Evolution of Viral Lysis Techniques Post COVID-19: A Review of Some Major Advancements

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DOI: https://dx.doi.org/10.51244/IJRSI.2025.1215PH000196

Received: 27 September 2025; Accepted: 04 October 2025; Published: 21 November 2025

ABSTRACT

Viral lysis is a critical step for obtaining nucleic acids and other components from viral particles. Prior to, and during the COVID-19 pandemic, viral lysis techniques required laboratory equipment and expertise, and especially required numerous washing steps post lysis for nucleic acid purification that significantly increase the overall turnaround time. Towards and during the Post COVID-19 era, novel and compelling lysis techniques revolutionised viral lysis. These innovations, born from the response to SARS-CoV-2, successfully overcame the numerous flaws of the ancient era, making viral lysis easier and safer to perform, less time consuming, cost-effective, and by far less demanding in terms of reagents, consumables, equipment, and expert personnel. This review presents and discusses some major advancements in viral lysis techniques in the post COVID-19 era. Emphasis is put on the innovation each technique brings and how it makes lysis better, safer and easier, and also how it shortens protocols and adaptability in point of care testing.

Key words: SARS-CoV-2 detection, Lysis techniques, Diagnostics, post COVID-19, Innovations

INTRODUCTION

In the context of diagnostics, lysis is a very important phase especially in diagnostic procedures involving nucleic acid analysis or other intracellular components such as proteins and amino acids [1]. In the specific context of nucleic acid extraction, lysis is used for the breaking down of cells or viral particles to release cellular components including their nucleic acids. At the core of viral molecular detection, such as through reverse transcription polymerase chain reaction (RT-PCR), lies the viral lysis step. A process meant for disrupting the viral envelope and capsid to specifically release the genetic material (RNA or DNA) for subsequent analysis [2]. Following this step, RT-PCR, sequencing, and other molecular assays can be performed. In most in vitro diagnostic testing methods, a lysis buffer is used to break open cells or viral particles [3].

The agent severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is responsible for the global coronavirus disease 2019 (COVID-19) pandemic. At the time of the outbreak, numerous reagents had been developed for the study of SARS-CoV infections but few were applicable for evaluating SARS-CoV-2 infection and immunity [4]. The COVID-19 pandemic presented an unparalleled global challenge, exposing critical limitations in traditional diagnostic procedures. It came along with the urgent need for rapid, sensitive, and affordable diagnostic tests for SARS-CoV-2, especially in resource limited countries [5]. Nucleic acid based tests, the gold standard for early detection of COVID-19, took several hours to complete, especially due to the necessary purification steps post lysis [6], and required extensive man power. In addition to these, RNA extraction kits became short in supply, especially in resource limited countries, and qPCR equipment was relatively scarce. Thus, there came the need to assess alternative protocols, reagents and approaches so that nucleic acid testing could continue and better still, scale up without being hampered by these challenges [7].

Prior to 2020, viral lysis techniques were often multi-step and required specialized laboratory environments, which proved to be a significant setback for mass, rapid testing. Numerous traditional methods though involving

chemical lysis, physical lysis, and enzymatic lysis [8], were gradually being relayed by methods such as direct lysis protocols, high-throughput and point of care testing, and CRISPR-based diagnostics [9]. The latter methods were more adapted to the rapid spread of the SARS-CoV-2 and the increasing demand for COVID-19 testing all over the world [10]. The urgent need for accessible and scalable diagnostic protocols catalysed significant innovation, fundamentally reshaping the landscape of viral lysis. The aim of this review is to explore the major advancements in viral lysis techniques that emerged in the post-COVID-19 era, focusing on the shift towards integrated chemical formulations, novel physical methods, and streamlined, point-of-care solutions.

METHODOLOGY

Original articles discussing post COVID-19 lysis techniques were critically appraised using the Critical Appraisal Skills Programme (CASP) checklist: For diagnostic test studies [11]. Using this checklist, articles were not assigned a formal score or grade as the questions in the checklist are answered with yes, partly, no, unclear, or NA (Not Applicable). Thus, the final decision on the evidence's strength and applicability rests entirely with the appraiser. Numerous yes answers hinted a strong study, whereas numerous "no" or "unclear" answers suggested potential issues with validity, applicability, or missing information requiring cautious interpretation. Based on the results retrieved from each of the critically appraised papers, we present scientific innovations in lysis techniques and how they make diagnostics better.

Articles searching was done using PubMed, Google Scholar, Science Direct, and Embase. The terms SARS-CoV-2 detection, lysis techniques, diagnostics, post COVID-19, innovations, were used during the search. The following criteria were used for including articles in the review; (1) articles published from 2020 onwards; (2) full length articles; (3) research articles that describe and discuss innovations in viral lysis technique; (4) articles that present strong evidence and applicability after appraisal. Exclusion criteria included; (1) review articles; (2) articles that describe innovations that do not fill gaps identified in studies from 2019 and earlier; (3) articles that describe innovations that are not yet applicable.

RESULTS

A total of five studies were selected to describe some innovations in viral lysis technique. The table below shows each included study and summarises their assessment, with overall answer under each theme of the CASP checklist.

Table 1: Summary of critical appraisal for each included study

Authors	**Study type**	**Result validity section**	**Result quality section**	**Result applicability section**	**Conclusion**
Ngaba et al.	Cross-sectional and comparative	Yes	Unclear	Yes	Adequate methodology, limitations on statistical precision, but highly applicable
Yu et al.	Experimental and applied research	Yes	Yes	Yes	Strong methodology and highly applicable
Fradique et al.	Experimental and applied research	Yes	Yes	Yes	Strong methodology and highly applicable
Welch et al.	Applied biomedical engineering and diagnostic accuracy	Yes	Yes	Yes	Remarkably rigorous and high impact diagnostic development
Qian et al.	Applied bioengineering and diagnostic development	Yes	Yes	Yes	Outstanding technical validity with transformative potential

Single-step, inactivating lysis buffers

Pre COVID-19 lysis methods often involved a number of washes and centrifugation steps which did not only add complexity but also high risks of cross-contamination [12]. As a counter measure, manufacturers produced new buffers that combined viral inactivation with nucleic acid stabilization within a single reagent. Such formulations, that typically contain chaotropic salts like guanidine thiocyanate or strong detergents, are very effective at denaturing viral proteins so that the virus becomes non-infectious, and at the same time they protect the RNA from degradation by RNases [13], [14]. This brought about simplified sample preparation and substantially upgraded safety for laboratory personnel by eliminating the handling of live virus. Additionally, these multipurpose buffers made direct transfer of the lysate into downstream amplification reactions easier, hence decreasing the turnaround time and facilitating high-throughput automation [15]. These pre-filled tubes in diagnostic kits became very popular and widespread, and therefore essential for large-scale testing operations.

A meaningful protocol that was introduced towards the post COVID-19 era is the Biosynex Ampliquick® for SARS-CoV-2 qualitative detection in saliva and nasopharyngeal samples [15], [16]. It is a double kit that contains a rapid RNA lysis kit and an amplification kit. This kit permits lysis without the need for washing and centrifugation steps. In the first step which is the lysis step, 50µl of sample is transferred into a well containing the reaction medium. This medium is then heated for 15 minutes during which lysis and inactivation take place. The next and final step involves transferring 10µl of the resulting mixture into the amplification medium. Amplification takes 33 minutes to completion. Ampliquick® permits the detection of two particular molecular targets of SARS-CoV-2 located on RdRp and E genes. Seeing the potential of Ampliquick® to scale up COVID-19 testing in Cameroon, Ngaba et al. (2021) evaluated its diagnostic performance against conventional reverse transcriptase polymerase chain reaction (RT-PCR). Their aim was to suggest it as an alternative diagnostic strategy in Cameroon [15]. During their evaluation, they assessed sensitivity, specificity, and turnaround time. They found that; with Ampliquick®, laboratory personnel could analyse a greater number of samples; Ampliquick® was more sensitive, and had significant agreement with conventional RT-PCR; Ampliquick® performed better than conventional RT-PCR as concerns early COVID-19 diagnosis. These findings showed that Ampliquick® was less time consuming, less complex, and less demanding in terms of consumables and laboratory personnel, and the technique is very reliable. Although COVID-19 was tamed before this protocol could be implemented nationally, it is a protocol that can, and should be experimented on other endemic infectious diseases.

Despite the significant advancement brought by single step inactivating buffers, there was yet the need for a laboratory setting and equipment such as qPCR machines, and critical personal protective equipment for the protocol. It could therefore not be used in non-clinical settings. Furthermore, some chemicals used came with serious health risks. Chemicals such as guanidine thiocyanate, if mishandled can cause oral, dermal, and respiratory track acute toxicity, and can be hazardous for aquatic environments [17]. Adequate and careful handling including waste management is required to avoid any inconvenience.

Microfluidic technologies and physical lysis

The post-COVID-19 era arrived with the need for a class of devices that combine two or more biomolecular steps that are normally performed in equipped laboratories into one miniaturized system, based on integrated microfluidic circuits. An objective in biotechnological research was the development of molecular diagnostic tools which are straight forward, easy to handle, and requiring minimal amounts of samples for operation [18]. The ‘lab-on-a-chip’ (LOC) approach is in line with these very essential requirements. The technologies based on LOC include microfluidics, microelectronics, photolithography and other fabrication techniques, physical methods for cell lysis and nucleic acid purification.

Physical lysis makes use of mechanical, thermal, or electrical forces to break viral particles, offering an up-and-coming alternative, especially for compact and automated systems [19]. Dedicated research groups developed and polished microfluidic devices able to lyse viruses on a chip using diverse physical principles. Examples of such devices include platforms that utilize acoustic waves to vibrate and break off virions, and those that use rapid thermal cycling to bring about structural damage [20]. The most commendable benefit of these miniature devices is their inherent capacity for point-of-care applications. With lysis directly integrated onto a little device, these technologies have the ability to perform sample preparation with the least possible user intervention, and

to exclude the necessity of an external laboratory [21]. This was a very important approach for sanctioning rapid and decentralized testing for remote or non-clinical settings.

A protocol presented by Yu et al. (2023) in their paper focusing on on-chip photothermal cell lysis shows an effective way of making use of microfluidic technologies [22]. They sought solutions for technical challenges such as reagent evacuation, complexity of design, and tremendous cost of manufacturing that held back microfluidic-based cell lysis for nucleic acid extraction. They used a highly efficient photothermal cell lysis chip (HEPCL chip) consisting of a PDMS microfluidic chamber and compact strongly absorbed plasmonic Au nanoislands (SAP-AuNIs) with broad diameters and small nanogaps that allow for broad-spectrum light absorption. Photothermal heat is activated by the SAP-AuNIs, bringing about a harmonized temperature distribution inside the chamber and expeditiously reaching the target temperature for cell lysis, typically within 30 seconds. Moreover, the confined plasmonic heating of SAP-AuNIs rapidly prompts phase transition and photoporation in the cell membrane's lipid bilayer, giving way to a fast and effective cell lysis. As high as 93% of PC9 cells were successfully lysed by The HEPCL chip at 90°C for 90 seconds without damaging the nucleic acid. With this successful demonstration, Yu et al. concluded that on-chip cell lysis provides a new platform for sample preparation and for use as integrated point-of-care molecular diagnostics. This conclusion is similar to that of Fradique et al. (2023), who explored the modular design of microfluidic devices by developing an integrated microfluidic chip [23].

Integration of viral lysis with downstream detection platforms

The COVID-19 pandemic showed the necessity to renovate the diagnostic pipeline such that any possible delay was eliminated [24]. Newly designed platforms in which lysis was not just a preliminary step but an integral part of the overall detection process were produced. This can be observed in rapid antigen and nucleic acid tests in which the sample is added to a cassette that contains a dry reagent pad. During an operation, the pad performs lysis, and launches the amplification or detection reaction in a single chamber. As molecular diagnostics is concerned, this innovation was central to developing loop-mediated isothermal amplification (LAMP) tests that had the ability to deliver results in minutes instead of hours [25]. This advanced but simplified technology was described and recommended for research during the COVID-19 era by numerous research groups. There had been some advances at the time, but setbacks such as effectiveness for on-site usage due to their large turnaround times, operational costs, and the need for laboratory equipment had to be overcome [26]. These all-in-one systems are the expression of a paradigm shift from a series of discrete laboratory procedures to a holistic and streamlined diagnostic platform that has speed, simplicity, and accessibility as priority.

Welch et al. (2022) worked on the microfluidic Combinatorial Arrayed Reactions for Multiplexed Evaluation of Nucleic acids (mCARMEN) which was a cost-effective virus and variant detection platform that combines CRISPR-based diagnostics and microfluidics and has a smooth workflow for clinical use [27]. The mCARMEN panel could test up to 21 viruses, including SARS-CoV-2, other coronavirus types, and influenza strains. The mCARMEN panel was later ameliorated and could also enable the identification of six SARS-CoV-2 variant lineages, including Delta and Omicron. Additionally, they implemented an associated Cas13 and Cas12 approach that facilitated the quantitative measurement of SARS-CoV-2 and influenza A viral copies in samples. The mCARMEN platform was expeditiously developed for the COVID-19 pandemic and despite challenges encountered during its clinical validation and approval, its ability to enable high-throughput surveillance of multiple viruses and variants simultaneously, and permitting rapid detection of SARS-CoV-2 variants has been verified.

Qian et al. (2025) on their part carried out a study on an acoustofluidic integrated molecular diagnostics (AIMDx) chip intended for a fast and extensive detection of viral antibodies and nucleic acids [28]. In this study, they presented the AIMDx on a chip, which is a platform that combines high speed and sensitivity to detect viral immunoglobulin A (IgA), G (IgG), and M (IgM), and nucleic acids. AIMDx makes use of acoustic vortexes and Gor'kov potential wells at a 1/10,000 sub-wavelength scale for isolating viruses and antibodies, and at the same time excluding cells, bacteria, and large vesicles found in saliva samples. This chip makes on-chip viral RNA enrichment easier, enables lysis within 2 minutes, and allows for detection through transcription loop–mediated isothermal amplification. All of these alongside performing electrochemical sensing of antibodies. Their results were highly appealing as the AIMDx could attain a close to 100% recovery of viruses and antibodies, a 32-fold enhancement of RNA detection, and an immunity marker sensitivity of 15.6 pg/ml. As their conclusion indicated,

this is a significant improvement that provides a life changing tool for multiplex diagnostics, making early infectious disease detection easier and better. Similar technologies have been used on other micro-organisms. For instance, Mehlawat et al. (2025) worked on a reagent-free, non-thermal acoustofluidic platform that makes use of bulk acoustic waves (BAWs) capable of swiftly lysing Gram-negative and Gram-positive bacteria through high energy acoustic waves and fixed shear forces [29].

SUMMARY

Each explored viral lysis technique from the first to the third brought its innovation to the process. Starting with single step inactivating buffers that shortened the process, needing less personnel and considerably reducing time of work. Microfluidic technologies made the process even shorter and safer by integrating lysis into small devices that require minimal user intervention. Ultimately, technologies that integrate viral lysis with downstream detection platforms made it possible to take the process out into the field as point-of-care testing. Every evolution of the viral lysis technique boosted the movement from complex laboratory processes to simplified bed side technologies.

CONCLUSION

This review aimed at discussing some major advancements in viral lysis techniques in the post COVID-19 era. The COVID-19 pandemic radically transformed viral lysis from a complex, manual procedure into a streamlined, integrated component of rapid diagnostic testing in the post COVID-19 era. These transformations went from safer, single-step chemical buffers to cutting-edge physical lysis on microfluidic chips which directly addressed the critical need for scalable, fast, and accessible solutions. These innovations, born from the urgency of a global crisis, have not only improved our response to the SARS-CoV-2 virus but have also laid the groundwork for a new generation of diagnostic tools that will be essential for future infectious disease surveillance and management.

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