



Research Article

Molecular Docking-Based Exploration of Green Tea Bioactive Compounds for Targeting Zucchini Yellow Mosaic Virus Genes: A Potential Control Strategy

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Abstract | Zucchini Yellow Mosaic Virus (ZYMV) is a major viral pathogen affecting zucchini and other cucurbit crops, resulting in substantial economic losses worldwide. This study aimed to identify potential antiviral compounds derived from green tea (*Camellia sinensis*) to combat ZYMV, utilizing silico molecular docking techniques. Five bioactive compounds, selected for their known phytochemical profiles, were docked against four key viral proteins encoded by the ZYMV genome-P1, HC-Pro, CI, and CP-to assess their binding affinities, interaction potential, and structural complementarity. Among the tested compounds, green tea polyphenols, particularly epicatechin gallate (ECG) and epigallocatechin gallate (EGCG), demonstrated the strongest binding affinities and molecular interactions with ZYMV proteins, surpassing the antiviral agent acyclovir. The docking analysis revealed that ECG and EGCG formed multiple stabilizing interactions, including hydrogen bonds, Pi-based interactions, and van der Waals contacts, with key amino acid residues across all four viral proteins, suggesting their potential to inhibit viral replication and movement. Polar surface area (PSA) results further supported these findings. ECG and EGCG exhibited higher PSA values (ECG: 130.61 Å², EGCG: 197.37 Å²) compared to simpler catechins and alkaloids, indicating a greater capacity for hydrogen bonding and stronger interaction with protein active sites. Compounds with lower PSA, such as caffeine (58.40 Å²) and theophylline (69.30 Å²), showed weaker binding and fewer stabilizing interactions, consistent with their limited antiviral potential. Overall, combination of strong binding affinities, diverse interaction profiles, and favorable PSA characteristics highlights ECG and EGCG as promising natural antiviral agents against ZYMV. These findings suggest the potential of green tea polyphenols as effective, and eco-friendly alternatives for viral control. However, additional *in vitro* and *in vivo* studies are necessary to validate their biological efficacy and explore their practical applications in agricultural virology and crop protection strategies.

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Introduction

Zucchini Yellow Mosaic Virus (ZYMV) is a substantial pathogen that affects cucurbit crops, particularly zucchini, causing severe agricultural losses worldwide (Farag *et al.*, 2025; Abdel Razek *et al.*, 2025a). The virus is transmitted by aphids and manifests a variety of symptoms, including yellowing of leaves, mosaic patterns, and stunted growth, reducing crop yield and quality (Ahsan *et al.*, 2023; Askora *et al.*, 2023; Farag *et al.*, 2024). Conventional control strategies, such as chemical pesticides and resistant cultivars, often fall short in their effectiveness due to the rapid adaptation of pests and pathogens, race-specific resistance, and environmental influences on resistance expression (Simmons *et al.*, 2013). These limitations have spurred the search for alternative, eco-friendly approaches to combat viral diseases in crops (Omidvari *et al.*, 2023).

Plant-derived compounds, particularly those from medicinal plants, have gained attention as potential antiviral agents due to their bioactive properties. Among these, green tea (*Camellia sinensis*) stands out as a promising source of natural antiviral compounds. This plant is rich in polyphenolic compounds, particularly catechins such as epigallocatechin gallate (EGCG), and has long been known for its powerful antioxidant, anti-inflammatory, and antiviral activities (Cheng *et al.*, 2020). Studies have demonstrated green tea's ability to inhibit a wide range of human, animal, and plant viruses, making it a valuable candidate for controlling viral infections in agricultural systems (Xu *et al.*, 2017; Cheng *et al.*, 2020; Mhatre *et al.*, 2021; Ahmed *et al.*, 2024; Abdel-Razek *et al.*, 2025b).

Recent studies have highlighted the potential of green tea compounds in combating various viral pathogens; however, their specific efficacy against ZYMV remains underexplored. Green tea's bioactive components, particularly EGCG, have shown broad-spectrum antiviral properties, including interference with viral replication and inhibition of viral entry into host cells (Xu *et al.*, 2017; Mhatre *et al.*, 2021). These properties make green tea an intriguing option for addressing viral infections in several crops like zucchini, susceptible to ZYMV.

In light of this, recent advancements in computational techniques, such as molecular docking, offer a powerful

tool to explore the antiviral potential of green tea compounds (Abdel Razek *et al.*, 2025b; Elshaer *et al.*, 2025). Molecular docking allows researchers to virtually screen a vast array of compounds and predict their binding affinity and interactions with viral proteins involved in replication and infection (Mahmoud *et al.*, 2025; Megahed *et al.*, 2025). The current *In silico* approach provides a cost-effective and time-efficient way to identify promising antiviral candidates, which can then be experimentally validated (de Ruyck *et al.*, 2016; Jamal, 2022). By evaluating the interactions between green tea compounds and key ZYMV proteins, such as the coat protein (CP) and RNA-dependent RNA polymerase (RdRp), molecular docking can reveal potential inhibitors of viral replication (Pathania *et al.*, 2022).

The objective of this study was to fill the gap in several research studies by utilizing molecular docking simulations to predict the antiviral effects of green tea compounds against ZYMV. Through this approach, we sought to identify compounds that can potentially block viral replication and reduce the severity of disease symptoms in infected plants. The findings of this study will provide valuable insights into the potential use of green tea as a natural antiviral agent for the management of ZYMV in agricultural settings.

Materials and Methods

Selected bioactive compounds of green tea

Eight bioactive compounds obtained from green tea including caffeine, catechin, epicatechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate, gallic acid, and theophylline were selected based on their reported antiviral properties in a previous study conducted by Ahmed *et al.* (2024). As a positive control acyclovir compound was used.

Selection of ZYMV genes for docking analysis

This study focused on 10 key proteins encoded by ZYMV, each playing a vital role in the virus life cycle, in reference to a previous study reported by Abdel Razek *et al.* (2025a). These proteins were selected based on their involvement in viral replication, movement, and interaction with plant cells. They were then evaluated for potential interactions with bioactive compounds from green tea using *In silico* molecular docking. The selected proteins included

ZYMV-P1 (BFF82028.1); involved in viral replication and translation/transcription processes, ZYMV-HC-Pro (BFF82029.1); encoding the helper component proteinase critical for viral replication and ZYMV-CI (BFF82032.1); a cytoplasmic inclusion protein playing a role in viral replication and RNA synthesis. Finally, ZYMV-CP (BFF82037.1); represents the coat protein that protects the viral genome and assists in viral entry into plant cells.

Protein sequence retrieval

The full-length protein sequences of the selected ZYMV genes were retrieved in FASTA format from GenBank using their corresponding accession numbers from the NCBI database (<https://www.ncbi.nlm.nih.gov>).

Preparation of protein structures in 2D and 3D formats

The 2D SDF format of the bioactive compounds was sourced from the PubChem database (<https://pubchem.ncbi.nlm.nih.gov>). The 3D structures of ZYMV proteins was performed in the Protein Data Bank (PDB) (<https://www.rcsb.org>). For proteins lacking experimentally determined structures; a homology modeling was used, utilizing tools like SWISS-MODEL or Phyre2. These platforms generated structural models by aligning the target protein sequences with those of homologous, well-characterized proteins. The quality and reliability of the generated models were assessed using validation methods, such as Ramachandran plot analysis.

Virtual screening of green tea-selected compounds

Virtual screening of selected green tea compounds, along with acyclovir, was carried out using PyRx software (<https://sourceforge.net/projects/pyrx/>) (Patel *et al.*, 2022). This tool utilizes energy minimization and molecular docking *via* the AutoDock Vina plugin to assess the binding potential of the compounds against ZYMV proteins. Compounds exhibiting the lowest binding energies, indicative of stronger interactions with the target proteins, were chosen for further analysis. It is important to note that before docking, the compounds were converted into 3D structures and underwent energy minimization using Open Babel and Chem3D.

Molecular docking of green tea-selected compounds

For docking studies, target proteins were prepared by removing water molecules and irrelevant ligands using PyMOL. Hydrogen atoms were added to

complete the protein structure, and partial charges were assigned using the Kollman method to enable accurate calculation of electrostatic interactions during molecular docking. The ligands underwent energy minimization with Open Babel or Chem3D. Docking simulations were performed using CB-Dock and AutoDock Vina, where the binding affinities (kcal/mol) for each protein-ligand interaction were recorded. CB-Dock was employed to automatically identify potential binding sites on the proteins, which enhanced the docking accuracy.

Analysis and visualization

The results from the docking simulations were analyzed and visualized using Discovery Studio 2022 (<https://10.0.142.116/Pharmaceutical-Sciences.543>). Interactions such as hydrogen bonds, hydrophobic contacts (Patil *et al.*, 2010), and ionic interactions were carefully examined to identify key binding sites and assess the stability of the protein-ligand complexes.

Results

Comparative binding analysis of green tea polyphenols against ZYMV proteins

The data in Table 1 present the binding affinities (BA) and molecular docking (MD) scores of various green tea polyphenols against different ZYMV proteins (P1, HC-Pro, CI, and CP) compared to acyclovir as a control. Polar surface area (PSA) values of the ligands are also provided. Caffeine and theophylline exhibited relatively low binding affinities across all ZYMV proteins (BA ranging from -4.1 to -6.0 kcal/mol). Their molecular docking scores mirror the weak interactions. This suggests that simple methylxanthines are less effective against ZYMV proteins.

Catechin and epicatechin (EC) showed improved binding affinities compared to caffeine and the control. BA values ranged from -5.8 to -8.0 kcal/mol. Notably, EC displayed slightly stronger binding to P1 (-8.0) and CI (-7.6), indicating potential inhibitory activity. Both epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) demonstrated the highest binding affinities among the tested ligands. EGCG, for instance, had a BA of -8.7 kcal/mol against P1 and -7.9 kcal/mol against CI. Molecular docking results support strong interactions with multiple ZYMV proteins. Their high polar surface areas (130–197 Å²)

Table 1: Binding affinities and molecular docking analysis of green tea polyphenols against ZYMV proteins compared to acyclovir.

Ligands	PSA (Å ²)	ZYMV-protein							
		P1	HC-Pro		CI		CP		
		BA	MD	BA	MD	BA	MD	BA	MD
Caffeine	058.40	-6.0	-6.0	-5.1	-4.3	-5.7	-3.3	-4.1	-4.0
Catechin	110.00	-7.9	-7.7	-6.5	-6.2	-7.2	-7.3	-5.9	-6.1
Epicatechin (EC)	110.38	-8.0	-7.8	-6.4	-6.2	-7.6	-7.4	-6.2	-5.8
Epicatechin gallate (ECG)	130.61	-8.6	-9.3	-6.9	-7.2	-8.2	-8.5	-6.6	-6.5
Epigallocatechin (EGC)	197.00	-8.1	-8.2	-6.3	-6.0	-7.5	-7.4	-6.0	-5.8
Epigallocatechin gallate (EGCG)	197.37	-8.7	-9.1	-7.4	-6.8	-7.9	-8.0	-6.5	-6.6
Gallocatechin	130.61	-8.0	-7.9	-6.4	-6.4	-6.9	-6.9	-5.9	-5.9
Theophylline	069.30	-6.0	-5.9	-4.8	-4.9	-5.5	-3.3	-4.5	-4.1
Acyclovir (as a control)	118.58	-6.3	-5.9	-5.6	-4.9	-5.9	-3.3	-4.4	-4.1

Where; PSA: Polar surface area. BA: Binding affinities. MD: Molecular docking. P1: Protein 1. HC-Pro: Helper Component-Protease. CI: Cylindrical Inclusion Protein. CP; Coat protein.

may facilitate multiple hydrogen bonding interactions with the protein active sites.

Epigallocatechin (EGC) and gallocatechin also displayed considerable binding, but generally lower than the gallate derivatives. EGC showed strong interaction with P1 (-8.1) and CI (-7.5), suggesting moderate inhibitory potential. Acyclovir showed moderate binding (BA ~ -5.6 to -6.3 kcal/mol), which was lower than most polyphenols, especially EGCG and ECG. This indicates that green tea polyphenols, particularly gallate derivatives, may have higher affinity for ZYMV proteins than conventional antiviral controls.

Overall, the results clearly suggest that green tea polyphenols, especially ECG and EGCG, possess strong binding potential to ZYMV proteins, surpassing the performance of acyclovir in both binding and docking analyses. These findings highlight their potential as plant-based antiviral agents against ZYMV

Antiviral potential of green tea bioactive compounds against ZYMV P1 protein

The experimental results shown in Table 2 and illustrated in Figures 1-3 outline the specific molecular interactions between eight green tea bioactive compounds and the ZYMV P1 protein, identifying the amino acid residues involved, their binding sites,

and the types of bonds formed. Acyclovir was included as a reference compound for comparison.

The data revealed that the green tea compounds interact with a broad range of amino acid residues through various types of non-covalent interactions, including conventional hydrogen bonds, Pi-related interactions (e.g., Pi-Alkyl, Pi-Pi Stacked), alkyl bonds, and some unfavorable contacts. These interactions suggested diverse and complex binding modes across different compounds. Among the most notable compounds, Epicatechin gallate (ECG) and Epigallocatechin gallate (EGCG) showed the most extensive and diverse interactions. ECG formed hydrogen bonds with key residues such as LYS1501, TYR1754, and HIS1762, in addition to Pi-Pi and Pi-Alkyl interactions. EGCG, while forming fewer interactions than ECG, bound to critical residues like VAL1345, THR1346, and GLY1478 using alkyl, Pi-Sigma and hydrogen bonds, supporting its strong binding affinity. Catechin and gallocatechin also interacted with multiple residues, including ARG1303, PHE1322, and HIS1328, through Pi-Cation, Alkyl, and hydrogen bonds. Interestingly, several interactions in these compounds involved aromatic and charged residues, indicating their potential to form stable complexes through both hydrophobic and electrostatic contributions.

Table 2: *Molecular interactions between green tea bioactive compounds and ZYMV P1 protein: Amino acid residues, binding sites and bond types.*

Green tea bioactive compounds	Amino acid residues	Bind-ing sites	Bond types
Caffeine	HIS	A:1631	Pi-Alkyl, Pi-Pi Stacked
	THR	A:1656	Conventional Hydrogen
	LEU	A:1786	Pi-Alkyl, Carbon Hydrogen
	SER	A:1787	Carbon Hydrogen
	ASP	A:1788	Attractive Change
	VAL	A:1806	Carbon Hydrogen
	SER	A:1807	Conventional Hydrogen
Catechin	ARG	A:1303	Pi-Cation
	PHE	A:1322	Alkyl
	HIS	A:1328	Pi-Pi T-shaped, Alkyl, Pi-Alkyl
	ASP	A:1347	Conventional Hydrogen
	ALA	A:1349	Pi-Sigma
	ALA	A:1554	Alkyl, Unfavorable Acceptor Acceptor, Pi-Pi T-shaped
	PHE	A:1587	Conventional Hydrogen
Epicatechin	THR	A:1278	Conventional Hydrogen
	VAL	A:1345	Alkyl, Pi-Sigma
	ASN	A:1473	Conventional Hydrogen, Conventional Hydrogen
	GLU	A:1476	Conventional Hydrogen, Pi-Sigma
	ASN	A:1477	Unfavorable Donor Donor
	GLY	A:1478	Conventional Hydrogen
	SER	A:1512	Conventional Hydrogen
Epigallocatechin	LYS	A:1501	Pi-Cation
	VAL	A:1504	Conventional Hydrogen
	TYR	A:1754	Pi-Donor Hydrogen
	THR	A:1759	Conventional Hydrogen
	HIS	A:1762	Pi-Pi- Stacked, Pi-Alkyl
Epicatechin gallate	SER	A:1807	Unfavorable Donor Donor
	LYS	A:1501	Conventional Hydrogen
	TRY	A:1506	Pi-Alkyl
	TYR	A:1754	Conventional Hydrogen, Conventional Hydrogen
	HIS	A:1758	Carbon Hydrogen
	HIS	A:1762	Pi-Pi T-shaped, Conventional Hydrogen, Conventional Hydrogen
	GLU	A:1805	Conventional Hydrogen
	VAL	A:1806	Pi-Alkyl
	SER	A:1807	Conventional Hydrogen

Table continues on next column.....

Green tea bioactive compounds	Amino acid residues	Bind-ing sites	Bond types
Epigallocatechin-gallate	VAL	A:1345	Alkyl, Pi-Sigma
	THR	A:1346	Conventional Hydrogen
	PRO	A:1374	Pi-Alkyl
	GLY	A:1478	Conventional Hydrogen
Gallocatechin	ARG	A:1303	Pi-Cation, Pi-Alkyl
	GLU	A:1319	Unfavorable acceptor acceptor
	PHE	A:1322	Alkyl
	HIS	A:1328	Alkyl, Pi-Sigma
	SER	A:1348	Carbon Hydrogen
	ALA	A:1349	Pi-Sigma
	ALA	A:1554	Conventional Hydrogen, Pi-Sigma, Alkyl
Theophylline	PHE	A:1587	Unfavorable Donor Donor
	LEU	A:1589	Conventional Hydrogen
	THR	A:1278	Conventional Hydrogen, Pi-Donor Hydrogen
	GLU	A:1342	Carbon Hydrogen, Attractive Change
	VAL	A:1345	Pi-Alkyl
	ASN	A:1473	Carbon Hydrogen
	ASN	A:1477	Conventional Hydrogen
Acyclovir (Control)	GLY	A:1478	Conventional Hydrogen
	GLU	A:1342	Attractive Change
	VAL	A:1345	Pi-Sigma
	ASN	A:1473	Conventional Hydrogen
	GLU	A:1476	Attractive Change, Conventional Hydrogen
	ASN	A:1477	Conventional Hydrogen, Conventional Hydrogen
	GLU	A:1478	Conventional Hydrogen

Where; ALA, Alanine; ARG, Arginine; ASN, Asparagine; ASP, Aspartic acid; GLU, Glutamic acid; GLY, Glycine; HIS, Histidine; LEU, Leucine; LYS, Lysine; PHE, Phenylalanine, PRO, Proline; SER, Serine; THR, Threonine; TYR, Tyrosine; and VAL, Valine.

On the other hand, Caffeine and theophylline, engaged in fewer and weaker interactions, primarily limited to Pi-Alkyl and conventional hydrogen bonds, aligning with their lower binding affinities. Caffeine's interaction with residues like HIS1631 and SER1807 seemed less structurally complex, which may explain its limited inhibitory potential. Acyclovir, used as the control, was bound to a small number of amino acid residues (e.g., ASN1473, GLU1476, and ASN1477) primarily through conventional hydrogen and electrostatic interactions. Its relatively simple and less diverse binding profile reinforced its weaker overall interaction with the P1 protein compared to the green tea polyphenols.

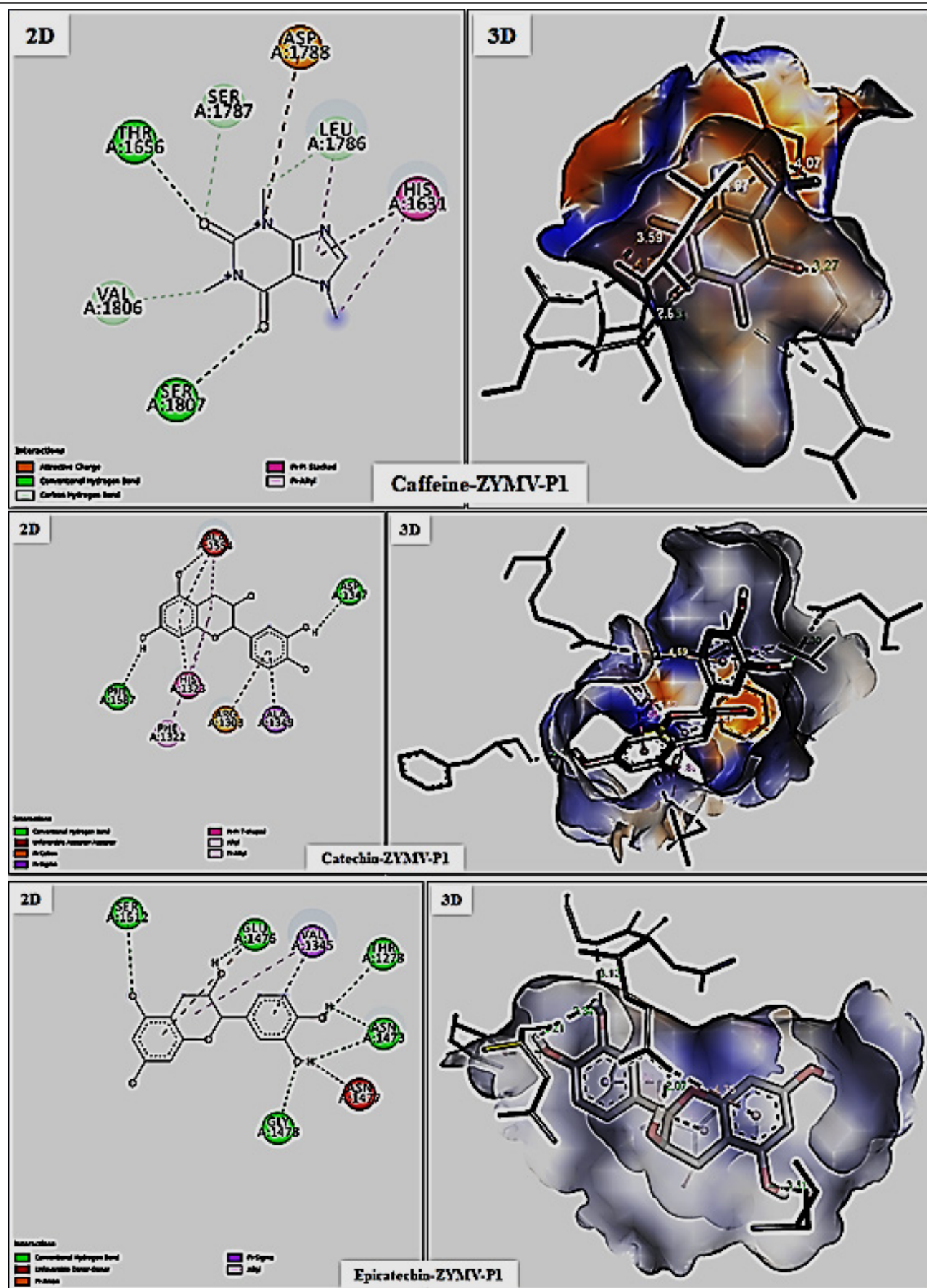


Figure 1: The docking visualization illustrating the interaction profiles of three phytochemicals—caffeine, catechin, and epicatechin—with the ZYMV-P1 protein presented in both 2D and 3D formats. The results show that caffeine has the weakest binding to the ZYMV-P1 protein, while catechin forms stronger interactions. Epicatechin shows the strongest and most stable binding, making it the most promising inhibitor among the three tested compounds.

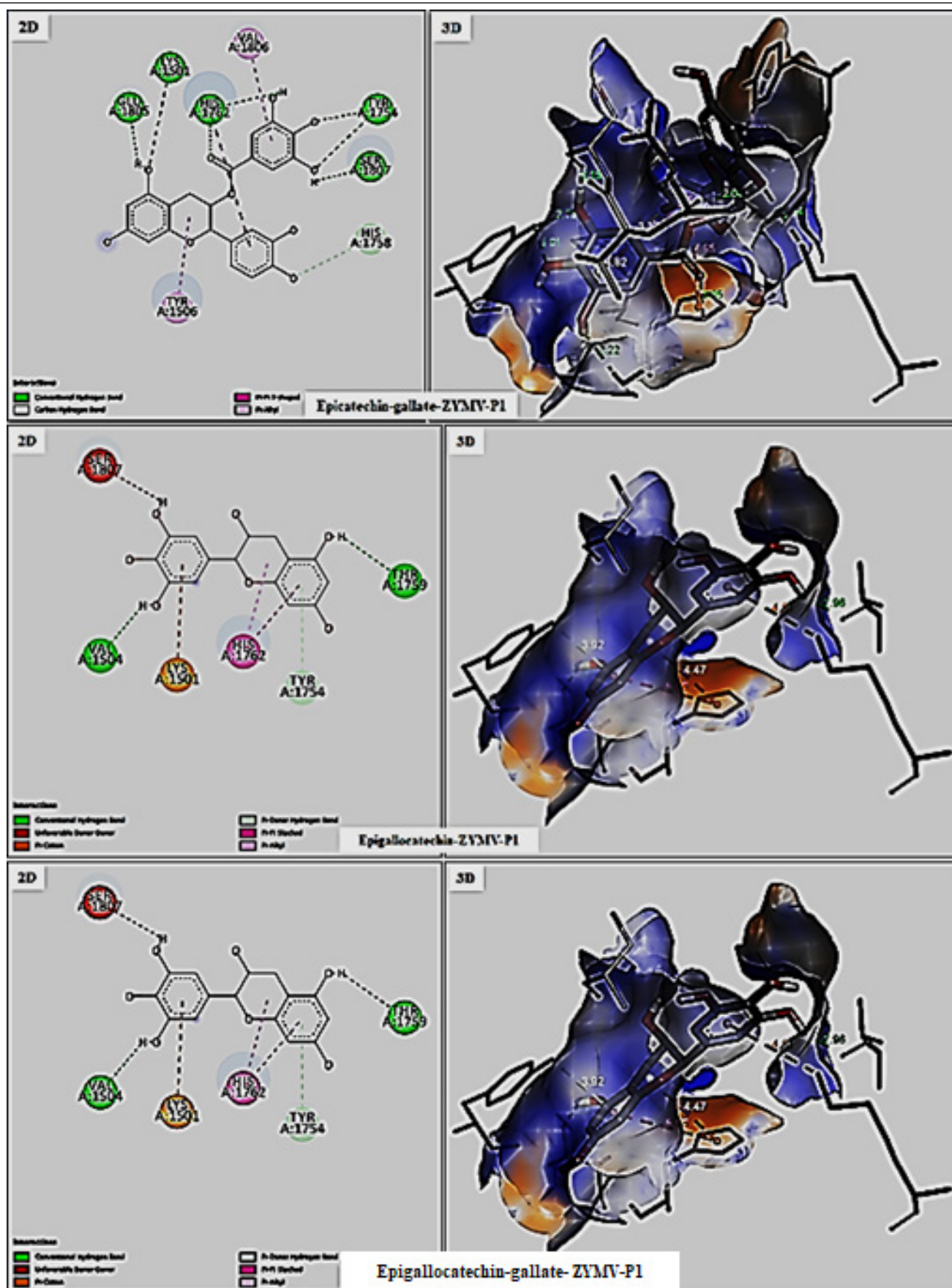


Figure 2: The docking visualization illustrates the interaction profiles of three phytochemicals– epicatechin-gallate, epigallocatechin, and epigallocatechin-gallate –with the ZYMV-P1 protein presented in both 2D and 3D formats. The results show that epicatechin-gallate forms the strongest and most stable interactions with the ZYMV-P1 protein, followed by epigallocatechin and epigallocatechin-gallate. All three compounds interact through multiple hydrogen bonds, indicating good binding potential, with epicatechin-gallate being the most promising inhibitor.

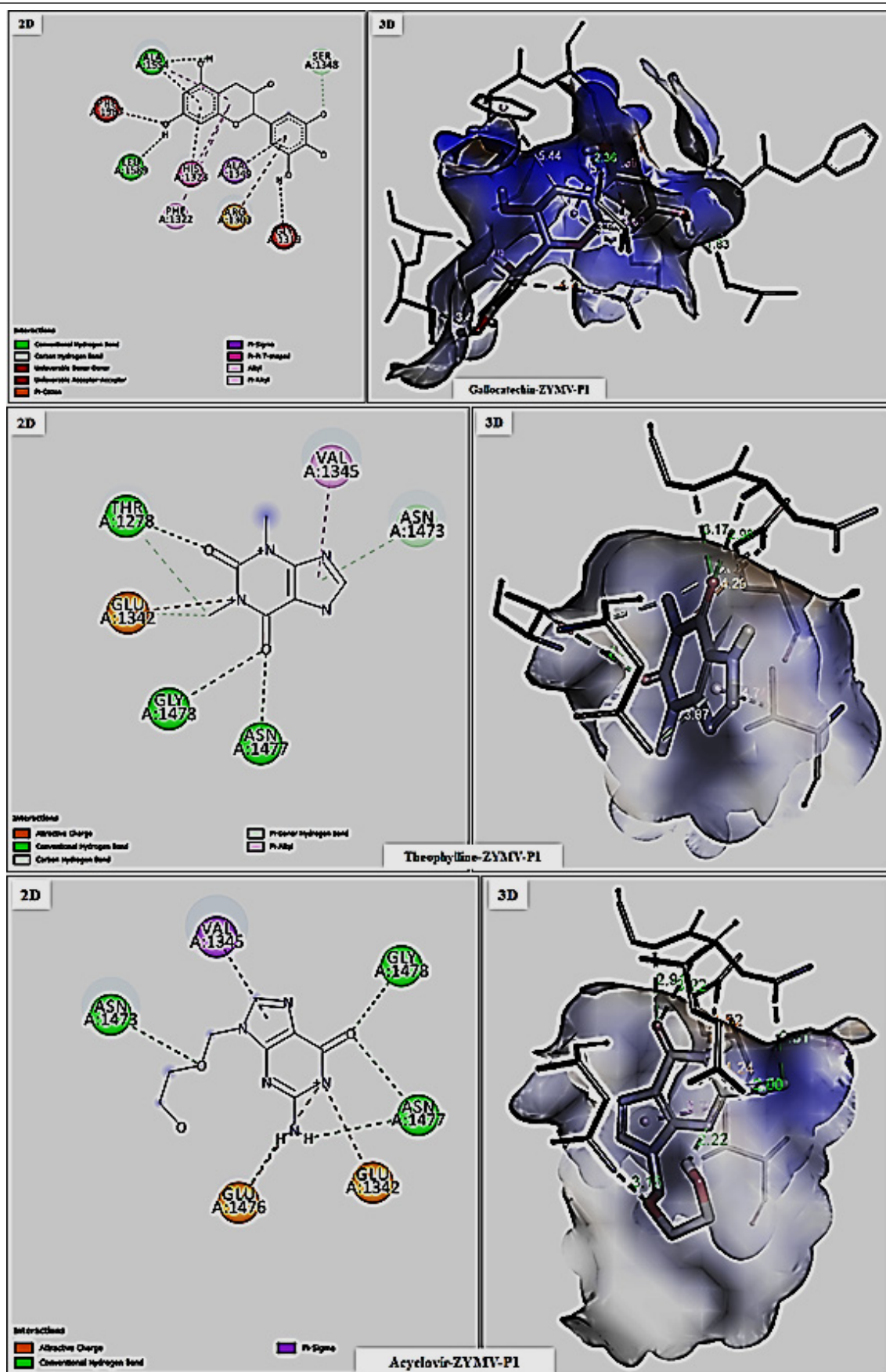


Figure 3: The docking visualization illustrates the interaction profiles of three phytochemicals– gallicatechin, theophylline, and Acyclovir–with the ZYMV-P1 protein presented in both 2D and 3D formats. Gallicatechin shows the strongest and most stable binding to the ZYMV-P1 protein through multiple hydrogen bonds and aromatic interactions. Theophylline and acyclovir also interact with the protein but with fewer bonds, indicating weaker binding compared to gallicatechin. Overall, gallicatechin appears to be the most promising inhibitor in this group.

Antiviral potential of green tea bioactive compounds against ZYMV HC-pro protein

Results presented in Table 3 and illustrated in Figures 4–6 outlines the detailed molecular interactions between various green tea bioactive compounds and the HC-Pro protein of the ZYMV, including the specific amino acid residues involved, their binding sites, and the types of bonds formed. Acyclovir, a standard antiviral reference compound was also included for comparative purposes. The data shows that green tea compounds engaged in a diverse range of interactions with the HC-Pro protein, involving multiple bond types such as conventional hydrogen bonds, Pi-related interactions (Pi-Alkyl, Pi-Anion, Pi-Sulfur), alkyl interactions, and some unfavorable contacts. These interactions suggested complex binding mechanisms that varied depending on the structure of each compound.

Table 3: Molecular interactions between green tea bioactive compounds and the ZYMV HC-Pro protein: amino acid residues, binding sites and bond types.

Green tea bioactive compounds	Amino acid residues	Bind- ing sites	Bond types
Caffeine	ALA	A:384	Carbon Hydrogen
	THR	A:385	Conventional Hydrogen
Catechin	MET	A:381	Pi-Alkyl
	ILE	A:439	Carbon Hydrogen
	ALA	A:442	Pi-Alkyl
	ASN	A:444	Conventional Hydrogen
	GLN	A:447	Conventional Hydrogen, Conventional Hydrogen, Conventional Hydrogen
Epicatechin	LYS	A:451	Unfavorable Donor-Donor
	ALA	A:337	Pi-Alkyl, Pi-Alkyl, Pi-Alkyl
	GLU	A:339	Unfavorable Donor-Donor
	CYS	A:342	Pi-Sulfur, Conventional Hydrogen, Alkyl, Pi-Alkyl
	ASN	A:345	Conventional Hydrogen
Epigallocatechin	ILE	A:417	Pi-Alkyl
	ASP	A:418	Conventional Hydrogen
	ALA	A:337	Alkyl, Pi-Alkyl
	CYS	A:342	Conventional Hydrogen, Alkyl, Pi-Alkyl
	ASN	A:345	Conventional Hydrogen
	VAL	A:416	Conventional Hydrogen
	ILE	A:417	Pi-Alkyl
	GLY	A:456	Conventional Hydrogen

Table continues on next column.....

Green tea bioactive compounds	Amino acid residues	Bind- ing sites	Bond types
Epicatechin gallate	TYR	A:338	Unfavorable Acceptor Acceptor, Carbon Hydrogen
	MET	A:381	Pi-Anion
	ILE	A:439	Carbon Hydrogen
	ALA	A:442	Pi-Alkyl
	ASN	A:444	Unfavorable Acceptor Acceptor
	ASP	A:445	Conventional Hydrogen, Unfavorable Donor-Donor
Epigallocatechin-gallate	GLN	A:447	Conventional Hydrogen, Unfavorable Donor-Donor
	ALA	A:337	Pi-Alkyl, Pi-Alkyl, Alkyl
	CYS	A:342	Carbon Hydrogen, Alkyl
	ASN	A:345	Conventional Hydrogen
	ILE	A:417	Pi-Donor Hydrogen, Alkyl
Gallocatechin	ASP	A:418	Conventional Hydrogen
	MET	A:381	Pi-Sulfur
	ALA	A:384	Conventional Hydrogen, Pi-Alkyl
	THR	A:385	Carbon Hydrogen
	ALA	A:442	Pi-Alkyl
	SER	A:443	Pi-Donor Hydrogen
	ASN	A:444	Conventional Hydrogen
	ASP	A:445	Conventional Hydrogen, Conventional Hydrogen
Theophylline	GLN	A:447	Unfavorable Donor-Donor
	LYS	A:451	Pi-Cation
	ALA	A:384	Pi-Alkyl
	ILE	A:439	Pi-Alkyl
Acyclovir (Control)	ALA	A:442	Amide-Pi Stacked
	SER	A:443	van der Waals
	ASP	A:418	Conventional Hydrogen
	GLU	A:339	Conventional Hydrogen, Salt Bridge
	GLY	A:456	Attractive Charge, Pi-Anion
	HIS	A:415	Conventional Hydrogen
	CYS	A:342	Pi-Donor Hydrogen
	VAL	A:416	Pi-Donor Hydrogen
	ILE	A:417	Carbon Hydrogen
	ASN	A:345	Unfavorable Donor-Donor
	ASP	A:418	Conventional Hydrogen

Where; ALA, Alanine; ASN, Asparagine; ASP, Aspartic acid; CYS, Cysteine; GLN, Glutamine; GLU, Glutamic acid; GLY, Glycine; HIS, Histidine; ILE, Isoleucine; LYS, Lysine; MET, Methionine; SER, Serine; THR, Threonine; TYR, Tyrosine; and VAL, Valine.

Among the compounds, Epicatechin gallate (ECG) and Epigallocatechin gallate (EGCG) again stood out

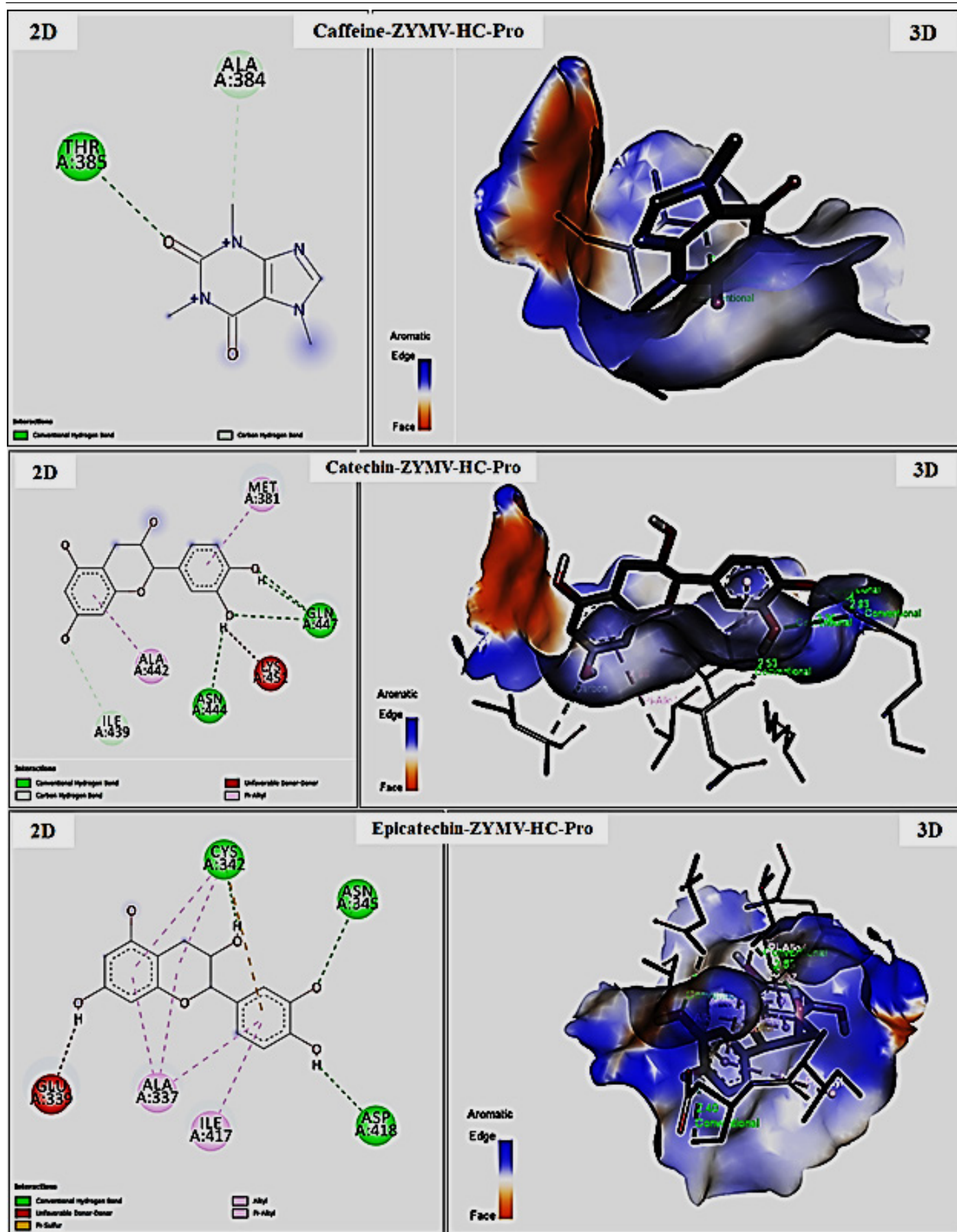


Figure 4: The docking visualization illustrates the interaction profiles of three phytochemicals—caffeine, catechin, and epicatechin—with the ZYMV- HC-Pro protein presented in both 2D and 3D formats. The 2D and 3D interaction maps clearly illustrate how caffeine, catechin, and epicatechin bind to ZYMV HC-Pro, highlighting key hydrogen bonds and aromatic interactions that may contribute to their inhibitory potential.

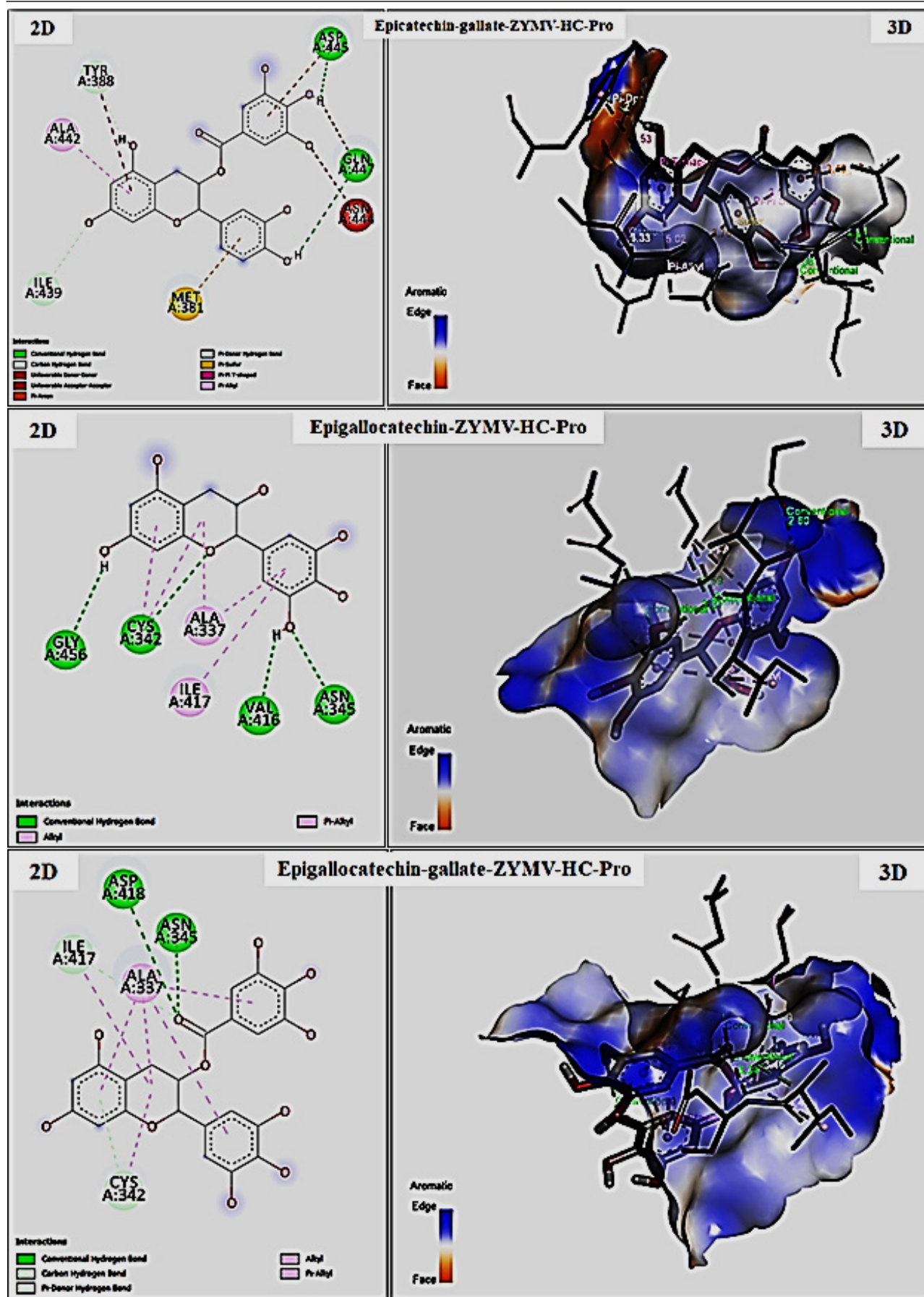


Figure 5: The docking visualization illustrates the interaction profiles of three phytochemicals- epicatechin-gallate, epigallocatechin, and epigallocatechin-gallate -with the ZYMV- HC-Pro protein presented in both 2D and 3D formats. Epicatechin-gallate, epigallocatechin, and epigallocatechin-gallate all show strong binding to ZYMV HC-Pro through multiple hydrogen bonds and aromatic interactions, indicating high inhibitory potential.

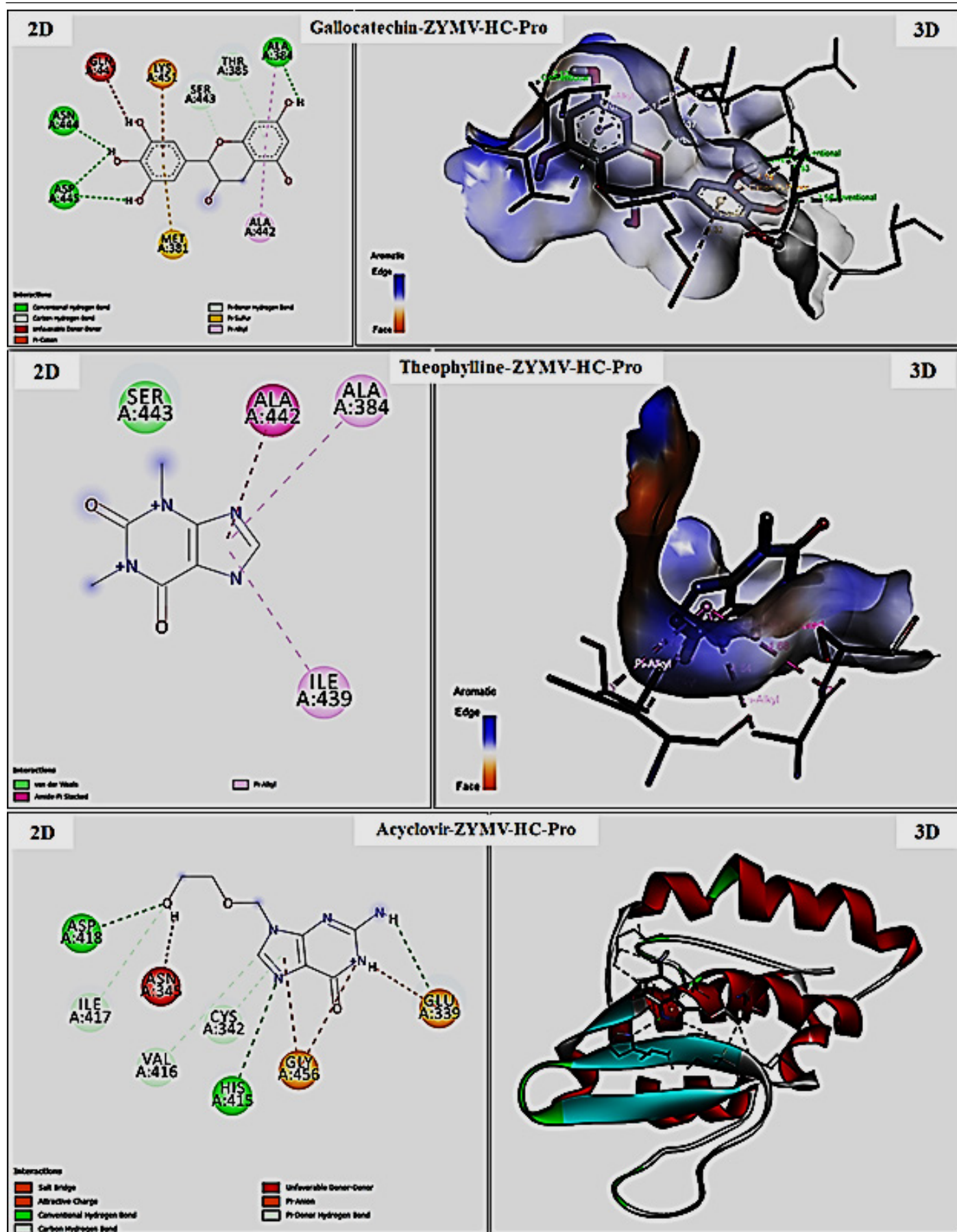


Figure 6: The docking visualization illustrates the interaction profiles of three phytochemicals– gallocatechin, theophylline, and Acyclovir–with the ZYMV- HC-Pro protein presented in both 2D and 3D formats. Gallocatechin, theophylline, and acyclovir each interact with ZYMV HC-Pro through several hydrogen bonds and π -interactions, but gallocatechin shows the strongest and most extensive binding among the three.

due to the diversity and strength of their interactions. ECG interacted with key residues like MET381, ILE439, and GLN447 through Pi-Anion, Pi-Alkyl, and hydrogen bonds. However, they also included a few unfavorable interactions, such as donor-donor and acceptor-acceptor clashes, possibly due to steric hindrance or charge repulsion. EGCG formed multiple stabilizing interactions, including Pi-Alkyl and hydrogen bonds with several residues including ALA337, CYS342, and ILE417, reinforcing its previously observed high docking affinity. Other catechins, such as epicatechin, epigallocatechin, and galliccatechin, showed substantial bonding as well, with interactions involving critical residues such as CYS342, ASN345, and ASP418. These interactions often included Pi-Sulfur bonds (notably with CYS), conventional hydrogen bonds, and alkyl interactions, suggesting that these compounds may effectively anchor themselves into the HC-Pro binding pocket through both polar and hydrophobic forces.

In contrast, caffeine and theophylline formed fewer and simpler interactions, with most bonds being limited to Pi-Alkyl or basic hydrogen bonds. This minimal interaction profile reflected their lower structural complexity and likely contributed to their weaker binding affinity. Acyclovir exhibited a moderate range of interactions, including conventional hydrogen bonds, Pi-Anion, and a salt bridge with GLU339, suggesting some degree of stability in binding. However, the number and diversity of its interactions was still less than that of the more complex green tea polyphenols. Additionally, unfavorable interactions with ASN345 may slightly hinder its binding efficiency.

Antiviral potential of green tea bioactive compounds against ZYMV CI protein

The data presented in [Table 4](#) and [Figures 7–9](#) provide an in-depth look at the molecular interactions between green tea-derived bioactive compounds and the CI (Cylindrical Inclusion) protein of the ZYMV. The [Table 4](#) identifies the specific amino acid residues, their binding sites, and the types of bonds formed during docking simulations. Acyclovir was included as a benchmark antiviral compound for comparative evaluation.

As observed in previous analyses, epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) displayed the richest and most diverse interaction

profiles. ECG interacted with residues like HIS177, VAL178, and ASN310 through hydrogen, alkyl, and carbon hydrogen bonds. Notably, ECG formed multiple stabilizing interactions, though it also included one unfavorable acceptor–acceptor contact at ASN306, which may slightly reduce its binding efficiency. EGCG was engaged in extensive hydrogen bonding with THR205, ASN306, ASN310, and SER376, highlighting its strong polar interaction capacity. These interactions reinforce its previously observed high affinity to the CI protein. Other catechin derivatives, such as epicatechin, epigallocatechin, and galliccatechin, also showed multiple stabilizing interactions. Epicatechin formed both conventional hydrogen and Pi-Anion bonds with residues such as THR205, PRO207, and GLU309. Epigallocatechin also was bound to GLU309 *via* Pi-Anion interaction and formed multiple hydrogen bonds, although it included an unfavorable donor–donor contact at GLY208. Galliccatechin exhibited Pi-Sigma and Pi-Alkyl bonding, with key contacts at PRO207, THR179, and GLU309.

Catechin, while forming fewer interactions than its gallate-containing counterparts, still bound effectively with VAL178, PRO207, and GLN351 *via* Pi-Alkyl and hydrogen bonds. The nature of these interactions indicated that even non-gallate catechins can establish stable complexes with the CI protein, though likely with somewhat reduced binding strength. In contrast, caffeine and theophylline once again showed a limited and simpler interaction pattern. Caffeine's interactions include conventional hydrogen bonding with THR205 and SER376, as well as a Pi-Anion interaction with GLU348. Theophylline's key interactions are confined to residues like THR205 and GLU384 through hydrogen bonds and electrostatic attraction, consistent with its overall lower docking performance.

Acyclovir, the reference compound, interacted with several residues including SER181, THR383, GLU384, and LEU388, forming mainly conventional hydrogen bonds and some Pi-Sigma interactions. While it was bound with a few more residues than caffeine or theophylline, its interactions lacked the diversity and depth observed in catechin derivatives, especially in terms of Pi-based and hydrophobic interactions.

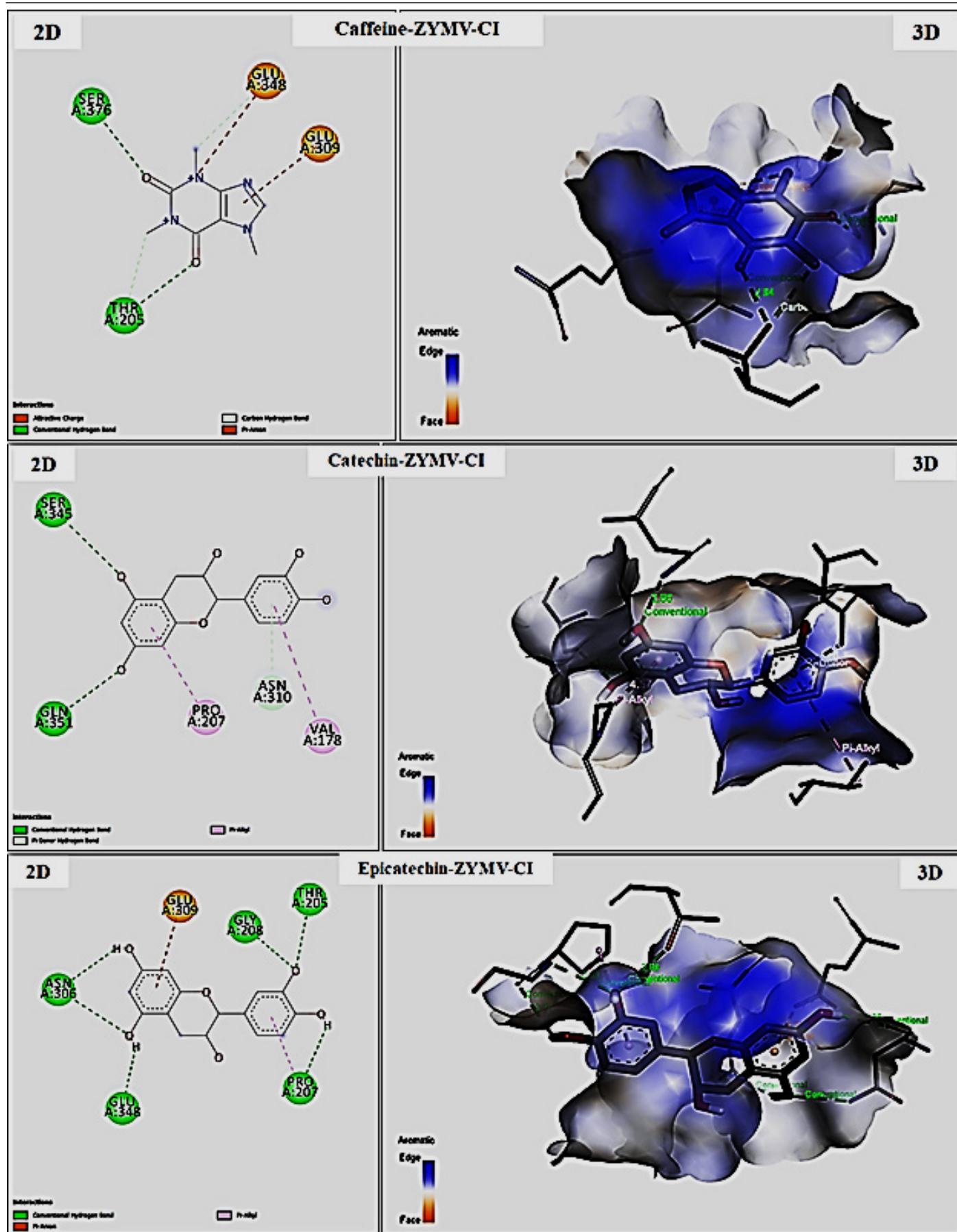


Figure 7: The docking visualization illustrates the interaction profiles of three phytochemicals—caffeine, catechin, and epicatechin—with the ZYMV-CI protein presented in both 2D and 3D formats. The 3D models confirm that catechin and epicatechin have more extensive interactions with the protein's active site than caffeine, which likely make them better inhibitors.

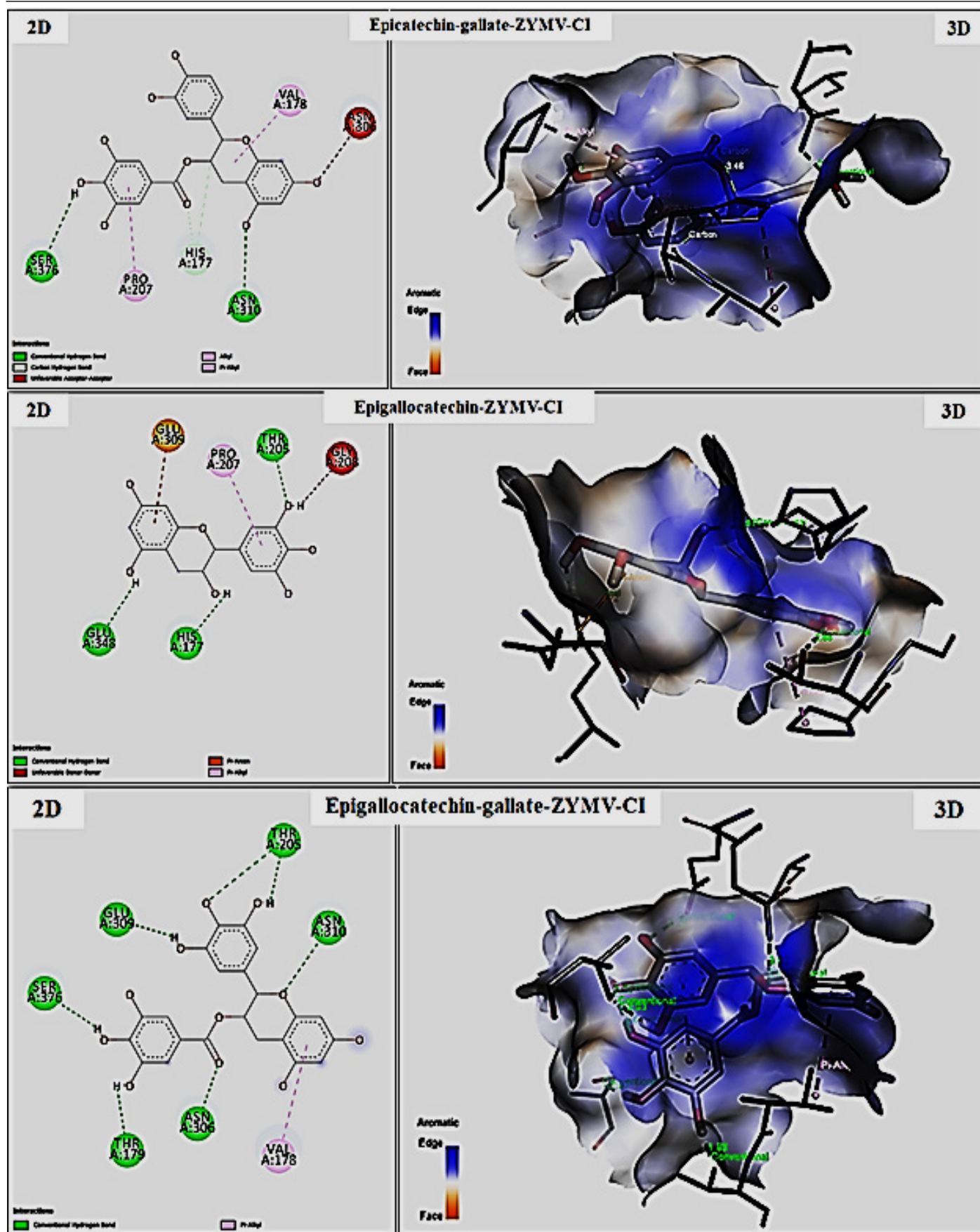


Figure 8: The docking visualization illustrates the interaction profiles of three phytochemicals- epicatechin-gallate, epigallocatechin, and epigallocatechin-gallate -with the ZYMV-CI protein presented in both 2D and 3D formats. Among the tested compounds, epigallocatechin-gallate appears to be the most promising inhibitor of ZYMV-CI due to its extensive interactions and optimal positioning in the active site. The other two compounds also show potential but with comparatively weaker binding.

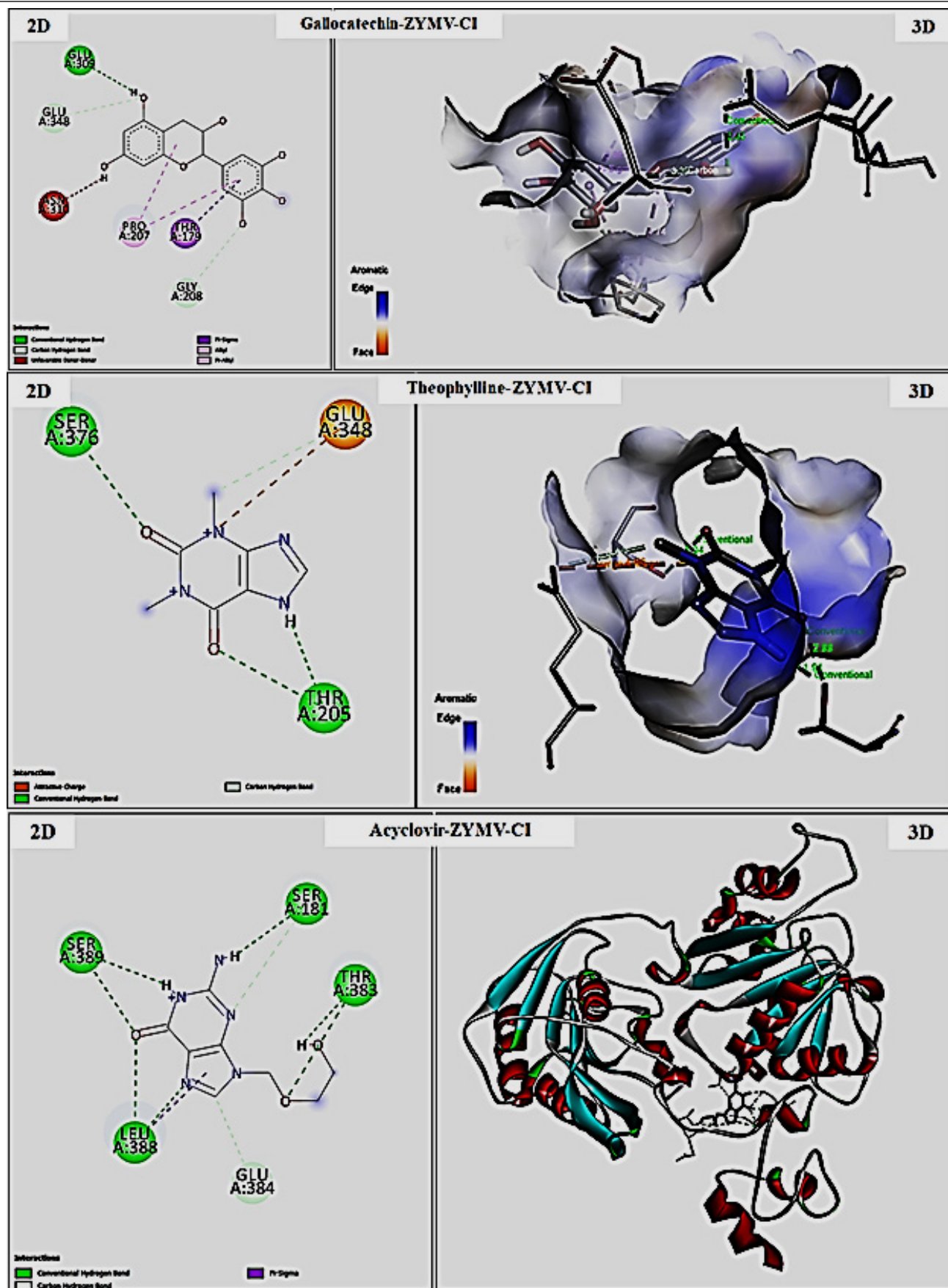


Figure 9: The docking visualization illustrates the interaction profiles of three phytochemicals– gallocatechin, theophylline, and Acyclovir–with the ZYMV-CI protein presented in both 2D and 3D formats. Among these compounds, gallocatechin demonstrates the strongest interaction with ZYMV-CI, while theophylline and acyclovir show weaker binding. This suggests that polyphenolic compounds may have better inhibitory potential than synthetic molecules like acyclovir for this target.

Table 4: *Molecular interactions between green tea bioactive compounds and the ZYMV CI protein: Amino acid residues, binding sites and bond types.*

Green tea bioactive compounds	Amino acid residues	Binding sites	Bond types
Caffeine	THR	A:205	Conventional Hydrogen, Carbon Hydrogen
	GLU	A:309	Attractive Change
	GLU	A:348	Pi-Anion, Carbon Hydrogen
	SER	A:376	Conventional Hydrogen
Catechin	VAL	A:178	Pi-Alkyl
	PRO	A:207	Pi-Alkyl
	ASN	A:310	Pi-Donor Hydrogen
	SER	A:345	Conventional Hydrogen
Epicatechin	GLN	A:351	Conventional Hydrogen
	THR	A:205	Conventional Hydrogen
	PRO	A:207	Conventional Hydrogen, Pi Alkyl
	GLY	A:208	Conventional Hydrogen
	ASN	A:306	Conventional Hydrogen, Conventional Hydrogen
	GLU	A:309	Pi Anion
Epigallocatechin	GLU	A:348	Conventional Hydrogen
	HIS	A:177	Conventional Hydrogen
	THR	A:205	Conventional Hydrogen
	PRO	A:207	Pi-Alkyl
	GLY	A:208	Unfavorable Donor Donor
Epicatechin gallate	GLU	A:309	Pi-Anion
	GLU	A:348	Conventional Hydrogen
	HIS	A:177	Carbon Hydrogen, Carbon Hydrogen
	VAL	A:178	Alkyl
	PRO	A:207	Pi Alkyl
Epigallocatechin-gallate	ASN	A:306	Unfavorable Acceptor Acceptor
	ASN	A:310	Conventional Hydrogen
	SER	A:376	Conventional Hydrogen
	VAL	A:178	Pi-Alkyl
	THR	A:179	Conventional Hydrogen
	THR	A:205	Conventional Hydrogen, Conventional Hydrogen
	ASN	A:306	Conventional Hydrogen
	GLU	A:309	Conventional Hydrogen
Gallocatechin	ASN	A:310	Conventional Hydrogen
	SER	A:376	Conventional Hydrogen
	THR	A:179	Pi-Sigma
	PRO	A:207	Pi-Alkyl, Alkyl
	GLY	A:208	Carbon Hydrogen

Table continues on next column.....

Green tea bioactive compounds	Amino acid residues	Binding sites	Bond types
Theophylline	GLU	A:309	Conventional Hydrogen
	ASN	A:310	Unfavorable Donor Donor
	GLU	A:348	Carbon Hydrogen
	THR	A:205	Conventional Hydrogen, Conventional Hydrogen
Acyclovir (Control)	SER	A:376	Conventional Hydrogen
	GLU	A:384	Attractive Change, Carbon Hydrogen
	SER	A:181	Conventional Hydrogen, Carbon Hydrogen
	THR	A:383	Conventional Hydrogen, Conventional Hydrogen
	GLU	A:384	Carbon Hydrogen
	LEU	A:388	Conventional Hydrogen, Conventional Hydrogen, Pi-Sigma
	SER	A:389	Conventional Hydrogen, Conventional Hydrogen

Where; ASN, Asparagine; GLN, Glutamine; GLU, Glutamic acid; GLY, Glycine; HIS, Histidine; LEU, Leucine; PRO, Proline; SER, Serine; THR, Threonine; and VAL, Valine.

Antiviral potential of green tea bioactive compounds against ZYMV CP Protein

The data provided in Table 5 and Figures 10–12 detail the molecular interactions between green tea bioactive compounds and the coat protein (CP) of the ZYMV, outlining the involved amino acid residues, binding sites, and the types of bonds formed. The antiviral compound acyclovir was included for reference, serving as a control to evaluate the relative performance of the natural compounds.

As with previous viral proteins analyzed, epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) exhibited the most complex and extensive binding interactions with the ZYMV-CP. ECG interacts with residues like ASN37, GLU26, ASP30, and LYS34 across multiple chains *via* conventional hydrogen bonds, Pi-Anion, and Pi-Alkyl interactions. EGCG also formed a rich network of interactions involving residues such as ARG23, GLU26, ASP30, and PHE31, combining hydrogen bonding, Pi-based interactions, and hydrophobic contacts. These multifaceted interactions likely underpinned their strong binding affinities and docking scores observed in earlier results.

Epicatechin and catechin formed several stabilizing interactions as well, including hydrogen bonds and Pi-Cation or Pi-Alkyl interactions with residues like

ARG42, ASP30, and ALA39. Notably, catechin also formed a Pi-Anion interaction with ASP30 and a Pi-Cation bond with ARG42, reinforcing its moderate binding efficiency. Gallicocatechin showed a similar interaction profile, forming both polar and Pi-based interactions, especially with ARG42 and ASP30-key charged residues that appeared repeatedly across effective compounds.

Table 5: *Molecular interactions between green tea bioactive compounds and the ZYMV coat protein (CP): amino acid residues, binding sites and bond types.*

Green tea bioactive compounds	Amino acid residues	Bind-ing sites	Bond types
Caffeine	ARG	A:42	Unfavorable Positive Positive, Unfavorable Positive Positive
	ARG	B:23	Carbon Hydrogen
	ALA	B:27	Alkyl
	ASP	B:30	Pi-Anion, Attractive Change, Unfavorable Positive Positive
	LYS	B:35	Conventional Hydrogen
	LYS	B:35	Conventional Hydrogen
	ASN	A:37	Conventional Hydrogen
	PRO	A:38	Pi-Alkyl
	ALA	A:39	Pi-Sigma, Alkyl
	ARG	A:42	Pi-Cation
Catechin	ARG	B:23	Conventional Hydrogen
	ALA	B:27	Unfavorable Donor Donor
	ASP	B:30	Pi-Anion
	ALA	A:27	Pi-Alkyl
	ASP	A:30	Conventional Hydrogen, Pi-Anion
	ASN	A:37	Conventional Hydrogen
	ALA	A:39	Pi-Sigma
	ARG	A:42	Conventional hydrogen, Pi-cation
	ALA	B:39	Alkyl, Pi-Alky
	ALA	C:27	Pi-Alkyl
Epigallocatechin gallate	ASN	B:37	Conventional Hydrogen
	ALA	B:39	Pi-Alkyl
	ARG	C:23	Conventional Hydrogen
	GLU	C:26	Conventional Hydrogen, Conventional Hydrogen
	ALA	C:27	Pi-Alkyl
	ASP	C:30	Pi-Anion, Conventional Hydrogen
	LYS	C:34	Pi-Alkyl
	ALA	B:39	Pi-Alkyl
	ARG	C:23	Conventional Hydrogen
	GLU	C:26	Conventional Hydrogen, Conventional Hydrogen

Table continues on next column.....

Green tea bioactive compounds	Amino acid residues	Bind-ing sites	Bond types
Gallicocatechin	ALA	C:27	Pi-Alkyl
	ASP	C:30	Pi-Anion, Pi-Alkyl
	PHE	C:31	Carbon Hydrogen
	LYS	C:34	Pi-Alkyl
	ASN	A:37	Conventional Hydrogen
	ASN	A:37	Conventional Hydrogen
	ALA	A:39	Pi-Sigma
	ARG	A:42	Pi-Cation
	ALA	B:27	Pi-Alkyl
	ASP	B:30	Pi-Anion
Theophylline	ASP	A:30	Attractive Change, Pi-Cation, Pi-Anion
	GLY	A:33	Conventional Hydrogen
	LYS	A:44	Conventional Hydrogen, Attractive Change
Acyclovir (Control)	ARG	A:42	Conventional Hydrogen, Carbon Hydrogen, Unfavorable Positive Positive, Pi-Cation
	ARG	B:23	Conventional Hydrogen
	GLU	B:26	Pi-Anion
	ASP	B:30	Pi-Cation, Attractive Change

Where; ALA, Alanine; ARG, Arginine; ASN, Asparagine; ASP, Aspartic acid; GLU, Glutamic acid; GLY, Glycine; LYS, Lysine; PHE, Phenylalanine; and PRO, Proline.

In contrast, caffeine and theophylline showed weaker and less favorable binding profiles. Caffeine, despite interacting with several residues (e.g., ARG42, LYS35, and ASP30), included multiple unfavorable interactions, particularly positive-positive repulsion between like-charged residues such as ARG42. These unfavorable interactions suggested poor binding stability. Theophylline displayed some electrostatic bonding (e.g., Pi-Cation and Attractive charge with ASP30 and LYS44), but overall was engaged in fewer interactions, consistent with its lower docking performance.

Acyclovir, used as the control, also bound to charged residues such as ARG42, GLU26, and ASP30. While it formed a mixture of conventional hydrogen bonds, Pi-Anion, and Pi-Cation interactions, it also included unfavorable positive-positive interactions with ARG42. This pattern suggested that although acyclovir was engaged in critical contacts, its binding stability was compromised by repulsive interactions, reflected in its relatively weak docking scores.

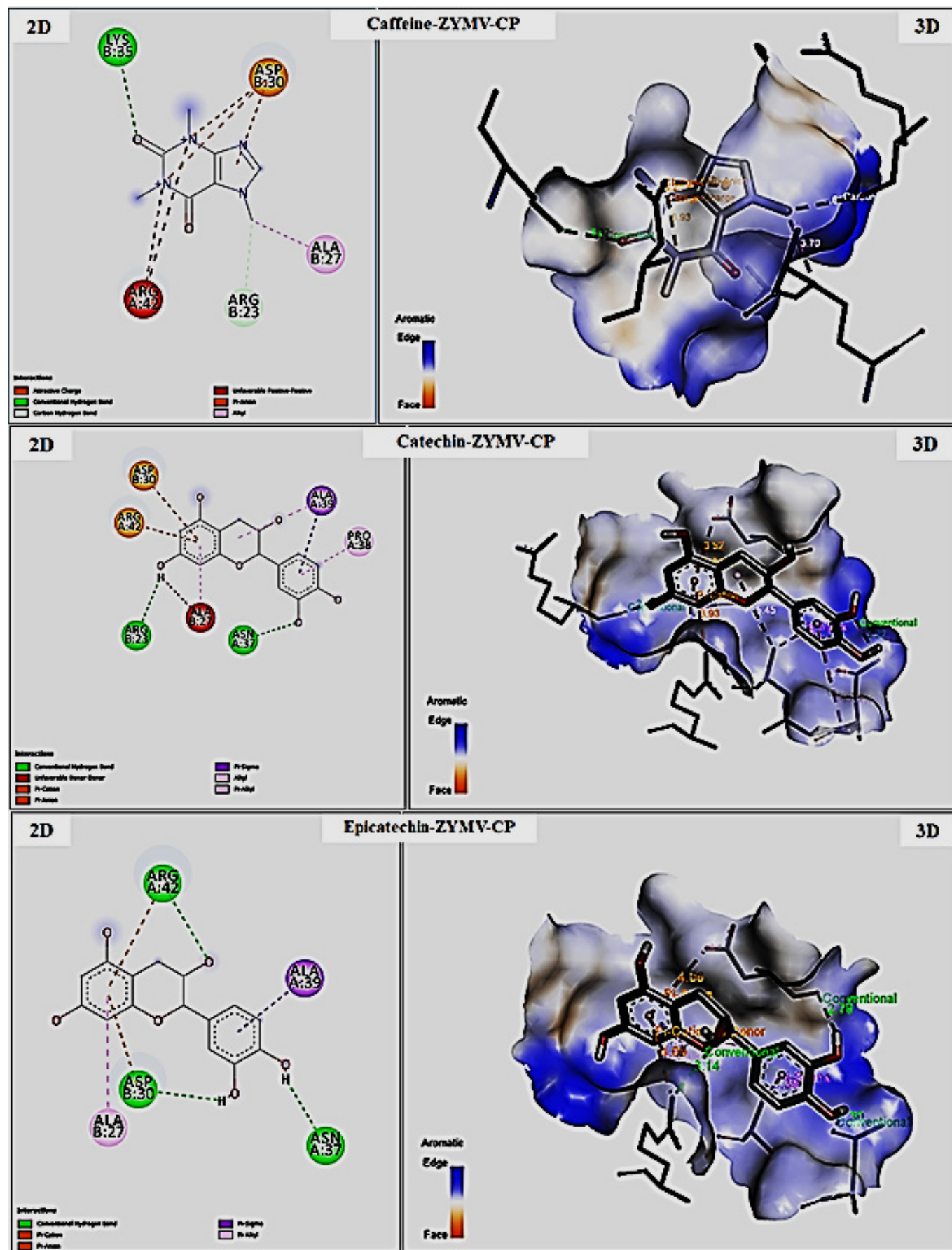


Figure 10: The docking visualization illustrates the interaction profiles of three phytochemicals—caffeine, catechin, and epicatechin—with the ZYMV-CP protein presented in both 2D and 3D formats. Polyphenolic compounds (catechin and epicatechin) show stronger and more stable interactions with ZYMV-CP compared to caffeine, suggesting that they may be more effective inhibitors of this viral protein.

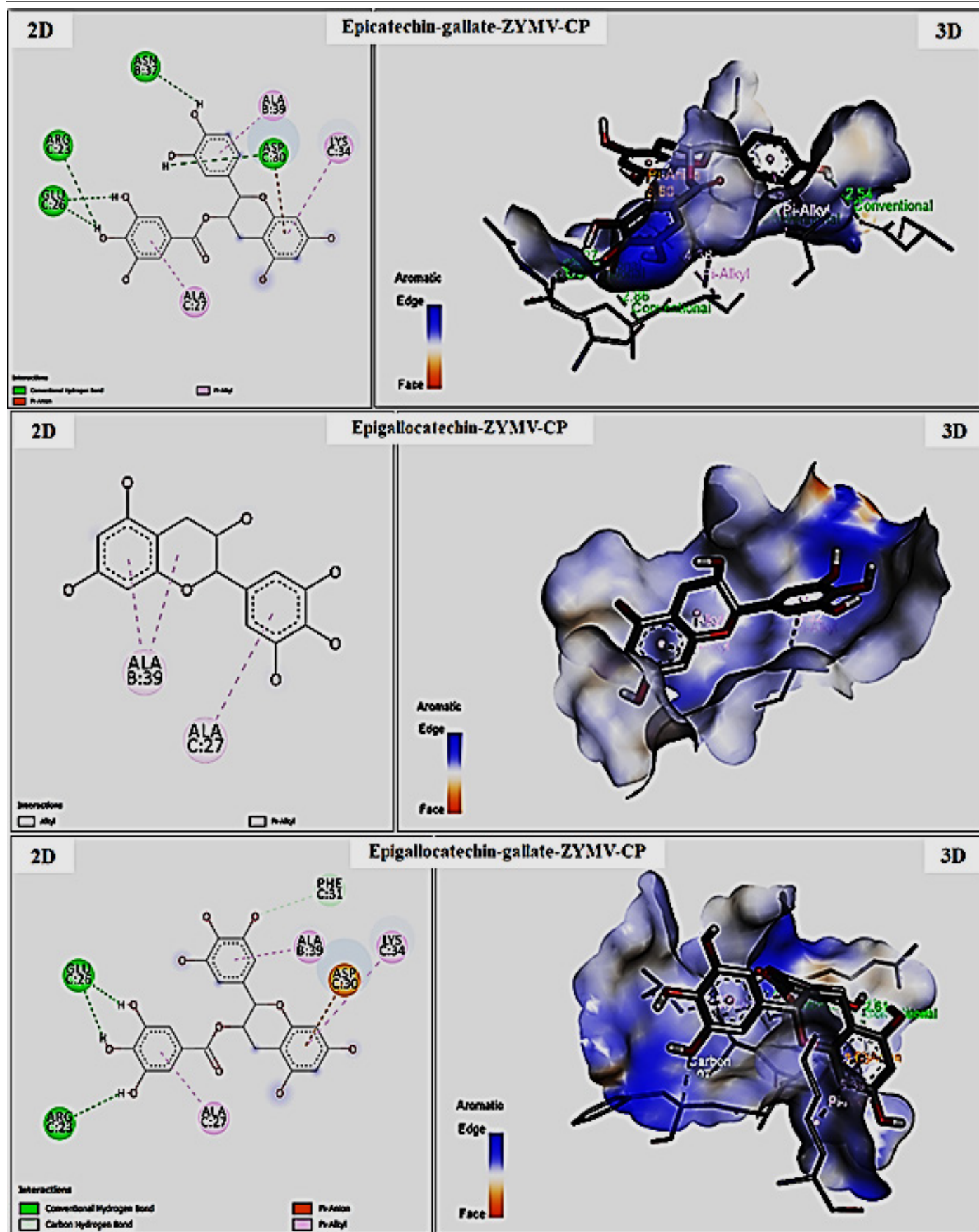


Figure 11: The docking visualization illustrates the interaction profiles of three phytochemicals- epicatechin-gallate, epigallocatechin, and epigallocatechin-gallate -with the ZYMV-CP protein presented in both 2D and 3D formats. Gallate derivatives (epicatechin-gallate and epigallocatechin-gallate) exhibit superior binding to ZYMV-CP compared to epigallocatechin alone. Epigallocatechin-gallate is likely the most potent inhibitor due to its extensive interactions and stable orientation in the active site.

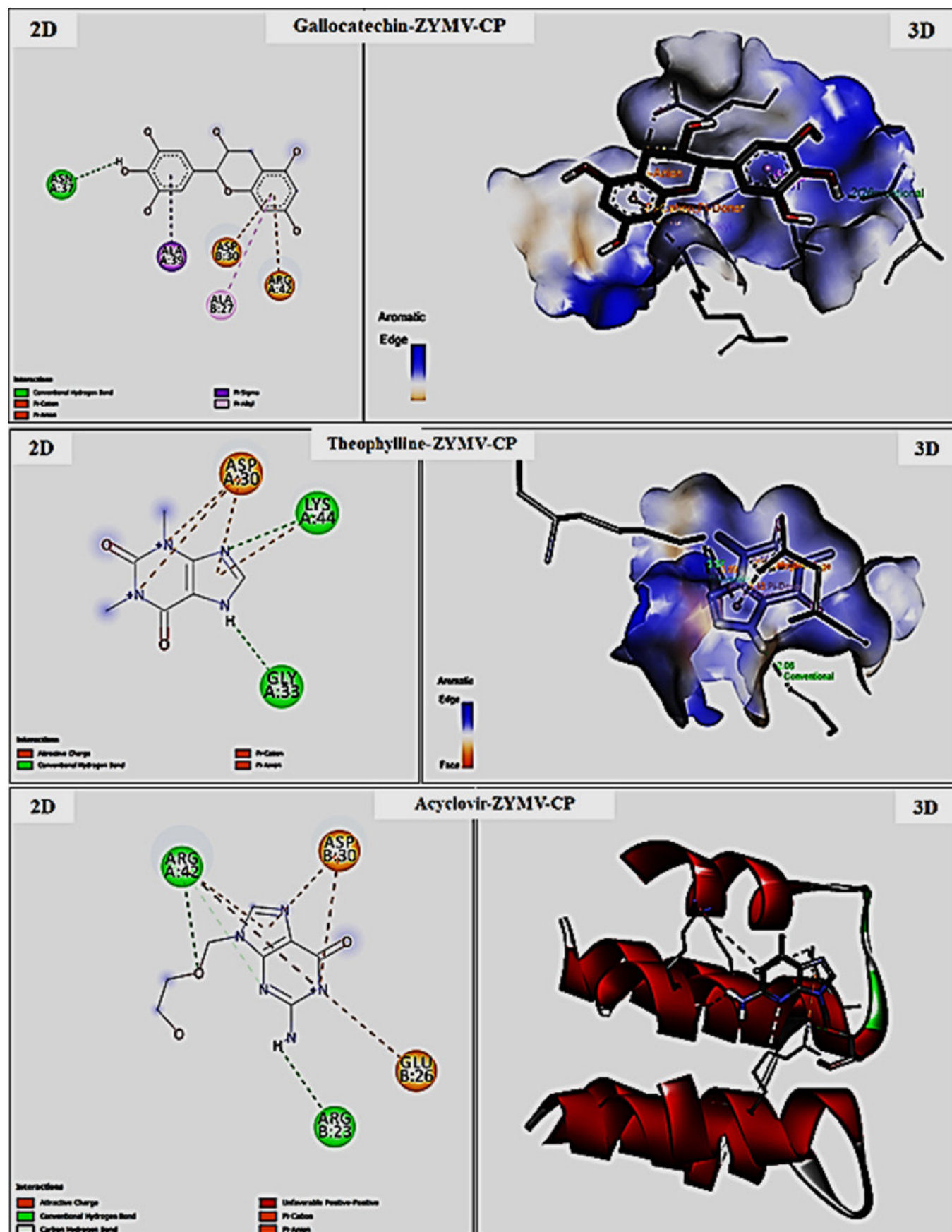


Figure 12: The docking visualization illustrates the interaction profiles of three phytochemicals– gallocatechin, theophylline, and acyclovir–with the ZYMV-CP protein presented in both 2D and 3D formats. Among these compounds, gallocatechin demonstrates the strongest interaction with ZYMV-CP, while theophylline and acyclovir show weaker binding. This supports the trend that polyphenolic compounds are more effective inhibitors than synthetic molecules like acyclovir for this viral protein.

Discussion

Zucchini yellow mosaic virus represents a remarkable threat to global cucurbit crops, particularly zucchini, cucumber, and melon, leading to considerable economic losses for farmers worldwide (Ahsan *et al.*, 2023; Moya-Ruiz *et al.*, 2023; Abdel Razek *et al.*, 2025a). This virus is primarily transmitted by aphids, which further complicates control measures (Moya-Ruiz *et al.*, 2023). Traditionally, aphid insecticides have been used to manage the spread of ZYMV, but these chemical treatments often have drawbacks, including environmental impact, resistance development, and non-target effects (Gisi and Leadbeater, 2010; Sternberg and Thomas, 2018). Given these limitations, there is an urgent need for alternative control strategies that are both effective and environmentally sustainable (Pretty and Pervez Bharucha, 2015; Thomas *et al.*, 2021). Recent advancements in molecular tools, particularly *In silico* molecular docking studies have provided a promising approach for identifying new bioactive compounds that can interfere with viral replication and transmission, offering a potential solution to managing ZYMV (Elbouzidi *et al.*, 2024).

The present *in silico* study demonstrated that green tea polyphenols, particularly epigallocatechin gallate (EGCG) and epicatechin gallate (ECG) exhibited strong binding potential against key ZYMV proteins, including P1, HC-Pro, CI, and CP. The presence of gallate moieties enhanced hydrogen bonding and van der Waals interactions, while their large polar surface areas improved complementarity with protein active sites, strengthening ligand–protein interactions. P1 and CI proteins showed consistently higher binding affinities, suggesting they were more susceptible to inhibition, whereas CP interactions were generally weaker.

These findings indicate that ECG and EGCG could effectively disrupt viral replication and movement, providing a natural antiviral strategy that reduces dependence on chemical pesticides as well as aphid control. This approach aligns with sustainable agricultural practices emphasizing plant health (Yang and Zhang, 2019; Abdulhassan *et al.*, 2022; Moya-Ruiz *et al.*, 2023). The obtained results are in agreement with previous reports of green tea polyphenols as potent antiviral agents (Xu *et al.*, 2017; Chojnacka *et al.*, 2021) and highlight their potential as eco-friendly

alternatives for crop protection against ZYMV.

This study highlights the potential of natural compounds derived from ecofriendly sources, such as green tea, as promising agents against viral diseases. In addition, molecular docking proved to be a valuable tool for the preliminary screening of bioactive compounds, supporting their potential integration into sustainable pest management strategies (El-Sayed, 2000; Mahmoud *et al.*, 2025). Further experimental validation and field trials are required to confirm their effectiveness under practical agricultural conditions. Overall, this *in silico* study suggests that green tea polyphenols, particularly ECG and EGCG, may represent promising lead compounds for the development of ecofriendly antiviral strategies against ZYMV. The significance of these findings lies in their potential application to sustainable plant disease management, addressing the persistent challenges posed by viral infections in cucurbit crops.

The strong interactions of ECG and EGCG with key ZYMV proteins suggest that these polyphenols may interfere with multiple stages of the viral life cycle, including viral replication, movement, and protein processing. Their superior binding affinities to functional viral proteins compared to acyclovir highlights the potential of natural compounds as multi-target antiviral agents in plant disease management, offering ecofriendly alternatives to conventional chemical treatments. This observation is important as it suggests that ECG and EGCG might inhibit viral replication through direct interaction with multiple critical viral proteins; a mechanism that has been previously observed for other plant viral inhibitors (Pardee *et al.*, 2004). The higher binding affinity of ECG and EGCG, especially in relation to P1 and CI proteins, may point to their ability to block the essential functions of these proteins in viral replication and movement, preventing the virus from spreading throughout the plant.

The HC-Pro protein; a multifunctional protein involved in the suppression of host RNA silencing and viral movement (Choi *et al.*, 2025) represented another key target in this study. ECG and EGCG demonstrated extensive and diverse interactions with key residues in HC-Pro, including Pi-Anion, Pi-Alkyl, and hydrogen bonds, particularly with residues such as MET381, ILE439, and GLN447. The diversity of interactions observed in these compounds

suggests that they can form stable complexes with HC-Pro, potentially disrupting its function in RNA silencing suppression and viral spread within plant tissues. This type of interaction is consistent with the broader role of polyphenolic compounds in inhibiting viral movement by interfering with essential viral proteins (Wu *et al.*, 2010).

Analysis of the CI protein, responsible for viral RNA replication, further supported the notion that ECG and EGCG are capable of disrupting critical viral processes. These polyphenols formed hydrogen bonds with THR205, ASN306, and ASN310 residues integral to the protein's ability to catalyze RNA replication. Their ability to form multiple stabilizing interactions, particularly through hydrogen and Pi-Sigma bonds, suggested a potential to inhibit polymerase function of the CI protein, essential for the viral replication cycle (Desbiez and Lecoq, 1997; Zhu *et al.*, 2022). Similar interactions with other viral proteins have been reported in several previous antiviral studies using flavonoid compounds, where the formation of multiple non-covalent bonds was a key for disrupting viral function (Zhou and Skolnick, 2013; Cheng *et al.*, 2020; Shahrajabian *et al.*, 2022; Abdel Razek *et al.*, 2025b). This further emphasizes the likelihood that ECG and EGCG could act as effective inhibitors of ZYMV replication.

Regarding the CP protein involved in the encapsidation of the viral genome and the formation of the viral particle, ECG and EGCG displayed strong binding affinities with key residues such as ASN37, GLU26, ASP30, and LYS34. The ability of these polyphenols to form complex interactions with both hydrophobic and charged residues suggested that they could prevent proper viral particle formation, reducing the ability of the virus to infect new host cells (Wu *et al.*, 2010). This finding aligns with similar studies, where polyphenolic compounds like ECG and EGCG inhibited the assembly of viral particles in other plant viruses (Xu *et al.*, 2017; Shahid *et al.*, 2022). This reinforces the idea that polyphenols can serve as effective inhibitors not only of viral replication but also of viral assembly, providing a multi-target mechanism for viral inhibition.

Caffeine and theophylline, despite being structurally similar to ECG and EGCG, demonstrated appreciably weaker binding interactions, in consistence with the simplicity of their structures and

their limited functional groups. The fewer and weaker interactions formed with ZYMV proteins further support the superior antiviral potential of the more complex catechin derivatives. This is an important consideration when designing antiviral strategies, as the structural complexity and diversity of the binding interactions directly correlate with the potency of the compound in blocking viral functions (Mahapatra *et al.*, 2024).

Compared to acyclovir; a synthetic antiviral agent known for its efficacy in treating human herpes viral infections (Klysik *et al.*, 2020), green tea polyphenols particularly ECG and EGCG displayed a broader and more diverse range of interactions with ZYMV proteins. Acyclovir's relatively weak binding affinity to the tested viral proteins further supports the hypothesis that plant-derived polyphenols may offer a more effective and sustainable solution for managing viral diseases. The lesser diversity of interactions observed with acyclovir likely limits its effectiveness in inhibiting the various functional roles of ZYMV proteins, confirming its comparatively lower docking scores.

Given these findings, ECG and EGCG, due to their high binding potential and diverse interaction profiles with viral proteins hold considerable promise as natural antiviral agents for the control of ZYMV. The use of these polyphenols in agriculture could present an ecofriendly and sustainable alternative to synthetic chemical treatments, which are often associated with environmental risks and resistance issues. Their ability to target multiple stages of the viral life cycle, including replication, movement, and assembly adds a layer of complexity to their antiviral mechanism, making them an attractive option for further development in plant virology.

However, despite the promising *In silico* results, it is crucial to perform further *in vitro* and *in vivo* studies to confirm the biological activity of ECG and EGCG against ZYMV. Testing these compounds under actual field conditions will help evaluate their stability, efficacy, and potential application as protective agents for cucurbit crops. Additionally, understanding the pharmacokinetics (Daina *et al.*, 2017) and toxicity profiles of these compounds will be essential for determining their practical feasibility as agricultural treatments. Further research could also explore the potential synergistic effects of ECG and

EGCG when used in combination with other natural or synthetic antiviral agents.

Conclusions and Recommendations

Molecular docking analyses of green tea compounds against ZYMV proteins (P1, HC-Pro, CI, and CP) revealed that epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) exhibited superior binding affinities and more diverse, stabilizing interactions compared to acyclovir. These polyphenols formed multiple hydrogen bonds and Pi-based interactions with key residues, suggesting their strong inhibitory potential against viral replication and spread. In contrast, simpler compounds like caffeine, theophylline, and acyclovir showed weaker binding and fewer interactions, highlighting the structural advantage of polyphenol-rich compounds in targeting viral proteins. To further explore the antiviral potential of green tea polyphenols such as ECG and EGCG against ZYMV, it is recommended to conduct *in vitro* validation studies to confirm their efficacy. Subsequently, several planta trials should evaluate their real-world impact on infected plants. Additionally, ecofriendly formulations of these compounds should be developed for practical application, and further mechanistic studies have to investigate how they inhibit ZYMV proteins. It is also crucial to assess their environmental safety, potential toxicity, and explore their synergistic combinations with other agents. Expanding these investigations to other plant viruses could broaden their application, offering sustainable, plant-based alternatives to traditional chemical pesticides.

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Novelty Statement

This study represents the first *In silico* investigation of green tea polyphenols, particularly epicatechin gallate (ECG) and epigallocatechin gallate (EGCG) as potential antiviral agents targeting key ZYMV proteins. The current work demonstrates the ability of these natural compounds to form strong molecular interactions with viral proteins, highlighting their

potential as ecofriendly alternatives for viral disease management in cucurbit crops.

Authors' Contribution

FSA: Conceptualization, methodology, molecular docking experiments, and data analysis.
SSAE: Literature review, data curation, and manuscript drafting.
SDI: Supervision, validation of docking procedures, and critical review of the manuscript.
ASS: Software setup, molecular modeling, and visualization of docking results.
NE: Interpretation of results and editing of the manuscript.
AM: Conceptualization, project administration, supervision, and final manuscript approval.
All authors have read and approved the final manuscript.

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Ethical approval

This study did not involve human participants or animals; therefore, ethical approval was not required. All research activities were conducted in accordance with institutional and international guidelines for laboratory safety and good scientific practice.

Generative AI and AI-assisted technology statement

AI tools were used only for language editing. All scientific content and conclusions are the authors' responsibility.

Conflict of interests

The authors have declared no conflicts of interest.

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