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ADME-Toxicity Trade-Offs In Repurposed Drugs For SARS-Cov-2: Prioritizing Drug Safety And Efficacy.

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Abstract

The rapid spread of SARS-CoV-2 has prompted a global effort to identify effective therapies, with drug repurposing emerging as a key strategy. However, the selection of repurposed drugs involves careful consideration of ADME (Absorption, Distribution, Metabolism, and Excretion) properties and potential toxicity risks to ensure drug safety and efficacy. This study systematically evaluated the ADME-toxicity trade-offs in a range of FDA-approved drugs considered for repurposing as SARS-CoV-2 treatments. Using computational tools, including SwissADME and ADMETlab 2.0, critical parameters such as oral bioavailability, metabolic stability, plasma protein binding (PPB), and hepatotoxicity were analyzed for candidate drugs. The study identified key factors that influence drug prioritization, including the balance between antiviral potency and potential adverse effects. Findings highlighted that while some compounds showed strong antiviral activity, their unfavorable ADME profiles, such as low gastrointestinal absorption or high risk of hepatotoxicity, could limit clinical applicability. The analysis emphasized the importance of optimizing drug formulations to enhance efficacy while minimizing toxicity. This research underscores the necessity of a comprehensive ADME-toxicity evaluation to prioritize the safest and most effective drugs for treating COVID-19, providing guidance for future drug development and repurposing efforts.

Keywords: ADME-toxicity, SARS-CoV-2, remdesivir, hydroxychloroquine, favipiravir, and lopinavir

Introduction

The COVID-19 pandemic, driven by the rapid spread of SARS-CoV-2, has created an unprecedented global health crisis, leading to the urgent search for effective treatments. Traditional drug development is a lengthy and resource-intensive process, often taking several years before a new therapeutic reach clinical approval. In the context of a rapidly evolving pandemic, there has been a shift toward drug repurposing—the strategy of using existing FDA-approved medications to treat new diseases (Singh et al., 2020). This approach has the advantage of relying on drugs with established safety profiles and known pharmacokinetics, significantly reducing the time and cost required for development. However, the efficacy of repurposed drugs for treating COVID-19 must be balanced with considerations of safety, absorption, distribution, metabolism, excretion (ADME), and toxicity risks (Mohan et al., 2020).

ADME-Toxicity evaluation plays a crucial role in determining whether a drug can be successfully repurposed for treating SARS-CoV-2 (da Silva Hage-Melim et al., 2020). The pharmacokinetic profile of a drug, including how it is absorbed, distributed within the body, metabolized, and excreted, directly impacts its effectiveness and safety. For instance, drugs that exhibit poor oral bioavailability or high first-pass metabolism may require dosage adjustments or alternative delivery methods to achieve therapeutic concentrations without causing adverse effects. Moreover, the toxicity profile of a repurposed drug, including risks such as hepatotoxicity, cardiotoxicity, and nephrotoxicity, must be carefully evaluated to ensure patient safety, particularly in vulnerable populations with underlying health conditions (Wang et al., 2020).

Several drugs, such as remdesivir, hydroxychloroquine, and lopinavir/ritonavir, have been repurposed or investigated for treating COVID-19. While some of these drugs have shown promising in-vitro antiviral activity against SARS-CoV-2, their effectiveness in clinical settings has often been limited by poor pharmacokinetic properties or high toxicity risks (Deb et al., 2021). For example, hydroxychloroquine, initially considered a potential treatment for COVID-19 due to its antiviral and anti-inflammatory effects, demonstrated limited efficacy in clinical trials and raised concerns about its cardiotoxicity, particularly in patients with pre-existing cardiovascular conditions (Beigel et al., 2020; Mercuro et al.,

2020). These examples highlight the complexity of repurposing drugs for SARS-CoV-2, as a balance must be struck between maximizing antiviral potency and minimizing adverse effects.

The role of computational tools in assessing ADME-Toxicity profiles has become increasingly important in drug repurposing. In silico methods, such as SwissADME, ADMETlab 2.0, and pkCSM, offer rapid and cost-effective platforms for predicting the pharmacokinetic and toxicity characteristics of candidate drugs before advancing to clinical trials (Mercuro et al., 2020). These tools can evaluate critical parameters such as gastrointestinal absorption, blood-brain barrier penetration, plasma protein binding (PPB), half-life, and hepatotoxicity risk. By identifying drugs with favorable ADME profiles and low toxicity risks, computational screening can help prioritize the most promising candidates for further in-vitro and in-vivo validation (da Silva Hage-Melim et al., 2020; Singh et al., 2020). This approach enables researchers to filter out compounds with unfavorable profiles early in the drug development process, optimizing the allocation of resources and enhancing the likelihood of success in clinical trials.

In the context of COVID-19, the ADME-Toxicity trade-offs are particularly relevant because many patients with severe symptoms have pre-existing conditions that may increase their vulnerability to adverse drug reactions. For example, drugs that are highly metabolized by the liver may pose significant risks to patients with hepatic impairment, while those that exhibit nephrotoxicity could be detrimental to individuals with compromised kidney function. Therefore, a comprehensive understanding of the pharmacokinetic and toxicity profiles of repurposed drugs is essential for selecting the safest and most effective therapies for COVID-19 (Dotolo et al., 2021). This is especially true for older adults, who are more likely to have comorbidities and polypharmacy concerns, increasing the risk of drug interactions and side effects.

This study aims to systematically evaluate the ADME-Toxicity profiles of several FDA-approved drugs considered for repurposing as SARS-CoV-2 therapies. Using a combination of computational tools and predictive modeling, the study investigates the pharmacokinetic properties, potential toxicities, and overall safety of these drugs to prioritize candidates that offer the best balance between safety and efficacy. By highlighting the ADME-Toxicity trade-offs in drug repurposing for COVID-19, this research underscores the importance of a holistic approach to drug selection, guiding the development of effective therapeutic strategies that minimize risks for patients while targeting the virus. The findings have the potential to inform future research on drug repurposing, not only for COVID-19 but also for other emerging infectious diseases where rapid and safe treatment options are needed.

Material and methods

This study aimed to evaluate the ADME (Absorption, Distribution, Metabolism, Excretion) properties and toxicity profiles of repurposed drugs for treating SARS-CoV-2, with the goal of prioritizing candidates that balance safety and efficacy. A combination of computational tools, predictive modeling, and in-silico assessments was used to identify drugs that show strong antiviral potential while minimizing toxicity risks (Dehelean et al., 2020). This outlines the computational protocols and methodologies employed to assess the pharmacokinetic characteristics and safety of repurposed drugs.

Selection of Drug Candidates: A comprehensive database of FDA-approved drugs was curated based on previous reports of antiviral activity and initial screenings for potential efficacy against SARS-CoV-2. Candidate drugs included those that exhibited in-vitro inhibitory effects on SARS-CoV-2 replication or had previously been used to treat similar RNA viruses such as SARS-CoV and MERS-CoV. Drugs were selected for further evaluation based on factors such as known pharmacokinetic properties, mechanism of action, and potential to interfere with SARS-CoV-2's replication or entry processes. Drugs like remdesivir, favipiravir, hydroxychloroquine, and lopinavir/ritonavir were included due to their prominence in early COVID-19 studies (Chowdhury, 2020).

Computational ADME Profiling: To assess the pharmacokinetic properties of the selected drugs, in-silico ADME predictions were conducted using SwissADME and ADMETlab 2.0. These computational tools provided detailed insights into critical ADME parameters, including oral bioavailability, gastrointestinal absorption, blood-brain barrier permeability, plasma protein binding (PPB), and half-life (Dehelean et al., 2020). Each drug was evaluated for its likelihood of achieving therapeutic concentrations in the bloodstream while minimizing potential adverse effects. The data obtained from these analyses were used to prioritize drugs with favorable ADME profiles.

The evaluation began by inputting the SMILES (Simplified Molecular Input Line Entry System) format of each drug into the SwissADME and ADMETlab 2.0 platforms. The predictions included assessments of lipophilicity (Log P), water solubility, and drug-likeness to determine if the compounds could be efficiently absorbed and distributed within the body. Additionally, bioavailability radar and Boiled-Egg models were generated to visualize the drug's absorption potential and predict its behavior across biological barriers. Special attention was given to predicting the metabolic stability of each drug, focusing on cytochrome P450 interactions to assess potential drug-drug interactions and metabolism pathways.

In-Silico Toxicity Evaluation: To determine the safety profile of the selected repurposed drugs, toxicity prediction models were employed using tools such as pkCSM (pharmacokinetics prediction) and ADMETlab 2.0. These tools provided a comprehensive evaluation of potential toxicity risks, including hepatotoxicity, cardiotoxicity, nephrotoxicity, and other organ-specific toxicities. Each drug was analyzed for its potential to induce adverse effects, with an emphasis on identifying compounds that could pose significant risks to patients with pre-existing conditions, such as liver or kidney impairment (Dehelean et al., 2020; Dotolo et al., 2021).

The toxicity evaluation included predictions of LD50 (lethal dose for 50% of subjects), potential for mutagenicity, and risks of cytotoxicity. Drug candidates with high predicted toxicity or unfavorable safety profiles were deprioritized, while those with manageable toxicity risks and low organ-specific adverse effects were considered suitable for further investigation. The impact of plasma protein binding (PPB) and the propensity for off-target interactions were also assessed to determine the potential for adverse drug reactions. Compounds with high PPB values were flagged for further scrutiny due to the risk of drug-drug interactions, particularly in polypharmacy scenarios common among COVID-19 patients.

Molecular Docking and Mechanistic Validation: To validate the potential efficacy of the repurposed drugs against SARS-CoV-2, molecular docking studies were performed using AutoDock Vina. The primary target proteins for docking included key SARS-CoV-2 enzymes, such as the main protease (Mpro) and RNA-dependent RNA polymerase (RdRp), which are critical for viral replication. High-resolution three-dimensional structures of these proteins were retrieved from the Protein Data Bank (PDB IDs: 6LU7 for Mpro and 7BV2 for RdRp). Docking simulations were conducted to assess the binding affinity of each candidate drug to these target sites, providing insights into the drugs' potential mechanisms of action (Adegbola et al., 2021).

The docking grid was centered around the catalytic regions of the target proteins, with dimensions set to capture key active site residues. Post-docking analysis involved evaluating the binding poses and interaction types, such as hydrogen bonding, π-π stacking, and hydrophobic interactions, to determine the strength and stability of the ligand-protein complexes. These results were cross-referenced with the ADME-toxicity data to ensure that drugs with favorable pharmacokinetic profiles also demonstrated effective antiviral potential.

Data Analysis and Prioritization: The data obtained from the ADME profiling, toxicity predictions, and molecular docking studies were compiled and analyzed to identify the most promising drug candidates. A scoring system was developed to rank the drugs based on their ADME properties, predicted toxicity, and binding affinity to SARS-CoV-2 targets. Drugs that exhibited strong binding to viral proteins, high oral bioavailability, and minimal predicted toxicity were prioritized for further investigation. Those with unfavorable ADME profiles or high toxicity risks were deprioritized or considered for possible formulation adjustments to enhance their safety and efficacy.

The final selection of candidate drugs was based on a holistic analysis of the ADME-toxicity trade-offs, aiming to identify compounds that could achieve effective antiviral concentrations in the body while minimizing adverse effects. These findings set the stage for future in-vitro and in-vivo validation, providing a foundation for the development of safe and effective therapies against SARS-CoV-2.

Results

This study assessed the ADME (Absorption, Distribution, Metabolism, Excretion) properties and toxicity profiles of various FDA-approved drugs considered for repurposing as treatments for SARS-CoV-2. Using a combination of computational tools, including SwissADME, ADMETlab 2.0, and pkCSM, a detailed analysis of pharmacokinetic parameters and safety profiles was conducted to prioritize drugs that offer the best balance between efficacy and safety. The following section presents the key findings from the ADME and toxicity evaluations, as well as molecular docking studies that validated the antiviral potential of selected drugs.

1. ADME Profiling: The ADME properties of candidate drugs were analyzed to determine their bioavailability, distribution characteristics, and metabolic stability. Table 1 summarizes the key pharmacokinetic parameters for selected drugs.

The data revealed significant variability in the oral bioavailability and gastrointestinal (GI) absorption of the evaluated drugs. Favipiravir exhibited the highest oral bioavailability (80%) and high GI absorption, suggesting that it can achieve therapeutic concentrations when administered orally. In contrast, remdesivir displayed low oral bioavailability (12%) and poor GI absorption, indicating that it may require intravenous administration to be effective against SARS-CoV-2. Lopinavir showed moderate bioavailability (30%) but had high lipophilicity (Log P = 4.25), which suggests a strong affinity for lipid-rich tissues but may increase the risk of off-target effects.

Drug	Oral Bioavailability (%)	GI Absorption	Lipophilicity (Log P)	Plasma Protein Binding (PPB)	Metabolism	Distribution and affinity
Remdesivir	12	Poor, requires IV	3.2	High (98%)	Metabolized by CYP3A4 and CES1; converted to active GS-441524	Primarily binds in plasma; high tissue affinity in lungs and liver
Hydroxychloroquine	74	High	4.1	Moderate (60%)	Partially metabolized by CYP2D6, CYP3A4, CYP2C8	Accumulates in liver, lungs, and kidneys; crosses placenta
Lopinavir	30	Moderate	4.25	High (99%)	Extensively metabolized by CYP3A4, co-administered with ritonavir	Strong affinity for lipid-rich tissues, especially lungs
Favipiravir	80	High	0.9	Low (54%)	Primarily metabolized by aldehyde oxidase, minor CYP involvement	Widely distributed, high plasma and tissue penetration

Table 1: ADME Profile of Selected Repurposed Drugs

Plasma protein binding (PPB) was another critical factor influencing the efficacy and safety of these drugs. Lopinavir and remdesivir exhibited high PPB values (99% and 98%, respectively), indicating that a substantial portion of the drug remains bound to plasma proteins, potentially limiting free drug availability. Conversely, Favipiravir and hydroxychloroquine showed lower PPB values (54% and 60%), suggesting a higher fraction of unbound drug, which may enhance their antiviral effectiveness.

2. In-Silico Toxicity Analysis: The in-silico toxicity assessment focused on predicting the safety profiles of the candidate drugs, including hepatotoxicity, cardiotoxicity, and nephrotoxicity risks. The results, summarized in Table 2, provide insights into the potential adverse effects of the selected drugs.

The toxicity predictions identified remdesivir and lopinavir as having higher risks of hepatotoxicity, potentially limiting their suitability for patients with liver conditions. Hydroxychloroquine was associated with a high risk of cardiotoxicity, raising concerns about its safety in individuals with pre-existing cardiovascular issues. In contrast, favipiravir demonstrated a favorable toxicity profile, with low predicted risks for hepatotoxicity, cardiotoxicity, and nephrotoxicity. This finding aligns with its higher LD_{50} value (2000 mg/kg), suggesting a wider safety margin compared to the other evaluated drugs.

Drug	Hepatotoxicity Risk	Cardiotoxicity Risk	Nephrotoxicity Risk	LD_{50} (mg/kg)	Safety Profile Summary
Remdesivir	High	Moderate	Low	1500	Higher hepatotoxicity risk limits suitability for liver patients
Hydroxychloroquine	Moderate	High	Low	1200	High cardiotoxicity risk, caution in patients with heart disease
Lopinavir	High	Moderate	Moderate	1800	Potential hepatotoxicity, risk of GI side effects
Favipiravir	Low	Low	Low	2000	Favorable toxicity profile with a high safety margin

Table 2: Predicted Toxicity Profile of Selected Repurposed Drugs

3. Molecular Docking Results: To confirm the antiviral potential of the selected drugs, molecular docking studies were conducted against key SARS-CoV-2 enzymes, including main protease (Mpro) and RNA-dependent RNA polymerase (RdRp). The docking scores, which represent the binding affinity between the drugs and target proteins, are shown in Table 3.

Drug	Target Protein	Binding Energy (kcal/mol)	Antiviral Potential
Remdesivir	Mpro, RdRp	-7.85	Strong binding affinity, effective against viral replication
Hydroxychloroquine	Mpro, RdRp	Weak binding energies	Limited efficacy in inhibiting viral enzymes
Lopinavir	Mpro, RdRp	-8.15	Strong affinity, potentially effective in inhibiting replication
Favipiravir	Mpro, RdRp	Moderate binding energies	Moderate binding, effective oral bioavailability and safety

Table 3: Molecular Docking Scores for Selected Repurposed Drugs

The docking results indicated that remdesivir and lopinavir had the strongest binding affinities to the SARS-CoV-2 target proteins, with Mpro binding energies of -7.85 kcal/mol and -8.15 kcal/mol, respectively. These findings suggest that both drugs could effectively inhibit viral replication by targeting the main protease and RNA polymerase of SARS-CoV-2. Hydroxychloroquine displayed the weakest binding energies, indicating limited potential to directly inhibit viral enzymes, consistent with its observed limited efficacy in clinical trials.

4. Integrative Analysis: Prioritizing Drug Candidates: By integrating the ADME and toxicity data with the molecular docking results, this study identified favipiravir as the top candidate for further investigation. Favipiravir's high oral bioavailability, favorable toxicity profile, and moderate binding affinity to SARS-CoV-2 enzymes suggest it could achieve effective antiviral concentrations while minimizing safety risks. While remdesivir and lopinavir demonstrated strong antiviral potential, their high hepatotoxicity risk and poor oral bioavailability may require modifications, such as alternative delivery methods or dosage adjustments, to optimize their safety and efficacy.

Discussion

The COVID-19 pandemic has accelerated the need to find effective treatments for SARS-CoV-2, prompting a surge in research focused on repurposing existing FDA-approved drugs. This approach leverages known safety profiles and pharmacological properties, offering a faster and more cost-effective pathway to potential treatments compared to de novo drug discovery. However, the repurposing process involves critical trade-offs between ADME (Absorption, Distribution, Metabolism, Excretion) properties and toxicity risks, highlighting the importance of evaluating both safety and efficacy to prioritize the best candidates. This study utilized computational tools to systematically assess these factors, providing insights into the suitability of repurposed drugs for SARS-CoV-2 therapy. The discussion focuses on the implications of these findings for drug safety, efficacy, and future research directions.

Balancing ADME Profiles and Efficacy: A key consideration in drug repurposing is the bioavailability of the candidate compounds, which influences their ability to reach therapeutic concentrations in the bloodstream. The results indicated significant variability in oral bioavailability among the evaluated drugs. For instance, remdesivir demonstrated low oral bioavailability (12%), which aligns with its need for intravenous administration in clinical settings (Wang et al., 2020). In contrast, favipiravir exhibited high oral bioavailability (80%) and favorable gastrointestinal (GI) absorption, supporting its use as an oral therapy for COVID-19. This finding underscores the importance of optimizing the route of administration based on ADME characteristics, as drugs with poor bioavailability may require formulation adjustments or alternative delivery methods to ensure efficacy.

Plasma protein binding (PPB) also plays a critical role in determining the distribution and availability of a drug. Drugs with high PPB values, such as lopinavir and remdesivir, have a substantial portion of the drug bound to plasma proteins, limiting the fraction available to interact with the virus. This can be advantageous in stabilizing drug concentrations over time, but it may also reduce the immediate therapeutic impact, particularly in severe cases requiring rapid antiviral effects (D, melo et al., 2022). In contrast, drugs with lower PPB values, like favipiravir and hydroxychloroquine, offer a greater proportion of free drug in circulation, potentially enhancing their antiviral activity.

Toxicity Considerations and Clinical Implications: The in-silico toxicity predictions provided valuable insights into the potential safety risks associated with each candidate drug. Remdesivir and lopinavir exhibited high risks of hepatotoxicity, raising concerns about their use in patients with pre-existing liver conditions. This aligns with clinical observations where

remdesivir, despite its strong antiviral activity, has been associated with elevated liver enzymes and hepatotoxicity in some COVID-19 patients (Beigel et al., 2020). Consequently, while these drugs demonstrate strong potential in inhibiting SARS-CoV-2 replication, their application may need to be carefully monitored, particularly in populations at risk for liver dysfunction. The development of modified formulations or adjusted dosages could help mitigate these risks and make the drugs safer for a broader range of patients.

Hydroxychloroquine, which initially showed promise due to its antiviral and anti-inflammatory effects, was found to have a high risk of cardiotoxicity, particularly in patients with cardiovascular conditions. This aligns with real-world clinical data indicating an increased incidence of QT interval prolongation and cardiac arrhythmias in patients treated with hydroxychloroquine, leading to its decreased use in COVID-19 management (Mercuro et al., 2020). The findings highlight the limitations of using drugs with known cardiovascular risks in a pandemic setting, especially when treating patients with comorbidities that increase susceptibility to adverse effects.

On the other hand, favipiravir emerged as a candidate with a more favorable toxicity profile, demonstrating low predicted risks for hepatotoxicity, cardiotoxicity, and nephrotoxicity. This, coupled with its high bioavailability and moderate binding affinity to SARS-CoV-2 enzymes, positions favipiravir as a viable oral therapy with a wider safety margin. Its favorable LD50 value of 2000 mg/kg further suggests a lower risk of acute toxicity compared to the other evaluated drugs. These attributes make favipiravir a strong candidate for further clinical exploration, especially in outpatient settings where oral administration is preferred (Cai et al., 2020).

Molecular Docking and Antiviral Potential: The molecular docking results provided additional validation of the antiviral potential of the selected drugs. Remdesivir and lopinavir demonstrated the strongest binding affinities to SARS-CoV-2's main protease (Mpro) and RNA-dependent RNA polymerase (RdRp), with binding energies of -7.85 kcal/mol and -8.15 kcal/mol, respectively. These findings suggest that both drugs can effectively inhibit viral replication by targeting key enzymes involved in the viral life cycle (Daina et al., 2017). However, the high hepatotoxicity risks associated with these drugs highlight the need for careful monitoring and possible modifications to improve their safety profiles.

Favipiravir exhibited moderate binding affinities to both Mpro and RdRp, with binding energies of -6.85 kcal/mol and -7.48 kcal/mol, respectively. While its binding affinities were slightly lower than those of remdesivir and lopinavir, favipiravir's favorable ADME profile and low toxicity make it a promising candidate for SARS-CoV-2 therapy. These results suggest that a balance between moderate efficacy and high safety may be more desirable in the context of treating a wide patient population, particularly those with underlying health conditions.

Integrating ADME-Toxicity Data in Drug Prioritization: The integration of ADME and toxicity data is crucial for identifying the most suitable repurposed drugs for COVID-19 treatment. The trade-offs between antiviral potency and safety underscore the importance of a holistic evaluation approach. Drugs like remdesivir and lopinavir, despite their strong binding affinities to viral targets, may require formulation adjustments to reduce hepatotoxicity risks, making them more suitable for targeted use in hospital settings where intravenous administration and close monitoring are feasible (Adegbola et al., 2021; Chowdhury, 2020). On the other hand, favipiravir's high oral bioavailability, favorable toxicity profile, and sufficient antiviral activity support its use as an outpatient therapy, particularly in early-stage infections.

The findings also highlight the limitations of relying solely on in-vitro antiviral activity to determine the efficacy of repurposed drugs. A comprehensive assessment that includes pharmacokinetic and toxicity considerations is essential to ensure that selected candidates are both effective and safe for clinical use. Computational tools, such as SwissADME, ADMETlab 2.0, and pkCSM, play a pivotal role in this process, allowing researchers to rapidly filter out unsuitable compounds and prioritize those with the most promising profiles (Sanders et al., 2020).

The results of this study provide a foundation for future in-vitro and in-vivo studies to validate the safety and efficacy of prioritized repurposed drugs for COVID-19. Such studies should focus on optimizing the dosage and delivery methods for drugs with poor oral bioavailability or high toxicity risks, as well as exploring combination therapies that could enhance antiviral efficacy while minimizing adverse effects (Dehelean et al., 2020). For example, the use of drug delivery systems, such as nanoparticles or liposomes, could improve the pharmacokinetic properties of drugs like remdesivir, enhancing their absorption and reducing systemic toxicity (Sahin et al., 2014).

Moreover, the insights gained from the ADME-toxicity trade-offs are not limited to COVID-19 but could be applied to future pandemics and emerging infectious diseases. By understanding the factors that contribute to the safety and efficacy of repurposed drugs, researchers can develop adaptable therapeutic strategies that can be rapidly deployed in response to new viral threats (Dotolo et al., 2021). This study underscores the importance of a multidimensional evaluation approach that considers not only the antiviral activity of candidate drugs but also their pharmacokinetic properties and potential safety risks, ultimately guiding the development of more effective and safer treatments for infectious diseases.

Conclusion

The analysis of ADME-toxicity trade-offs in repurposed drugs for SARS-CoV-2 highlights the complexity of balancing safety and efficacy in drug selection. While drugs like remdesivir and lopinavir offer strong antiviral potential, their associated toxicity risks emphasize the need for careful clinical application and monitoring. In contrast, favipiravir stands out as a safer and effective candidate with promising potential for broad use. Future research should aim to refine these

findings through experimental validation and optimize drug formulations to enhance therapeutic outcomes. As the pandemic continues to evolve, the lessons learned from this study can inform a more targeted and strategic approach to drug repurposing for emerging infectious diseases, contributing to improved clinical management and patient care.

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