ of curcumin, with interactions with Arg191, Glu192 and Asn263 in a different model of FtsZ. In sum, the current studies suggest a feasible molecular mechanism of curcumin-FtsZ interaction, but direct biochemical and microbiological data are still required for target engagement and antibacterial mechanism.

KEYWORDS

Curcumin; keto-enol tautomerism; density functional theory; molecular electrostatic potential; FtsZ; molecular docking; medicinal plants.

1. Introduction

1.1. Background of the Study

A clear relationship between chemical character, biochemical action, and predictable biological response is essential to medicinal plant studies. Relevant botanical contexts include holy basil (*Ocimum sanctum*), turmeric (*Curcuma longa*), and guava (*Psidium guajava*); however, extracts from these botanicals are chemically variable mixtures. The chemical profiling published is used for the investigation of these plants but does not determine that the selected marker is responsible for all activity of the extract (Chaudhary et al., 2020; Wichitnithad et al., 2009; Metwally et al., 2010).

The only compound analyzed by computation in this manuscript is curcumin. In its conjugated structure with oxygen-containing functional groups and keto–enol alternatives, the molecular form–electronic structure correlation is particularly relevant. FtsZ is a biologically motivated target as experimental studies have shown that curcumin is associated with modified bacterial cell division and FtsZ assembly (Rai et al., 2008). Electronic Descriptors and Docking can be used to suggest an interaction hypothesis, but this hypothesis must be tested by direct biochemical and cellular measurements.

1.2. Problem Statement

One of the frequent interpretive issues is a good docking score or small frontier-orbital gap is taken as proof of antibacterial activity. These types of conclusions ignore molecular form, conditions of calculation, receptor state, type of exposure, and interference in the assays. The current study overcomes this by combining traceable structural and electronic evidence from curcumin with receptor-specific docking and experimental results. This changes the problem at the site's heart: which conclusions are still true for the various systems of computation and biology that the evidence describes?

1.3. Objectives of the Study

This study aims to:

- i. Establish the structural identity of curcumin and investigate the diketo and keto–enol molecular forms using conformational and quantum-chemical analysis;
- ii. Assess the relative electronic energy, frontier molecular orbital characteristics and global molecular descriptor for curcumin using density functional theory;
- iii. Describe the molecular electrostatic potential surface of curcumin and pinpoint the chemically credible regions expected to participate in intermolecular interactions;
- iv. Use molecular docking simulation to explore the possible interaction between curcumin and *Staphylococcus aureus* FtsZ (PDB 4DXD), and validate the docking simulation protocol by redocking the crystallographic reference ligand 9PC.
- v. Correlate the computational results with experimental and biological literature and judge their significance in reference to the possible anti-bacterial activity of curcumin.

1.4. Research Questions

The main questions of the present study are related to structural stability and the difference in the electronic properties between the diketo and keto–enol forms of curcumin if assessed in the same computational environment, and what effect the different molecular forms have on frontier molecular

orbital characteristics, global molecular descriptors, and electrostatic-potential distribution. The study also investigates whether a receptor specific docking approach is available using the *Staphylococcus aureus* FtsZ structure 4DXD that can offer a consistent framework to assess putative interactions of curcumin with the region associated to 9PC. One more question is what do these simulation results mean in comparison with experimental data reported on curcumin and FtsZ, and how far can one extrapolate the findings of such compounds to chemically variable plant extracts?

1.5. Chemical Composition of Selected Plants

The word plant does not indicate concentration of constituents. The distinction between marker selection and measured composition needs to be conveyed clearly in the analytical characterization. Turmeric requires separation of curcumin from other curcuminoids before a dose of curcumin can be assigned. Background botanical examples are kept and not included for DFT and docking comparison. The chemical-composition framework and the computational scope are summarized in Table 1.

Table 1. Botanical context and analytical priorities.

Plant material	Relevant constituents	Interpretive priority
Holy basil leaves	Phenolic and volatile constituents; eugenol as a candidate marker	Verify the actual profile and marker abundance.
Turmeric rhizome	Curcumin, demethoxycurcumin, and bisdemethoxycurcumin	Resolve curcuminoids analytically; compute curcumin only.
Guava leaves	Flavonoids including quercetin-related constituents	Distinguish aglycones, glycosides, and mixture effects.

Sources: Chaudhary et al. (2020), Wichitnithad et al. (2009), and Metwally et al. (2010). Entries identify analytical targets, not measured composition in project samples.

1.6. Electronic Structure and DFT Analysis

Within the scope of a well-founded hypothesis, the structural and electronic properties of curcumin were studied using density functional theory (DFT) calculations. Some forms of the molecules investigated were subsequently geometry optimized at the dispersion-corrected B3LYP level with an aqueous continuum-solvation model and then subjected to higher basis-set electronic-structure analyses. Relative electronic energies, frontier molecular orbital energies, global molecular descriptors, and molecular electrostatic potential characteristics were calculated and evaluated.

Calculated orbital-based descriptors are viewed as model dependent, quantum-chemical properties and not as measured ionization energies, excitation energies, binding affinities, antibacterial potencies, etc. These global descriptors are complemented by molecular electrostatic potential analysis, which

identifies regions of comparatively negative and positive electrostatic potential in space that might participate in intermolecular interactions.

1.7. Molecular Docking and Target Selection

Here, FtsZ is investigated specifically because of the experimental literature on the interaction between curcumin and FtsZ, rather than through a general screen of phytochemicals. The 4DXD structure shows the inhibitor PC190723 represented by ligand identifier 9PC bound to the *S. aureus* FtsZ and GDP. This represents a unique validation opportunity — recovery of the crystallographic 9PC pose in its own binding cleft (Tan et al., 2012; RCSBPDB, 4DXD). Docking to another site or species asks another structural question.

1.8. Antibacterial Mechanisms and Experimental Evidence

An experimental support for a molecular target is more mechanistically relevant than a favorable docking score alone. The FtsZ-associated changes in assembly and bacterial division warrant further study of this target but are not an indication that every curcumin-containing preparation is functioning primarily through the FtsZ pathway. Membrane effects and other responses are also relevant to the broader plant literature and therefore cannot be attributed to an uncharacterized botanical identity extract alone.

1.9. Integration and Remaining Knowledge Gaps

The DFT calculations take into account the molecular-form-dependent structural stability, electronic energies, frontier molecular orbitals, global molecular descriptors, and electrostatic-potential characteristics, whereas receptor-specific molecular docking leads to a structural framework to assess the potential interactions between curcumin and *Staphylococcus aureus* FtsZ.

These computational findings collectively support a viable hypothesis of curcumin interaction with FtsZ, but do not represent experimental binding, target occupancy, or antibacterial activity. Uncertainties include conformational or tautomeric sampling, solvent representation, receptor flexibility, docking-score approximations, and lack of direct structural or biochemical confirmation of the predicted interaction.

2. Results and discussion

2.1. Chemical Composition and Extract Comparability

The botanical literature specifies constituent groups and analytical priorities, while the evidence assessed here lacks measurements of matched extraction batches. Thus it does not provide composition percentages or a potency ranking of the extracts selected. Curcumin is not a turmeric extract, but a well-defined molecular subject. Any comparative assessment of extract activity should account for losses due to precipitation or degradation, and should take into account measured concentrations of constituents during exposure. Keep inactive preparations and uncertain assignments to avoid selective mechanistic interpretation.

2.2. Interpretation of Electronic Properties

2.2.1. Curcumin structure and keto enol forms

The diketo and keto–enol molecular forms of curcumin were considered in the computational study since the process of proton transfer within the central β -dicarbonyl-derived system affects its conjugation, intramolecular hydrogen bonding, and the distribution of electron density without changing the elemental composition. Conformational preparation and quantum-chemical optimization were carried out for candidate structures, and representative geometries were selected for electronic-property analysis.

Table 2. Computational definition of curcumin structures investigated in the present study.

Property	Computational specification
Identity	Curcumin; PubChem CID 969516; C ₂₁ H ₂₀ O ₆ ; 368.4 g mol ⁻¹
Molecular forms	Diketo and keto–enol curcumin
Molecular charge	0
Spin state	Singlet
Geometry optimization	B3LYP-D3BJ/6-31+G(d,p)
Solvent environment	IEF-PCM water
Frequency analysis	Performed following geometry optimization
Final electronic calculation	B3LYP-D3BJ/6-311++G(d,p)
Electronic-property analysis	HOMO, LUMO, global descriptors and MEP

Optimized enol structure revealed a longer conjugated framework with a central enol group joined to the central-chain oxygen groups via an intramolecular hydrogen-bonding arrangement, while selected diketo structure had another central-chain geometry and the oxygen groups in another orientation. These structural differences can explain the observed variation in calculated electronic energy and frontier orbital properties. The illustrated geometries show selected optimized conformers and cannot be interpreted as the full set of equilibrium geometries of curcumin in water.

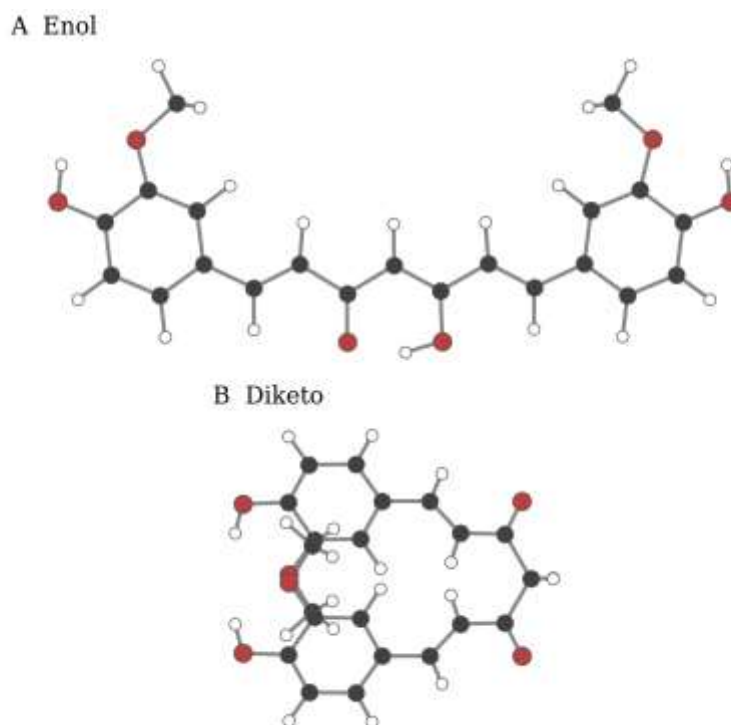


Figure 1. Representative DFT-optimized geometries of the investigated curcumin molecular forms. A, enol form; B, diketo form. Carbon is dark grey, Oxygen is red, and Hydrogen is white. The structures shown are selected optimized conformers from the calculation workflow and are not intended to depict the equilibrium population of tautomers or conformers in solution.

2.2.2. DFT methodology and electronic energies

Table 3. Method-specific electronic properties of curcumin.

Dataset and molecular form	Quantity	Obtained value
B3LYP-D3/SMD water; diketo	Electronic energy	−1264.004354 hartree
B3LYP-D3/SMD water; enol	Electronic energy	−1264.008247 hartree
Same B3LYP-D3 dataset	$E(\text{diketo}) - E(\text{enol})$	2.01 kcal mol ^{−1}
APFD water; keto conformer 1	HOMO–LUMO gap, Table S4	3.719 eV
APFD water; enol conformer 1	HOMO–LUMO gap, Table S5	3.237 eV

These two structures of diketo-curcumin and enol-curcumin were then selected and quantum chemically optimized at aqueous-phase computational conditions. The computed electronic energies were −1264.004354 Hartree for the diketo form and −1264.008247 Hartree for the selected enol form. It was therefore found that the difference in the two electronic energies, $E(\text{diketo}) - E(\text{enol})$, was about 2.01 kcal mol^{−1}, showing that under

these computational conditions, the chosen enol form possessed the lower electronic energy.

The answer to this is that the adopted enol geometry is stabilized by a combination of effects of extended conjugation and intramolecular hydrogen bonding. However, the calculated difference is an electronic-energy difference between specific optimized structures and should not be taken as an aqueous equilibrium constant or tautomer population. A full thermodynamic description would take into account conformational ensembles, vibration/thermal contributions and solvation effects, and the associated free-energy treatment.

The calculated energy difference thus helps to show relative stabilization of the enol form selected here as representable in the computational model and still depends on the level of theory, solvent representation and conformational sampling.

2.2.3. HOMO LUMO and global molecular descriptors

Table 4. Calculated frontier-orbital quantities and global molecular descriptors for selected enol curcumin.

Quantity	Value
HOMO energy	−5.6869 eV
LUMO energy	−2.7154 eV
HOMO–LUMO gap	2.9715 eV
Ionization potential, I	5.6869 eV
Electron affinity, A	2.7154 eV
Electronegativity, χ	4.2012 eV
Chemical potential, μ	−4.2012 eV
Hardness, η	1.4857 eV
Softness, S	0.3365 eV ^{−1}
Electrophilicity, ω	5.9397 eV

$$\Delta E = E(\text{LUMO}) - E(\text{HOMO}) \quad I \approx -E(\text{HOMO}) \quad A \approx -E(\text{LUMO})$$

$$\chi = (I + A)/2 \quad \mu = -\chi \quad \eta = (I - A)/2 \quad S = 1/(2\eta) \quad \omega = \mu^2/(2\eta)$$

For the selected enol structure, the calculated values of HOMO and LUMO were − 5.6869 eV and − 2.7154 eV, respectively, with an HOMO–LUMO energy gap of 2.9715 eV, as obtained from the frontier molecular orbital analysis. In the adopted orbital approximation, the corresponding ionization potential and electron affinity were 5.6869 and 2.7154 eV, respectively.

The calculated electronegativity was 4.2012 eV and the chemical potential was −4.2012 eV. The Hardness value was 1.4857 eV, the Softness value was 0.3365 eV^{−1}, and the calculated electrophilicity index value was 5.9397 eV. These descriptors build on one another repeatedly from the same frontier-

orbital energies and thus summarize related features of the same model of the electronic structure, rather than making repeated experimental measurements.

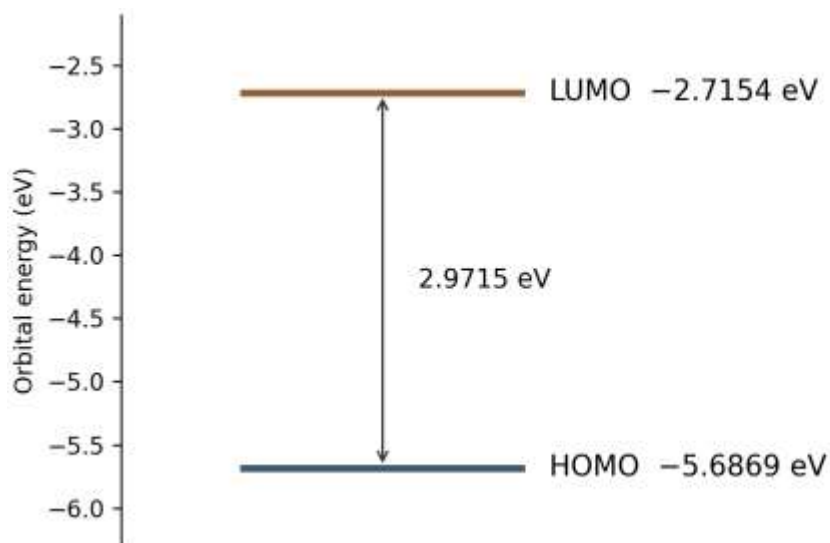


Figure 2. Frontier molecular orbital energy-level diagram of the selected enol curcumin structure. The calculated HOMO – LUMO energies were found to be -5.6869 and -2.7154 eV, respectively, with a gap of 2.9715 eV. This diagram is a calculated orbital-energy-level diagram and not an optical excitation spectrum.

The HOMO–LUMO gap describes the difference between the frontiers occupied and unoccupied orbitals under the applied computational conditions. A small gap orbital may suggest higher electronic polarizability or more efficient distribution of electron density in comparative series of molecules, but should not be directly correlated with optical excitation energy, experimental chemical reactivity, binding affinity, or antibacterial activity.

2.2.4. Molecular electrostatic potential

Table 5. Principal molecular electrostatic potential features of curcumin.

Feature	Present-study interpretation
Oxygen-containing regions	Predominantly negative electrostatic potential
Carbonyl/ether oxygen atoms	Plausible hydrogen-bond acceptor regions
Phenolic/enolic OH groups	Potential hydrogen-bond donor regions
Tautomeric dependence	Local electrostatic distribution changes with molecular form
Binding interpretation	Supports evaluation of complementary polar contacts during docking

Molecular electrostatic potential analysis was done to explore the distribution of electrostatic character on the curcumin molecular surface. The resultant MEP distribution revealed relatively negative electrostatic potential around the oxygen containing functional groups, especially the carbonyl, ether, phenolic and enolic oxygen regions. These are electron-rich zones that can form potential binding sites with opposite positively polarized or hydrogen-bond donor regions.

2.3. Molecular Docking Evaluation

2.3.1. FtsZ structure and receptor preparation

Molecular docking was performed with the crystallographic structure of *Staphylococcus aureus* FtsZ (PDB 4DXD) as a receptor. The structure includes an interdomain binding cleft containing the inhibitor, PC190723 (Ligand 9PC), which gives a direct crystallographic reference for the docking-pose recovery assessment.

The receptor was prepared for docking without discarding the structural definition of the 9PC-binding region. The crystallographic 9PC ligand was extracted from its binding site and served as reference ligand for the redocking process. Docking search region was centered on the crystallographic 9PC site, and the search-space definition was then applied to curcumin docking, to the same receptor.

Table 6. 4DXD receptor and docking-protocol specifications.

Component	Specification
Receptor	<i>S. aureus</i> FtsZ; PDB 4DXD; protein chain A
Reference ligand	9PC
Binding region	Crystallographic 9PC interdomain cleft
Docking engine	AutoDock Vina
Exhaustiveness	32
Number of modes	20
Energy range	4 kcal mol ⁻¹
Random seed	314159
Validation procedure	Redocking of crystallographic 9PC

2.3.2. Binding Hypotheses and Pose Quality

Table 7. Published curcumin–FtsZ docking evidence used for external comparison.

Item	Published evidence	Applicability to 4DXD
Curcumin docking score	Glide score –5.273 kcal mol ⁻¹	Different species, receptor model, and scoring function

Item	Published evidence	Applicability to 4DXD
Hydrogen-bond contacts	Arg191, Glu192, Asn263	Residue labels belong to the source model
Contact distances	Distances not verified for the cited curcumin pose.	No distances assigned
Validation comparator	GDP redocking to 4M8I: RMSD 0.4302 Å	Different ligand and site; heavy-atom and symmetry conventions not established

For poses generated for the 4DXD system, the 9PC redocking calculation was used as a receptor-specific quality-control calculation before interpretation. Pose recovery was evaluated against the crystallographic 9PCs coordinates based on the predefined heavy-atom RMSD criterion. This validation procedure is useful for assessing, on a system-specific basis, whether the docking protocol is able to mimic the ligand conformation found in the experimentally determined reference structure within the cleft of interest.

After redocking, curcumin was re-docked to the same 9PC associated area. Generated poses were graded based on docking score, receptor ligand contacts and orientation in the binding pocket. The interaction pattern was interpreted in the light of MEP, especially for the oxygen containing groups of curcumin which are capable of polar interactions.

$$RMSD = \sqrt{[(1/N) \sum_i \|r_i(docked) - r_i(crystal)\|^2]}$$

N is the number of mapped non-hydrogen ligand atoms. Where symmetry allows, equivalent atoms should be accounted for in the proposed calculation and the mapping and software documented. The output columns rmsd l.b. and rmsd u.b. reported by AutoDock Vina in most such cases are for comparison to the best predicted mode, not a redocking comparison to the crystal ligand (AutoDock Vina, n.d.). This means that a best mode of zero does not indicate crystallographic validation.

Therefore the current 4DXD docking results do not purport to be based on a direct numerical comparison with the published Glide score or GDP redocking result but rather on their own receptor-specific validation and interaction geometry.

2.3.3. Linking Predictions to Antibacterial Response

The three methods DFT, MEP and molecular docking give complementary molecular information. Electronic-structure calculations describe the inherent characteristics of curcumin and MEP analysis localizes regions capable of engaging in beneficial electrostatic interactions. Molecular docking is then used to test whether the molecular features can 'dock' into the structural context of the FtsZ receptor.

The inherent chemical consistency in the computational model stems from the agreement between the electrostatically favorable regions of curcumin and complementary receptor contacts. However, a predicted docking pose is not proof of experimental occupancy of the 9PC binding cleft. Actual

interaction may be affected by desolvation, flexibility of the receptor, entropy of the ligand, protonation state, tautomeric state, and limitation of the scoring function.

The curcumin–4DXD interaction model obtained should therefore be considered a testable structural hypothesis. The biochemical and cellular observations of both curcumin and FtsZ support this hypothesis but were not meant to test the binding pose described in the present computation.

Table 8. Published mechanistic precedents and limits of extract attribution.

Compound	Mechanistic precedent	Unresolved inference
Eugenol	Membrane disruption by plant-oil aromatics (Gill and Holley, 2006)	The mechanism of a particular holy basil extract requires direct testing.
Curcumin	FtsZ assembly and cell-division effects (Rai et al., 2008)	The relevant binding site and contribution to turmeric-extract activity remain unresolved.
Quercetin	DNA gyrase binding and inhibition studies (Plaper et al., 2003)	The activity of a guava extract cannot be assigned to quercetin alone.

2.4. Antibacterial Activity and Integrated Interpretation

In *Bacillus subtilis* system, the presence of curcumin was linked to filamentation and to abnormalities in Z-ring formation. Purified-protein studies revealed decreased FtsZ assembly and bundling in addition to higher GTPase activity, with a reported dissociation constant of $7.3 \pm 1.8 \mu\text{M}$. Together, these support perturbation of FtsZ assembly dynamics and should not be described as simple inhibition of GTP hydrolysis. This does not detect occupational PC190723 in *S. aureus* either.

The Biolog data supports the FtsZ-related hypothesis more so than electronic descriptors alone. But the evidence for that spans various molecular shapes, species, and experimental conditions. The existing data do not provide a causal link from the enol orbital gap to the 4DXD binding to bacterial killing. Matched exposure, direct binding or functional measurements, and cellular evidence that discriminates FtsZ effects from nonspecific stress, would be needed to establish that sequence.

The obtained binding and assembly studies do not provide us with the minimum inhibitory concentrations, inhibition zones, or bactericidal endpoints for the plant extracts assayed. When referring to a mixture, apparent enhancement also must have concentration matched comparison, and explicit additivity model before it can be said to be synergy.

3. Conclusion

3.1. Conclusions

The present computational investigation shows that the molecular form of curcumin affects its structural and electronic properties. The calculated electronic energy of the enol structure was about 2.01 kcal mol^{−1} lower than that of the diketo structure (−1264.008247 versus −1264.004354 Hartree). Based on

the selected enol form, the obtained HOMO and LUMO energy were -5.6869 and -2.7154 eV with the HOMO–LUMO gap of 2.9715 eV respectively.

In the MEP study, the oxygen-rich regions of curcumin were determined as the key electron-rich sites that can participate in the electrostatic and hydrogen-bonding interactions. Using 9PC redocking with *Staphylococcus aureus* FtsZ (PDB 4DXD), molecular docking generated a structural framework for assessing potential interactions with the inhibitor binding region of curcumin.

The results from electronic structure analysis, the electrostatic potential and the docking studies support a feasible molecular-interaction hypothesis between FtsZ and curcumin. The published studies suggested that curcumin induced changes in FtsZ assembly and bacterial cell division, which provided biological support for further investigation, and direct biochemical, structural, and microbiological validation was still pending to prove the proposed mechanism.

3.2. Limitations of the Study

Computational results rely on the models, molecular structures, and sampling strategies employed for the study. The choice of exchange-correlation functional, basis set, dispersion treatment, solvent representation, and conformational selection can lead to different calculated DFT properties. The implicit aqueous-solvation model has the disadvantage that it cannot represent individual solvent molecules or all specific solute–solvent interactions, and optimized solute structures represent only a restricted thermodynamic ensemble of curcumin conformers and tautomers. Therefore, the energy differences between electronic states are not directly convertible to an experimental population of tautomers.

The limitations of molecular docking are also related to receptor preparation, ligand state, receptor flexibility, solvent treatment, search completeness and empirical docking scoring functions. Redocking of a crystallographic reference ligand serves as a tool for pose-recovery evaluation, but it doesn't imply that curcumin experimentally binds the same receptor site and with affinity corresponding to the calculated docking score.

3.3. Future Scope of Research

The present work should be extended by future computational studies, which should sample more conformations and tautomers, compare with alternative density functionals and basis sets, and examine both implicit and explicit solvent representations. The quantum-chemical calculations carried out so far are limited to lower levels, and their results could give further insights into the relative stability and electronic properties of the investigated curcumin forms.

In the case of FtsZ system, receptor-ensemble docking and molecular-dynamics simulations may be performed to examine the stability of the predicted curcumin pose and the effect of receptor conformational flexibility. When adequate sampling can be performed, binding free energy may also in principle give more quantitative information and report convergence and uncertainty explicitly.

Experiment validation should be extended to direct curcumin – FtsZ binding assays, FtsZ polymerization and GTPase assays and biological testing with chemically defined curcumin exposures. Mutational analysis of residues proposed by reproducible computational poses could then evaluate the predicted interaction network. These could help to establish structure–activity relationships; comparisons with

related curcuminoids may clarify these relationships, and studies involving authenticated extraction, chemical profiling, fractionation, depletion and reconstitution would be necessary before properties of botanical extracts could be attributed specifically to curcumin.

4. Material and methods

4.1. Materials and Chemical Composition

Rather than estimating the composition of newly collected material, botanical evidence was used to identify constituent classes and analytical requirements. This analysis was not based on any plant collection, extraction, or chromatographic measurement. A matched extract investigation needs to involve material that has been authenticated, voucher records, controlled handling and storage, and validated profiling. Curcuminoid separation is crucial to assigning exposure specifically to curcumin (Wichitnithad et al., 2009). Any comparison based on concentration should be supported by recovery, calibration, blanks, repeatability and stability.

The current investigation incorporated original computational analysis of curcumin and targeted integration of published chemical, structural and biological evidence. The molecular identity of curcumin was established through PubChem and the structure of the *Staphylococcus aureus* FtsZ was obtained from the RCSB Protein Data Bank for use in molecular docking. Where relevant, biological context and external computational comparisons were provided from the primary research papers and official supporting information.

This computational workflow produced the DFT calculations, frontier molecular orbital analysis, global molecular descriptors, molecular electrostatic potential analysis, receptor-specific docking workflow, and curcumin docking evaluation reported as present-study findings. Past computational and experimental work was kept only when explicitly attributed as comparative or contextual evidence and not as newly produced data.

4.2. Computational Design and DFT Procedure

Curcumin was modeled as a neutral molecule with a total charge of 0 and singlet multiplicity. Conformational screening of diketo and keto–enol molecular forms was carried out before quantum-chemical optimization. The representative conformers were chosen for subsequent DFT analysis based on the conformational and energetic criteria used in the computational workflow.

B3LYP-D3BJ/6-31+G(d,p) was used for geometry optimization with IEF-PCM continuum-solvation model for water. The geometry optimizations were followed by harmonic-frequency calculations to assess the stationary structures and to guide further structural selection. Thermochemical quantities, if applicable, were determined at 298.15 K.

The chosen optimized geometries were then put into final B3LYP-D3BJ/6-311++G(d,p) single-point calculations, again in the same IEF-PCM water environment. No final single-point geometry optimization was done. Calculated electronic energies were used for comparison of the selected molecular forms.

The final electronic-structure calculations provided HOMO and LUMO orbital energies. From these values, the HOMO–LUMO gap and other global molecular parameters such as ionization potential,

electron affinity, electronegativity, chemical potential, hardness, softness, and electrophilicity were calculated. The electrostatic potential analysis of the molecules was carried out using the calculated electronic density, which allowed the identification of spatial variations in electrostatic character of the molecular surface.

All calculated values were analyzed based on the stated quantum-chemical model. The experimental free energies were not compared with electronic energies and the orbital descriptors were not interpreted as direct measures of biological activity or binding affinity.

4.3. Molecular Docking Procedure

The crystal structure of *Staphylococcus aureus* FtsZ (PDB 4DXD) was retrieved from the RCSB Protein Data Bank and served as the receptor model for molecular docking. Protein chain A was kept for receptor preparation, and the 9PC crystallographic inhibitor ligand was used for docking-protocol validation. The binding region was determined by the crystallographic location of 9PC inside the interdomain inhibitor cleft.

The receptor and ligand structures were prepared using the preparation procedure implemented in the computational workflow for AutoDock Vina docking. Before Curcumin docking was interpreted, the crystallographic 9PC ligand was removed from its bound position and re-docked into the prepared receptor. Heavy-atom RMSD was used to assess the crystallographic reference with the predicted 9PC pose, using 2.0 Å as the acceptable limit.

AutoDock Vina calculations were run using an exhaustiveness value of 32, 20 binding modes generated, an energy range of 4 kcal mol⁻¹, and a fixed random seed of 314159. After the reference-ligand validation, the chosen DFT-optimized curcumin structures were docked into the same receptor and binding-site definition.

The resulting curcumin poses were assessed based on docking score, position in the cleft in 9PC, and predicted receptor-ligand contacts. The actual 4DXD poses from this study were used to create interaction assignments. Docking scores were considered as outputs of the empirical scoring function, not as experimentally measured binding free energies.

5. Data availability

The data generated by computation during this study include molecular input files, optimized geometries, quantum-chemical calculation output files, electronic energies, frontier molecular orbital data, global molecular descriptors, molecular electrostatic potential results, receptor preparation files, ligand preparation files, docking configuration files, reference-ligand redocking results, curcumin docking poses, docking scores, and related output files for interaction analysis.

The main numerical results used for the conclusions of the present study are included in the body of the paper. At this stage of the research project the full computational output files are not deposited in a public repository but are held by the authors. The corresponding author, if publication, intellectual-property, and ongoing-research requirements so warrant, may consider access to additional computation records.

Data used to establish molecular and structural identity is publicly available and is represented by the curcumin entry in PubChem (CID 969516) and the crystal structure of *Staphylococcus aureus* FtsZ (PDB 4DXD) with the crystallographic ligand 9PC, both obtained from RCSB Protein Data Bank.

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Conflict of interest

All authors have no conflict of interest.

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