

Applications of comparative genomics in the surveillance of bacterial resistance

Aplicaciones de la genómica comparada en la vigilancia de la resistencia bacteriana

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ABSTRACT

In recent decades, bacterial resistance to antibiotics has become one of the greatest challenges to global public health, as it could cause 10 million deaths annually by 2050 if effective control measures are not implemented immediately. In this context, there is a need for accurate, rapid tools to monitor, understand, and combat the problem. Its application in surveillance has revolutionized the way bacterial resistance is monitored through the analysis of whole genome sequences. A systematic review was conducted to provide a detailed analysis based on the available scientific evidence. The search was conducted in recognized databases such as Scielo, PubMed, Scopus, and Google Scholar, focusing on scientific articles published in English, Portuguese, and Spanish. Comparative studies analyzing genomics were included. The articles were critically appraised to extract relevant data on the applications of comparative genomics in bacterial resistance surveillance. The data obtained were analyzed using an evidence matrix. Finally, it is important to note that their integration into health systems strengthens outbreak response capacity and helps create clearer and more useful rules for proper antibiotic use. Furthermore, their combination with bioinformatics tools and global genomic databases has enabled the development of collaborative international data surveillance networks, which are essential for responding to health problems.

Keywords: Comparative genomics, Bacterial resistance, Bioinformatics, Epidemiological surveillance.

RESUMEN

En las últimas décadas, la resistencia bacteriana a los antibióticos se ha convertido en uno de los mayores desafíos para la salud pública mundial, ya que, podría causar 10 millones de muerte al año para 2050 sino se implementan medidas efectivas de control de inmediato. En este contexto, la necesidad de herramientas precisas, rápidas para monitorear, comprender y combatir la problemática. Su aplicación en el ámbito de la vigilancia ha revolucionado en la forma que se monitoriza la resistencia bacteriana, mediante el análisis de secuencias completas del genoma. Se realizó una revisión sistemática con el fin de proporcionar un análisis detallado y fundamentado en la evidencia científica disponible. La búsqueda se realizó en bases de datos reconocidas, como Scielo, Pubmed, Scopus y Google Académico enfocándose en artículos científicos publicados en los idiomas inglés, portugués y español. Se incluyeron estudios que analizaran la genómica comparada. Los artículos fueron evaluados críticamente para extraer datos pertinentes sobre las aplicaciones de la genómica comparada en la vigilancia de la resistencia bacteriana. Los datos obtenidos se analizaron mediante una matriz de evidencia. Finalmente, es importante señalar que su integración en los sistemas de salud fortalece la capacidad de respuesta ante brotes y ayuda a crear reglas más claras y útiles para usar bien los antibióticos. Además, su combinación con herramientas bioinformáticas y bases de datos genómicas globales ha posibilitado el desarrollo de redes colaborativas de vigilancia de datos internacionales, fundamentales para responder ante problemas sanitarios.

Palabras clave: Genómica comparada, Resistencia bacteriana, Bioinformática, Vigilancia epidemiológica.

INTRODUCTION

In recent decades, bacterial resistance to antibiotics has become one of the greatest challenges to global public health, as it could cause 10 million deaths per year by 2050 if effective control measures are not implemented immediately. The World Health Organization (WHO) defines antibiotic resistance as a natural phenomenon where bacteria mutate and become resistant to the effect of these drugs, making infections more difficult to treat, thus increasing the morbidity and mortality associated with bacterial infections and generating a significant socioeconomic impact. In this context, the need for accurate, rapid tools to monitor, understand, and combat the evolution of bacterial resistance has become important to reduce the problem (Murray et al., 2022).

Comparative genomics involves the systematic and detailed analysis of genomic sequences from different bacterial strains with the aim of identifying similarities and differences that allow us to better understand their biology, evolution, and pathogenicity. Similarly, it is a tool that allows us to observe the genetic material of different bacteria and better understand how the genes that give them resistance to antibiotics arise and spread. Thanks to this approach, we can not only determine which bacteria are resistant, but also discover where they got those genes from, whether they inherited them from other microbial species or passed them directly from an organism, this is known as horizontal transfer (Zhang and Zhang, 2019 & Cedeño et al., 2020).

Furthermore, it involves the use of bioinformatics tools, which consists of the search for orthologs, genes with functional and structural homology to other known genes from other genomes. This approach has been successfully applied in the surveillance of antimicrobial resistance, facilitating the discovery of the genetic mechanisms involved in resistance and the early detection of emerging strains (Cedeño et al., 2020).

However, its application in the field of surveillance has revolutionized the way bacterial resistance is monitored, through the analysis of complete genome sequences (WGS). Genome Sequencing), scientists can track outbreaks of resistant infections with an unprecedented level of precision, its use has made it possible to discover transmission chains that could not previously be detected with traditional methods, therefore, it allows not only to understand the current dynamics of antimicrobial resistance, but also to predict possible future scenarios based on the genetic evolution of bacteria (Su et al., 2019).

Comparative genomics therefore not only represents a powerful tool for better understanding the evolutionary dynamics of resistant bacteria, but has also become a fundamental pillar for effective surveillance of antibiotic resistance. Its integration into health systems and reference laboratories allows for improved responses to health emergencies, optimized antibiotic use, and protected populations against the threat of untreatable infections.

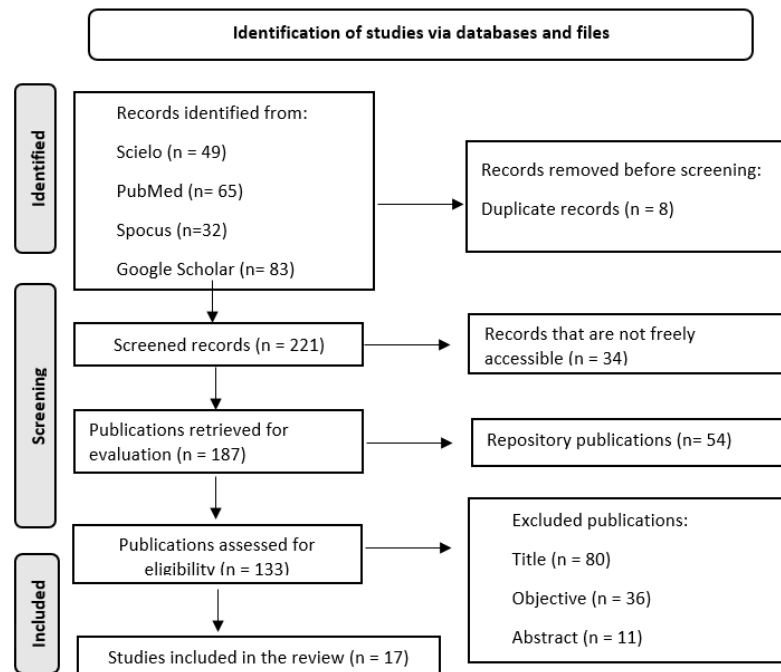
METHODOLOGY

A systematic review was conducted to provide a detailed, evidence-based analysis of the available scientific evidence, which will help understand the context of comparative genomics applications in bacterial resistance surveillance. The search was conducted in recognized databases such as Scielo, PubMed, Scopus, and Google Scholar, focusing on studies published in English, Portuguese, and Spanish.

To ensure the relevance of the studies included in the review, specific inclusion and exclusion criteria were defined. The inclusion criteria considered were original scientific articles, systematic reviews and case studies, and open-access publications. Regarding exclusion criteria, studies that included repository articles, theses or non-peer-reviewed papers, unverified gray literature, and duplicate works were excluded.

In addition, to search for information in the aforementioned databases, DeCs terms such as "comparative genomics," "bacterial resistance," "bioinformatics," and "epidemiological surveillance" were used, combined with the Boolean operators AND and OR to ensure a precise and relevant search. Of the studies initially identified, 229 articles were found, of which 70 were selected after applying the inclusion and exclusion criteria. Ultimately, 20 studies were deemed suitable for in-depth qualitative analysis (See Figure 1).

The application of these criteria during the selection of studies was evidenced by using the flowchart of the PRISMA 2020 methodology (Preferred Reporting Items for Systematic reviews and Meta- Analyses) to ensure a valid approach in systematic reviews.

Figure 1. PRISMA flowchart for item selection

Source: PRISMA Declaration, 2020.

RESULTS AND DISCUSSION

Once selected, the articles were critically appraised to extract relevant data on the applications of comparative genomics in bacterial resistance surveillance. The data obtained were analyzed using an evidence matrix from the total of 17 reviewed articles, which used a qualitative research methodology and followed a systematic review or literature review format.

Table 1. Classification by author, year, title, type of study, findings and DOI/URL

Authors	Year	Qualification	Type of Study	Findings	DOI/URL
Jauneikaite E., Baker K., Nunn J., Midega J., Hsu L., Singh S.	2023	Genomics for antimicrobial resistance surveillance to support infection prevention and control in health-care facilities	Systematic review of the literature	Pathogen surveillance is a key component of infection prevention and control strategies, particularly in detecting and responding to outbreaks. However, at the facility level, pathogen identification resolution typically occurs only at the species level, offering very limited discriminatory power for epidemiological analysis and little insight into the genetic basis of the AMR properties of the pathogen under investigation. Genomic surveillance of AMR in pathogens isolated from healthcare-associated infections can transform the accuracy with which the causative agent of the infection is routinely characterized, far exceeding that provided by species-level identification typically offered by diagnostic laboratories.	https://doi.org/10.1016/S2666-5247(23)00282-3
Vallejo D., Galarza J., Lalaleo L., Calero W.	2025	Beyond clinical genomics: addressing critical gaps in One Health AMR surveillance. <i>Frontiers in Microbiology</i>	Systematic review of the literature	The advent of whole genome sequencing (WGS) has simplified these processes, providing a single, comprehensive method for detecting antimicrobial resistance genes (ARGs), mobile genetic elements (MGEs), virulence traits, clonal relatedness, and phylogenetic profiles in a single sequencing run. WGS is now a cornerstone of AMR surveillance in clinical settings, facilitating outbreak detection, strain characterization, and retrospective epidemiological investigations. It encompasses sample processing, sequencing methodology, and bioinformatics workflows.	https://doi.org/10.3389/fmicb.2025.1596720
Landman F., Jamin C., Haan A., Witteveen S., Bos J., Heide H., Schouls L., Hendrickx A.	2024	Genomic surveillance of multidrug-resistant organisms based on long-read sequencing	Systematic review of the literature	These classical typing methods had low typing resolution, were laborious and expensive, and not all were suitable for high-throughput MDR typing on a daily basis. In the last decade, these classical methods are being replaced by whole genome sequencing (WGS) based methods, such as core genome (cg) or whole genome (wg) MLST and cg and wg single nucleotide polymorphisms (SNPs), as these methods significantly increased typing resolution.	https://doi.org/10.1186/s13073-024-01412-6
Fernandez R., Bolivar H., Hoyos C., Carrillo L., Serrano María., Abdellah E.	2021	Antibiotic resistance: the role of humans, animals, and the environment	Systematic review of the literature	The overuse of antibiotics in human and veterinary medicine, agriculture, and aquaculture, coupled with the lack of wastewater treatment plants to eliminate bacteria and antibiotic compounds, has allowed these compounds to enter the environment, leading to an increase in bacterial resistance, largely due to the selective pressure that antibiotics exert on microorganisms.	https://doi.org/10.14482/sun.36.1.615
Calero W., Ortuño N., Sunyoto T., Gomes A., Bastidas C., Ramírez M., Harries A.	2023	Whole-genome sequencing for surveillance of antimicrobial resistance in Ecuador: present and future implications.	Systematic review of the literature	In Ecuador, surveillance of bacterial pathogens and antimicrobial resistance in the clinical setting is primarily carried out at the Antimicrobial Resistance Reference Laboratory of the National Institute of Public Health, using conventional and molecular techniques. This laboratory supports the country's hospital network in the characterization of human pathogens.	https://doi.org/10.26633/RPSP.2023.8
Nikoline S., Riber L.	2025	Metagenomics as a Transformative Tool for Antibiotic Resistance Surveillance: Highlighting the Impact of Mobile Genetic Elements with a Focus on the Complex Role	Systematic review of the literature	Along with traditional AST methods, rapid and efficient molecular tools have been developed to study the hallmarks of AMR. While phenotypic characterization relies on culture-based techniques, excluding many pathogens and microbial communities from detection, genotypic approaches such as polymerase chain reaction (PCR) and DNA microarrays offer alternative detection strategies. Next-generation sequencing (NGS) platforms have significantly advanced both approaches, with second- and third-generation technologies playing important	https://doi.org/10.3390/antibiotics14030296

		of Phages		roles and offering complementary strengths.	
Lirola L., Ávila A., Fernández M., Reinoso A., Martínez S.	2022	Bacterial resistance: Overview, carbapenemases, and current status: A narrative review.	Systematic review of the literature	Antibiotic resistance is a direct consequence of the inappropriate use of these drugs. Antibiotics were designed to eliminate bacterial infections through various mechanisms. However, due to their overuse, they are causing selective pressure on bacterial populations, favoring the "survival of the fittest." Bacteria can acquire resistance through mutations (point or structural). These mutations are subjected to selective pressure by antimicrobials. This selective pressure favors the survival of the most resistant strains and leads to "vertical evolution."	http://hdl.handle.net/10481/75043
Zumbado R., Barquero A., Hidalgo O.	2022	Antibiotic resistance	Systematic review of the literature	The value of antimicrobial agents lies in the fact that diseases that once caused widespread death could be controlled, thereby reducing the fear and possibility of dying from a common infection for generations. However, this great achievement began to be undermined when bacteria, followed by fungi and viruses, began to develop the ability to adapt to the onslaught of antibiotics. This is possible because these microorganisms' ability to modify their DNA through mutation processes that allow them to acquire resistance to antimicrobial agents.	https://doi.org/10.34192/cienciaysalud.v6i3.500
Araújo P., Silva C., Lima R., Carneiro A., Costa J., Fernandes D., Brito L., Gancalves L., Nascimento R., Barros F.	2023	resistance resulting from indiscriminate use of antibiotics: integrative review	Systematic review of the literature	Microbial resistance to antibiotics has been gaining ground, showing rapid growth mainly in hospital environments, thus generating the so-called superbacteria, which are microorganisms that have genetically adapted to the action of antibiotics that are used on a large scale to treat infections.	https://doi.org/10.25110/arqsaude.v27i5.2023-076
Hernández M., Quijada N., Rodríguez D., Eiros J.	2020	Application of massive sequencing and bioinformatics to clinical microbiological diagnosis	Systematic review of the literature	The application of massive sequencing, in addition to reducing costs and analysis time, generates a large amount of information, which is changing the way microbiology research is conducted and inevitably demands the application of bioinformatics in microbiological diagnosis and analysis. The variety and quantity of software programs that provide a graphical interface are limited and reduce the computational power required for development, making it necessary to use programs run from a terminal. Although this is a new discipline for many microbiologists, the scientific community has developed numerous open-source software programs.	https://doi.org/10.1016/j.ram.2019.06.003
Ramos U., Silva J., Martínez E.	2019	Genetics and genomics focused on the study of bacterial resistance	Systematic review of the literature	Early detection of antibiotic resistance in bacteria that cause nosocomial infections provides relevant information for instituting appropriate and successful treatment. In the field of microbiology, various laboratory tests have been developed, such as E-test strips, antibiotic-impregnated discs, chromogenic media, and so on. Bioinformatic analysis of more than three dozen microbial genomes has identified some unique targets in pathogenic bacteria that are targeted by antibiotics. This narrows the therapeutic options, which directly impacts the success of antimicrobial therapy to combat secondary infections caused by these pathogens, in addition to leading to high rates of morbidity, mortality, and hospital costs.	https://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0036-3634200900090009#:~:text=A%20partir%20del%20an%C3%A1lisis%20de,que%20inhiban%20el%20crecimiento%20bacteriano.
Rubio S., Pacheco R., Gómez A., García R.	2020	Next-generation DNA sequencing (NGS): present and future in clinical practice	Systematic review of the literature	To understand the process and results of NGS-based testing: coverage and depth. There is still confusion in the use of these terms, which are commonly used interchangeably in the literature. Coverage (<i>coverage or breadth</i>) of Coverage refers to the percentage of bases in the reference genome that are being sequenced a given number of times. On the other hand, <i>depth of coverage</i> represents the average number of times each base in the genome is sequenced in the DNA fragments.	https://doi.org/10.11144/javeriana.umed61-2.sngs
Su M., Satola S., Read T.	2019	Genome-Based Prediction of Bacterial Antibiotic Resistance	Systematic review of the literature	While culture-based antimicrobial susceptibility testing (AST) remains the primary method employed by clinical laboratories, whole genome sequencing for antimicrobial susceptibility testing (WGS-AST) offers the potential to provide rapid, consistent, and accurate predictions of every known resistance phenotype for a strain. WGS-AST follows selective cultivation of the bacterium of interest from a clinical specimen, can determine genome-wide antibiotic resistance phenotypes simultaneously, and phenotypes contributed by multiple loci can be easily examined (as opposed to performing multiplex PCR).	https://doi.org/10.1128/JCM.01405-18
Shen X., Lundborg C., Sun X., Hu X., Dong H.	2019	Economic burden of antibiotic resistance in ESKAPE organisms: a systematic review	Systematic review of the literature	These microorganisms consistently evade the effects of commonly used antibiotics and pose a critical threat to public health. It is important to pay attention to these pathogens, as some studies have shown that patients with ESKAPE ABR microorganisms are more likely to receive inadequate antibiotic treatment, resulting in higher mortality rates and a greater likelihood of transmitting the disease to other patients.	https://aricjournal.biomedcentral.com/articles/10.1186/s13756-019-0590-7
Sherry N., Lee J., Giulieri S., Lane C., Carter G., Seemann T., Howde B.	2025	Genomics for antimicrobial resistance—progress and future directions	Systematic review of the literature	AMR research and surveillance using genomic methods have initially focused on separate sectors, such as human and animal health. The interconnectedness of humans, animals, and the environment is increasingly recognized. Consequently, to overcome these data silos, genomics has emerged for AMR surveillance in a One Health context. The concept of "One Health" is an important concept for understanding the transmission and evolution of AMR in different sectors and has been recently revised.	https://doi.org/10.1128/aac.01082-24
Naghavi M., Vollset S., Wool E., Han C., Chung E., Altay U., Smith G., Araki D., Alzoubi K., Amos B., Ahmend S.	2024	Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050	Systematic review of the literature	It provides a representative sample of the burden, limiting the ability to understand historical trends in AMR and evaluate policies implemented to reduce its impact. So far, temporal trends in AMR have been limited to selected high-income locations for a small number of pathogen-drug combinations. Using these components, we estimate the disease burden attributable to and associated with AMR, which we define based on two counterfactuals; respectively, an alternative scenario in which all drug-resistant infections are replaced by drug-susceptible infections, and an alternative scenario in which all drug-resistant infections were replaced by no infections.	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)01867-1/fulltext
Baker K., Jauneikaite E., Hopkins K., Lo S., Sánchez L., Getino M.	2023	Genomics for public health and international surveillance of antimicrobial resistance	Systematic review of the literature	Genomics also facilitates the detection of AMR genetic determinants (and their carriers; e.g., plasmids), virulence, and other relevant phenotypic markers previously explored only by molecular techniques, such as PCR. The electronic nature of genomic data also enables sequencing results to be shared and analyzed between laboratories and in bioinformatics centers (whether physical or cloud-based), for retrospective and international data comparisons, and for external quality assessments of genomic and bioinformatics processes.	https://doi.org/10.1016/S5247(23)00283-5
Murray C., Shunji K., Sharara F., Swetchinski L., Aguila G.	2022	Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis	Systematic review of the literature	Information on the current magnitude of the bacterial AMR burden, trends in different parts of the world, and the main pathogen-drug combinations that contribute to the bacterial AMR burden is crucial. If left unchecked, the spread of AMR could make many bacterial pathogens much more lethal in the future than they are today. A major challenge in addressing AMR is understanding the true burden of resistance, especially in settings where surveillance is minimal and data are scarce. There is a large literature estimating the effects of AMR on incidence, deaths, length of hospitalization, and healthcare costs for selected pathogen-drug combinations in specific settings.	https://doi.org/10.1016/S0140-6736(21)02724-0

Source: the authors.

The reviewed studies demonstrate the applications of comparative genomics in monitoring bacterial resistance to understand how resistance spreads between bacteria and to predict its potential eradication.

The evolution of microorganisms, especially bacteria, toward multidrug-resistant profiles is a direct consequence of the inappropriate and excessive use of antibiotics in human, veterinary, agricultural, and aquaculture medicine. This phenomenon has led to the emergence of "superbugs," organisms that have developed complex genetic mechanisms that allow them to survive even in the face of multiple therapeutic agents (Araújo et al., 2023 & Lirola et al., 2022). This approach not only limits available therapeutic options but also increases morbidity, mortality, and associated healthcare costs.

In this context, comparative genomics has emerged as a fundamental tool for understanding, monitoring, and combating this phenomenon. Through the detailed analysis of genetic sequences from different bacterial strains, this discipline allows for the identification of genes associated with resistance mechanisms. As mentioned in Medical Microbiology in 2020, it indicates that comparative genomics allows us to understand the genetic variability of microorganisms from the perspective of mutation and recombination. This is especially relevant when analyzing bacteria that rapidly acquire resistance, such as *Escherichia coli* or *Klebsiella pneumoniae*. In addition, environmental factors such as contamination by antibiotic residues constitute the survival of resistant strains (Fernández et al., 2021 & Sherry et al., 2025).

In this regard, Su et al., in 2019, indicated that traditional AMR surveillance is mainly based on phenotypic techniques such as antimicrobial susceptibility testing (AST), which identify whether a pathogen is sensitive or resistant to certain antibiotics using bacterial cultures. However, these tests have limitations in terms of speed, sensitivity, and specificity, which delays crucial clinical decision-making. On the other hand, molecular methods such as PCR have made it possible to detect specific genes associated with resistance, but their scope is limited because they can only analyze a small number of genetic targets (Nikoline & Riber, 2025).

In this context, whole genome sequencing (WGS) is emerging as a revolutionary tool that provides detailed information on the genetic identity of microorganisms, including resistance genes, mobile genetic elements (MGEs), virulence traits, and phylogenetic relationships between strains. One of the major advances associated with the implementation of WGS is its ability to overcome the limitations of traditional bacterial typing methods, such as pulsed-field electrophoresis (PFGE) or multilocus sequence typing (MLST), which offered low resolution and were laborious and expensive (Vallejo et al., 2025 & Landman et al., 2024).

Thanks to WGS, much greater discrimination between epidemiologically related strains can be achieved, thus facilitating the early detection of hospital outbreaks and the accurate characterization of local or international transmission events. Furthermore, this technology allows not only the identification of known resistance genes, but also the exploration of new genetic variants that may be emerging in clinical or environmental settings (Baker et al., 2023 & Vallejo et al., 2025). The use of WGS is also transforming the way integrated AMR surveillance is carried out by an approach that recognizes the interconnectedness between human, animal and environmental health.

Therefore, another key aspect is the proper interpretation of genomic data. Although WGS provides rich and comprehensive information, its clinical value largely depends on the ability to correlate genetic profiles with the resistance phenotypes observed in AST. This requires up-to-date databases, precise algorithms, and standardized criteria that allow for confidently predicting resistance from the genetic sequence. In this sense, the development of accessible and easy-to-use bioinformatics tools is essential to democratize access to genomics in low- and middle-income countries (Su et al., 2019 & Rubio et al., 2020).

However, it is important to understand that the integration of whole genome sequencing into bacterial resistance surveillance represents a qualitative leap in the fight against this global crisis. Its systematic application in clinical, veterinary, and environmental settings not only improves outbreak detection and response but also allows for a better understanding of the evolutionary dynamics of resistant microorganisms.

CONCLUSION

Comparative genomics is emerging as an innovative tool in the fight against bacterial resistance. It not only allows us to identify resistance genes and track their spread, but also to understand the molecular mechanisms behind microbial adaptation.

For this reason, it is important to understand that it not only contributes to scientific knowledge but also has fundamental practical applications in epidemiological surveillance and health decision-making.

Finally, it is important to note that their integration into health systems strengthens outbreak response capacity and

helps create clearer and more useful rules for proper antibiotic use. Furthermore, their combination with bioinformatics tools and global genomic databases has enabled the development of collaborative international data surveillance networks, which are essential for effectively responding to health problems affecting the entire world.

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