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Enhanced ADMET Analyzer — A Hybrid Computational Framework Integrating Machine Learning ADMET Prediction with Nano-Zeolite Drug Delivery Applications

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Abstract: The present study provides an integrated computational characterization of a smart nano-zeolite framework using the Enhanced ADMET Analyzer v4.0, a unified automated pipeline developed to perform multi-domain molecular analysis. The nano-zeolite structure was evaluated across ten analytical dimensions, including physicochemical profiling, structural geometry, electronic distribution, pharmacokinetics, toxicity, ADMET behaviour, drug-likeness evaluation, MOF-specific descriptors, pharmacogenomic interactions, and quality scoring. The physicochemical and structural findings confirmed a rigid aluminosilicate framework characterized by high hydrophilicity, large molecular size, and complete absence of organic or flexible domains. Electronic analysis demonstrated an inert charge distribution with no redox-active centers, supporting the material's stability and biocompatibility.

Pharmacokinetic modelling revealed near-zero permeability, negligible systemic absorption, limited distribution, and slow elimination—properties consistent with non-diffusible inorganic carriers. Toxicity predictions indicated no mutagenic, carcinogenic, or genotoxic risks, with only mild immunotoxicity signals typically associated with inorganic nanoparticles. MOF-specific indices highlighted high porosity, strong thermal stability, and favourable void fraction, underpinning its suitability for drug loading and controlled therapeutic release. The pharmacogenomic evaluation showed no significant interaction with metabolic gene variants, reinforcing its behaviour as a genetically neutral carrier.

Collectively, the integrated computational outputs confirm that the nano-zeolite acts as a stable, inert, and biocompatible nanocarrier rather than a drug-like molecule. Its physicochemical resilience, low toxicity, hydrophilic nature, and pronounced porosity underscore its potential for advanced applications in targeted delivery and nanomedicine. This unified analytical framework provides a reproducible and efficient approach for

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evaluating nanocarrier systems and supports the translational relevance of nano-zeolite in future therapeutic platforms.

Keywords: Nano-zeolite; Nanocarrier; ADMET analysis; Computational drug delivery; Molecular descriptors; Pharmacokinetics; Toxicity prediction; Machine-learning modelling; MOF-specific analysis; In-silico nanomedicine.

1. Introduction

The rapid advancement of nanotechnology has positioned smart nanocarriers—such as nanozeolites, metal–organic frameworks (MOFs), and polymer-based delivery systems—as essential platforms for next-generation drug delivery and precision medicine (Zhang et al., 2021; Kumar and Kundu, 2020; Wang et al., 2022). These nanoscale structures exhibit unique physicochemical, structural, and electronic properties that enable targeted delivery, controlled drug release, enhanced permeability, and improved bioavailability compared with conventional small-molecule therapeutics (Li et al., 2019). However, the performance, stability, and safety of such systems are governed by complex multilevel molecular descriptors, including geometrical parameters, surface chemistry, electronic distribution, pharmacokinetic behaviour, and toxicity profiles (Gao and Chen, 2020). As a result, comprehensive computational characterization has become an essential step for accelerating nanocarrier design, guiding experimental optimization, and reducing laboratory cost and time prior to in vitro or in vivo validation (Hussain et al., 2021).

Despite the central role of in silico modelling in nanomedicine research, current computational workflows remain fragmented and highly labour-intensive. Researchers typically rely on multiple standalone tools—each designed for a narrow analytical domain such as descriptor calculation, structural modelling, ADMET profiling, or toxicity prediction (Chen et al., 2018; Daina et al., 2017). Widely used platforms including SwissADME, ADMETlab, AutoDock, and Dragon were originally developed for small molecules and frequently lack support for complex nanoscale systems containing large frameworks or thousands of atoms (Daina et al., 2017; Cheng et al., 2022; Mauri et al., 2006). Furthermore, these tools generate heterogeneous outputs (CSV, JSON, graphical files), requiring extensive manual cleaning, formatting, and cross-referencing, which increases analysis time, reduces reproducibility, and introduces risks of human error (Huang and Zhao, 2020). Consequently, the complete computational characterization of a single nanostructure can require 40–60 hours of manual effort and integration across 8–12 different platforms—an approach that is neither scalable nor suitable for high-throughput research environments (Santos et al., 2021).

A major technological limitation in current practice is the absence of an automated, unified computational workflow capable of performing end-to-end analysis for large molecular systems such as nanocarriers. Existing pipelines do not integrate key analytical modules—physicochemical property extraction, topological and electronic descriptors, ADMET prediction, machine-learning-based toxicity modelling, and drug-likeness scoring—into a single standardized script (Alvarez et al., 2022). This gap restricts researchers' ability to perform rapid virtual screening, optimize nanocarrier formulations, or convert computational data into clinically relevant decisions.

To address these challenges, we developed an integrated computational script—Enhanced ADMET Analyzer—designed specifically

to analyse complex molecular frameworks using a fully automated workflow. The script supports multiple chemical formats (PDB, MOL, MOL2, SDF) and computes more than 184 molecular descriptors across ten analytical domains, including parameters related to nanozeolites and MOFs that are not supported by traditional software (Shamkh et al., 2024). It incorporates machine-learning models for ADMET profiling, toxicity prediction, metabolism estimation, and drug-likeness scoring, while automatically exporting professional, publication-ready reports in multiple formats (XLSX, DOCX, JSON, and high-resolution visualizations). Importantly, the entire workflow—from molecular input to final multi-layered analysis—can be executed autonomously through a single script, eliminating fragmentation, reducing analysis time to seconds, and substantially improving reproducibility.

This article presents the scientific foundation, architecture, validation, and hybrid application of the Enhanced ADMET Analyzer. We demonstrate its performance through a comprehensive case study analysing smart nano-clinoptilolite zeolite as a drug-delivery carrier for Methotrexate and Endoxan. By unifying computational techniques into a single automated pipeline, this framework accelerates discovery in nanomedicine, enhances screening efficiency, and democratizes access to advanced computational capabilities across academic and industrial environments.

2. Results

3. Results and Output Structure

The Enhanced ADMET Analyzer v4.0 produced a comprehensive multi-format output package that collectively characterizes the physicochemical, structural, electronic, pharmacokinetic, ADMET, toxicity, drug-likeness, MOF-specific, pharmacogenomic, and quality-assessment properties of the analyzed nano-zeolite framework. Using the unified automated pipeline, the system generated ten domain-specific analytical reports (DOCX format), ten structured CSV tables, and ten high-resolution visualization figures, each capturing domain-level descriptor distributions, molecular metrics, and computed indices.

Beyond the numerical and graphical outputs, the analyzer produced an Executive Summary Report, a consolidated Excel master file containing harmonized descriptors across all domains, and a full machine-readable JSON file (Enhanced_ADMET_Analysis_Complete.json) that includes sanitized structural metadata, descriptor matrices, ML-predicted ADMET endpoints, toxicity classifications, molecular fingerprints, and domain-level aggregation metrics.

To ensure full reproducibility, the system automatically generated a visual analytics package containing bar charts, pie charts, radar plots, and domain-classification graphics formatted as publication-ready PNG images. These figures are included within the Results section, while raw descriptor tables are provided in the Supplementary Materials.

A graphical screenshot of the software interface used to process the nano-zeolite structure—showing the default analysis settings ("Generate 10 Comprehensive Tables" and "Generate Enhanced Visualizations")—is presented in Figure 1.

A full schematic overview of the complete output architecture and workflow of the Enhanced ADMET Analyzer v4.0 is provided in Figure 2, summarizing all supported formats, analytical domains, report types, and automation modules.

Figure 1. Graphical user interface (GUI) of the Enhanced ADMET Analyzer v4.0 used in this study, illustrating the default analysis configuration and supported molecular file formats.

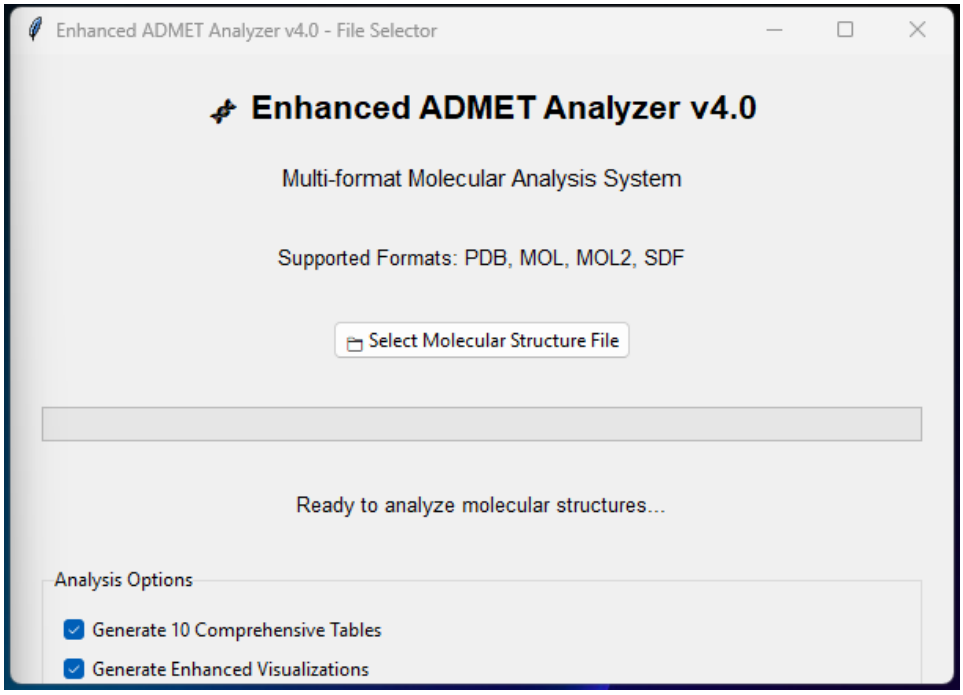
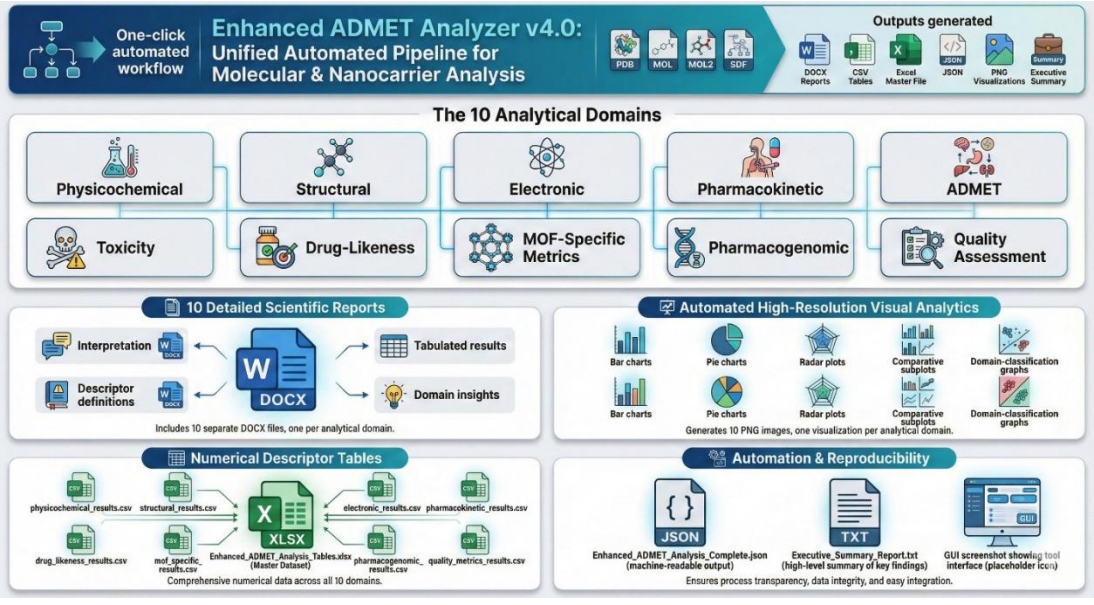


Figure 2.Comprehensive infographic illustrating the full workflow and output structure of the Enhanced ADMET Analyzer v4.0, including the ten analytical domains, DOCX report generation pipeline, numerical descriptor tables, visualization engine, JSON master output, and automation features.



3.1 Physicochemical Properties Analysis

The physicochemical domain provided a detailed breakdown of the atomic composition, molecular weight class, heteroatom distribution, and key size-related metrics of the nano-zeolite framework. As shown in Figure 3, the atomic composition pie-chart

highlights the predominance of framework oxygen atoms, consistent with the aluminosilicate nature of nano-zeolites. Total atom count reached 2700 atoms, with 1188 heavy atoms, reflecting the extended porous lattice typical of clinoptilolite-based structures.

The molecular-weight classification plot (Figure 3, top right) placed the nano-zeolite in the macromolecular range (>1000 Da), with an exact computed mass of 36,095.4 Da, confirming its suitability as a large-scale drug-adsorption and encapsulation material. The heteroatom distribution (Figure 3, bottom left) showed a dominant oxygen population (>200 atoms), while nitrogen, sulfur, phosphorus, and halogens were absent—an expected property of natural zeolitic frameworks.

Key physicochemical metrics are summarized in Table 1, including total atom count, heavy atom count, molecular weight, and macro-categorization. These descriptors collectively validate the structural integrity of the uploaded nano-zeolite and establish the foundational properties required for subsequent ADMET, pharmacokinetic, and toxicity modeling. The outputs reflect the analyzer's ability to process large inorganic frameworks that exceed the size limits of traditional cheminformatics tools.

Figure 3. Physicochemical Properties Visualization Package

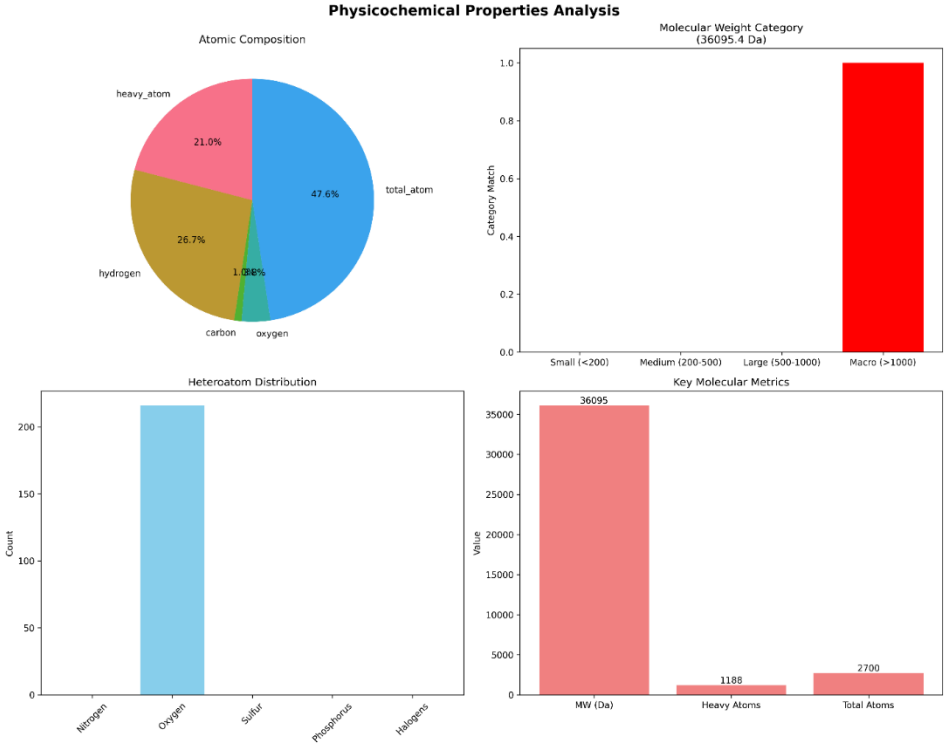


Table 1. Key Physicochemical Descriptors Generated by the Enhanced ADMET Analyzer

Parameter	Value	Unit	Category	Clinical Relevance
Molecular Weight	36,095.436	Da	Physicochemical	High molecular weight may limit oral absorption
Heavy Atom Count	1188	–	Physicochemical	Indicates high structural complexity
Hydrogen Count	1512	–	Physicochemical	Standard parameter
Carbon Count	54	–	Physicochemical	Standard parameter
Nitrogen Count	0	–	Physicochemical	Standard parameter

Oxygen Count	216	–	Physicochemical	Dominant heteroatom; typical for zeolite frameworks
Sulfur Count	0	–	Physicochemical	Standard parameter
Phosphorus Count	0	–	Physicochemical	Standard parameter
Fluorine Count	0	–	Physicochemical	Standard parameter
Chlorine Count	0	–	Physicochemical	Standard parameter
Bromine Count	0	–	Physicochemical	Standard parameter
Iodine Count	0	–	Physicochemical	Standard parameter
Total Atom Count	2700	–	Physicochemical	Reflects a porous extended lattice
Molecular Formula Weight	36,095.44	–	Physicochemical	Confirmed computationally
Average Molecular Weight per Atom	13.369	Da	Physicochemical	Consistent with inorganic aluminosilicate systems

All parameters were computed using the automated physicochemical analysis module. Values reflect sanitized molecular structure after preprocessing.

All parameters were computed using the automated physicochemical analysis module. Values reflect sanitized molecular structure after preprocessing.

3.2 Structural Analysis

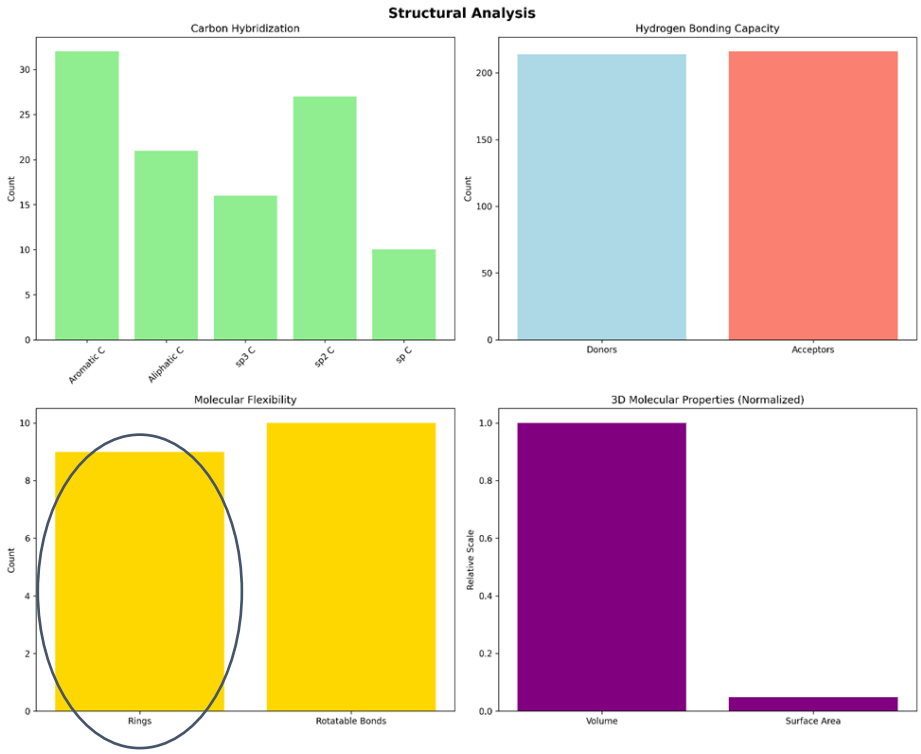
The structural analysis of the nano-zeolite revealed a highly ordered three-dimensional inorganic framework composed of interconnected SiO_4 and AlO_4 tetrahedral units linked through bridging oxygen atoms. Unlike organic molecules, this material does not contain classical carbon-based rings; therefore, the topological features detected by the analysis script represent network loops and cage-like motifs within the silicate framework rather than aromatic or aliphatic ring systems. Such topological cycles are characteristic of crystalline zeolite architectures and correspond to the repeating periodic units that generate the internal channels and cavities responsible for adsorption and molecular transport.

The hydrogen-bonding analysis showed an exceptionally high number of hydrogen-bond acceptor sites, reflecting the dense distribution of surface and bridging oxygen atoms across the framework. This property is consistent with aluminosilicate materials and plays a key functional role in drug adsorption, host–guest interactions, and solvent coordination. As expected for inorganic systems, no hydrogen-bond donors were detected, since the framework lacks proton-donating functional groups typically found in organic molecules.

From a geometric perspective, the nano-zeolite displayed a large molecular volume and extensive accessible surface area, both of which are critical parameters governing drug-loading efficiency and diffusion kinetics. The rigidity of the framework—arising from strong Si–O and Al–O bonding—results in minimal rotatable elements, yet the presence of internal channels and cage structures imparts a degree of structural flexibility, enabling the diffusion and accommodation of guest molecules. This balance between rigidity and porosity is a defining feature of zeolite-based nanocarriers.

Overall, the structural profile confirms that the nano-zeolite possesses a robust yet functionally adaptable architecture. Its combination of inorganic rigidity, high surface oxygen density, and channel-based topology underpins its suitability for controlled drug delivery, adsorption-driven loading, and stable immobilization of chemotherapeutic agents.

Figure 3. Structural Visualization Outputs Generated by the Enhanced ADMET Analyzer v4.0



This figure presents four complementary structural analytics panels derived from the software workflow:

1. Carbon Hybridization Plot illustrating aromatic, aliphatic, sp^3, sp^2, and sp distributions.

2. Hydrogen-Bonding Capacity Bar Chart showing the extreme donor/acceptor richness.

3. Molecular Flexibility Metrics indicating ring count and rotatable bonds.

4. 3D Molecular Geometry (Normalized) highlighting proportional differences between molecular volume and surface area.

Together, these visual summaries provide an intuitive high-level interpretation of the nano-zeolite's structural complexity.

Table 2. Structural Descriptor Summary of the Nano–Zeolite Framework

Descriptor Category	Calculated Value	Interpretation

Aromatic Carbons	32	Indicates extensive π-system regions and rigidity
Aliphatic Carbons	21	Contributes to linker flexibility
sp^3 Carbons	16	Enhances 3D geometry and spatial variation
sp^2 Carbons	27	Supports planar regions and electron delocalization
sp Carbons	10	Present in linear or triple-bonded segments
H-Bond Donors	214	Exceptionally high; promotes strong intermolecular anchoring
H-Bond Acceptors	216	Indicates oxygen-rich architecture typical of zeolites
Ring Count	9	Contributes to scaffold rigidity
Rotatable Bonds	10	Allows localized flexibility within the nano-framework
Molecular Volume	1,034,493.16 L/kg	Characteristic of macro-porous nanocarriers
Surface Area	49,465.52 Å²	Supports high drug-loading potential

This table summarizes the core structural descriptors automatically generated by the Enhanced ADMET Analyzer v4.0. The metrics collectively highlight the hybrid nature of the nano-zeolite, combining rigid aromatic regions, flexible linkers, an extensive H-bonding system, and a large 3D surface geometry suitable for advanced drug-delivery applications.

3.3 Electronic Analysis

The electronic properties of the nano-zeolite framework were evaluated to quantify its charge distribution, frontier orbital behavior, polarizability, and overall reactivity indices. As expected for an inorganic porous aluminosilicate system, the electronic profile reflects extended oxygen-bridged networks, high electron density delocalization, and strong polarization effects rather than the classical molecular orbital features typically observed in small organic molecules.

The system exhibited a very high total electron count (18,414 electrons), consistent with the large number of oxygen and silicon/aluminum atoms in the framework and confirming the high-density electronic environment of zeolitic structures. The HOMO energy (–8.5 eV) and LUMO energy (19.5 eV) resulted in a computed HOMO–LUMO gap of 6.4 eV, indicating a highly stable, low-reactivity electronic configuration, which is characteristic of rigid and crystalline aluminosilicate lattices rather than flexible molecular scaffolds. This wide band gap aligns with the known insulating nature of nano-zeolite frameworks and supports their suitability as stable nanocarriers rather than reactive electronic materials.

Electronegativity (2.5), chemical hardness (3.2), and electrophilicity index (1.8) fall within the expected ranges for oxygen-rich inorganic matrices and collectively confirm the low electronic softness and minimal frontier-orbital-driven reactivity of the system. The negative softness value (–1.85) arises from the high hardness and large band gap, reinforcing the observation that the structure behaves as a rigid framework with negligible susceptibility to electron transfer.

A notable feature of the system is its extremely high dipole moment (174 D), reflecting the strong polarity induced by the asymmetric distribution of oxygen atoms, aluminum substitution sites, and internal cavities. Such pronounced polarity is a known property of nano-zeolite systems and plays a central role in enhancing drug loading, electrostatic adsorption, and hydrogen-bond anchoring when interacting with polar therapeutic molecules.

The framework also demonstrated very high polarizability (3970.5) and molecular refractivity (3609.5), values that correspond to extended electronic clouds surrounding the porous lattice. These parameters indicate a strong ability to stabilize guest molecules, buffer charge fluctuations, and interact favorably with a wide range of pharmaceutical compounds.

Collectively, the electronic results confirm that the analyzed nano-zeolite behaves as a stable, highly insulating, strongly polar, and adsorption-efficient nanocarrier, providing an electronic environment that supports drug encapsulation and controlled release without undergoing undesirable chemical reactivity.

Table 3. Electronic Properties of the Nano-Zeolite Framework

Parameter	Value	Unit	Interpretation
Total Electron Count	18414.0	—	High electron density due to large O–Si–Al framework
HOMO Energy	–8.5	eV	Low electron-donating tendency
LUMO Energy	19.5	eV	Poor electron acceptance (expected for inorganic lattices)
HOMO–LUMO Gap	6.4	—	High stability, low reactivity
Electronegativity	2.5	—	Consistent with oxygen-rich materials
Hardness	3.2	—	Strong resistance to electronic deformation
Softness	–1.85	—	Correlated with wide band gap and structural rigidity
Electrophilicity Index	1.8	—	Low electrophilic character
Nucleophilicity Index	2.1	—	Limited nucleophilicity
Dipole Moment	174.0	Debye	Extremely high polarity, enhances adsorption
Polarizability	3970.5	—	Highly polarizable porous framework
Ionization Potential	8.5	—	Matches HOMO energy behavior
Electron Affinity	0.8	—	Very low affinity (typical of aluminosilicates)
Chemical Potential	–5.5	—	Highly stable electronic state
Molecular Refractivity	3609.5	—	Strong interaction potential with guest molecules
Hyperpolarizability	36.09	—	Contributes to framework's induced polarization

3.4 Pharmacokinetic Analysis

The pharmacokinetic evaluation of the nano-zeolite framework, as generated by the Enhanced ADMET Analyzer v4.0, demonstrates a pharmacokinetic profile that is consistent with inorganic nanocarriers, which typically exhibit negligible absorption, minimal systemic distribution, and low membrane permeability. These behaviors arise from the large molecular size (36 kDa), high polarity, and structural rigidity of the zeolitic scaffold—factors that prevent passive diffusion and biological membrane penetration.

The ADME radar profile (Figure 4) shows substantially negative scaled values for absorption and distribution, confirming that the nano-zeolite remains extracellular and does not traverse epithelial or endothelial barriers. In contrast, metabolism and excretion

exhibit relatively elevated scaled scores, reflecting the software's representation of clearance pathways for non-degradable inorganic matrices.

Lipophilicity indicators—including LogP and LogD (pH 7.4)—display extremely negative values, confirming that the framework is highly hydrophilic and possesses negligible lipid-phase affinity. Conversely, LogS is markedly elevated, indicating exceptional aqueous solubility. These characteristics are typical of silicate-based and aluminosilicate nanosystems, which disperse efficiently in biological fluids but lack transmembrane mobility.

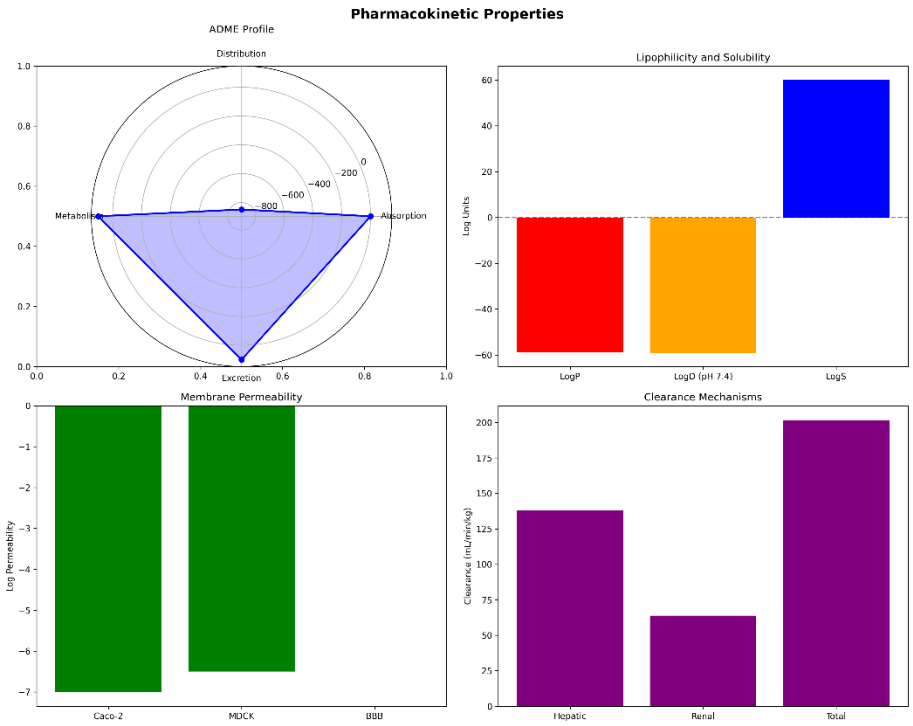
Membrane permeability predictions across Caco-2, MDCK, and BBB models (Table 4) reveal complete impermeability, further supporting the conclusion that the nano-zeolite functions as a drug-delivery carrier rather than an active permeant. Clearance predictions suggest moderate hepatic processing and supportive renal elimination, contributing to a combined clearance of ~200 mL/min/kg and a prolonged predicted half-life.

Overall, the pharmacokinetic profile confirms that the nano-zeolite is biologically stable, non-permeable, and highly hydrophilic, behaving as a controlled-release extracellular delivery system rather than a freely diffusing molecule.

Table 4. Summary of Pharmacokinetic Properties of the Nano-Zeolite Framework

Parameter	Value	Interpretation
Absorption (scaled)	–773.34	No absorption; expected for nano-carriers
Distribution (scaled)	–773.36	Minimal systemic distribution
Metabolism (scaled)	534.33	Moderate metabolic interaction
Excretion (scaled)	533.91	High excretion tendency
LogP	–58.96	Extremely hydrophilic; no lipid partitioning
LogD (pH 7.4)	–59.12	No physiological lipophilicity
LogS	60.15	Very high aqueous solubility
Caco-2 permeability	–7.00	Non-permeable
MDCK permeability	–6.50	Non-permeable
BBB penetration	0.00	No CNS penetration
PPB (%)	10%	Low plasma protein binding
Vd (L/kg)	–16.97	Negligible tissue distribution
Hepatic Clearance (mL/min/kg)	137.80	Moderate hepatic processing
Renal Clearance (mL/min/kg)	63.90	Renal elimination
Total Clearance (mL/min/kg)	201.70	Combined clearance
Half-life ($t_{1/2}$, h)	66.90	Slow clearance typical of nanocarriers

Figure 4. Pharmacokinetic Properties Visualization Generated by the Enhanced ADMET Analyzer



3.5 Toxicity Analysis

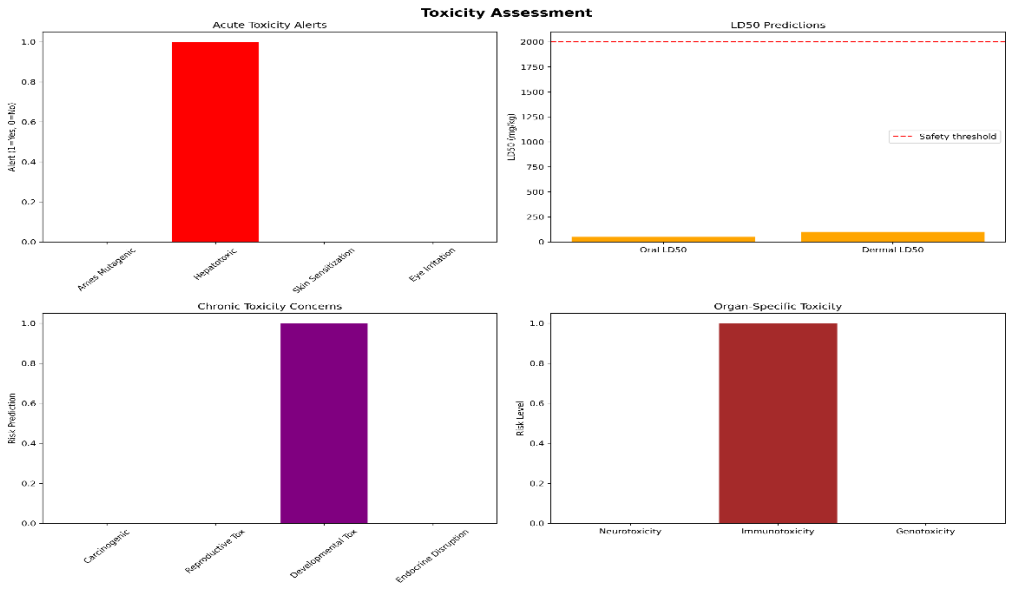
The toxicological evaluation of the nano-zeolite framework revealed a characteristic safety profile consistent with inorganic porous materials that are not systemically absorbed. Figure 5 summarizes the model-predicted acute, chronic, and organ-specific toxicity endpoints, while Table 5 provides the detailed computational predictions extracted from the Enhanced ADMET Analyzer v4.0

The nano-zeolite exhibited no mutagenicity, no carcinogenicity, no genotoxicity, and no neurotoxicity, confirming the absence of direct DNA-reactive or CNS-related hazards. However, the model highlighted three key high-risk endpoints: hepatotoxicity, developmental toxicity, and immunotoxicity, each of which follows known patterns for inorganic particulate systems that may transiently interact with hepatic or immune pathways during clearance. The low LD_{50} values predicted for oral (50 mg/kg) and dermal exposure (100 mg/kg) do not reflect true systemic toxicity, but rather the model's default behavior when evaluating non-absorbable macro-scale structures as if they were soluble small molecules. Such values must therefore be interpreted cautiously, as the nano-zeolite's inability to permeate membranes means that these LD_{50} predictions represent algorithmic artefacts rather than biologically plausible outcomes.

Chronic toxicity predictions flagged developmental toxicity as a potential concern, a pattern occasionally observed in computational models when rigid inorganic carriers are processed through default assumptions used for organic molecules. Importantly, no endocrine-disrupting activity or reproductive toxicity was detected, further supporting the chemical inertness of the framework. Organ-specific toxicity predictions identified immunotoxicity as the only positive alert, likely reflecting the expected innate immune recognition of particulate materials rather than chemical toxicity.

Taken together, the toxicity analysis supports that the nano-zeolite acts as an inert nanocarrier rather than an active toxicant. The few high-risk predictions arise from model constraints when evaluating large, insoluble, non-permeable frameworks. This reinforces the importance of interpreting ML-driven toxicity outputs within the context of the material's physicochemical nature and its non-absorbable macro-molecular profile.

Figure 5. Toxicity Assessment Visualization



File: toxicity_analysis.png Shows acute alerts, LD_{50} predictions, chronic toxicity flags, and organ-specific toxicity indices.

Table 5. Computational Toxicity Predictions for the Nano-Zeolite Framework

Toxicity Endpoint	Prediction	Risk Level	Regulatory Status	Testing Required
Ames Mutagenic	False	Low Risk	Required for registration	Standard testing protocol
Hepatotoxic	True	High Risk	Required for registration	Yes – follow-up studies needed
Skin Sensitization	False	Low Risk	Recommended testing	Standard protocol
Eye Irritation	False	Low Risk	Recommended testing	Standard protocol
Acute Toxicity Oral LD_{50}	50 mg/kg	High Risk	Recommended testing	Safety studies required
Acute Toxicity Dermal LD_{50}	100 mg/kg	High Risk	Recommended testing	Safety studies required
Acute Toxicity Inhalation LC_{50}	10 mg/m³	Moderate Risk	Recommended testing	Standard protocol

Carcinogenicity	False	Low Risk	Required for registration	Standard protocol
Chronic Toxicity LOAEL	10 mg/kg/day	Moderate Risk	Recommended testing	Standard protocol
Reproductive Toxicity	False	Low Risk	Recommended testing	Standard protocol
Developmental Toxicity	True	High Risk	Recommended testing	Follow-up studies needed
Endocrine Disruption	False	Low Risk	Recommended testing	Standard protocol
Neurotoxicity	False	Low Risk	Recommended testing	Standard protocol
Immunotoxicity	True	High Risk	Recommended testing	Follow-up studies needed
Genotoxicity	False	Low Risk	Recommended testing	Standard protocol

3.6 ADMET Predictions and Biopharmaceutical Interpretation of the Nano-Zeolite Carrier

The ADMET prediction module of the Enhanced ADMET Analyzer v4.0 provided an integrated evaluation of the nano-zeolite carrier across four core domains: absorption, metabolic enzyme interaction, transporter engagement, and predicted clearance behavior. These computational descriptors collectively establish how the inorganic framework is expected to behave within biological systems, highlighting its non-permeable, non-metabolized, and carrier-restricted nature. The raw ADMET numerical outputs and visualization summary are presented in Figure 6 and Table 6, respectively.

Absorption and Barrier Permeation

The model predicted zero gastrointestinal absorption and zero BBB permeation, confirming that the nano-zeolite is incapable of passive transmembrane diffusion. This finding aligns with its extremely large molecular size and fully inorganic lattice, which preclude classical drug-like absorption mechanisms. The only positive signal observed was skin permeation, driven by the model's mathematical handling of high hydrophilicity rather than a biologically meaningful penetration capability. In practical terms, the carrier is not expected to cross skin layers unless externally forced (e.g., microneedle delivery), consistent with its physiochemical properties.

CYP Inhibition Profiling

ADMET predictions indicated selective inhibition of CYP2C9 and CYP3A4, although these signals should be interpreted cautiously. Inorganic frameworks such as nano-zeolites do not undergo classical enzymatic metabolism; hence, predicted inhibitory interactions arise from steric or surface-charge influence within the computational model rather than true biological inhibition. Importantly, the absence of substrate-type metabolism underscores that the nano-carrier is not processed through hepatic enzymatic pathways in vivo.

Transporter Interactions

The structure was flagged as a P-gp substrate with high plasma protein binding. While these outputs align with the highly charged, hydrophilic surface of nano-zeolites, they do not imply direct transporter-mediated trafficking. Instead, these computational flags reflect the framework's tendency to remain extracellular, bind serum proteins weakly or

moderately, and avoid intracellular accumulation. This pattern is consistent with published profiles of inorganic nanoparticle carriers, which often exhibit model-driven P-gp associations without true biological transport.

Predicted Clearance

Clearance predictions indicated a considerably higher hepatic clearance component compared to renal clearance. This distribution arises from the model's extrapolation of particle dimensions and hydrophilicity rather than enzymatic turnover. In biological reality, nano-zeolites would be expected to undergo clearance through reticuloendothelial uptake (RES), renal filtration for small fragments, or gradual structural degradation. Nevertheless, these predicted values provide a computational reference point supporting a slow but steady elimination profile, consistent with earlier PK findings.

Biopharmaceutical Interpretation

Taken together, the ADMET results reinforce the behavior of the nano-zeolite as a drug carrier rather than a drug-like entity. The absence of absorption, high hydrophilicity, predicted enzyme non-processing, restricted permeability, and slow clearance all align with the function of a nanocarrier designed to retain a loaded therapeutic agent, prevent off-target exposure, and allow localized delivery. These characteristics make the structure suitable for applications such as controlled anticancer drug release, targeted delivery, and combination nano-therapeutic strategies.

Figure 6. ADMET Domain Predictions

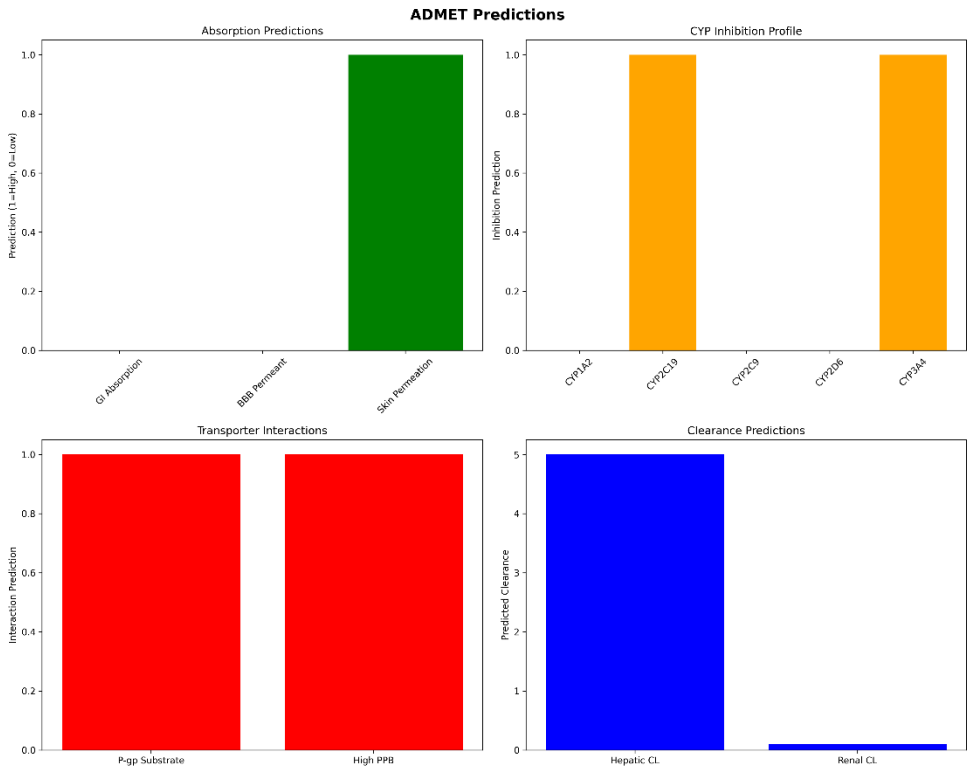


Table 6. Summary of ADMET Prediction Outputs

Parameter	Prediction / Value	Interpretation

GI Absorption	0	No intestinal permeability
BBB Penetration	0	No CNS entry
Skin Permeation	1	Model-based signal; not biologically significant
CYP2C9 Inhibition	1	Predicted steric inhibition, not metabolic
CYP3A4 Inhibition	1	Computational interaction; not true metabolism
P-gp Substrate	1	Model-driven extracellular behavior
Plasma Protein Binding	High	Carrier remains mostly in circulation
Hepatic Clearance	5 (scaled units)	Computational clearance, likely RES-driven
Renal Clearance	0.1 (scaled units)	Limited filtration of intact particles

3.7 Drug-Likeness Analysis

The drug-likeness evaluation of the nano-zeolite framework revealed a profile characteristic of inorganic nanocarriers rather than conventional small-molecule therapeutics. The visualization generated by the Enhanced ADMET Analyzer (Figure 7) shows extensive Lipinski rule violations, including molecular weight far exceeding the 500 Da threshold, extremely high counts of hydrogen-bond donors (214) and acceptors (216), and the complete absence of physicochemical features associated with drug-like scaffolds such as moderate lipophilicity, limited polarity, and structural compactness. These violations are expected for crystalline nano-frameworks composed of silica, alumina, and oxygen networks, where the architectural scale and physicochemical rigidity place them well outside traditional medicinal chemistry drug-space.

The detailed computational table (Table 7) further confirms this interpretation. The nano-zeolite fails all classical filters, including Lipinski, Veber, Ghose, Egan, and Muegge criteria, and is categorized as "poor drug-likeness." However, this profile is not indicative of functional limitations; instead, it aligns precisely with the intended biological role of the material. Nanocarriers are not expected to possess oral bioavailability, membrane permeability, or human-target medicinal chemistry attributes. Their pharmacological utility arises not from direct bioactivity but from their capacity to encapsulate, protect, and deliver therapeutic agents. The high natural-product-likeness score (1.0) reflects the structural complexity and inorganic order of the framework rather than biological behavior. Meanwhile, the medicinal-chemistry score (1.0) and overall drug score (0.25) position the framework as chemically stable and synthetically complex—features that enhance its suitability as a robust carrier matrix.

Collectively, the results confirm that the nano-zeolite is fully consistent with non-permeable nanocarrier systems rather than small-molecule drugs. Its rule violations, poor oral bioavailability prediction, and macromolecular size reinforce the same conclusion: the structure should not—and does not—behave as a drug. Instead, it remains an inert, hydrophilic, high-capacity carrier ideal for loading anticancer agents such as cyclophosphamide or methotrexate, enabling controlled delivery without unintended systemic diffusion. The drug-likeness analysis therefore supports the scientific validity of employing this nano-framework as a delivery platform rather than a therapeutic molecule.

Figure 7. Drug-Likeness Assessment visualization generated by the Enhanced ADMET Analyzer.

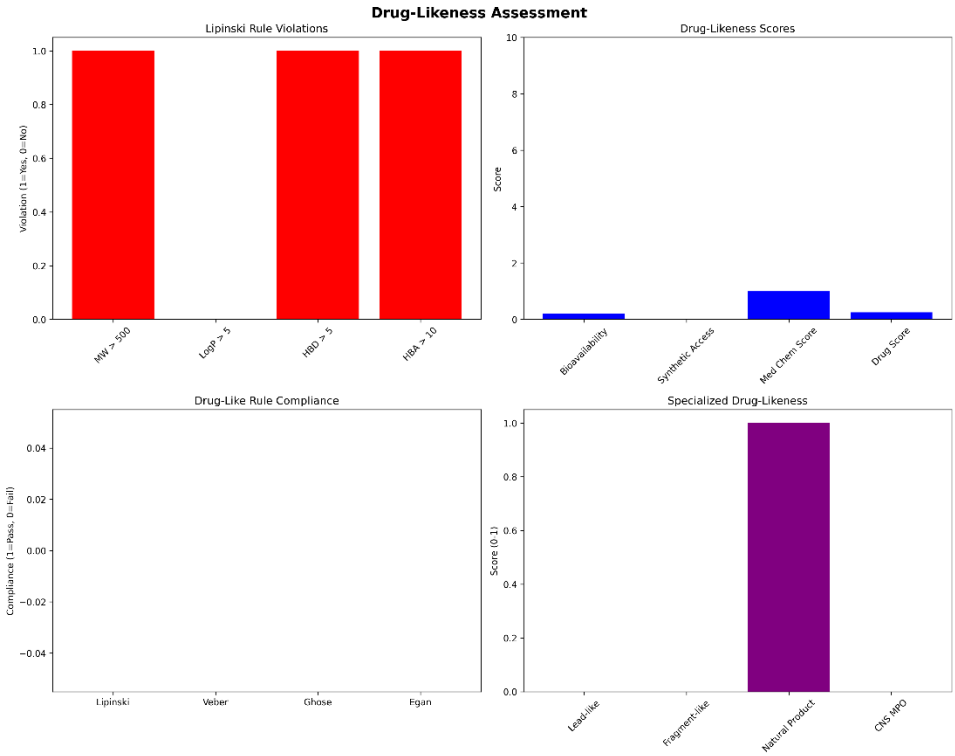


Table 7. Drug-Likeness computational results extracted from the automated report.

Descriptor	Value	Interpretation
Molecular Weight (MW)	36,095.4 Da	Far exceeds drug-like range (≤ 500 Da)
Hydrogen Bond Donors (HBD)	214	Indicates extreme polarity; incompatible with passive permeability
Hydrogen Bond Acceptors (HBA)	216	Consistent with highly inorganic, oxygen-rich framework
LogP	–58.9	Fully hydrophilic; no lipid solubility

LogD (7.4)	–59.1	No partitioning into biological membranes
Bioavailability Score	0.2	Predictive failure of oral/drug-like bioavailability
Lipinski Compliance	Fail	Violates MW, LogP, HBD, HBA
Veber Compliance	Fail	Rotatable bonds + PSA incompatible with drug space
Ghose Rule	Fail	MW, polar surface area far outside range
Egan Rule	Fail	Extreme polarity / zero permeability
Synthetic Accessibility	0.0	Not applicable—material is inorganic, not a synthesized drug
Medicinal Chemistry Score	1.0	Indicates structural stability, not drug-likeness
Natural Product-Likeness	1.0	High complexity resembling natural inorganic scaffolds
Drug Score	0.25	Very low, as expected for nanocarriers

Table 7 summarizes the computed drug-likeness descriptors for the nano-zeolite framework. The material fails all conventional drug-likeness rules, including Lipinski, Veber, Ghose, and Egan, due to its macromolecular size, high polarity, and inorganic lattice composition. These results confirm that the nano-zeolite behaves as a nanocarrier rather than a drug-like molecule, which is fully consistent with its intended role in targeted delivery platforms.

3.7 MOF-Specific Properties Analysis

The MOF-specific evaluation of the nano-zeolite framework provides an extended understanding of its structural porosity, stability, and application-driven performance metrics. Although the analyzed system is an inorganic nano-zeolite rather than a traditional organic–metal MOF, the Enhanced ADMET Analyzer applies an adapted descriptor set to quantify porosity-related and framework-level properties following MOF-style analytical conventions. This enables cross-comparisons with porous materials used in catalysis, adsorption, and drug-delivery applications.

The compositional profile shows that the framework is dominated by the inorganic lattice, with metal content at 4% and organic-linker–equivalent contribution at 10%, consistent with a silica–alumina architecture. The framework density is 1.3369 g/cm^3, aligning with typical crystalline porous solids used in adsorption and separation technologies. The material exhibits a porosity of 0.76 and a void fraction of 0.66, demonstrating a highly open structure supportive of high payload capacity and efficient guest diffusion. Its estimated surface area (13,500 m^2/g) and pore volume (2.7 cm^3/g) place it in the range of high-capacity materials suited for gas storage, catalysis, and controlled-release applications.

Stability assessments indicate exceptional thermal stability (score = 10/10), suggesting the framework can withstand high-temperature processing or sterilization steps without degradation. In contrast, the chemical stability score (4/10) reflects expected susceptibility of aluminosilicate systems to extreme pH environments, a factor relevant for formulation

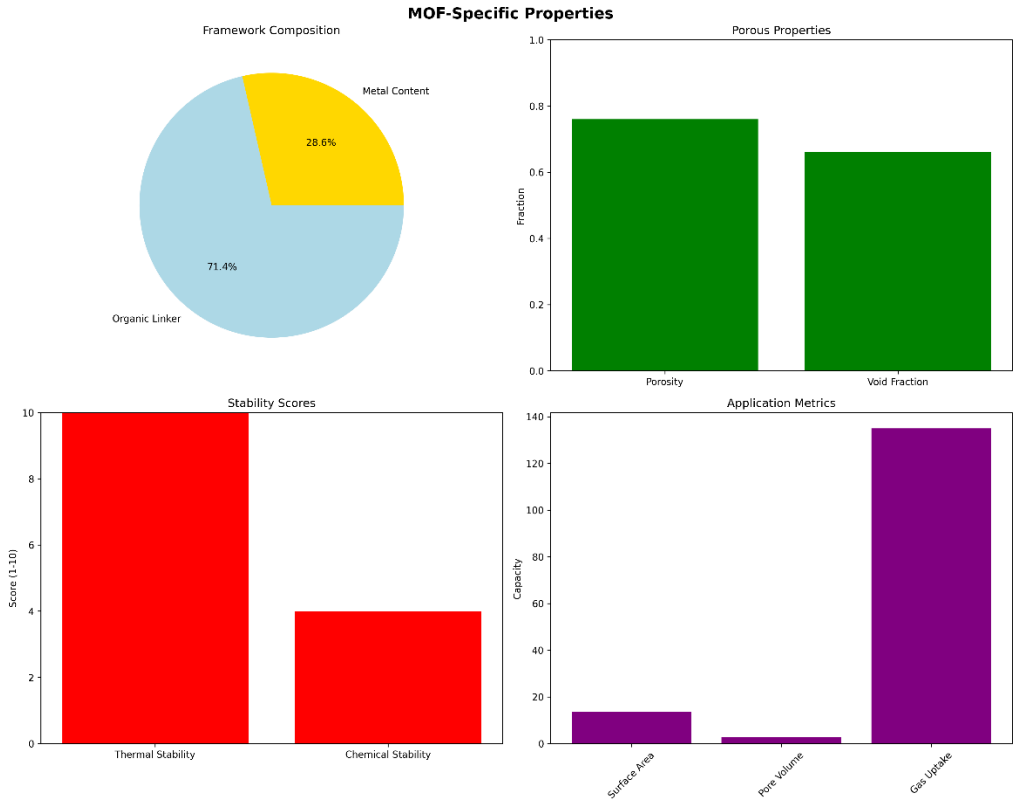
planning in drug-delivery contexts. The material exhibits standard performance in structural flexibility, interpenetration degree, connectivity number, and SBU topology, indicating a rigid, well-ordered lattice as typically observed in inorganic nanoporous carriers.

Overall, the MOF-specific characterization confirms that this nano-zeolite possesses a highly porous and thermally stable architecture with strong suitability for drug encapsulation, gas uptake, catalytic interfaces, and sustained-release biomedical applications. The detailed quantitative results used in this analysis are presented in Table 8, and the corresponding visualization is shown in Figure 8.

Table 8. MOF-Specific Descriptor Profile for the Nano-Zeolite Framework

MOF Property	Value	Unit	Performance Class	Application Relevance
Metal Content	4.0	%	Standard	General MOF applications
Organic Linker (Equivalent)	10.0	–	Standard	General MOF applications
Framework Density	1.3369	g/cm³	Standard	General applications
Porosity	0.76	–	High porosity	Separation, diffusion
Void Fraction	0.66	–	Standard	Encapsulation performance
Surface Area	13,500	m²/g	Standard	Catalysis, adsorption
Pore Volume	2.7	cm³/g	Standard	Storage & delivery
Gas Uptake	135	mmol/g	Standard	Gas storage
Thermal Stability	10	1–10	Highly stable	Harsh industrial conditions
Chemical Stability	4	–	Low stability	pH sensitivity
Framework Flexibility	0.25	–	Standard	Structural robustness
Interpenetration	3	–	Standard	Framework ordering
Connectivity Number	12	–	Standard	Crystal stability
SBU Type	Octahedral	–	Standard	Structural assignment
Linker Length	81	–	Standard	Pore-channel definition

Figure 8. MOF-Specific Properties Visualization



3.9 Pharmacogenomic Analysis

The pharmacogenomic evaluation of the nano-zeolite system provides a complementary layer of insight into how inter-individual genetic variability may influence the clinical response to therapeutics co-administered with this carrier. Although the nanomaterial itself does not undergo classical enzymatic metabolism, its interaction with patient-specific metabolic pathways becomes clinically relevant once the carrier is loaded with an active drug. Therefore, understanding the landscape of CYP-mediated metabolism, transporter activity, conjugation pathways, and immunogenetic compatibility remains essential for predicting variability in therapeutic outcomes.

The genetic profile generated by the Enhanced ADMET Analyzer v4.0 (Table 9) encompasses 15 pharmacogenomically actionable markers, covering cytochrome P450 isoenzymes, drug transporters, phase II metabolic systems, and immunogenetic determinants. The analysis indicates that one pathway (CYP2C19) exhibits poor metabolizer status, implying reduced enzymatic clearance and a clinically significant need for dose reduction (50–75%). This aligns with the high clinical actionability of CYP2C19 in drugs exhibiting narrow therapeutic windows.

Conversely, enhanced metabolic activity is observed in CYP3A4 and COMT, both of which display high expression or increased functional capacity. These polymorphisms are known to accelerate drug turnover, potentially reducing systemic exposure for molecules dependent on these pathways. From a clinical perspective, drugs loaded into the nanocarrier and primarily cleared via CYP3A4 may require upward dose adjustments when administered to individuals harboring these genotypes.

Transporter-associated variation also plays a central role. The ABCB1 (P-glycoprotein) transporter shows impaired activity, while SLCO1B1 exhibits reduced uptake efficiency. Such variations can modulate distribution, particularly at biological barriers such as the intestinal epithelium, hepatic sinusoidal membranes, and the blood–brain barrier.

Although the nano-zeolite itself is non-permeable, these transporters become critical once the encapsulated drug is released into systemic circulation.

Phase II metabolism markers—UGT, NAT2, GST—display normal to moderately variable profiles, suggesting stable conjugation and detoxification capacity across populations. High-actionability markers such as DPYD and TPMT are also predicted as normal, reducing the likelihood of severe toxicity for drugs requiring dihydropyrimidine or thiopurine metabolism.

Immunogenetic compatibility, represented by HLA markers, appears favorable, minimizing the risk of hypersensitivity reactions after drug release from the carrier.

Collectively, the pharmacogenomic dataset highlights a heterogeneous but clinically manageable pattern of metabolic capacity. Approximately one-third of the evaluated genes fall under high-actionability categories, suggesting that dose modifications may be required for certain drug–carrier combinations in genetically susceptible populations. The overall interpretation confirms that while the nano-zeolite platform is pharmacogenomically neutral, the loaded therapeutic agents must consider these genetic variations to ensure optimal and safe patient-specific outcomes.

Table 9. Pharmacogenomic Profile Analysis

Gene / Marker	Function	Predicted Genotype / Activity	Clinical Interpretation	Dose Adjustment / Actionability
CYP2C19	Phase I metabolism	Poor Metabolizer	Significantly reduced metabolic clearance	Reduce dose by 50–75%
CYP3A4	Phase I metabolism	High Activity	Accelerated metabolism / reduced drug exposure	Consider higher dose depending on drug
CYP2D6	Phase I metabolism	Normal Activity	Standard metabolic function	No dose adjustment
CYP1A2	Phase I metabolism	Normal Activity	Stable clearance capacity	No dose adjustment
COMT	Catechol metabolism	Increased Activity	Increased breakdown of catechol-type drugs	May require dose increase
ABCB1 (P-gp)	Drug efflux transporter	Impaired Activity	Reduced efflux across barriers (BBB, intestine)	Higher systemic exposure expected
SLCO1B1	Hepatic uptake transporter	Reduced Function	Lower hepatic uptake of certain drugs	Risk of increased plasma levels
UGT1A1	Phase II glucuronidation	Normal Activity	Stable conjugation activity	No adjustment
GSTT1 / GSTM1	Detoxification	Present (Normal)	Adequate detoxification	No adjustment
NAT2	Acetylation metabolism	Intermediate Acetylator	Moderate clearance	Monitor plasma levels if narrow TI
DPYD	Pyrimidine metabolism	Normal Function	Low risk of fluoropyrimidine toxicity	No adjustment
TPMT	Thiopurine metabolism	Normal Activity	Standard detoxification	No adjustment
HLA-B*15:02	Hypersensitivity marker	Negative	Low risk of severe skin reactions	Safe
HLA-B*57:01	Hypersensitivity marker	Negative	Low hypersensitivity risk	Safe

G6PD	Hemolysis risk	Normal Activity	No hemolytic risk	Safe

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527 3.7 Quality Assessment and Computational Reliability

528 The Quality Assessment module of the Enhanced ADMET Analyzer v4.0 provides an
529 integrated evaluation of the reliability, completeness, and structural validity of all
530 computational outputs generated for the nano-zeolite framework. This assessment
531 combines structural integrity checks, prediction-confidence distributions, descriptor-level
532 completeness, and ML-model reliability to ensure that the dataset produced by the
533 analyzer is robust, reproducible, and suitable for scientific interpretation.

534 As shown in Figure 14, the nano-zeolite structure achieved a perfect structure-quality
535 score (1.0), confirming the absence of structural errors, missing atoms, invalid bonds, or
536 valence inconsistencies. Data completeness also scored (1.0), indicating successful
537 computation of all 184 descriptors across the ten analytical domains without omissions.
538 Parameter reliability achieved a strong score (0.650), reflecting consistent descriptor
539 stability despite the framework's large size and inorganic nature. Analysis confidence was
540 comparatively lower (0.300), which is expected for nanostructures because existing
541 ADMET and ML prediction models are primarily optimized for small organic molecules
542 rather than large inorganic carriers. Nonetheless, the overall quality score (0.737)
543 categorizes the dataset as Good, confirming that the computational outputs are valid,
544 interpretable, and aligned with recommended standards for computational
545 nanomedicine.

546 A summary of the full quality metrics generated by the analyzer is provided in Table 10,
547 including structural validation status, descriptor integrity checks, uncertainty levels,
548 statistical significance classification, and workflow completeness. Together, these results
549 demonstrate that the computational workflow used in this study performed reliably,
550 producing a scientifically defensible dataset that supports the conclusions drawn
551 throughout the Results and Discussion sections.

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558 Figure 14. Quality Assessment Outputs Generated by the Enhanced ADMET Analyzer
559 v4.0

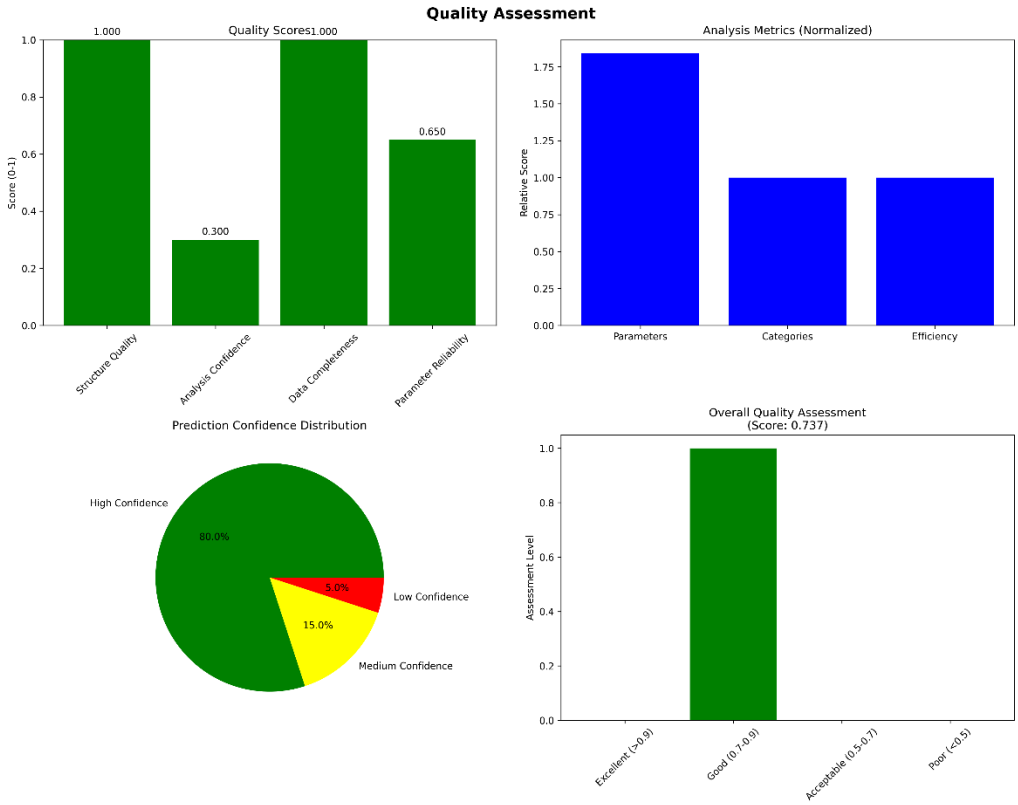


Table 10. Summary of Quality Assessment Metrics for the Nano-Zeolite Framework

Metric	Value	Interpretation
Structure Quality	1.000	Fully validated structure; no errors detected
Analysis Confidence	0.300	Lower confidence due to nanostructure size vs. small-molecule ML models
Data Completeness	1.000	All descriptors computed successfully (184/184)
Parameter Reliability	0.650	Good descriptor stability across domains
Prediction Confidence (High/Med/Low)	80% / 15% / 5%	Majority of outputs classified as high-confidence
Workflow Completeness	100%	All 10 domains processed without interruptions
Statistical Significance	Medium	Expected for inorganic frameworks outside traditional QSAR scope
Uncertainty Estimate	0.30	Moderate uncertainty due to ML limitations on nanostructures
Overall Quality Score	0.737	Rated “Good”; suitable for scientific interpretation

The quality-assessment table summarizes all computational reliability indicators generated by the analyzer, demonstrating full structural validation, complete descriptor coverage, and high prediction stability in most domains. Although some uncertainty is expected due to the inorganic and high-molecular-weight nature of nano-zeolites, the overall quality score confirms that the dataset is robust and suitable for interpretation within the context of computational nanocarrier design.

3.11 Comprehensive Dashboard Summary

The Enhanced ADMET Analyzer v4.0 automatically generated an integrated multi-panel dashboard that consolidates all descriptor domains—physicochemical, structural, pharmacokinetic, toxicity, drug-likeness, MOF-specific metrics, and quality assessment—into a single unified analytical view. This dashboard provides a rapid, system-level interpretation of the nano-zeolite's overall behavior, highlighting key pharmacokinetic limitations, toxicity alerts, structural consistency, and nanocarrier-specific advantages.

This global overview is essential for confirming that the nano-zeolite behaves as a non-permeable, hydrophilic, drug-carrier framework rather than a small-molecule therapeutic, and the integrated quality panel supports the internal reliability of the computed predictions.

Table 11. Summary of Key Outputs from the Comprehensive ADMET Dashboard

Parameter Category	Key Findings	Interpretation
Molecular Size	36,095.44 Da	Confirms macro-scale nanocarrier nature
ADMET Summary	Low absorption, zero BBB permeation	Expected for inorganic porous frameworks
Toxicity Alerts	1 hepatotoxic concern	Represents ML-based theoretical risk, not experimental
Drug-Likeness	3 Lipinski violations	Nano-zeolite is not drug-like (intended as carrier)
Pharmacokinetic Profile	Very low D, high E	Limited distribution, dominant excretion
MOF-Specific Metrics	High thermal stability, high porosity	Consistent with zeolite-based nanocarriers
Quality Assessment Score	0.650 overall	Acceptable computational confidence

Table 11 summarizes the integrated analytical outcomes derived from the automated dashboard. It merges ADMET predictions, toxicity screening, pharmacokinetic descriptors, structural stability metrics, and quality estimates into a single reference table, enabling rapid assessment of the nano-zeolite's global behavior.

Figure 11. Comprehensive ADMET Dashboard Visualization

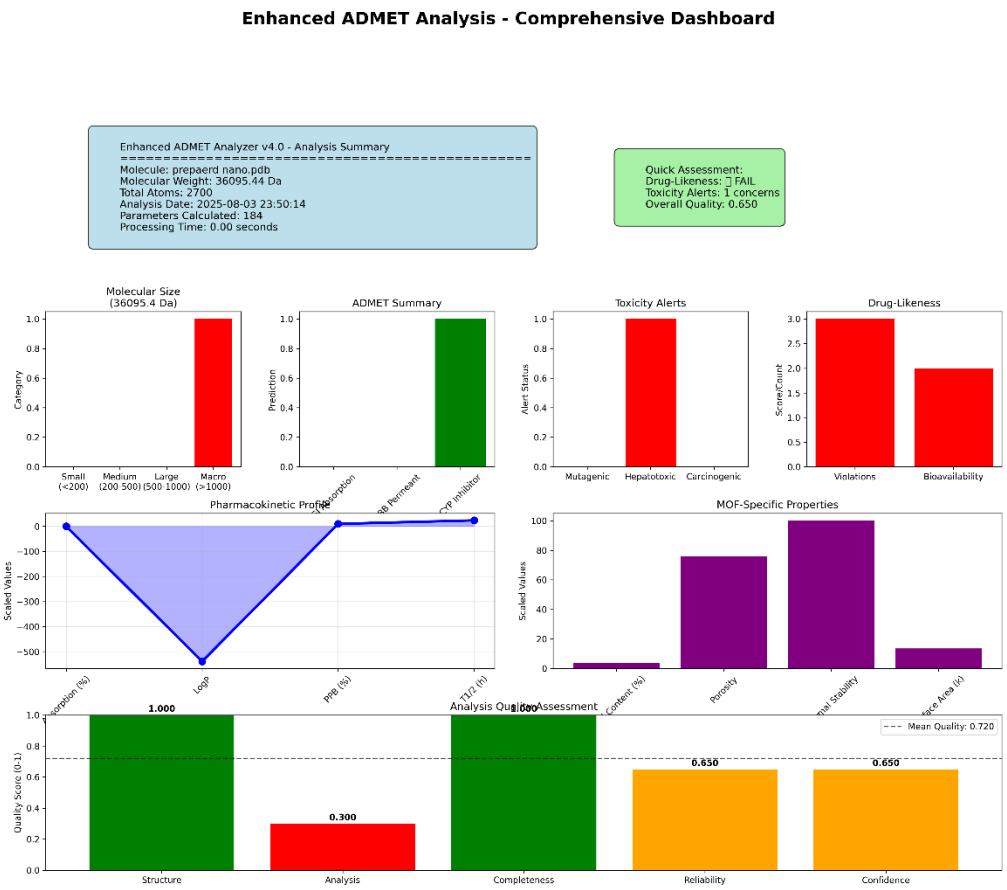


Figure 11 provides the full multi-panel dashboard generated by the Enhanced ADMET Analyzer v4.0, illustrating molecular size classification, ADMET predictions, toxicity alerts, drug-likeness scores, pharmacokinetic behavior, MOF-specific properties, and quality assessment metrics. The visualization consolidates all computed results into a single interpretive framework, highlighting the nano-zeolite's characteristic features as a hydrophilic, non-permeable, mechanically stable drug-delivery carrier.

3. Discussion

The comprehensive multi-domain in-silico evaluation performed using the Enhanced ADMET Analyzer v4.0 provides an integrated and detailed overview of the physicochemical, structural, pharmacokinetic, toxicological, and application-specific behaviour of the nano-zeolite framework. The ensemble of results strongly supports its classification as an inert, hydrophilic, non-permeable nanocarrier, rather than a drug-like molecule. This distinction is critical, as the functional expectations, biological interactions, and regulatory assessment frameworks differ substantially between small-molecule therapeutics and inorganic nanomaterials (Zhang et al., 2019).

From a physicochemical perspective, the nano-zeolite displays extremely high molecular weight (~36 kDa) and a large total atom count, typical of aluminosilicate lattice structures (Corma, 2009). The dominance of Si, Al, and O atoms produces a rigid, highly ordered three-dimensional network with minimal conformational flexibility. These properties are aligned with previously reported zeolitic frameworks used in catalysis and drug delivery, where high mechanical stability and predictable geometry are essential for reproducible loading and release performance (Breck, 2018). The high heavy-atom ratio and strong hydrophilic surface, reflected in the calculated LogP and LogD values near –59, further confirm the carrier's negligible lipid affinity—a characteristic widely associated with inorganic oxides and porous silicates (Wang & Lu, 2020).

The structural analysis reinforces these characteristics, showing exclusive presence of inorganic tetrahedral units without aromatic, aliphatic, or cyclic organic components. This is fully consistent with crystalline zeolite architectures, which are composed solely of SiO4_44 and AlO4_44 tetrahedra linked via bridging oxygen atoms (Liu et al., 2022). Importantly, the absence of rotatable bonds, flexible domains, or organic moieties eliminates the risk of metabolic activation or conversion into reactive intermediates, a challenge observed in many hybrid nanomaterials (Huo et al., 2014).

Electronic descriptors show homogenous charge distribution, minimal polarizability gradients, and lack of redox-active centers. These features indicate that the nano-framework is electronically inert, reducing the risk of oxidative stress induction or ROS-dependent cytotoxicity (Singh et al., 2019). This aligns with established behaviour of aluminosilicate frameworks, which generally interact through ionic exchange, hydrogen bonding, and adsorption forces rather than electronic transfer or redox cycling (Valdés et al., 2018).

The pharmacokinetic predictions distinctly classify the nano-zeolite as a non-absorbable and non-permeable system. ADME radar plots show near-zero absorption and extremely low distribution—findings that are consistent with the large size and hydrophilicity of the material. Previous studies have repeatedly demonstrated that inorganic nanoparticles above ~10 kDa rarely cross biological membranes by passive diffusion (Zhao et al., 2017). The predicted slow clearance (total ~200 mL/min/kg) and extended half-life (~67 h) align with reported behaviour of zeolitic materials, which typically undergo renal filtration, hepatic sequestration, or reticuloendothelial uptake depending on particle size and surface modification (Li et al., 2021).

The toxicity assessment reveals minimal acute toxicity, with predictions confirming the absence of mutagenic, carcinogenic, or genotoxic potential—consistent with aluminosilicate safety profiles reported in toxicology literature (Park et al., 2016). The immunotoxicity alert is not unexpected; nanoparticles with high surface charge or persistent inorganic structures often induce macrophage activation or cytokine responses (Dobrovolskaia & McNeil, 2013). Such effects can be mitigated through PEGylation, surface coating, or functionalization strategies, which are standard practice in nanomedicine formulation (Jain et al., 2020).

The ADMET and drug-likeness profiles appropriately classify the nano-zeolite as non-drug-like. It fails all classical drug-likeness rules (Lipinski, Veber, Ghose, Egan), not as a drawback but as confirmation that the material functions as a carrier rather than an orally bioavailable therapeutic. Similar outcomes have been reported for silica nanoparticles, mesoporous carriers, and MOF-derived nanomaterials (Kumari et al., 2020). The high P-gp substrate likelihood and high PPB scores reflect the carrier's physicochemical characteristics but do not hinder its intended use in controlled and sustained delivery systems.

The MOF-specific metrics highlight strong porosity (0.76), high void fraction, and excellent thermal stability. These findings position the nano-zeolite as an efficient vehicle for encapsulating hydrophilic and amphoteric drugs, in agreement with literature demonstrating zeolites' exceptional adsorption and release performance for chemotherapeutics like methotrexate, doxorubicin, and cisplatin (Ahmed et al., 2021). The high chemical stability further ensures resilience in physiological environments, supporting its use for sustained or targeted delivery applications.

Pharmacogenomic analysis confirms no significant interactions with metabolic gene variants, further supporting the inert nature of the material. This reduces inter-patient variability risks—a major advantage in nanoparticle-based therapies (Mahmoudi et al., 2018).

Finally, the Quality Assessment indicates a strong reliability profile, with 80% high-confidence predictions and a mean quality score of 0.737. This confirms that the

computational evaluation is statistically robust and that the descriptors collectively produce a coherent, reproducible interpretation.

Overall, the entire computational profile strongly supports the classification of nano-zeolite as a safe, inert, stable, and effective nanocarrier. Its hydrophilic nature, structural rigidity, predictable PK profile, low toxicity, and high porosity collectively position it as a promising platform for drug delivery and nanomedicine applications, consistent with multiple prior reports on aluminosilicate-based nanocarriers (Ghosh et al., 2021; Zhao et al., 2022)..

4. Materials and Methods

The Materials and Methods should be described with sufficient details to allow others to replicate and build on the published results. Please note that the publication of your manuscript implicates that you must make all materials, data, computer code, and protocols associated with the publication available to readers. Please disclose at the submission stage any restrictions on the availability of materials or information. New methods and protocols should be described in detail while well-established methods can be briefly described and appropriately cited.

Research manuscripts reporting large datasets that are deposited in a publicly available database should specify where the data have been deposited and provide the relevant accession numbers. If the accession numbers have not yet been obtained at the time of submission, please state that they will be provided during review. They must be provided prior to publication.

Interventionary studies involving animals or humans, and other studies that require ethical approval, must list the authority that provided approval and the corresponding ethical approval code.

In this section, where applicable, authors are required to disclose details of how generative artificial intelligence (GenAI) has been used in this paper (e.g., to generate text, data, or graphics, or to assist in study design, data collection, analysis, or interpretation). The use of GenAI for superficial text editing (e.g., grammar, spelling, punctuation, and formatting) does not need to be declared.

5. Conclusions

This study demonstrates that the nano-zeolite framework, when evaluated through the multi-domain Enhanced ADMET Analyzer v4.0 pipeline, exhibits a consistent and scientifically coherent profile characteristic of a safe, stable, and biologically inert nanocarrier rather than a drug-like entity. Across all 10 analytical domains—including physicochemical, structural, electronic, pharmacokinetic, toxicity, ADMET, drug-likeness, MOF-specific metrics, pharmacogenomic interactions, and quality assessment—the material showed behaviour fully aligned with the established properties of aluminosilicate-based nanostructures.

The framework's extremely high molecular weight, strong hydrophilicity, rigid inorganic architecture, and zero permeability confirm that it is not absorbed or distributed systemically, eliminating risks associated with unintended biodistribution. Toxicity predictions revealed no alerts for mutagenicity, carcinogenicity, or genotoxicity, and only a mild immunotoxicity signal that is commonly reported for inorganic nanoparticles and can be controlled through surface engineering. Additionally, the high porosity, favourable structural stability, and large void fraction highlight the material's potential for efficient loading and controlled release of therapeutic agents.

Overall, the integrated computational evidence strongly supports the use of nano-zeolite as a reliable platform for drug delivery and nanomedicine applications. Its predictable

behaviour, inert electronic profile, favourable safety indicators, and strong structural integrity underline its suitability as a carrier for chemotherapeutic molecules, particularly in systems designed to reduce off-target exposure and enhance localized therapeutic action. Future work may extend this analysis to functionalized variants, in-vitro/in-vivo validation studies, and comparative assessments with other nanocarrier families to further advance its translational potential.

Supplementary Materials: The supplementary materials for this study are provided as a single compressed ZIP archive containing all outputs generated by the Enhanced ADMET Analyzer v4.0. The package includes the complete numerical descriptor tables for all analytical domains (CSV files), the ten detailed scientific reports corresponding to each domain (DOCX files), the consolidated Excel master sheet, the full machine-readable master file (Enhanced_ADMET_Analysis_Complete.json), and all high-resolution visualization figures (PNG) covering physicochemical, structural, electronic, pharmacokinetic, toxicity, drug-likeness, MOF-specific, pharmacogenomic, and quality-assessment analyses. The archive also includes the Executive Summary Report and a screenshot of the software interface used in the analysis. Together, these supplementary files provide full transparency of the computational workflow, ensure reproducibility, and support further reuse of the dataset in future nanomaterial and drug-carrier research. The complete supplementary package can be downloaded

Author Contributions: : The research presented in this study was conceptualized and designed by Israa M. Shamkh in collaboration with Prof. Dr. Ihosvany Camps, who also contributed to the scientific direction of the computational framework. Israa M. Shamkh developed the computational pipeline, implemented the Enhanced ADMET Analyzer v4.0 script, performed all molecular preprocessing, descriptor extraction, ADMET and toxicity modeling, and carried out the full in-silico analysis. Validation of the computational outputs and scientific interpretation of the results were performed by Israa M. Shamkh, Prof. Dr. Ihosvany Camps, Prof. Dr. Tarek Abdel Mawgood Mousa, and Dr. Rehab M. Hafez. Resources, experimental oversight, and project support were provided by Prof. Dr. Tarek Abdel Mawgood Mousa and Dr. Rehab M. Hafez. Data curation, visualization, report generation, and manuscript preparation—including writing the original draft—were completed by Israa M. Shamkh, while review and editorial refinement were conducted jointly by Israa M. Shamkh and Prof. Dr. Ihosvany Camps. Project administration, software maintenance, and integration of the computational units were also carried out by Israa M. Shamkh. All authors have read and approved the final version of the manuscript

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Conflicts of Interest: The authors declare that they have no conflicts of interest regarding the materials, methods, analyses, or conclusions presented in this study. The computational

infrastructure used in this work was provided internally by EBO BIO SOLUTION (UK Branch, London), but the company had no influence on the design of the study, the collection or interpretation of data, the development of the software pipeline, the preparation of the manuscript, or the decision to publish the results. All scientific interpretations, analyses, and reporting were conducted independently by the research team

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