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Quantum Computing in Drug Discovery: A Comparative Analysis of Classical, Quantum, and Hybrid Approaches

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Abstract: Drug discovery is a complex, costly, and data-intensive process that depends increasingly on computational methods for molecular modelling, virtual screening, property prediction, and lead optimisation. Classical high-performance computing, molecular simulation, and machine-learning methods currently provide the practical foundation for computer-aided drug discovery; however, their accuracy and scalability can be constrained when electronic correlation, large conformational spaces, or combinatorial optimisation must be treated explicitly. Quantum computing offers an alternative computational paradigm in which molecular electronic states and selected optimisation problems may be represented more naturally. This narrative comparative review examines the respective roles of classical, quantum, and hybrid classical-quantum approaches across major drug-discovery tasks. The analysis considers computational accuracy, scalability, hardware maturity, data requirements, interpretability, workflow integration, and evidence of practical utility. Current evidence indicates that classical methods remain superior for routine high-throughput screening and production-scale modelling, whereas quantum methods are presently restricted mainly to small molecular systems, proof-of-concept studies, and carefully selected subproblems. Variational quantum eigensolvers, quantum machine-learning models, and hybrid optimisation workflows are promising, but their performance remains sensitive to noise, circuit depth, data encoding, active-space selection, and benchmark design. The most credible near-term pathway is therefore not wholesale replacement of classical computing, but targeted integration of quantum routines into validated classical pipelines. Progress toward pharmaceutical utility will require chemically meaningful benchmarks, fair comparisons against strong classical baselines, uncertainty reporting, reproducible software stacks, and experimental validation of quantum-generated candidates.

Keywords: Quantum Computing, Drug Discovery, Computational Chemistry, Quantum Machine Learning, Molecular Simulation, Hybrid Computing; Lead Optimisation, NISQ Devices.

1. Introduction

Drug discovery requires the identification and optimisation of molecules that interact selectively with biological targets while satisfying efficacy, safety, pharmacokinetic, and manufacturability constraints. Computational methods reduce the search burden by supporting target analysis, molecular docking, molecular dynamics, quantitative structure-activity relationship modelling, virtual screening, de novo design, and absorption-distribution-metabolism-excretion-toxicity prediction [1- 3]. Artificial intelligence has further expanded this toolkit by enabling representation learning, molecular generation, and data-driven prediction across large chemical and biological datasets [1]. Nevertheless, classical approaches remain dependent on approximations, available training data, and substantial computational resources, particularly when high-accuracy electronic-structure calculations or extensive conformational sampling are required [2, 3].

Quantum computing has attracted interest because molecular systems are intrinsically quantum mechanical and because selected quantum algorithms offer favourable theoretical scaling for electronic-structure, sampling, and optimisation problems [4, 5]. In contrast to classical bits, qubits may occupy superposition states and exhibit entanglement, allowing quantum circuits to encode and transform information in ways that have no direct classical analogue. However, present-day noisy intermediate-scale quantum devices have limited qubit counts, short coherence times, restricted connectivity, and non-negligible gate and measurement errors [6]. Consequently, the practical value of quantum computing in pharmaceutical research must be assessed against realistic hardware capabilities rather than against idealised asymptotic speed-ups alone.

Recent pharmaceutical perspectives have identified electronic-structure calculation, molecular property prediction, generative chemistry, combinatorial optimisation, and selected machine-learning tasks as potential application areas [7-10]. Proof-of-concept hybrid pipelines have also been reported for real-world drug-design problems, although such studies generally operate at modest scale and do not yet establish broad quantum advantage over state-of-the-art classical methods [9]. Quantum machine learning is developing rapidly, but its utility depends on data encoding, circuit expressibility, trainability, measurement cost, and comparison with appropriately tuned classical baselines [10, 11].

Against this background, this article provides a critical comparative analysis of classical, quantum, and hybrid approaches to drug discovery. It evaluates where each paradigm is currently useful, distinguishes demonstrated capability from theoretical potential, and identifies the technical and evidentiary requirements for responsible pharmaceutical adoption. The central premise is that quantum computing should be treated as a specialised emerging resource within a broader computational ecosystem, rather than as an immediate substitute for classical high-performance computing.

2. Review Scope and Comparative Framework

This article adopts a narrative comparative-review approach. The analysis is organised around peer-reviewed foundational studies, major reviews, pharmaceutical perspectives, and recent proof-of-concept applications published primarily between 2017 and 2026, while retaining seminal earlier work where necessary.

The comparison focuses on six criteria: (i) scientific task addressed, (ii) expected accuracy, (iii) scalability and computational cost, (iv) hardware and software maturity, (v) reproducibility and validation, and (vi) readiness for integration into pharmaceutical workflows. Because the literature is heterogeneous and does not use common datasets, hardware, or evaluation metrics, the article does not perform a meta-analysis and does not claim a quantitative cross-study performance ranking.

3. Classical Computing in Drug Discovery

3.1 Molecular Modelling and Simulation

Classical computing currently supports nearly every stage of computer-aided drug discovery. Molecular docking rapidly evaluates candidate binding poses and approximate interaction scores, while molecular dynamics simulates atomistic motion to examine conformational stability, binding-site flexibility, solvent effects, and kinetic behaviour [2, 3]. More computationally demanding approaches, including free-energy perturbation and quantum mechanics/molecular mechanics calculations, can improve energetic accuracy for selected systems but require extensive sampling and careful force-field or electronic-structure choices. Classical high-performance computing is therefore mature, scalable, and supported by established validation practices, but computational cost grows sharply with system size, simulation duration, and the level of physical detail.

3.2 Machine Learning and Virtual Screening

Machine-learning methods accelerate virtual screening and property prediction by learning relationships between molecular representations and experimentally measured outcomes [1]. Graph neural networks, transformer-based molecular models, kernel methods, and ensemble learners are used for activity prediction, molecular generation, toxicity assessment, and drug-target interaction modelling. Their practical strengths include rapid inference and compatibility with large compound libraries. Their limitations include dataset bias, domain shift, uncertain extrapolation, limited mechanistic interpretability, and the possibility that high benchmark performance does not translate into prospective experimental success.

4. Quantum Computing Foundations for Drug Discovery

4.1 Electronic-Structure Algorithms

Quantum simulation of molecular electronic structure is one of the best-established theoretical motivations for quantum computing. Early work demonstrated that molecular energies could be estimated with quantum phase estimation using resources that scale polynomially under suitable assumptions [12]. Fault-tolerant quantum phase estimation can, in principle, provide systematically improvable energy estimates, but its circuit depth and error-correction requirements exceed current hardware capabilities. Near-term research therefore emphasises variational quantum algorithms, particularly the variational quantum eigensolver, which combines a parameterised quantum circuit with a classical optimiser [13]. Hardware-efficient ansätze reduce circuit depth but may introduce optimisation and accuracy trade-offs [14].

4.2 Quantum Machine Learning and Optimisation

Quantum machine-learning approaches use quantum feature maps, variational circuits, quantum kernels, or hybrid neural architectures for classification, regression, and molecular generation [10, 11]. Potential applications include activity prediction, ADME-Tox modelling, molecular property estimation, and chemical-space exploration. Quantum optimisation algorithms have also been proposed for molecular docking, conformer selection, and combinatorial design. At present, however, most studies use small datasets, low-dimensional molecular encodings, simulators, or limited quantum hardware. Consequently, observed performance differences may arise from modelling choices rather than from an intrinsic computational advantage.

5. Comparative Analysis of Classical and Quantum Approaches

Table 1 summarises the comparative position of classical, quantum, and hybrid approaches.

Classical methods offer the highest operational maturity and remain preferable when millions of compounds must be screened, when validated software and force fields are available, or when regulatory traceability is required.

Quantum methods are potentially valuable for electronically complex subproblems and specialised optimisation tasks, but present performance is constrained by hardware noise and resource limitations.

Hybrid approaches are currently the most realistic strategy because they allocate data preparation, large-scale search, and workflow orchestration to classical systems while reserving selected subproblems for quantum processing [8, 9].

Table 1. Comparative characteristics of classical, quantum, and hybrid computing in drug discovery

Criterion	Classical computing	Quantum computing	Hybrid classical-quantum
Current maturity	Production-ready for routine modelling and screening	Experimental; mainly proof-of-concept	Early integration stage
Primary strengths	Scalability, mature software, reproducibility, large datasets	Natural representation of quantum states; potential algorithmic advantages	Combines mature classical workflows with targeted quantum routines
Primary limitations	Approximation error, sampling cost, difficult high-level electronic correlation	Noise, limited logical qubits, circuit depth, measurement overhead	Integration complexity, latency, benchmark dependence
Best-supported tasks	Docking, molecular dynamics, virtual screening, ML prediction	Small-molecule electronic structure and exploratory QML	Active-space calculations, selected optimisation and molecular-design subroutines
Evidence of advantage	Established practical utility	No general pharmaceutical quantum advantage established	Promising in selected demonstrations; requires stronger validation
Near-term role	Default computational platform	Research and benchmarking platform	Most plausible adoption pathway

6. Role in Lead Identification and Optimisation

Lead identification requires efficient traversal of chemical space, whereas lead optimisation requires accurate prediction of how structural modifications affect potency, selectivity, solubility, metabolism, toxicity, and synthetic feasibility. Classical generative models and optimisation algorithms can propose large numbers of candidates, but their rankings remain dependent on learned priors and approximate scoring functions. Quantum-enhanced workflows may contribute by refining electronic energies, representing difficult correlation effects, or solving constrained optimisation subproblems. A recent hybrid pipeline demonstrated how quantum routines can be embedded within a broader drug-design workflow, but such results should be interpreted as feasibility evidence rather than proof of scalable superiority [9].

The strongest near-term use case is therefore selective quantum refinement. A classical pipeline may first reduce a library from millions of compounds to a manageable set, after which higher-accuracy classical quantum chemistry or quantum-assisted electronic-structure calculations can be applied to a small number of chemically important candidates. This staged design avoids using scarce quantum resources for tasks that classical methods already perform efficiently.

7. Chemical-Space Exploration and Quantum Machine Learning

Chemical space is extraordinarily large, and practical drug discovery relies on guided sampling rather than exhaustive enumeration. Quantum kernels and variational quantum models may transform molecular descriptors into high-dimensional feature spaces, potentially improving the separation of complex activity classes [10, 11]. Quantum generative models have also been proposed for producing novel molecular structures. Nevertheless, a useful comparison must account for training-set size, descriptor construction, hyperparameter optimisation, model capacity, sampling cost, and uncertainty. Claims of quantum advantage are not persuasive when quantum models are compared only with weak or untuned classical baselines.

Prospective validation is especially important. A model that performs well on a retrospective benchmark may fail to identify experimentally active compounds because of data leakage, chemical-series overlap, assay heterogeneity, or distribution shift. Quantum-generated or quantum-ranked molecules should therefore be assessed using the same medicinal-chemistry filters, synthesis constraints, biophysical assays, and cellular validation procedures applied to conventionally designed candidates. Recent experimental studies indicate that quantum-assisted workflows can contribute to candidate identification, but the field still lacks broad, independently replicated evidence across targets and therapeutic areas [15].

8. NISQ Devices and Hybrid Pipelines

Current quantum processors belong largely to the NISQ regime [6]. Their limited coherence and gate fidelity restrict the number of operations that can be executed before noise dominates the result. Error-mitigation techniques, circuit compilation, qubit tapering, symmetry reduction, and active-space selection can improve performance, but each introduces additional assumptions or computational overhead. Variational algorithms are comparatively compatible with shallow circuits, yet they may suffer from barren plateaus, optimiser instability, shot noise, and ansatz bias.

Hybrid pipelines address these limitations by partitioning the workload. Classical systems perform molecular featurisation, dataset management, large-scale screening, optimisation control, and post-processing, while the quantum processor evaluates a circuit-based subroutine. This model aligns with current cloud-access architectures and allows gradual

adoption. However, hybridisation does not automatically confer advantage: data-transfer cost, repeated measurements, queue latency, and classical optimisation may dominate total runtime. End-to-end cost and accuracy must therefore be reported, not only the execution time of the quantum circuit.

9. Software Frameworks, Reproducibility, and Benchmarking

Practical quantum-drug-discovery research depends on interoperable software connecting cheminformatics, electronic-structure packages, machine-learning libraries, and quantum software development kits. Reproducibility requires disclosure of molecular geometries, basis sets, active spaces, fermion-to-qubit mappings, ansätze, optimisers, circuit depths, shot counts, hardware calibration data, error-mitigation procedures, random seeds, and classical baselines. Without these details, apparently favourable results cannot be independently assessed.

Benchmarking should use chemically meaningful tasks and report accuracy, computational resources, uncertainty, scalability, and failure modes. For electronic-structure studies, quantum results should be compared with appropriate classical reference methods rather than with deliberately low-level approximations. For machine learning, evaluations should include scaffold or temporal splits where relevant, repeated runs, confidence intervals, ablation studies, and strong classical models. For docking or optimisation, the full pipeline should be assessed using experimentally grounded poses, affinities, or prospective hit rates. Standardised benchmark suites are required before the field can distinguish hardware progress from dataset- or implementation-specific effects.

10. Industrial Adoption, Security, and Societal Considerations

Pharmaceutical companies are exploring quantum computing through collaborations with hardware providers, software developers, and academic groups. Current activity is primarily exploratory and focuses on capability building, algorithm development, and identification of commercially relevant subproblems. Broad deployment will depend on evidence that quantum-assisted methods improve decision quality, turnaround time, or research productivity relative to existing high-performance-computing workflows. Regulatory use will additionally require validation, auditability, version control, and clear documentation of model limitations.

Quantum adoption also raises security and equity considerations. Sensitive chemical structures, proprietary assay results, and patient-derived datasets require strong governance when processed through external cloud services. Future cryptographically relevant quantum computers may threaten conventional public-key systems, making migration to post-quantum cryptography an important organisational consideration. Unequal access to advanced hardware could also concentrate innovation within well-resourced organisations. Shared benchmarks, transparent

reporting, public research infrastructure, and workforce development are therefore important for equitable scientific progress.

11. Challenges and Limitations

The principal limitations are hardware noise, insufficient logical qubits, costly error correction, limited circuit depth, measurement overhead, and uncertain scaling from toy systems to drug-like molecules. Algorithmically, quantum chemistry calculations require careful orbital and active-space selection, while quantum machine learning faces data-loading, trainability, and generalisation challenges. At the evidence level, many publications rely on simulators or small datasets and report task-level metrics without demonstrating end-to-end pharmaceutical value. The literature also contains substantial heterogeneity in hardware, datasets, baselines, and evaluation procedures, which prevents straightforward comparison.

This review is narrative rather than systematic and is therefore not an exhaustive bibliometric account. Its conclusions should be interpreted as a critical synthesis of representative literature rather than as a quantitative estimate of effect size. Rapid hardware and algorithmic development may also change the assessment of particular applications. Even so, the present evidence supports a cautious conclusion: quantum computing is scientifically relevant to drug discovery, but broad practical advantage has not yet been established.

12. Future Research Directions

Future research should prioritise error-corrected architectures, lower-overhead algorithms, chemistry-informed circuit design, robust active-space strategies, and end-to-end hybrid workflows. Benchmark datasets should include molecules that are difficult for classical methods for scientifically identifiable reasons, rather than merely molecules small enough to fit available devices. Resource estimates should report logical and physical qubit requirements, circuit depth, measurement demand, wall-clock time, energy use, and classical preprocessing. For quantum machine learning, future studies should compare against strong classical baselines under identical data splits and optimisation budgets. Prospective experimental validation should become a central criterion, particularly for generated molecules and predicted activities. Industrial studies should report whether quantum components change project decisions, reduce failed synthesis, improve hit quality, or accelerate lead optimisation. Progress will be most credible when quantum algorithms are evaluated as components of complete, reproducible, and experimentally validated drug-discovery pipelines.

13. Conclusion

Quantum computing offers a scientifically compelling route for addressing selected challenges in molecular simulation, chemical-space exploration, and optimisation. Its most

important conceptual advantage is the ability to represent and manipulate quantum states directly, which may ultimately improve the treatment of electronically complex molecular systems. However, contemporary drug discovery continues to depend on classical high-performance computing, molecular simulation, cheminformatics, and machine learning because these technologies are mature, scalable, and extensively validated. Present quantum devices remain limited by noise, circuit depth, qubit quality, measurement overhead, and the absence of broadly accepted pharmaceutical benchmarks. Accordingly, general claims that quantum computing is already faster, more accurate, or more economical than classical computing are not supported across routine drug-discovery tasks. The most realistic near-term strategy is a hybrid architecture in which classical systems conduct data-intensive screening, workflow management, and optimisation, while quantum processors address carefully selected subproblems for which a credible computational rationale exists. Future progress should be judged through fair classical comparisons, transparent resource accounting, reproducible implementation, uncertainty analysis, and prospective experimental validation. Quantum computing may eventually become an important component of pharmaceutical research, but its impact will depend less on theoretical promise than on demonstrable improvements in chemically and clinically meaningful decisions.

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The Author's have no conflicts of interest to declare that they are relevant to the content of this article.

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