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Research paper

Using biosensors for the early diagnosis of arboviruses: a scoping review

Uso de biossensores no diagnóstico precoce de arboviroses: uma revisão de escopo

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ABSTRACT: Mapping scientific knowledge about the development of biosensors to be used for the early diagnosis of arboviruses. Scoping review based on studies searched in Lilacs, PubMed, SciELO and Web of Science databases. Nineteen (19) articles were selected, in total. The selected studies presented different types of biosensors used to detect arboviruses and their variants, with emphasis on dengue and Zika viruses. Electrochemical, optical and plasmon resonance were the biosensors mostly used for the aforementioned purpose due to their little margin of error. They enable reliable and fast diagnosis processes, besides being easy to handle and its low cost. Biosensors capable of identifying arboviruses are not yet available in health services, since they still require advancements to be achieved at practical research stages.

Keywords: Biosensors; Dengue; Zika virus; arboviruses; early diagnosis.

RESUMO: *Mapear o conhecimento científico sobre o desenvolvimento de biossensores para o diagnóstico precoce de arboviroses. Trata-se de uma revisão de escopo, onde, as buscas foram realizadas nas bases de dados Lilacs, PubMed, SciELO e Web of Science. Foram selecionados ao todo, 19 artigos. Os estudos apresentaram os diversos tipos de biossensores para a detecção da arbovirose e suas variantes, destacando-se dengue e zika. Os mais utilizados devido à pouca margem de erro são os eletroquímicos, ópticos e de ressonância de plasmons. Trazem confiabilidade e rapidez no diagnóstico além de serem fáceis de manusear e de baixo custo. Conclui-se que ainda não há nenhum biossensor para identificação de arboviroses disponíveis nos serviços de saúde, uma vez que necessitam avançar nas fases práticas das pesquisas.*

Palavras-chave: *Biossensores; Dengue; Zika Vírus; Arboviroses; diagnóstico precoce.*

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INTRODUCTION

Population growth, urbanization, global warming, increased livestock farming, anthropogenic changes and pristine habitats' destruction have worsened the outspread of re-emerging and emerging infectious diseases, such as Dengue, Zika and Chikungunya. Arboviruses trigger a group of viral diseases that are mainly transmitted by arthropods, such as mosquitoes and ticks, and that have similar symptoms. These factors make it hard to clinically diagnose them; therefore, tests enabling quickly diagnosing these virus types play key role in clinical practice (Khan, 2020).

Arboviruses' impact on morbidity and mortality rates gets stronger as epidemics involve large numbers of affected individuals. In addition, these virus types lead to implications for health services, mainly in absence of treatment, vaccines, among other effective prevention and control measures (Donalisio; Freitas; Von Zuben, 2019).

The clinical diagnosis of flaviviruses (Dengue and Zika Viruses), as well as of some viruses belonging to genus Alphavirus, such as Chikungunya virus, is overall carried out by analyzing common symptoms like high fever, in combination to retro-orbital and joint pain. However, these common symptoms make it hard to get specific diagnoses (Naresh; Lee, 2020). Therefore, laboratory diagnosis should be used to help differentiating infections caused by viruses belonging to genus Flavivirus from those caused by other genera, such as Alphavirus, since they have similar symptoms (Vidic, 2021).

Serology tests based on the Enzyme-Linked Immunosorbent Assay (Elisa) method is currently used to diagnose dengue, zika and chikungunya infections. They must be requested from the sixth day of symptoms' emergence, onwards, whereas tests focused on detecting viral antigens (Structural Antigen 1) NS1, viral isolation RT-PCR (Reverse Transcription followed by Polymerase Chain Reaction) and immunohistochemistry tests should be requested up to the fifth day after symptoms' onset.

It is worth emphasizing that positive results in any of these tests confirm the investigated case; however, in case of negative results, a new sample should be subjected to IgM serology to confirm or rule out the diagnosis (Brasil, 2021). All the tests, as well as the collection of a new sample to confirm the results, imply late diagnosis, since the sample must be collected from the sixth day after symptoms' emergence, onwards. Tools, such as biosensors, have been developed to detect these diseases since the first day of symptoms' onset (at low cost) and with higher result sensitivity (Kaya *et al.*, 2021).

Biosensors are analytical devices presenting bioreceptor molecules (probes) immobilized on the transducer surface of the biosensor that specifically bind to the target (Mollarasouli, 2019).

Accordingly, there has been increase in the number of studies aimed at developing techniques to ensure the fast diagnosis of the most prevalent arboviruses in the country (Ying-Pei *et al*., 2019; Mazlan *et al*., 2019; Faria; Mazon, 2019). It is worth emphasizing that early diagnosis of arboviruses mainly contributes to the proper clinical management of these diseases to prevent symptoms' worsening, as well as to plan health surveillance actions. Thus, the aim of the current study was to map scientific knowledge about the development of biosensors used to early diagnose arboviruses.

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MATERIAL AND METHOD

Scoping review conducted by following all six methodological steps described by Joanna Briggs Institute, namely: (1) identifying the research question; (2) identifying relevant studies; (3) selecting studies; (4) extracting data; (5) separating, summarizing and reporting results; and (6) sharing results (Aromataris, 2020).

The PCC (population, context and concept) strategy was used to identify the research question: P (not applicable), C (dengue, zika and chikungunya) and C (biosensors and diagnosis). The following research question was defined: What biosensors have been developed to diagnose dengue, zika and chikungunya?

Articles were searched in Lilacs, PubMed, SciELO and Web of Science databases based on using descriptors deriving from the Health Sciences Descriptor (DeCS) and Medical Subject Headings (MeSH) (**Table 1**).

Table 1. Search strategies applied to the databases. São Carlos-SP, 2024.

Database	Search Strategies
Web of Science	(“Biossensores OR biossensor OR biosensores OR biosensors ") AND ("Diagnóstico OR diagnostico OR diagnosis”) AND (“Precoce OR precoz OR early”) AND (“Arboviroses OR arbovirose OR arboviruses OR arbovirus OR arbovirus”)
Pubmed	(“Biossensores OR biossensor OR biosensores OR biosensors ") AND ("Diagnóstico OR diagnostico OR diagnosis”) AND (“Precoce OR precoz OR early”) AND (“Arboviroses OR arbovirose OR arboviruses OR arbovirus OR arbovirus”)
Lilacs	(“Biossensores OR biossensor OR biosensores OR biosensors ") AND ("Diagnóstico OR diagnostico OR diagnosis”) AND (“Precoce OR precoz OR early”) AND (“Arboviroses OR arbovirose OR arboviruses OR arbovirus OR arbovirus”)
SciELO	("Zika Virus Infection" OR "Zika Virus Fever" OR "Zika Virus Disease") AND ("Changes" OR "aspects" OR "manifestation") AND (Kids OR Children rbctiOR Child)

Primary studies published in Portuguese, English and Spanish, between 2005 and 2020, were included in the current review, whereas articles whose titles and abstracts did not fall within the research scope, as well as opinion articles, editorials and reviews, were excluded from it. The reference lists of all identified studies were also checked. The identified references were exported to the Mendeley reference manager, version X7, in order to select the studies after implementing the search strategy in each database.

The references of the herein selected studies were exported to the StArt web application (State of the Art through Systematic Review) to select the studies at two different levels.

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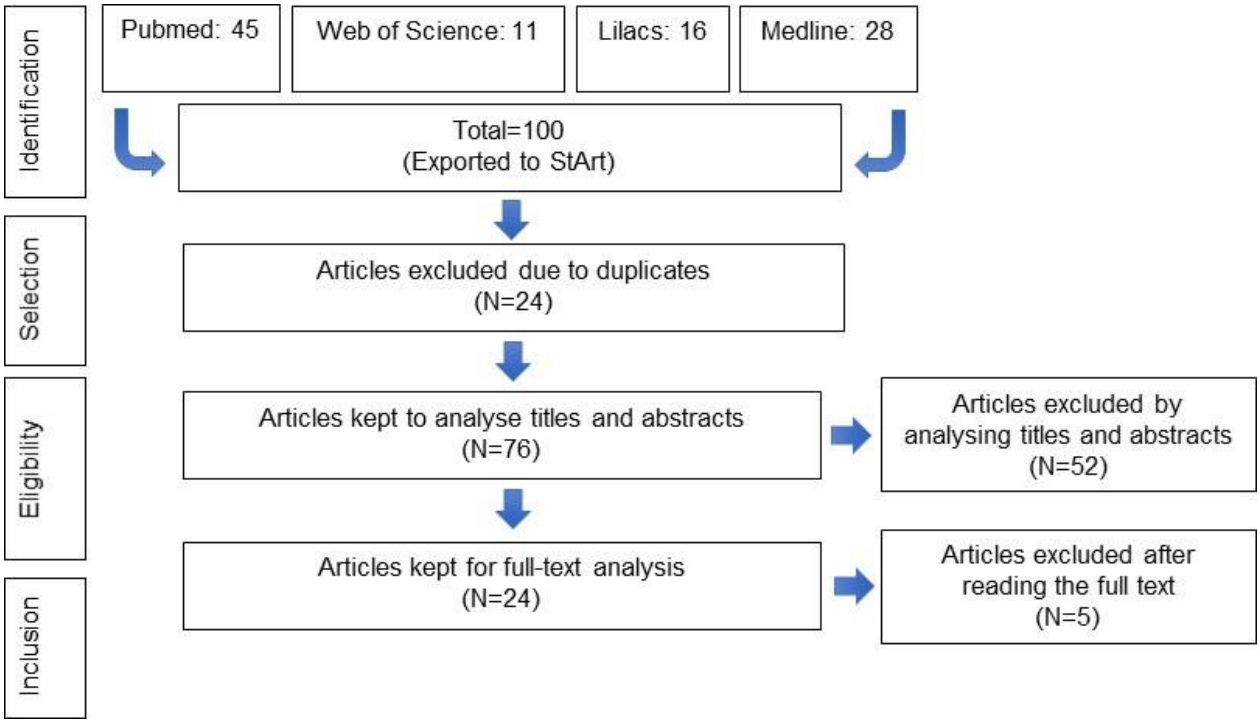
RESULTS

In total, 100 articles were identified in the investigated databases, but 24 of them were excluded from this review because they had been published in duplicate, 52 articles were excluded after analyzing their titles, abstracts and keywords, and 5 articles were excluded after full–text reading. The final sample comprised 19 selected studies (**Figure 1**).

Figure 1. Reference flowchart: inclusion and exclusion of articles. São Carlos-SP, 2023.



All 19 publications included in this scoping review were published in English. Four (21%) studies were carried out in Brazil and Malaysia; 3 (15.7%), in the United States; 2 (10.5%), in Taiwan and India; and only 1 (5.2%), in Thailand, Austria, Australia, Colombia, Israel, the Philippines, Sweden and France. On the other hand, 12 (63.15%) studies were published in the Netherlands; 5 (29.31%), in Switzerland; and 02 (10.5%), in the United Kingdom. All 19 articles regarded experimental studies (**Table 2**).

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Table 2. Description of the analyzed articles of experimental studies, based on author, publication year, country, aim, sample type and main results. São Carlos - SP, 2021.

Authors, year and country	Aims	Mains results
Sz-Hau *et al.,* 2009, Taiwan, Reino Unido	Developing a circulating-flow quartz crystal microbalance (QCM) biosensing method combining oligonucleotide-functionalized gold nanoparticles (i.e. AuNP probes) used to detect DENV (Dengue DNA).	In the DNA–QCM method, two kinds of specific AuNP probes were linked by the target sequences onto the QCM chip to amplify the detection signal, i.e. oscillatory frequency change (ΔF) of the QCM sensor. The target sequences amplified from the DENV genome act as a bridge for the layer-by-layer AuNP probes' hybridization in the method. Besides being amplifiers of the detection signal, the specific AuNP probes used in the DNA–QCM method also play the role of verifiers to specifically recognize their target sequences in the detection. The effect of four AuNP sizes on the layer-by-layer hybridization has been evaluated and it is found that 13 nm AuNPs collocated with 13 nm AuNPs showed the best hybridization efficiency. According to the nanoparticle application, the DNA–QCM biosensing method was able to detect dengue viral RNA in virus-contaminated serum as plaque titers being 2 PFU ml−1 and a linear correlation (R2 = 0.987) of ΔF versus virus titration from 2 × 100 to 2 × 106 PFU ml−1 was found.
Navakul *et al.,* 2017, Amsterdã	Perform electrochemical impedance spectroscopy (EIS) as an alternative method for detecting total dengue (DENV) and antibody assay through protein recognition.	A detector is constructed by applying the polymer compound graphene oxide (GO) to an EIS electrode. The experimental protocol is relatively simple, with no need for expensive reagents or conditions, but it can detect the virus up to the limit of 0.12 pfu / mL (P = 0.05). At this detection limit, the method can confirm the presence of DENV at an early stage of infection. The method was able to discriminate between DENV and the other subtypes, as well as H5N1. In addition, the experiments also showed that when a DENV antibody is added to the corresponding DENV virus solution, this led to a decrease in resistance compared to the pure virus sample, indicating that the antibody inhibited the binding of the virus to the GO polymer. The results suggest that this method can be used to screen for antibodies against dengue virus and could be of general benefit in DENV vaccine research.
Oliveira *et al*., 2015, Suíça	Developing an electrochemical DNA biosensor for the detection of dengue virus serotype 3 (DENV-3) sequences.	The results showed that the 22-m sequence was the best DNA probe for identifying DENV-3. The optimum concentration of the DNA probe immobilized on the electrode surface is 500 nM and a low detection limit of the system (3.09 nM). In addition, this system allows the selective detection of DENV-3 sequences in buffer solutions and human serum.
Steinmetz *et al.,* 2019, Amsterdã	Developing a DNA biosensor to detect Zika Virus (ZIKV) in real human serum samples, using an oxidized glassy carbon electrode (ox-GCE)	Due to the high surface area and high electrical conductivity of AuNPs, the amount of charge of the DNA probes was increased, resulting in a significantly improved electrochemical response of the developed biosensor. This proposed biosensor platform proved to be quite simple and suitable for proper immobilization of ZIKV ssDNA probes (through the formation of Au-S covalent bonds) and was able to efficiently detect ZIKV in real human serum samples. The device demonstrated an adequate LOD of 0.82 pmol L-1 by EIS and exhibited stability for 90 days.

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Dias *et al.*, 2013, Amsterdã	Developing an immunosensor for the non-structural protein 1 (NS1) of the Dengue Virus based on carbon nanotube printed electrodes (CNT-SPE).	A homogeneous mixture containing carboxylated carbon nanotubes was dispersed in carbon ink to prepare a screen-printed working electrode. The Anti-NS1 antibodies were covalently linked to the CNT-SPE by an ethylenediamine film strategy. Amperometric responses were generated at -0.5 V vs. Ag / AgCl by reaction of hydrogen peroxide with peroxidase (HRP) conjugated to anti-NS1. An excellent detection limit (in the order of 12 ng mL^{-1}) and a sensitivity of 85.59 **µ**A mM^{-1} cm^{-2} were achieved, allowing the diagnosis of dengue according to the required clinical range.
Lim *et al.*, 2018, Amsterdã	Develop a test using a drop of blood, an immunosensor, to specifically detect ZIKV without cross-reacting with other FLAVs.	The analysis was carried out using a drop of blood added to an immunosensor. A high sensitivity of 1 pg/mL, desirable specificity, data storage and geographic location surveillance were achieved simultaneously. And the POC test can easily distinguish ZIKV infection from FLAV blood samples with cross-reactivity by visual detection. This simple, convenient, inexpensive, instrument-free and portable POC test has the potential to meet urgent needs at ports of entry, airports and endemic regions with few resources.
Mazlan, 2019, Amsterdã	To develop an optical genosensor based on the Schiff base complex DNA marker for Dengue Virus serotype 2.	This design basis provided good selectivity in distinguishing one-base variation in nucleotide sequence, high sensitivity screening at low tcDNA concentrations and fast hybridization time to give observable color change on the DNA biosensor surface. Furthermore, the demonstration of the DNA biosensor in the testing of the DEN-2 genome in clinical samples of blood, urine and saliva from dengue-positive patients was carried out in comparison with the RT-PCR reference method with no statistically significant difference in the results generated by both methods.
Faria; Mazon, 2019, Amsterdã	Developing an electrochemical immunosensor based on ZnO nanostructures immobilized with ZIKV antibody	The biosensor developed allows rapid detection of Zika virus in undiluted urine, without cross-reactivity with the DENV-NS1 antigen, with a linear range of 0.1 ng mL^{-1} to 100 ng mL^{-1} . The detection limit is less than 1.00 pg mL^{-1}. It showed high specificity for ZIKV-NS1. The dot-blot assay approved the non-reactivity of the immunosensor based on ZnO NRs with the dengue antigen. Testing in urine allows the immunosensor to be performed as a rapid and immediate test, without the need for specialists. This immunosensor has shown adequate stability and reproducibility with other ZIKV tests.
Rahman *et al.,* 2016, Amsterdã	Demonstrate highly effective molecular electronics-based detection using silicon nanowire (SiNW) integrated with complementary metal oxide semiconductor process	By using this enhancing technique, the results show that the detection limit for the 60-second plasma-treated SiNW device can be reduced to 1.985 x 10^{-14} M compared to 4.131 x 10^{-13} M for the untreated SiNW device. It is believed that these findings can greatly promote the use of plasma treatment as enhancement platforms. In addition, the modified SiNW biosensor can distinguish different base target sequences from DENV DNA oligomer 27-mers and is stable with respect to the denaturation and rehybridization circle. The developed biosensor was also able to detect the DENV RT-PCR product in real samples, indicating its potential applications as a diagnostic tool.

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Alzate *et al.,* 2020, Amsterdã	Report on the development of genosensors for differential detection of ZIKV and its discrimination from homologous dengue (DENV) and chikungunya (CHIKV,) arboviruses	The results show that the designed molecular primers were specific for the efficient amplification of synthetic ZIKV target probes compared to a reference molecular weight ladder and negative control with non-genetic material. In fact, these primers also efficiently amplified cDNA transcribed from ZIKV RNA strands replicated in cell cultures. The primers also specifically amplified RNA from infected cell culture samples and discriminated them from DENV and CHIKV genetic material by real-time PCR. These results demonstrated that the high specificity of the designed primers allows us to detect ZIKV RNA and discriminate it from the phylogenetically related DENV and CHIKV arboviruses.
Michelson *et al*., 2019, Reino Unido	Evaluate new ZIKV serological assays using the NS1 biosensor modulation antigen	MMB assays for Zika have a sensitivity of 88% -97%, much higher than the current EUROIMMUN ELISA assays (38% -74%). In addition, specificity is 100% and cross-reactivity with West Nile and dengue viruses is minimal (0% -4%). MMB assays have detected IgM antibodies to Zika as early as 5 days and up to 180 days after the onset of symptoms, significantly extending the number of days in which antibodies are detectable.
Darwish *et al.*, 2018, Amsterdã	Developing an immunofluorescence biosensor for the detection of the Dengue non-structural protein 1 biomarker in clinical samples obtained in the early stages of infection	The linear detection range for the NS1 antigen was between 15 and 500 ng mL^{-1}, with coefficients of determination (R2) = 0.92 and LOD of 15 ng mL^{-1}, which is much lower than that of a previously reported localized surface plasmon resonance (LSPR)-based biosensor (74 ng mL^{-1}) for NS1 detection. The present optical NS1 immunosensor provided good reproducibility, with a relative standard deviation of 2%, and high stability (up to 21 days) during storage at 4°C. In addition, this immunosensor effectively determined the NS1 antigen in complex plasma samples from DENV-infected patients, with high selectivity for the NS1 antigen and low cross-reactivity with JEV (Japanese Encephalitis Virus) and Zika Virus.
Suthanthiraraj; Sen, 2019, Amsterdã	To produce a biosensor based on localized surface plasmon resonance to detect the Dengue antigen in whole blood.	Specifically in a two-fold concentration range in plasma. By integrating the proposed biosensor with membrane-based blood plasma separation, we have developed a lab-on-chip device that facilitates rapid NS1 diagnosis (within 30 minutes) from just 10 µL of whole blood. In addition to reducing sample volume and assay time, the biosensor can also reduce the cost of the assay, since metal deposition and annealing are performed en masse, and several biosensors can be fabricated from a single substrate.
Afsahi *et al.*, 2018, Amsterdã	Developing a portable and inexpensive graphene-based biosensor to detect Zika Virus with a highly specific immobilized monoclonal antibody.	The covalent binding of anti-Zika NS1 to a graphene biosensor chip allows the portable and low-cost acquisition of kinetic binding data in real time using Field Effect Biosensor (FEB) technology. The Agile R100 biosensor chip functionalized with anti-Zika NS1 detects ZIKV NS1 at concentrations as low as 0.45 nM. Furthermore, when the device was tested with Japanese encephalitis (JEV) NS1, there was no measurable cross-reactivity. The LLOD and specificity of the ZIKV NS1 antigen provide an opportunity for early-stage detection of active disease in presumptive Zika infection. The Agile R100 FEB platform offers a promising basis for the development of clinical applications for Zika and improved diagnostic tests early in infection.

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Ariffin *et al.*, 2018, Suíça	Developing a reflectometric biosensor for dengue virus DNA based on the DNA immobilization matrix and the optical marker.	The reflectometric DNA biosensor demonstrated a wide linear response range for the target DNA in the concentration range of 1.0×10^{-16} - 1.0×10^{-10} M (R2 = 0.9879) with an ultra-low limit of detection (LOD) at 0.2 aM. The response of the optical DNA biosensor was stable and sustainable at 92.8% of its initial response for up to seven days of storage with a response time of 90 minutes. The reflectance DNA biosensor obtained promising recovery values of around 100% for the detection of synthetic dengue virus (DENV-2) DNA concentration in non-invasive human samples, indicating the high accuracy of the proposed DNA analytical method for early diagnosis.
Wasik; Mulchandan; Yates, 2018, Reino Unido	To present a label-free chemosensor for the detection and free quantification of Dengue (DENV) NS1 protein markers in saliva.	Unlike commercially available Rapid Diagnostic Tests (RDTs), the presented immunosensor is compatible with saliva collection, a non-invasive sampling technique that is much more likely to be accepted by patients and can be collected by untrained personnel. With a quantification range of ~1 ng/mL to 1000 ng/mL of NS1 in artificial human saliva, the proposed biosensor can quantify DENV NS1 in a clinically relevant way, with a salivary concentration range and 10 min incubation of 10 µL of saliva. As such, the immunosensor will improve clinical utility and point-of-care diagnostics, especially when blood collection is not available, and can distinguish dengue from severe dengue.
Kumbhat *et al.*, 2017, Amsterdã	Proposing a surface plasmon resonance immunobiosensor for Dengue Virus serological diagnosis.	The results were compared with those obtained by MAC-ELISA. Regeneration was achieved by pepsin solution in glycine-HCl buffer (pH 2.2) and the sensor surface exhibited a high level of stability during repeated immunoreaction cycles. The proposed biosensor being simple, effective and based on the use of natural antigen-antibody affinity, this study presents an encouraging scope for the development of biosensors for the diagnosis of dengue and dengue hemorrhagic fever (DHF).
Yrad *et al.*, 2019, Suíça	Developing a colorimetric lateral flow biosensor (LFB) for the visual detection of Dengue-1 RNA.	The positive test generated a red test line on the lateral flow biosensor (LFB) strip, which allowed visual detection. The optimized biosensor has a cut-off value of 0.01 µM using the synthetic Dengue-1 target. The proof-of-concept application of the biosensor detected Dengue-1 virus in pooled human sera with a cut-off value of 1.2×10^{4} pfu / mL. The extracted viral RNA, when coupled with nucleic acid sequence-based amplification (NASBA), was detected in the LFB within 20 min. This study demonstrates for the first time the applicability of dextrin as a marker for lateral flow assays.
Palomar *et al.*, 2020, Suíça	Developing an electrochemical biosensor for the detection of Dengue toxin	The system exhibits a high sensitivity of - 0.44 ± 0.01 µA per decade with a wide linear range between 1×10^{-12} and 1×10^{-6} g/mL with a working potential of 0.22 V vs Ag / AgCl. The extremely low detection limit (3×10^{-13} g/mL) ranks this immunosensor as one of the most efficient reported in the literature for the detection of recombinant Dengue Virus 2 NS1. This biosensor also offers good selectivity, characterized by a low response to various non-specific targets and assays in human serum.

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DISCUSSION

Early disease identification is essential to properly treat individuals infected with arboviruses. Thus, it is necessary developing biosensors capable of contributing to the fast and accurate diagnosis of these diseases. Biosensors are suitable for detecting pathogenic viruses at excellent response/specificity rates, as well as allow rapid testing based on simple, reliable and miniaturization procedures.

Biosensors' configuration comprises devices capable of detecting antigens in a faster, simpler and more economical way, based on antigen-antibody interaction, according to which, antibodies are immobilized by the transducer so it can detect the antigen. Biosensors can be built with a biological element capable of capturing the virus, as well as with a transducer used to convert the virus that had been previously captured in the sample into a detectable signal. Subsequently, the systems amplify and express the signal for quantitative detection purposes. These biorecognition elements are formed by enzymatic reactions, whole cells, virus genetic material, such as DNA and RNA, and by products deriving from patients' immune response system, such as antibodies.

Electrochemical biosensors are simpler, more sensitive and reliable, as well as present rapid diagnostic efficacy and response to detect viral infections caused by arboviruses, such as yellow fever. This type of procedure can already be used in health services; however, there may be interference between electrochemically and electrophysiologically detected signals, since some viral proteins can share the same sequence identity as other viral species, and it would require repeating the process.

Optical biosensors used to identify arboviral infections can also be used to diagnose and monitor throat cancer. These biosensors can detect non-electrical remote signals in sensitive environments, without the need of active elements in the biolayer. Thus, they can respond to more than one analyte by using reagents that absorb or emit at different wavelengths, although the optically active reagents used by them are often unstable. However, they can suffer interference from ambient light, as well as present long response times, reagent release under continuous use, low immobilization matrix stability, high manufacturing and reagent costs, as well as high complexity.

Localized surface plasmon resonance biosensors can detect diseased exosomes, as well as present results that can be seen by the naked eye and responses in real time, besides being easy to handle, fast and accurate.

These biosensors act at temperature and detect electromagnetic oscillations taking place at the metal-dielectric interface in the interaction between the ligand immobilized on the biosensor chip and the target analyte. It is worth emphasizing that they can be used to detect different biomarker types, such as nucleic acids, proteins and antibodies; however, it is necessary conducting further tests to validate their applicability to each specific pathology.

According to a study carried out by the Federal University of Ouro Preto (UFOP) in 2019, the localized surface plasmon resonance biosensor was capable of specifically and sensitively detecting arboviruses (mainly at acute infection stage), in purified virus samples, as well as in human serum samples added with these viruses. In addition, it was capable of distinguishing diseases with similar clinical symptoms, such as Influenza, Dengue, Zika and Chikungunya, besides presenting fast results (15 minutes, on average) and low cost.

Thus, this biosensor has great potential to be used to develop a new and effective diagnostic approach to be applied to Flaviviruses (Ribeiro; Silva, 2019).

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There is also the field effect biosensor, which comprises electrodes measured by biotechnology concentration and transistor technology, and target molecules that bind and identify both the analyte and its composition.

These biosensors are highly sensitive to identify viral infections, such as hepatitis, influenza, dengue, chikungunya and Zika.

Studies have shown that the ZIKV protein conformation has a unique feature in comparison to proteins found in other Flaviviruses. It can be detected in urine since the onset of the first symptoms, even before the production of specific antibodies, a fact that rules out the need of performing invasive blood collection to complete the diagnosis.

A study carried out by Universidade Estadual Paulista Júlio de Mesquita Filho (UNESP, 2014) was able to prove that electrochemical biosensors can detect viruses that have invaded individuals' bodies.

However, regardless of the dilution state of the sample collected from the infected person since the first day of symptoms' emergence, using microfluidic technology in these devices can infer the positivity of the viral disease affecting the body. It happens because the dilution-level control allows detecting molecules at wide concentration range based on using small sample volume, in a fast, efficient, sensitive and portable way, besides allowing savings on both samples and reagents.

Limitations of the current study lie on the fact that the herein conducted review only included studies written in Portuguese, English and Spanish, articles that were available in full text, as well as on not including indexing databases other than the herein included ones.

Finally, none of these biosensors aimed at identifying arboviruses are currently available in healthcare services, since they still require advancements at practical research stages. It is important applying these biosensors in the early and differential diagnosis of different arbovirus types, as well as making practical, easy-to-use and effective devices available to health services, in order to provide more effective and appropriate treatments for patients affected by arboviruses-related diseases.

CONCLUSIONS

Based on studies focused on investigating biosensors' features and advantages, it is necessary implementing them in the daily routine of healthcare services, since they can contribute to accurate and easy-to-handle diagnosis processes. In addition, they can provide fast diagnosis to favor proper symptoms' treatment, besides contributing to epidemiological and health assessments and to reduce the number of underreported cases of these diseases.

Despite the reliability, speed and low cost of biosensors, there is a gap in the literature, when it comes to studies focused on investigating their practical feasibility, since their reliability and reproducibility must be thoroughly analyzed in order to guarantee more specific and stable results, even for the most common diseases.

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