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THEORETICAL ANALYSIS OF THE ELECTRONIC PROPERTIES AND REACTIVITY OF GLYPHOSATE AND ITS DERIVATIVES USING DFT

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ABSTRACT

This study examines the electronic properties of glyphosate, several structural analogues, and three glycosylated derivatives using density functional theory (DFT). Molecular geometries were optimized at the CAM-B3LYP/6-31G level. The resulting structures were analyzed using frontier molecular orbitals (HOMO and LUMO), global reactivity descriptors, and Fukui indices to compare how structural modifications affect electron distribution and reactive sites. For the non-glycosylated analogues, the reported HOMO–LUMO gaps range from 8.385 to 10.512 eV. For the glycosylated derivatives, they range from 4.716 to 8.824 eV, with M329 showing the smallest gap. These differences indicate variation in the calculated electronic properties across the series. Frontier-orbital distributions and local indices also suggest that substitution can alter the location and relative contribution of regions potentially involved in chemical interactions. The results therefore provide a theoretical comparison of the effects associated with substitution and glycosylation of glyphosate. They offer a basis for examining relationships between molecular structure and electronic response, but do not, on their own, establish affinity for EPSPS, herbicidal efficacy, or biological selectivity. The Fukui indices and thermochemical quantities should be interpreted in light of the computational conventions, protonation states, and reference reactions actually used. Further work, including solvent effects and experimental validation, is needed to determine the scope of these theoretical trends.

Keywords: Glyphosate; DFT; Fukui Indices; Frontier Orbitals; Molecular Reactivity

1 INTRODUCTION

Weed management remains a major challenge in crop production. Weeds can reduce yields by competing with crops for available resources [1, 2]. Herbicides remain widely used to manage weeds [3, 4], and glyphosate is among the most important. Studying its molecular properties can help characterize its chemical interactions and those of its analogues. Glyphosate, or N-(phosphonomethyl)glycine, primarily inhibits 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), an enzyme in the shikimate pathway involved in aromatic amino acid biosynthesis in plants, fungi, and many bacteria [5, 6]. Structural and biochemical studies indicate that glyphosate binds to the enzyme–substrate complex and occupies a site associated with phosphoenolpyruvate [6, 7]. Its phosphonate, amine, and carboxylate groups contribute to its acid–base properties. Its ionic forms vary with pH, which can affect its electron distribution and interactions [8]. Previous work has examined EPSPS inhibition and the relationship between glyphosate structure and activity. Some structural changes can reduce enzyme inhibition, underscoring the role of molecular structure in target recognition [7, 9, 10]. More recently, glyphosate glycosylation has been reported in rice as a transformation pathway associated with tolerance in some plants [11]. These findings motivate a comparative study of the electronic properties of glyphosate and its glycosylated derivatives.

Density functional theory (DFT), developed through the work of Hohenberg, Kohn, and Sham, is widely used to study molecular electronic structure [12, 13]. Reviews and textbooks describe its application across chemistry and related fields [14, 15]. Conceptual DFT extends this approach with global descriptors that characterize tendencies to donate or accept electron density [16–18]. Related descriptors, including those used in HSAB theory and electrophilicity analysis, provide additional ways to compare electronic behavior [19, 20]. Fukui indices describe the electronic response of individual atomic sites [21]. Used together, these tools allow calculated trends to be compared across related molecules. They nevertheless require cautious interpretation. A HOMO–LUMO gap or Fukui index is not a direct measure of herbicidal activity, reaction rate, or affinity for EPSPS. Results may also depend on protonation state, solvent, and the conventions used to calculate local indices. Calculated electronic trends must therefore be distinguished from biological properties, which require experimental validation.

Despite progress in understanding glyphosate's mode of action, its analogues, and its glycosylation, comparing their global and local electronic properties within a common theoretical framework remains useful. Joint analysis of frontier orbitals, global descriptors, and Fukui indices can show how structural modifications affect electron distribution and the relative ranking of reactive sites. This approach also enables comparison of glyphosate with substituted analogues, analogues modified by heteroatom replacement, and glycosylated derivatives

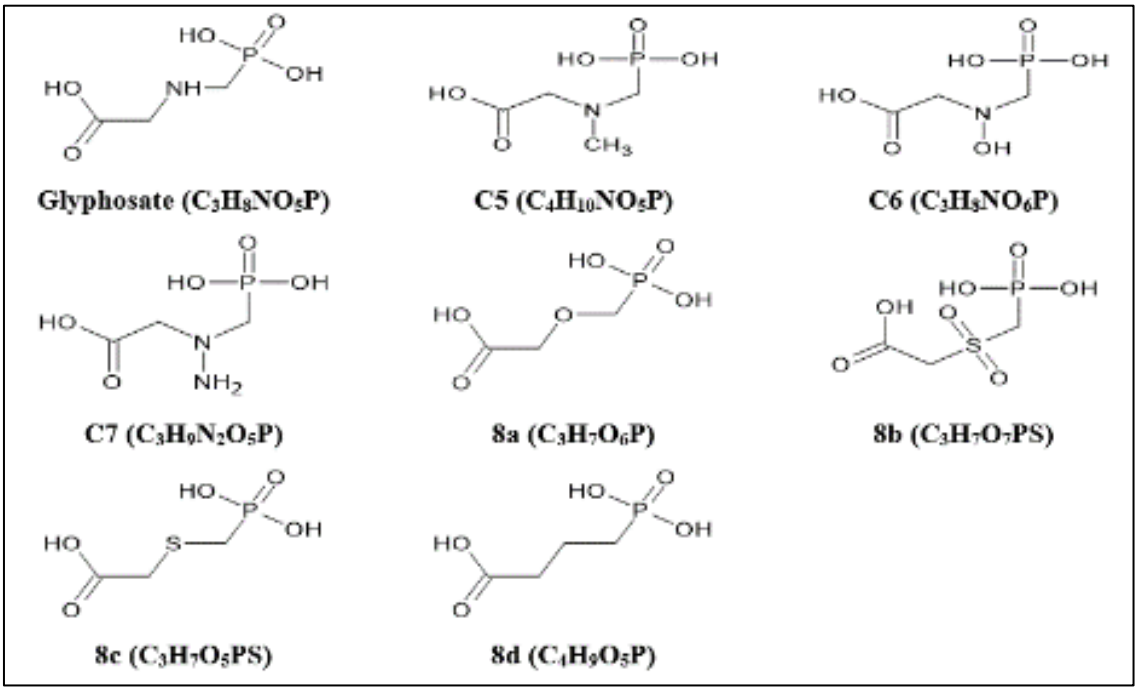


Figure 1: Structures of glyphosate and its analogues.

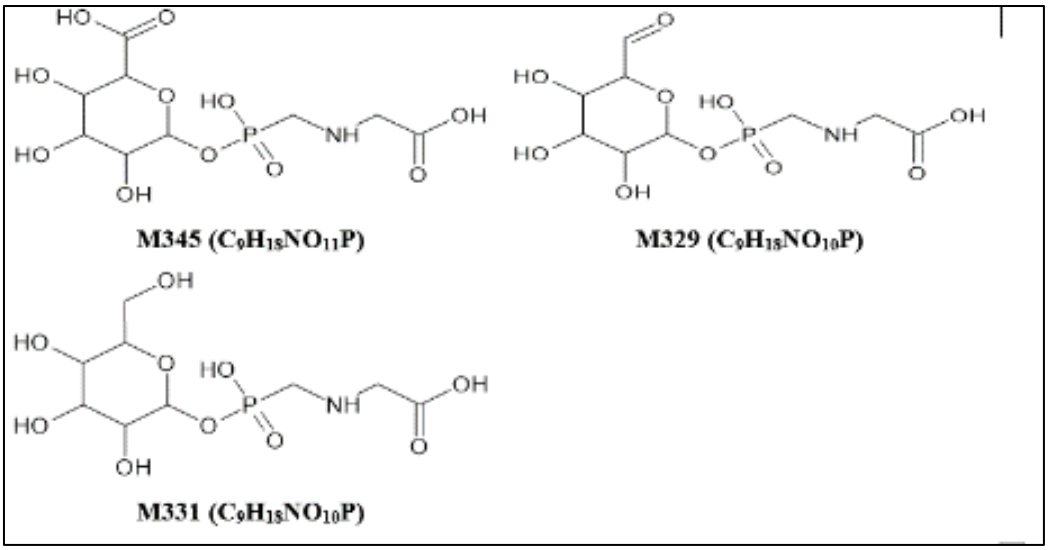


Figure 2: Structures of the glycosylated derivatives of glyphosate.

Here, DFT is applied to glyphosate, several structural analogues, and three glycosylated derivatives at the CAM-B3LYP/6-31G level. Following geometry optimization, we examine the HOMO and LUMO, global reactivity descriptors, Fukui indices, and calculated thermochemical properties. Molecular electrostatic potential maps are also used to visualize regions of positive and negative potential.

The overall aim is to compare the electronic properties of glyphosate and its derivatives and to assess trends associated with the structural modifications considered. The contribution of this work lies in comparing structural analogues and glycosylated derivatives within a shared theoretical framework using global and local descriptors. The conclusions concern calculated trends and do not replace direct investigation of interactions with EPSPS or experimental validation.

2 MATERIALS AND METHODS

2.1 Quantum-chemical approach

Quantum chemistry describes molecular structures and properties using the principles of quantum mechanics. In this study, DFT is used to compare the species through their electron densities and molecular orbitals [12, 15].

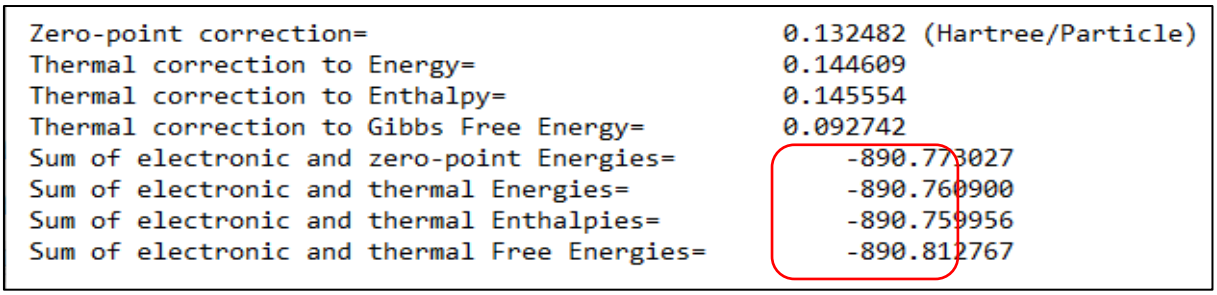
DFT describes the ground state of an electronic system in terms of its electron density. In the Kohn–Sham formulation, the system is represented by independent particles moving in an effective potential; exchange and correlation effects are incorporated through an approximate functional [12, 15]. Results depend, among other factors, on the choice of functional and orbital basis set.

2.2 Computational methods and level of theory

The molecular geometries were fully optimised at the CAM-B3LYP/6-31G theoretical level [22], using the Gaussian 09 software [23]. The initial molecular structures were constructed and visualised using GaussView 5.0.8 [23]. Vibrational frequency calculations were then carried out at the same theoretical level (CAM-B3LYP/6-31G) to verify the nature of the stationary points and to confirm that the optimised structures correspond to energy minima. The 6-31G basis set is a separated valence basis set without polarisation or diffuse functions. The charges, multiplicities, convergence criteria and calculation parameters for the ionised species must be reported to ensure reproducibility. The 6-31G basis set separates the valence functions into two sets (3 and 1 primitive functions) and uses six primitive functions for the core orbitals. It contains neither polarisation functions nor diffuse functions; its suitability for ionised species must therefore be justified, particularly for anions.

2.3 Determination of molecular thermodynamic quantities

Harmonic frequencies and thermochemical contributions were extracted from the Gaussian output at 298 K. Values should be clearly associated with the relevant species, units, and computational conditions. A quantity calculated for an isolated molecule does not, by itself, represent an experimental standard enthalpy or Gibbs free energy of formation.



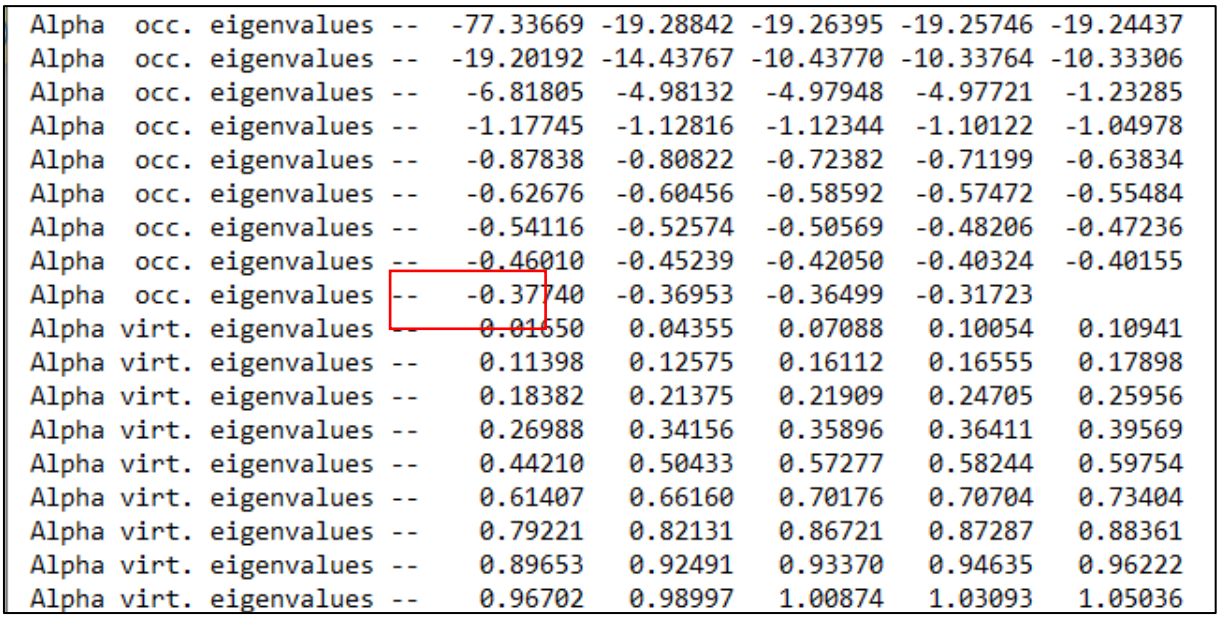
```
Zero-point correction=                          0.132482 (Hartree/Particle)
Thermal correction to Energy=                   0.144609
Thermal correction to Enthalpy=                 0.145554
Thermal correction to Gibbs Free Energy=        0.092742
Sum of electronic and zero-point Energies=           -890.773027
Sum of electronic and thermal Energies=              -890.760900
Sum of electronic and thermal Enthalpies=            -890.759956
Sum of electronic and thermal Free Energies=         -890.812767
```

Figure 3: Excerpt from a Gaussian output file following geometry optimization and frequency calculation.

For a defined reaction, enthalpy and Gibbs free-energy changes are calculated from the quantities for the products and reactants, weighted by their stoichiometric coefficients. The reaction equation and standard states must be specified before interpretation. Without a balanced reference reaction, the reported values are discussed as calculated properties of the species considered.

$$\Delta r\Phi 0(298K) = \sum_{Produits} \Delta_f\, \Phi^0\,(298K) - \sum_{Réactifs} \Delta_f\, \Phi^0(298K) \quad (1)$$

The frontier molecular orbitals, HOMO and LUMO, were identified from the Gaussian output. Their energies were then used to calculate the reactivity descriptors presented in the following sections.



```
 Alpha  occ. eigenvalues --  -77.33669 -19.28842 -19.26395 -19.25746 -19.24437
 Alpha  occ. eigenvalues --  -19.20192 -14.43767 -10.43770 -10.33764 -10.33306
 Alpha  occ. eigenvalues --   -6.81805  -4.98132  -4.97948  -4.97721  -1.23285
 Alpha  occ. eigenvalues --   -1.17745  -1.12816  -1.12344  -1.10122  -1.04978
 Alpha  occ. eigenvalues --   -0.87838  -0.80822  -0.72382  -0.71199  -0.63834
 Alpha  occ. eigenvalues --   -0.62676  -0.60456  -0.58592  -0.57472  -0.55484
 Alpha  occ. eigenvalues --   -0.54116  -0.52574  -0.50569  -0.48206  -0.47236
 Alpha  occ. eigenvalues --   -0.46010  -0.45239  -0.42050  -0.40324  -0.40155
 Alpha  occ. eigenvalues --   -0.37740  -0.36953  -0.36499  -0.31723
 Alpha virt. eigenvalues --   -0.01650   0.04355   0.07088   0.10054   0.10941
 Alpha virt. eigenvalues --    0.11398   0.12575   0.16112   0.16555   0.17898
 Alpha virt. eigenvalues --    0.18382   0.21375   0.21909   0.24705   0.25956
 Alpha virt. eigenvalues --    0.26988   0.34156   0.35896   0.36411   0.39569
 Alpha virt. eigenvalues --    0.44210   0.50433   0.57277   0.58244   0.59754
 Alpha virt. eigenvalues --    0.61407   0.66160   0.70176   0.70704   0.73404
 Alpha virt. eigenvalues --    0.79221   0.82131   0.86721   0.87287   0.88361
 Alpha virt. eigenvalues --    0.89653   0.92491   0.93370   0.94635   0.96222
 Alpha virt. eigenvalues --    0.96702   0.98997   1.00874   1.03093   1.05036
```

Figure 4: Excerpt from a Gaussian output file used for molecular-orbital analysis.

The HOMO and LUMO energies were used to estimate the ionization energy, electron affinity, electronegativity, chemical potential, hardness, softness, and electrophilicity according to the relationships given below.

2.4 Reactivity indices

2.4.1 Global reactivity descriptors

Conceptual DFT describes reactivity trends using global descriptors, including chemical potential, electronegativity, hardness, softness, and electrophilicity [17–19]. The equations and conventions must be applied consistently, particularly when defining hardness and using HOMO and LUMO energies [20].

$$\mu = \left(\frac{\partial E}{\partial N}\right)_{V(r)} = -\chi \qquad (2)$$

The finite-difference approximation can be used to estimate chemical potential and electronegativity from the energies of neutral, anionic, and cationic species. The sign conventions and equations adopted are specified in the expressions below.

$$\boldsymbol{\mu = -\frac{PI + AE}{2} = -\chi} \quad (3)$$

Chemical hardness describes the change in chemical potential with electron number; softness is defined in relation to its inverse [18]. The numerical expressions used in the analysis should be consistent with these definitions.

$$\boldsymbol{\eta = \left(\frac{\partial \mu}{\partial N}\right)_{V(r)} = \left(\frac{\partial^2 E}{\partial N^2}\right)_{V(r)} = \frac{1}{\sigma}} \quad (4)$$

In the finite-difference approximation, hardness and softness are expressed in terms of ionization potential and electron affinity. These descriptors are also used in hard and soft acids and bases (HSAB) theory to interpret some acid–base trends qualitatively [19].

$$\boldsymbol{\eta = \frac{1}{\sigma} = (PI - AE)} \quad (5)$$

The electrophilicity index, ω, is a global descriptor of a species' capacity to accept electron density [20]. It is calculated using the expression shown below.

$$\boldsymbol{\omega = \frac{\mu^2}{2\eta} = \frac{\chi^2}{2\eta}} \quad (6)$$

The energy associated with electron transfer is estimated using the following relationship:

$$\boldsymbol{\Delta E_T = -\frac{\eta}{4}} \quad (7)$$

Under Koopmans' approximation, the HOMO and LUMO energies are used to estimate ionization and electron acceptance, respectively [17]. These estimates provide comparative indicators and do not replace experimental measurements.

- $AE = -E_{BV}$ The lowest unoccupied molecular orbital (LUMO) characterizes a molecule's susceptibility to electrophilic attack.
- $PI = -E_{HO}$ The highest occupied molecular orbital (HOMO) characterizes a molecule's susceptibility to nucleophilic attack.

The hard and soft acids and bases (HSAB) principle can be used to interpret certain preferences in chemical interactions and selectivity qualitatively [19].

2.4.2 Fukui indices and local reactivity

Condensed Fukui indices describe the local electronic response of a site when an electron is added or removed [21]. Their interpretation depends on the atomic quantity used (electron population or atomic charge) and the corresponding sign convention. The expressions below must therefore be checked for consistency with the NBO data analyzed.

- $\mathbf{f^+(k) = q(k, N+1) - q(k, N)}$ **(8):** Fukui index for nucleophilic attack (response to electron addition)
- $\mathbf{f^-(k) = q(k, N) - q(k, N-1)}$ **(9):** Fukui index for electrophilic attack (response to electron removal)
- $\mathbf{f^0(k) = [f^+(k) + f^-(k)] / 2}$ **(10):** Fukui index for radical attack

The quantities q(k,N), q(k,N+1), and q(k,N−1) denote the natural atomic charges on atom k in the neutral, anionic, and cationic systems, respectively. The index expressions must be adapted to these charges and checked against the electron populations used. Calculations for anionic and cationic species were performed at the CAM-B3LYP/6-31G level, as were those for the neutral molecule.

3 RESULTS AND DISCUSSION

3.1 Geometries of glyphosate and its analogues

The optimized geometries of AMPA (aminomethylphosphonic acid), glyphosate, and the analogues studied are shown in Figure 5. Based on the calculated frequencies, the selected structures correspond to local minima when no imaginary frequency is present.

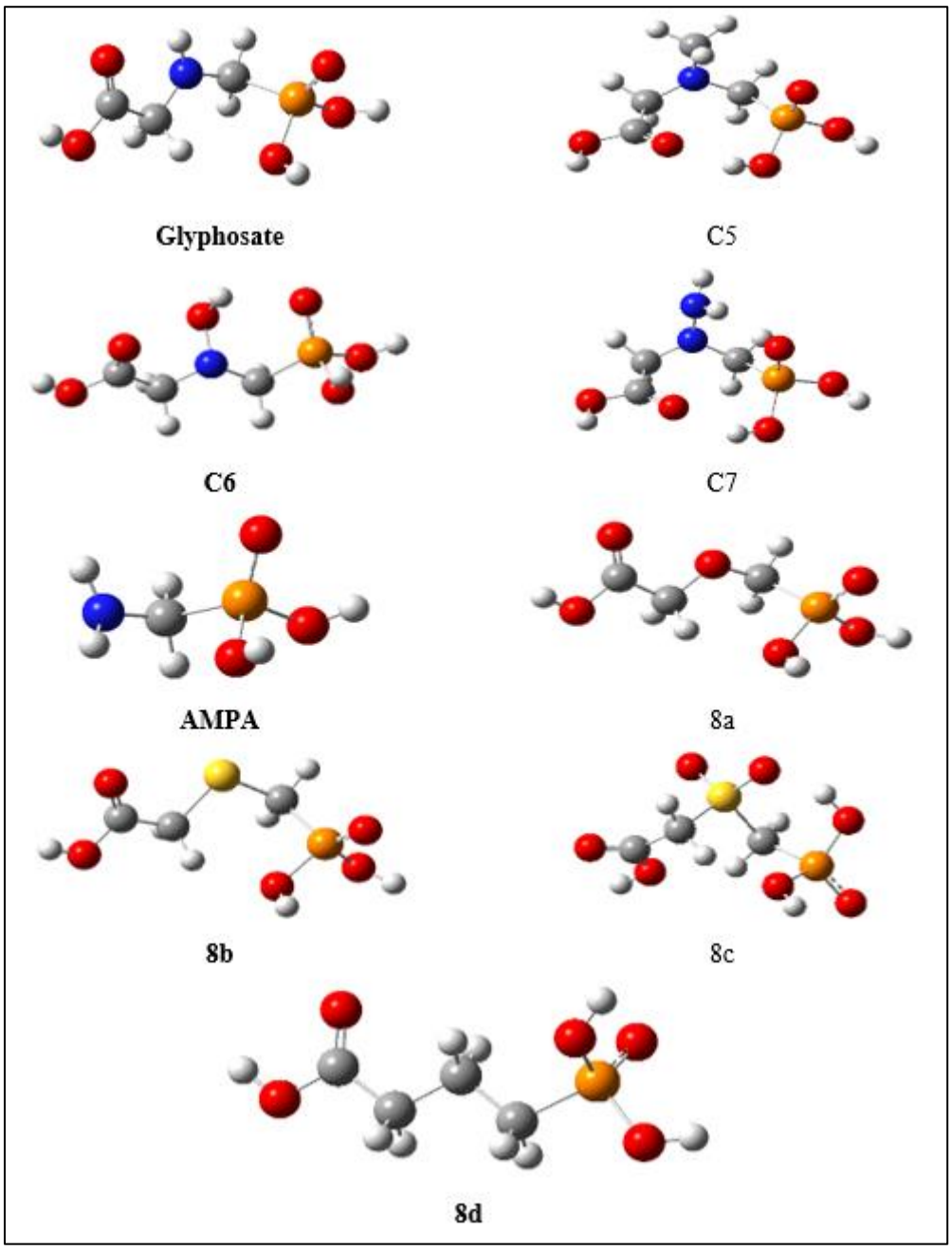


Figure 5: Optimized geometries of AMPA, glyphosate, and the analogues studied.

Analogues C5, C6, and C7 were generated by replacing the hydrogen attached to the glyphosate nitrogen with a methyl, hydroxyl, and amino group, respectively. Compounds 8a–8d correspond to the nitrogen substitutions described in the experimental section. The calculated geometries show conformational differences among these structures. Attributing these differences to steric hindrance or other effects should be done cautiously in the absence of a detailed conformational energy analysis.

3.2 Thermodynamic properties

The calculated thermochemical parameters are presented in Table 1. Their interpretation requires distinguishing properties of an isolated species from changes associated with a defined reaction. The values reported here do not, on their own, establish that formation of each molecule is spontaneous or exothermic; that conclusion requires a balanced reference reaction and explicitly defined standard states. The thermochemical table also requires a unit and reference-state check: the header reports atomic units for enthalpy and Gibbs energy and calorie-based units for entropy, but the manuscript should confirm that these are the intended quantities and that all species are treated consistently.

Table 1: Standard thermodynamic quantities of formation for glyphosate and its analogues

Compounds	$\Delta_f H°$(ua)	$\Delta_f G°$(ua)	$\Delta_f S°$(cal.mol^{-1}.K^{-1})
Glyphosate	-890.760	-890.813	111.150
C5	-930.005	-930.060	115.876
C6	-965.870	-965.925	115.195
C7	-946.023	-946.077	111.813
AMPA	-663.102	-663.144	87.417
8a	-910.613	-910.666	111.138
8b	-1233.619	-1233.673	113.460
8c	-1383.778	-1383.833	116.270

Thermochemical quantities describe different properties: enthalpy reflects the energy balance of a defined transformation, whereas Gibbs free energy can be used to assess spontaneity under specified conditions. Absolute values for isolated species should therefore not be interpreted as reaction enthalpies or free energies unless the formation reaction and thermodynamic reference states are specified.

$$\Delta fS°(\text{glyphosate}) < \Delta fS°(C7) < \Delta fS°(C6) < \Delta fS°(C5)$$

AMPA is a known transformation product of glyphosate. However, thermochemical values for isolated molecules are insufficient to establish the mechanism or spontaneity of this transformation; a balanced reaction and reference conditions are required.

3.3 Global chemical reactivity

Frontier orbitals help interpret electron-transfer tendencies qualitatively. Figure 6 compares their distributions across the molecules studied. In glyphosate, the HOMO is mainly distributed over the molecule outside the carboxyl group, whereas the LUMO has a substantial contribution from that group. Analogues C5 and C7 show distributions similar to glyphosate, while C6 has a different distribution. These maps describe orbitals of isolated molecules and do not, on their own, demonstrate actual charge transfer in a reaction medium.

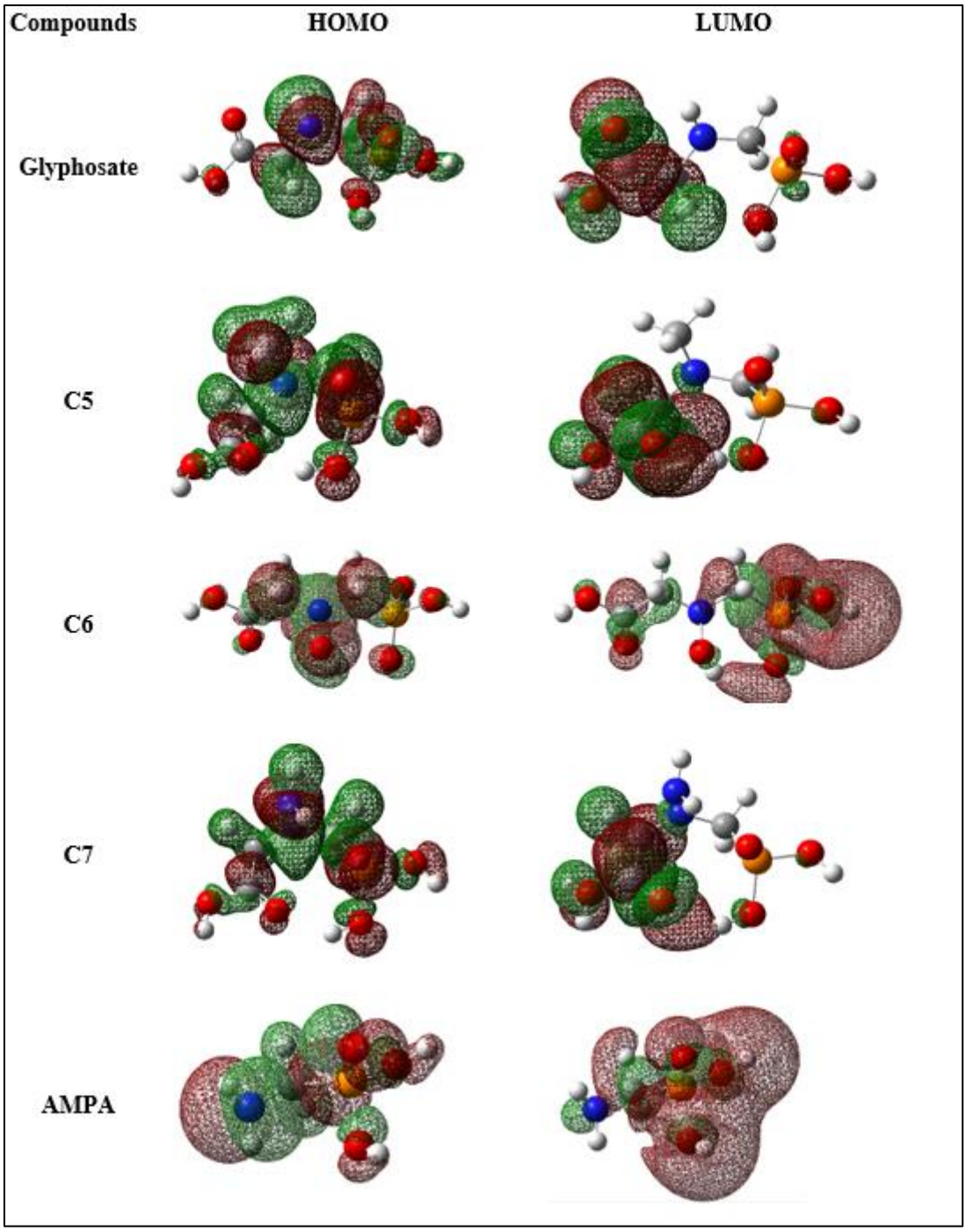


Figure 6: Comparison of the isodensity surfaces of glyphosate and its analogues.

Table 2: Global reactivity descriptors (eV) for glyphosate and its analogues

Compounds	HOMO	LUMO	ΔE	μ	η	ω
Glyphosate	-8.632	0.449	9.081	-4.0915	9.081	0.922
C5	-8.248	0.472	8.720	-3.888	**8.720**	0.867
C6	-8.547	0.742	9.289	-3.9025	9.289	0.820
C7	-8.271	0.981	9.252	**-3.645**	9.252	0.718
8a	-9.588	0.292	9.880	-4.648	9.880	**1.093**
8b	-7.847	0.538	**8.385**	**-3.655**	**8.385**	0.796
8c	-9.551	-0.080	9.471	-4.816	9.471	**1.224**

8d	-9.671	0.841	10.512	-4.415	10.512	0.927
AMPA	-8.184	1.307	9.491	-3.439	9.491	0.623

The frontier-orbital energies and associated descriptors are listed in Table 2. Nitrogen substitution changes the HOMO and LUMO energies as well as the energy gap. Among the analogues considered, 8b has the smallest reported gap (8.385 eV). This value enables comparison at the chosen level of theory but is not a direct experimental measure of reaction rate.

The global descriptors suggest differences in the calculated tendencies of the molecules to donate or accept electron density. Compounds C7 and 8b have the least negative chemical potentials in the table, while 8b has the smallest HOMO–LUMO gap among the non-glycosylated analogues. These trends depend on the computational method and the conventions used for hardness and electrophilicity. They do not, by themselves, establish experimental reactivity or herbicidal activity. In Table 2, the reported hardness (η) values are numerically identical to the HOMO–LUMO gaps (ΔE); because hardness is commonly defined as half the gap under the stated frontier-orbital approximation, these entries and any dependent descriptors should be checked against the equations and original calculation outputs before submission.

3.4 Local reactivity

Local reactivity was assessed using the Fukui indices in Table 3 and the molecular electrostatic potential maps in Figure 7. Substitution can alter the calculated electronic responses and the relative ranking of sites. These assignments are interpreted according to the sign convention and atomic populations actually used.

Table 3: Fukui indices for glyphosate and its analogues

Atoms	**q(N)**	**q(N+1)**	**q(N-1)**	**f-**	**f+**
Glyphosate					
C7	-0.589	-0.583	-0.653	0.064	0.006
C12	-0.389	-0.371	-0.441	0.052	0.019
C5 (N-methylglyphosate)					
C11	-0.376	-0.344	-0.421	0.045	0.032
C6 (N-hydrox glyphosate)					
C7	-0.632	-0.637	-0.675	0.043	-0.005
C11	-0.394	-0.377	-0.433	0.039	0.016
C7 (N-aminoglyphosate)					
C11	-0.375	-0.342	-0.413	0.038	0.033
8a (O-glyphosate)					
C10	-0.246	-0.233	-0.268	0.022	0.013
8b (glyphosate sulfate)					
C7	-1.005	-1.005	-1.042	0.037	0.000
C10	-0.713	-0.695	-0.730	0.017	0.018
8c (carba-glyphosate)					
O5	-1.026	-1.011	-1.000	-0.026	0.015
S17	1.763	1.663	1.712	0.051	-0.101
AMPA (aminomethylphosphonic acid)					
C7	-0.605	-0.618	-0.644	0.038	-0.013

Figure 7 shows the molecular electrostatic potential. Colors represent potential values according to the selected scale and do not directly indicate electron density. Regions of negative potential are generally more favorable for interactions with electrophilic species, whereas regions of positive potential may favor interactions with nucleophilic species. The legend should specify the scale and color scheme.

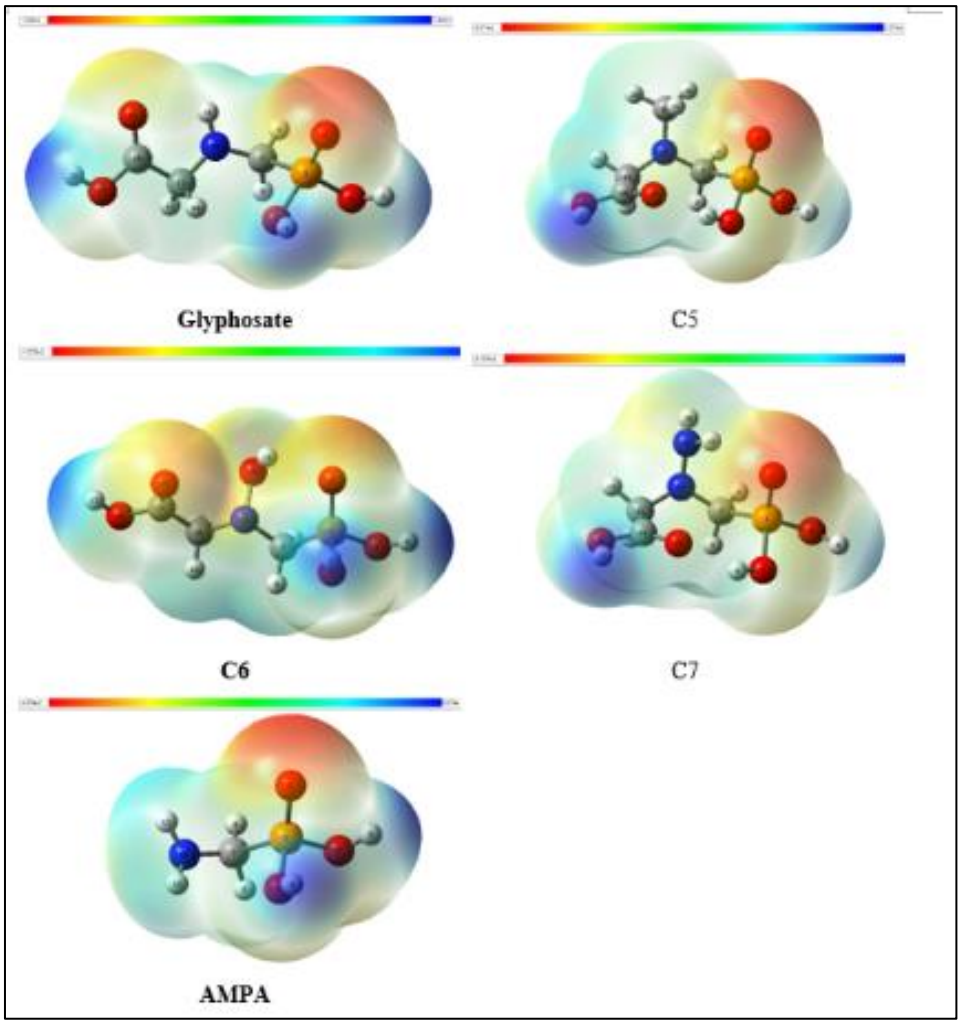


Figure 7: Molecular electrostatic potential map of glyphosate and its derivatives.

3.5 Effect of glycosylation

3.5.1 Geometric analysis

Glycosylation is the attachment of a carbohydrate residue to a molecule. Experimental studies have described this transformation of glyphosate in rice and its association with herbicide tolerance [11]. In the present work, M345, M329, and M331 are examined as molecular structures; the calculations alone do not demonstrate their biological formation or their effect on plant tolerance. The geometries optimized at the CAM-B3LYP/6-31G level are shown in Figure 8.

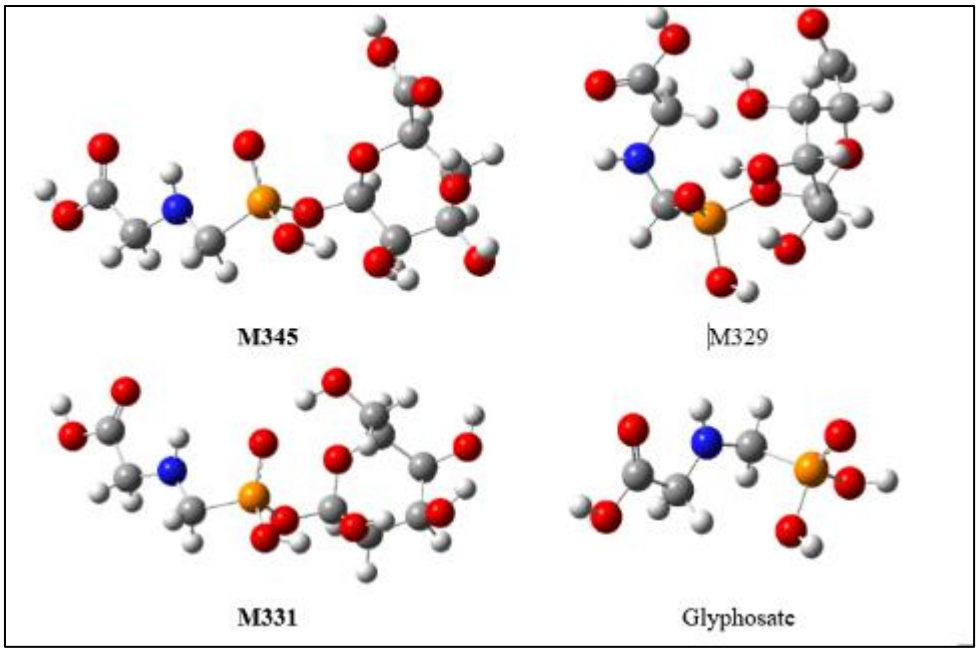


Figure 8: Optimized geometries of glyphosate and its glycosylated derivatives.

The optimized structures of M345 and M331 are nearly planar, whereas M329 is non-planar (Figure 8). The thermochemical quantities in Table 4 describe the calculated species. They do not establish that glycosylation is spontaneous without a balanced reference reaction and clearly defined standard states.

Table 4: Standard thermodynamic quantities of formation for glyphosate and its analogues

Compounds	$\Delta_f H°$(ua)	$\Delta_f G°$(ua)	$\Delta_f S°$(cal.mol^{-1}.K^{-1})
Glyphosate	-890.760	-890.813	111.150
M345	-1574.872	-1574.950	164.590
M329	-1499.697	-1499.768	150.140
M331	-1500.876	-1500.951	157.738

3.5.2 Chemical reactivity

Figure 9 compares the frontier orbitals of glyphosate and its glycosylated derivatives. In the calculated structures, the HOMO remains mainly localized on the glyphosate moiety. The LUMO distribution varies: it is located on the carbohydrate residue in M345 and M329, whereas M331 shows a larger contribution from the carboxyl group. M329 has the smallest HOMO–LUMO gap in this series (4.716 eV). This difference describes a calculated electronic variation but does not establish greater chemical or biological activity.

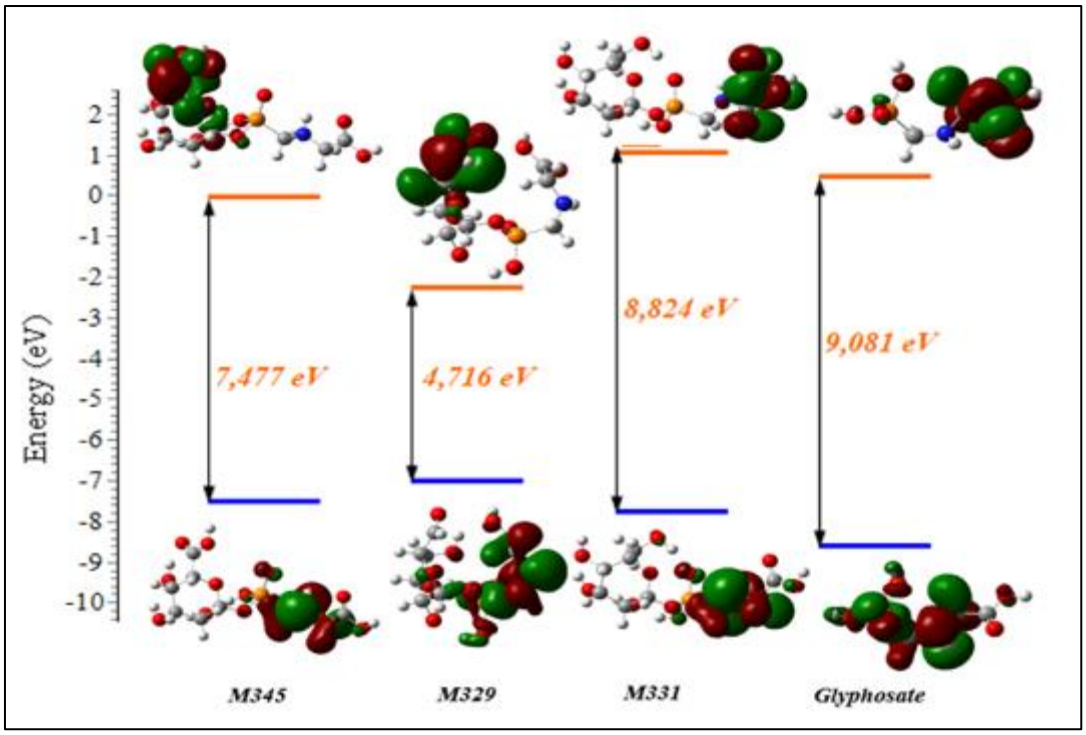


Figure 9: Energy-level diagram of the frontier orbitals of the glycosylated derivatives.

The global descriptors in Table 5 were calculated from the HOMO and LUMO energies using the relationships presented in the section on global reactivity.

Table 5: Global reactivity descriptors (eV) for the glycosylated derivatives of glyphosate

Compounds	HOMO	LUMO	ΔE	μ	η	ω
Glyphosate	-8.632	0.449	9.081	-4.092	9.081	0.922
M345	-7.542	-0.065	7.477	-3.804	7.477	0.967
M329	-7.024	-2.308	4.716	-4.666	4.716	2.308
M331	-7.807	1.017	8.824	-3.395	8.824	0.653

According to the descriptors in Table 5, M345 has the least negative chemical potential, whereas M329 has the smallest HOMO–LUMO gap and the highest electrophilicity value among the derivatives modeled. These descriptors do not directly measure reaction rate. Comparisons require the same definitions and conventions for every species.

Table 6: Fukui indices for the glycosylated derivatives of glyphosate

Atoms	q(N)	q(N+1)	q(N-1)	f^-	f^+
M345					
P_1	2.159	2.158	2.117	0.042	-0.001
O_{35}	-0.775	-0.772	-0.765	-0.010	0.003
M329					
P_1	2.114	2.266	2.257	-0.143	0.152
C_{30}	0.372	-0.117	0.251	0.121	-0.489
M331					
C_6	-0.613	-0.630	-0.679	0.066	-0.017
O_5	-0.818	-0.769	-0.810	-0.008	0.049

The local reactive sites of the glycosylated derivatives were also examined using the Fukui indices in Table 6. Their assignment must follow the sign convention and atomic populations used in the calculation.

The indices in Table 6 show differences in the relative ranking of sites across the three glycosylated derivatives. The reported nucleophilic and electrophilic assignments should be checked against the original atomic charges or populations because the sign of the indices depends on the computational convention. Subject to this qualification, the results suggest that modification of the phosphate group may redistribute local electronic responses and warrant a closer analysis of the sites involved.

ABBREVIATIONS

- AMPA, aminomethylphosphonic acid;
- DFT, density functional theory;
- EPSPS, 5-enolpyruvylshikimate-3-phosphate synthase;
- HOMO, highest occupied molecular orbital;
- LUMO, lowest unoccupied molecular orbital;
- MEP, molecular electrostatic potential;
- NBO, natural bond orbital.

4 CONCLUSION

This study set out to compare the electronic properties and reactive sites of glyphosate, several structural analogues, and three glycosylated derivatives. Molecular geometries were optimized using DFT at the CAM-B3LYP/6-31G level. The structures were then characterized using frontier orbitals, global descriptors, Fukui indices, electrostatic potential maps, and calculated thermochemical parameters. The results show that structural modifications are accompanied by changes in HOMO–LUMO gaps and frontier-orbital distributions. Among the non-glycosylated analogues, the reported gaps range from 8.385 eV for 8b to 10.512 eV for 8d. For the glycosylated derivatives, they range from 4.716 eV for M329 to 8.824 eV for M331. The local indices and electrostatic maps also suggest that substitution can alter electron distribution and the relative ranking of reactive sites.

These findings provide a theoretical comparison of the relationships between structure and electronic properties in this series of molecules. They suggest that glycosylation and the other modifications studied may affect local electronic response. The contribution remains theoretical: the calculated descriptors do not directly measure EPSPS inhibition, herbicidal activity, or biological selectivity. Interpretation is also limited by aspects of the protocol that require clarification or verification, including the protonation states used, the full settings for calculations on charged species, and the sign conventions applied to the Fukui indices. In addition, thermochemical quantities support conclusions about reaction spontaneity only when based on balanced reference reactions and clearly defined standard states.

Future work should verify the atomic populations and local indices using the original calculation files, then examine solvent effects and the relevant ionic forms of glyphosate. Calculations of interactions with EPSPS, followed by biochemical or biological assays, would help determine whether the electronic trends observed correspond to differences in activity or selectivity.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

Disclosure of conflict of interest

Authors have declared that no competing interests exist.

Declaration of AI use

This manuscript was prepared through the intellectual contributions of the author(s) to the study design, data analysis, interpretation of results, and scholarly content. Grammarly and ChatGPT were used solely to assist with grammatical refinement and reference formatting during manuscript revision. The author(s) accept full responsibility for the accuracy, integrity, and final content of the manuscript.

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