**Supplementary**

**Text S1 Modified molecular docking and function predictions of viral proteins**

Computational docking tools, including PyRx (v.08), QuickVina2, and BIOVIA Discovery Studio (v.21.1), were used for molecular docking and interaction analyses following the modified approach of Kuo et al. (2023)[[1]](#footnote-1). The modified approach involved blind docking of each target structural protein with the antiviral drug remdesivir using PyRx, and the generated binding configuration was further utilized for batch docking with QuickVina2. The ligand structures of chemical disinfectants (SDF format) were obtained from the NCBI PubChem database, and protein structures (PDB format) were obtained from the RCSB PDB database. Remdesivir was used as a benchmark to establish the antiviral efficacy of disinfectants against diverse viruses.

**Text S2 Proposed eco-pharmaco-economic analysis (EPEA) of disinfectants**

The eco-pharmaco-economic analysis (EPEA) involved a combination of Weighted Score Method (WSM) and Multicriteria Decision Analysis (MCDA): Six critical environmental and safety profiles were conducted for the most effective chemical disinfectants, employing the US EPA Estimation Program Interface (EPI) Suite (v4.11). These profiles included the atmospheric hydroxylation rate (logOH), soil adsorption coefficient (logKoc), fish biotransformation half-life (HLN), bioconcentration factor (logBCF), bioaccumulation factor (logBAF), and biodegradation half-life (DT50). The outcomes of these profiles were classified into three tiers (i.e., safe, mild, and danger) according to criteria derived from established environmental and toxicological benchmarks integrated within the EPI Suite. This stratification facilitated a detailed assessment of their specific ecological and health-related effects, thereby providing a nuanced understanding of the potential risks associated with each profile. For each profile, a categorical scoring system was proposed (safe, 1; mild, 2; and danger, 3). The cumulative scores of these categories were then compared with the maximum possible score (max. Categorical score (3) × number of impact profiles (6)). This comparison is expressed as a percentage to ascertain the overall environmental impact, as illustrated in Equation (1):

*Environmental Impact (EI, %) = (Tot. Profile Score / Max. Assigned Score) x 100%* (Eq.1)

Where: *EI* utilized the WSM and delineated into three classifications: safe (≤ 33.33%), mild (33.34-66.66%), and danger (≥66.67%). *Tot. Profile Score* refers to the aggregated scores from the six environmental profiles, while *Max. Assigned Score* indicates the highest possible score.

Moreover, the cost-effectiveness of prominent disinfectant was evaluated. Prices per kilogram (US$/kg) for the most effective chemicals were sourced from Chemicalbook[[2]](#footnote-2), and the price for remdesivir was acquired from Gilead Sciences[[3]](#footnote-3). The cumulative performance of each chemical, including affordability (*C*), environmental safety (*S*), and antiviral efficacy (*E*), was ranked in ascending order by using MCDA. This ranking was established to highlight the overall performance (*O*) of each chemical, using proposed Equation (2):

*O(%) = wE x Enorm + wS x Snorm + wC x Cnorm* (Eq.2)

Where: *wE*, *wS*, and *wC* signify the weighted contributions of antiviral efficacy, environmental safety, and cost, respectively. Equal weights were allocated to *C*, *S* and *E* (i.e., *wE + wS + wC = 1* or *1/3E + 1/3S + 1/3C =1*) and normalized to a uniform scale (0 to 100) using proposed Equations (3), (4), and (5).

*Enorm = E - min(E) / max(E) - min(E) x 100* (Eq.3)

Where: *E* represents the LBE of a chemical with *min(E)* and *max(E)* denoting the most negative and least negative LBE values in the dataset, respectively. This normalization ensures that a score of 100 corresponds to the highest efficacy (most negative LBE), whereas a score of 0 indicates the lowest efficacy.

*Snorm = 100 - (S - min(S) / max(S) - min(S) x 100)* (Eq.4)

Where: *S* refers to the environmental safety of a chemical as determined by its impact assessment percentage. *min(S)* and *max(S)* are the lowest and highest impact percentages in the dataset, indicating the best and worst safety profiles, respectively. A lower impact percentage is synonymous with a better safety profile.

*Cnorm = 100 - (S - min(C) / max(C) - min(C) x 100)*  (Eq.5)

Where: *C* represents the cost of the chemical. *min(C)* and *max(C)* represent the lowest and highest costs in the dataset, respectively, with lower costs indicating higher affordability. This normalization ensures that a lower cost translates to a higher score, reflecting better affordability.

Table S1 Different categories of disinfectant and their chemicals

|  |  |  |
| --- | --- | --- |
| Types | Name | PubChemCID |
| Alcohol-Based Disinfectants | Ethanol |  702  |
|  | Isopropanol |  3776  |
|  | 2,4-Dichlorobenzyl Alcohol | 15684 |
| Aldehydes | Formaldehyde |  712  |
|  | Glutaraldehyde |  3485  |
| Antiviral drugs (reference) | Remdesivir  | 121304016 |
| Chlorine & chlorine compounds | Chlorine |  24526  |
|  | Chlorine Dioxide |  24870  |
|  | Monochloramine |  25423  |
| Iodophors | Iodine |  807  |
| Miscellaneous inactivating agents | L-Lactic Acid |  107689  |
|  | Amylmetacresol |  14759  |
|  | 2-Dodecylbenzenesulfonic acid  |  25457  |
|  | Potassium Permanganate |  516875  |
|  | Triethylene Glycol |  8172  |
|  | Chlorhexidine Gluconate |  9552081  |
| Oxidizing Agents | Hydrogen Peroxide |  784  |
|  | Peracetic Acid |  6585  |
|  | Ozone |  24823  |
|  | Potassium peroxymonosulfate  | 156589072  |
| Phenolic Compounds | Triclosan |  5564  |
|  | Hexachlorophene |  3598  |
| Phytochemicals | Rutin | 5280805 |
|  | Thymol |  6989  |
| Quaternary Ammonium Compounds | Benzyldimethyltetradecylammonium chloride | 8756 |

Table S2 Surface proteins of pivotal human pathogenic viruses

|  |  |  |
| --- | --- | --- |
| Virus  | Surface proteins |  PDB ID  |
|  Human Parainfluenza Virus 3  | Hemagglutinin-neuraminidase (HN)  |  1V3B |
|  SARS-CoV-2  | Spike (S) protein  |  6VXX  |
|  Human Immunodeficiency Virus (HIV)  | Envelope glycoprotein gp120  |  6MEO  |
|  Hepatitis C Virus  | Envelope glycoproteins E1  | 4N0Y  |
|  Influenza A Virus  | Hemagglutinin (HA)  | 4WE9  |
|  Hepatitis B Virus  | Surface protein (HBsAg)  |  7TUK |
|  Human Papillomavirus  | L1 capsid protein  |  1DZL  |
|  Epstein-Barr Virus  | Glycoprotein gp350  |  2H6O |
|  Human Cytomegalovirus  | Glycoprotein B (gB)  |  7KDP |
|  Human T-lymphotropic Virus  | Glycoprotein gp21 |  1MG1  |
|  Herpes Simplex Virus | Glycoprotein D (gD) |  1JMA |
|  Human Adenovirus  | Hexon protein  |  1P30  |
|  Human Rhinovirus  | Capsid proteins  | 1AYM  |
|  Human Norovirus  | Capsid protein VP1  | 7MRY |
|  Human Rotavirus  | VP8  |  7C8P |
|  Human Respiratory Syncytial Virus  | Fusion (F) glycoprotein  | 1G2C |
|  Human Metapneumovirus  | Fusion (F) glycoprotein  |  7SEJ |
|  Zika Virus  | Envelope (E) protein  |  5JHM |
|  Dengue Virus  | Envelope glycoprotein  |  4UTC |

Table S3 Eco-pharmaco-economic analysis (EPEA) of candidate chemical disinfectants

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Disinfectant category | Chemical/drug | Avg. ligand binding energy (kcal/mol) | Environmentalimpact (%) | Avg. Price (US$/Kg/Vial) | EPEA ranking (%) |
| Miscellaneous inactivating agents | 2-Dodecylbenzenesulfonic acid | -7.5 | 77.78 | 100.00 | 68 |
|  | Amylmetacresol | -7.05 | 88.98 | 7.00 | 61 |
|  | Chlorhexidine gluconate | -7.81 | 66.67 | 17.5 | 71 |
| Phenolic compounds | Hexachlorophene | -7.63 | 83.33 | 12.5 | 54 |
| Antiviral drug (reference) | Remdesivir | -7.85 | 61.11 | 5.2 M\* | 43 |
| Phytochemicals | Rutin | -8.49 | 66.67 | 33.52 | 93 |

\*M denotes million US$, where 1 vial is equal to 100 mg and priced at US$520.

1. Kuo, H. W. D., Zure, D., & Lin, C. R. (2023). Occurrences of similar viral diversity in campus wastewater and reclaimed water of a university dormitory. Chemosphere, 330, 138713. https://doi.org/10.1016/j.chemosphere.2023.138713 [↑](#footnote-ref-1)
2. Chemicalbook (2024). Chemicalbook. Chemicalbook. url: <https://www.chemicalbook.com/> [↑](#footnote-ref-2)
3. Gilead Sciences (2024). Gilead Sciences. Gilead Sciences Inc. url: https://www.gilead.com/ [↑](#footnote-ref-3)