Collaboration for Environmental Evidence

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Systematic Map Protocol

Title
What impact does concentration methods have on the study of viruses in different environmental samples types?

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viral concentration, methods, flocculation, ultracentrifugation, yield

Background
The recent COVID-19 pandemic caused by SARS-CoV-2, has underscored the risk posed by viruses and other pathogenic microorganisms to public health, the environment, and global economy. This situation has raised growing concerns about the spread of these pathogens, especially in densely populated areas. Environmental surveillance has regained its role as a fundamental tool for detecting and monitoring potential epidemiological outbreaks, with a particular focus on the analysis of environmental matrices. However, traditional surveillance methods have significant technical and detection limitations, especially when it comes to non-cultivable microorganisms. Additionally, these methods are at times time-consuming and costly, making their implementation in routine monitoring, challenging. In contrast, molecular-based techniques have made significant advancements, enhancing their sensitivity and reducing response times in the detection of various pathogens. Today, thanks to technological progress, it is possible to simultaneously analyze thousands or even millions of sequences, enabling a detailed characterization of organisms present in an environmental sample. As a result, they are a cost-effective long-term option in the fields of public and environmental health. However, challenges persist in the detection and characterization of microbial communities, especially viruses, due to the difficulty of obtaining adequate concentrations that allow for their subsequent amplification and identification. To address this issue, protocols for viral particle concentration have been developed and optimized, maximizing the cost-effective detection of viral groups without compromising viral recovery performance in different environmental systems. There are several reviews discussing the methods of concentrating viral particles in various environmental samples that highlight the difficulties in monitoring viruses in environmental systems. However, the information in these reviews has some limitations, and they may not include the latest advancements that originated from the SARS-CoV-2 pandemic, where new methods, approaches, and studies in different environmental samples have emerged. As a result, the available information may have significant biases.

Theory of change or causal model
Despite the advantages of implementing environmental monitoring with microorganisms to detect potential health risks, there is a need to enhance these monitoring plans, particularly by deepening

and optimizing the available information on the concentration methods for viral particles. This should take into account the various types of environmental matrices that can be analyzed, the methods employed, yields obtained, and availability of existing data. See attached figures named "environmental_surv_virus.png" and "mapping_model.png"

Stakeholder engagement

It is imperative to enhance the success of monitoring programs for potentially pathogenic microorganisms, particularly in terms of the ability to concentrate viruses, which, as demonstrated in the recent pandemic caused by SARS-CoV-2, represent a powerful tool for increasing our understanding of present microorganisms as well as the speed of response in decision-making. The formulation of this research question and scoping of systematic map was discussed with different Mexican research institutions from different perspectives (ecological, biological, biotechnology, marine sciences and limnology) and a Non-Governmental Organization specialized in citizen science (Global Water Watch Mexico), in order to improve monitoring design, and generate data relevant for stakeholders and decision makers. The aim is to provide a solid and up-to-date foundation for future research in this area, enabling better-informed decision-making, in identifying and characterizing viruses. Additionally, it aims to develop more effective strategies for environmental monitoring that promote public and environmental health.

Objectives and review question

Primary: How much information is available regarding viral particle concentration methods in the processing of environmental samples? Secondaries: What are the spatiotemporal trends in the publication of this type of studies? What are the most commonly used concentration methods for virus concentration? Which environmental matrices are most frequently processed with those methods? Which viruses are the most extensively studied using these concentration methods? What molecular and bioinformatic tools are employed to facilitate the study of viruses once viral particles have been concentrated? Which ecosystems have been the most extensively studied?

Definitions of the question components

Population: Any type of environmental system in which viruses have been studied, extracted, concentrated, and identified. Intervention: Studies in which the use of at least one viral particle concentration method is reported and employed. Comparator: taxonomic groups studied, environmental matrix studied (water, sediment, air, mixed sample, etc.), type of technique applied (flocculation, ultracentrifugation, commercial kit, etc.) Outcome: All outcomes related to the studied population, including data about taxonomic groups studied, sequencing platforms, other molecular techniques employed, environmental matrix used, community structure, detected pathogens, obtained yields and concentrations.

Search strategy

The strategy designed for this systematic map protocol and its corresponding systematic map is designed in accordance with the Guidelines and Standards for Evidence Synthesis in Environmental Management, following the ROSES format for Reporting Standards for Systematic Map Protocols. Those guidelines aim to capture a wide range of sources and ensure its replicability and transparency. A search in 3 bibliographic databases and 1 web-based search engine will be conducted. Also for the searches, in each of the databases and search engines, a general word string will be used. The selected search string will be reviewed and tested by the whole team in order to secure a good "specifity" level of returned studies that allows us to identify relevant studies. In the platform, the field "topic" that includes title, abstract, and keywords will be used. The scoping search string will use the Web of Science format, considering English-Spanish language studies, using the following Booleans (AND, OR) and the wildcards: Virus OR Viral OR Particle* AND concentrat* OR recover* OR detect* AND Method* AND Ultracentrifugation OR Flocculation OR

Polyethileneglycol OR PEG OR Commercial Kit AND environment* OR sample* OR matri* For the other bibliographic database and search engine (SCOPUS, PubMed and Google Scholar), the search string will use the same terms, only to be adapted in accordance to the format of the database, as long as the search includes the title, abstract, and keywords. The date of searches using these databases was on June 2023.

Bibliographic databases
A search in three bibliographic databases will be conducted (Web of Science, SCOPUS and PubMed). The first two databases were selected because of their renowned relevance as databases for this type of studies, and the third one was selected as the main medical database that could include studies regarding to viruses studies. It is worth to mention that we count with institutional subscriptions to those platforms, those are provided by the Universidad Nacional Autónoma de México digital library and digital database (comprises publications since 1900). Searches will consider full text, English or Spanish language, and the search strings provided in the previous search strategy.

Web-based search engines
The search engine Google Scholar will be used to identify additional literature that cannot be found in the bibliographic databases. We will focus only on the grey literature launched by this search engine. As in the Bibliographic databases section, our searches will consider full text, English language, and the search strings provided in the search strategy.

Organisational websites
N/A

Comprehensiveness of the search
The comprehensiveness of our search string was tested using 10 papers considered relevant (by the whole team) as an indicator of a successful search. If those key papers, or the majority (at least 8), were returned by the search string, it was considered an optimum. However, if that search string did not return the majority of papers, it was modified. See the "key_papers_virus" document.

Search update
There are plans to update the launched results in the searches, during the conduct of the review, to improve the quantity and spatiotemporal resolution of the systematic map, once the present protocol is submitted to this repository and accepted as valid (October 2023). Actual results cover until June 2023.

Screening strategy
In our screening strategy, there will be two stages: The first one is focused on a review of the title and abstract presented in the studies, in order to determine their inclusion or exclusion, based on a decision tree that was designed by all the review team (see image "decision_tree”), in concordance with the proposed objectives of the study. Prior to determine if the documents passed the first screening stage, the whole team reunited for a general training focused on the review of articles. After that, each study will be reviewed by double-screening. The studies that were considered with "uncertainty" about their inclusion/exclusion, as well that those who did pass it will pass to stage two of the screening. Stage two of the screening process involves a full text review of the articles that passed the first stage and those that are categorized as "uncertain". However, if those studies cover at least one of the exclusion criteria, they will be excluded, even if they pass the first stage. For those studies where the uncertainty continues, a second review by another two members of the team will proceed.

Eligibility criteria
Eligibility criteria are showed in the "inclusion_criteria" document. -Inclusion criteria: Type of studies: Original articles, preprints, and studies presented in theses. Language: English and Spanish Population: Studies where viral concentration methods (ultracentrifugation, ultrafiltration, commercial concentration kit with a concentration step, flocculation, etc.) have been applied to concentrate viruses present in various environmental matrices (e.g., soil, water, air, sediments, sludge, etc.) Intervention: Use of viral concentration methods with the purpose of characterizing the viral community and/or detecting specific viruses in environmental matrices. Outcome: Reports relevant details about viral particle concentration methods (e.g., concentration method yield, virus recovery capacity, advantages and disadvantages, etc.). Geography: There was no limitation for geographic areas. Period: There was no time limit for studies. -Exclusion criteria: Type of study: Books, chapters, letters to the editor, review studies (systematic reviews, meta-analysis), modeling studies that did not take environmental samples. Language: Non-English nor Spanish Population: Studies where viral concentration methods have not been applied in various environmental matrices. Intervention: There was no use of viral concentration methods for the purpose of characterizing the viral community and/or detecting specific viruses in environmental matrices. Outcome: No report any of the outcome inclusion criteria.

Consistency checking
10% of the articles screened by a reviewer will be selected randomly and screened by two other reviewers in order to check the consistency of eligibility. All discrepancies regarding screened articles will be discussed by the 2 members of the review team, and if there is no final consensus about it, the whole team will be consulted if necessary. Consistency of reviewers' screening will be measured by the Kappa coefficient.

Reporting screening outcomes
Screening outcomes will be reported in a ROSES diagram, a list of eligible articles and the list of full text articles excluded with the reasons of their exclusion (watch the "ROSES flow diagram_virus" diagram).

Study validity assessment
We will not be critically appraising the validity of robustness of the included articles. First, due to the big number of studies that will be encountered in the searches; secondly, because the included articles will be reviewed by all the team in order to identify if there is a study that did not fulfill the criteria; third, because the aim of this study is to describe the location of existent studies and not to analyze the results; and finally, because of the great variability in design, approach, and objectives of the several studies. However, considering the first and prospective review of results launched by the databases, an estimated number of studies that meet the inclusion criteria and could be used for the database construction ranges between 400-500 studies.

Consistency checking
Consistency of reviewers' screening will be measured by the Kappa coefficient. A value of Kappa coefficient higher to 0.69 will be considered as an accepted value for quality and unbiased assessment.

Data coding strategy
For each of the studies that passes the screening stages, data extraction and codification will proceed. Any of the members of the team will have a data sheet where meta-data and information about relevant variables will be placed. Once a reviewer finishes the review of the articles, 10% of those studies will be reviewed by the other two members of the team in order to ensure that the data extraction was done correctly. Also, in these formats, a commentary section will be available, so the

rest of the team can review and decide if data remains on the data sheet or will be removed

Meta-data to be coded
Data extracted from each of the studies will be included: -Bibliographic details (author affiliations, keywords, etc.) -Study location: country, type of ecosystem -Intervention: concentration method and extraction method employed -Outcome: concentration method yield, type of virus studied, etc. -Study design: number of samples used, used volume, previous steps used for concentration, etc. -Year of publication -Data availability: repositories, primers used, geographic coordinates, etc. -Taxonomic groups of virus studied These variables are captured in a standardized Excel form (View "BD_virus_data" file) that the reviewers will use to fill with the corresponding information.

Consistency checking
Once a reviewer finishes the review of the articles, 10% of those studies will be reviewed by other two members of the team in order to ensure that the data extraction was done correctly.

Type of mapping
The data set generated via data extraction will be analyzed in R in order to provide a narrative synthesis that summarizes searchable databases and visual outputs reflecting the actual evidence of the use of different concentration methods in the study of viral particles in different type o environmental samples. Data extracted for any of the studies will be available in a database, so that users can filter, analyze and evaluate the existent evidence

Narrative synthesis methods
The findings will be summarized in the form of tables, graphs (comparison of variables), and maps (geographic distribution of actual evidence) that allow visualizing the generated evidence. These representations will allow the identification of gaps, thematic synthesis, major taxonomic groups that are studied, sequencing platforms used, etcetera.

Knowledge gap identification strategy
Generated evidence will be analyzed and discussed in order to find evidence gaps, geographic bias of generated evidence, and try to synthesize the presented evidence to understand where and how different methods have been applied. The trends shown by the data will serve as a preliminary tool in the form of a narrative synthesis that helps the scientific community, non-governmental organizations, stakeholders, and decision makers to take better action in the way viral communities can be studied depending the nature of the environmental matrix to be sampled.

Demonstrating procedural independence
In case there is a member of the review team who could be listed as an author on an article considered for the review, that member will not be involved in the review process or any of the decisions of inclusion or exclusion related to that article.

Competing interests
All authors declare they have no competing interests.

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Author’s contributions

CASB, RICC, MK, HAPM and LBD developed the concepts and framework for the systematic map. CASB and RICC wrote the manuscript. All authors contributed for decision tree construction based on their expertise and discussion of ideas. MK, HAPM and LBD contributed with ideas, proof-reading, and review, assuring the protocol applicability. All authors have read and approved the information embodied in the document.

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