

## VACCINES AGAINST COVID-19 USING NANOTECHNOLOGY: A LITERATURE REVIEW<sup>1</sup>

### VACINAS CONTRA A COVID-19 UTILIZANDO NANOTECNOLOGIA: UMA REVISÃO DA LITERATURA

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#### ABSTRACT

In March 2020, it was declared a state of pandemic coronavirus disease (COVID-19) by the World Health Organization, which represents a public health concern. Some vaccines were created to fight the COVID-19 disease and use nanotechnology in their composition. Vaccines approved in clinical trials that are currently available for the population using nanotechnology are BNT162b2 (Pfizer, 95% effective), and mRNA-1273 (Modern, 94, 5% effectiveness). These vaccines use lipid nanoparticles, loaded with RNA (mRNA) to fight SARS-Cov-2. Nanotechnology can have several advantages in creating vaccines, for example, antigen protection by premature degradation to increase the immune response, control release kinetics, provide site-specific antigens, and facilitate intracellular absorption. This review article seeks to present applications of nanostructures in the production of vaccines against COVID-19 that are in the clinical testing phase and also those that have already been approved.

**Keywords:** *Virus, pandemic, SARS-CoV-2, nanoparticles.*

#### RESUMO

*Em março de 2020, foi declarado estado de pandemia da doença coronavírus (COVID-19) pela Organização Mundial de Saúde, o que representa um problema de saúde pública. Algumas vacinas foram criadas para combater a doença COVID-19 e utilizam nanotecnologia em sua composição. As vacinas aprovadas em ensaios clínicos que estão atualmente disponíveis para a população e usam nanotecnologia são BNT162b2 (Pfizer, 95% eficácia) e mRNA-1273 (Moderna, 94,5% de eficácia). Essas vacinas utilizam nanopartículas lipídicas, carregadas com RNA (mRNA) para combater a SARS-Cov-2. A nanotecnologia pode apresentar várias vantagens na criação de vacinas, por exemplo, proteção de antígeno por degradação prematura para aumentar a resposta imune, controlar a cinética de liberação, fornecer antígenos específicos do local e facilitar a absorção intracelular. Este artigo de revisão tem como objetivo apresentar aplicações de nanoestruturas na produção de vacinas contra COVID-19 que estão em fase de testes clínicos e vacinas já aprovadas.*

**Palavras-chave:** *Vírus, pandemia, SARS-CoV-2, nanopartículas.*

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## INTRODUCTION

In December 2019, coronavirus disease (COVID-19) was first recognized as a disease caused by severe acute respiratory syndrome (SARS-CoV-2) with the main site of infection in Wuhan, Hubei Province, China (ZHU *et al.*, 2020). The virus that caused the outbreak was recognized as ‘coronavirus’. However, this is the name of the virus family to which it belongs (Coronaviridae). Within this family, there are other variations of the virus, such as Severe Acute Respiratory Syndrome Coronavirus (Sars-CoV) and Middle East Respiratory Syndrome (Mers-CoV), which are known to scientists. To differentiate this new variation that emerged recently, at first, many experts referred to it as the ‘new coronavirus’. Until it had its official name defined: Sars-CoV-2, which means ‘severe acute respiratory syndrome - coronavirus 2’. The World Health Organization (WHO), defined that the respiratory disease caused by the new coronavirus infection should be called Covid-19. The name of the disease results from the words ‘corona’, ‘virus’, and ‘disease’, indicating the year in which it appeared (2019). It was initially believed that the disease was confined to China alone, but it quickly spread around the world and was declared a pandemic by the World Health Organization in March 2020. Currently with 247,219,391 confirmed cases of COVID-19, and 5,016,369 people have died worldwide from the disease (as of November 2021) (DONG *et al.*, 2020; HOPKINS, 2021).

There have been several attempts to find an effective treatment against COVID-19 since then, however, most results have been disappointing and others controversial. Even unveiling some mechanisms involving COVID-19, the scenario is still quite challenging (PACHECO *et al.*, 2020). As shown during the current COVID-19 pandemic, reliable and efficient vaccine delivery systems are urgently needed for the development of vaccines against COVID-19 as well as other emerging pathogens (PARK *et al.*, 2021). Developing a vaccine takes time, as vaccines must be not only protective but also safe. Unlike other drugs that are administered to sick patients, vaccines are administered to healthy patients and require very high safety margins (SINGH; MEHTA, 2016). Therefore, the development of a safe and effective vaccine that can prevent SARS-CoV-2 infection and transmission has quickly become a priority (BROUWER *et al.*, 2021).

According to the human body’s immune response mechanism, a vaccine considered effective must contain antigens, immunological enhancers (adjuvants), and/or target-specific delivery systems, for example using carrier nanostructures (PASHINE *et al.*, 2005). Adjuvants are pharmacological or immunological agents used to activate the innate immune system, allowing it to respond quickly to infections and boosting adaptive immune responses that are specific to viral infections (MAO *et al.*, 2021). However, there are few licensed adjuvants for human vaccines (SHI *et al.*, 2019), making the

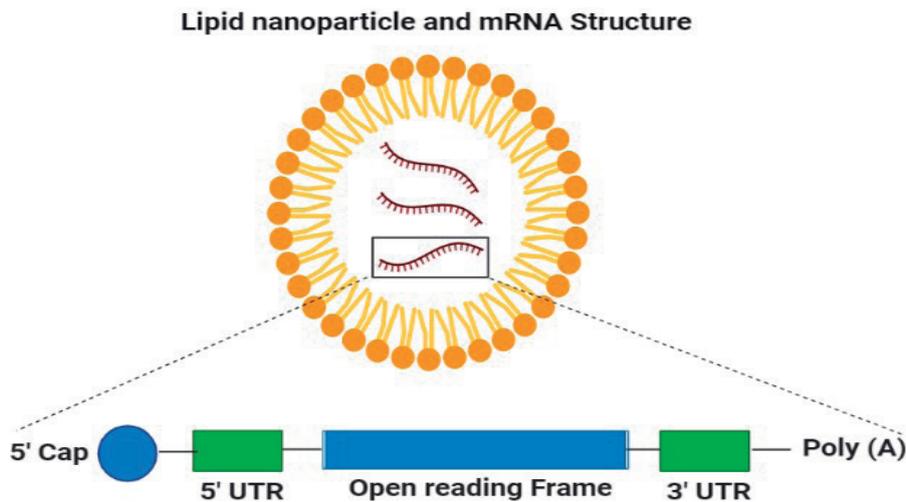
development of vaccines against viruses difficult. In recent years, nanoparticles have attracted attention and were developed as adjuvants against several viruses (MAO *et al.*, 2021).

The structure of the nanoparticle can be controlled to become a depot for loading antigens, preventing degradation and prolonging exposure to the antigen. Different sizes and morphology of nanoparticles allow them to induce different immune responses and deliver antigens to target or specific sites (MAO *et al.*, 2021).

Vaccines can be prophylactic or therapeutic, with some possible classifications: live attenuated vaccines, that is, where microorganisms remain alive (pathogenic microbe), but altered in a way that can cause an immune response and not lead to infection (LASRADO *et al.*, 2021); inactivated vaccines, which are those where the microorganisms are dead, but deceive the immune system with the dead infectious agent or part of it, triggering a protection process (HOFFMANN *et al.*, 2021); subunit or protein vaccines (purified antigens) are made up of protein fragments or parts of coronavirus proteins that mimic its structure (FERRAZ, 2021; LARSEN *et al.*, 2021), or toxoid vaccines, that is, made with modified toxins, unable to cause disease. Toxoids usually generate a weak immunization, requiring some reinforcement after a few years, for example, the tetanus vaccine (TICHA *et al.*, 2021).

Nucleic acid-based vaccines, i.e., DNA (as plasmids) and RNA (as messenger RNA -mRNA) vaccines, pave the way for safe and effective biological products to mimic inoculation with live organism-based vaccines, particularly for stimulation of immune-mediated cells (CHANDLER *et al.*, 2020; JAHANAFROOZ *et al.*, 2019). Although nucleic acid-based vaccines demonstrate significant advantages over traditional vaccines in terms of safety, efficacy, induction of B and T cell responses, and specificity, it is important to mention that mRNA vaccines have advantages when compared to vaccines based on other types of nucleic acids. Furthermore, DNA vaccines present a potential risk of integration into the host genome, which can result in insertional mutagenesis (JAHANAFROOZ *et al.*, 2019). In contrast, mRNA vaccines are only targeted for cytoplasmic delivery, bypassing the risk of genomic integration (PARDI *et al.*, 2018; JAHANAFROOZ *et al.*, 2019).

The mRNA vaccines have emerged in recent years as an option in cancer treatment (HOECKE *et al.*, 2021). In combination with nanoparticle-based formulations that increase transfection efficiency (insertion of nucleic acids into cells) and facilitate targeting of the lymphatic system, nucleoside-modified mRNA provides effective delivery of cytokines, costimulatory receptors, or therapeutic antibodies (BECK *et al.*, 2021).

**Figure 1** - Structural elements of mRNA therapy.

Source: Author construction (Created in Biorender.com)

Figure 1 shows structural elements of mRNA therapy. At the top is the schematic structure of the lipid-based mRNA nanoparticle (LNP - *Lipid Nanoparticles*) and at the bottom the structure of the synthetic mRNA, comprising a cap 5', 5' and 3' UTRs (UTR - *Untranslated Region*), the *Open Reading Frame* (ORF) and a 'poly (A)' tail. The adjustable structural elements that influence mRNA translation are the 5' cap, 3' and 5' UTRs, and the codon used in the ORF, in the case of SARS-CoV-2 the ORF is a nucleoside encoded by spike protein (S). Innate immune activation is related to nucleoside modification, and stability is related to the 5'cap and 'Poly(a)' tail (BECK *et al.*, 2021).

Therapeutic strategies based on nanotechnology represent a promising approach to overcome the limitations found in prevention, diagnosis, and therapies against COVID-19 (WEISS *et al.*, 2020). In therapy with COVID-19, nanotechnology has wide application and can act at different stages of the disease, with the potential to inhibit virus-cell interaction, membrane fusion, cell internalization, transcription, translation, and viral replication, in addition to activating intracellular mechanisms that cause virus irreversible damage (MAINARDES; DIEDRICH, 2020).

The mRNA vaccines are largely coupled with immunological adjuvant and various delivery strategies that can increase antigen reactivity. The delivery strategies most used by researchers in recent years are mRNA vaccines based on lipid transporters (LNP), polymers, peptides, pseudovirus particles (VLP - *Virus-like Particle*), cationic nanoemulsions, and newly developed dendritic cells to induce adaptive immunity (WANG *et al.*, 2021).

This review aims to discuss the presence of nanotechnology in vaccine production, the challenges and opportunities of the manufacturing processes, and the delivery platforms that are needed for global vaccination. The advantages of using nanotechnology over other technologies used and perspectives regarding mRNA vaccines against viruses and other diseases.

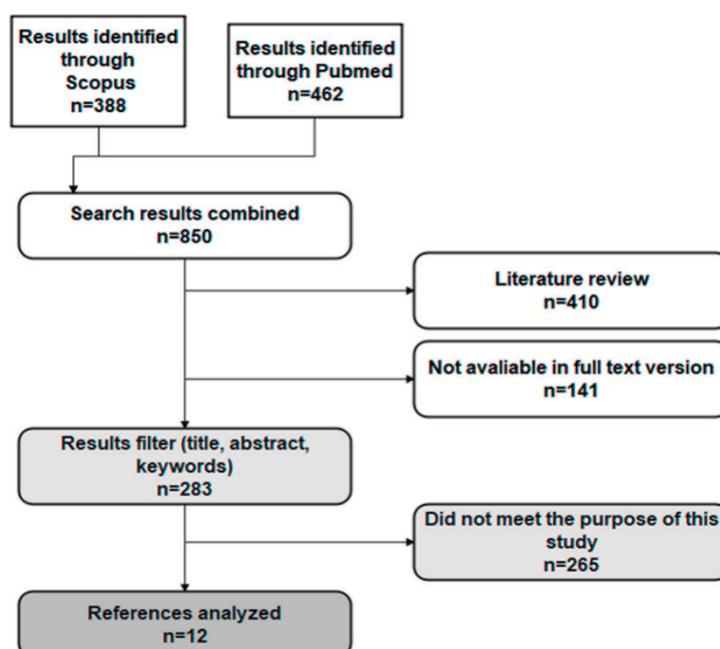
## METHODOLOGY

This study is defined as exploratory of the type of integrative review in the literature. The search was based on Boolean descriptors or operators, using the following words (English): ‘*SARS-CoV-2 AND vaccines AND nano\**’, (\*Main descriptor), among others. The research took place between March and July 2021 in electronic databases: Scopus and PUBMED (US National Library of Medicine).

Some inclusion criteria were used to select the articles, such as complete articles and available in full text, with a publication date close to the current date, not being a review article, and being articles with title, abstract, and/or keywords similar to the context of the research.

After searching the chosen databases, titles and abstracts were evaluated and articles that met the prerequisites defined in this study were selected for a full reading. The following characteristics of the publications were recorded: Year of publication, name(s) of the author(s), type of biological application of nanostructures in the creation of vaccines against COVID-19, advantages of using nanotechnology in the creation of vaccines against COVID -19.

Figure 2 - Flowchart with the article selection strategy



Source: Author construction.

The search in the chosen databases resulted in the collection of 850 articles, of which 12 met the criteria and were selected for inclusion in the study. Figure 2 shows the flowchart with the strategy for selecting the articles included. The publications that made up this study were published between 2020 to 2021.

## RESULTS AND DISCUSSIONS

This study presents current research related to the use of nanotechnology applied in vaccines against COVID-19. The chosen references show different types of nanoparticles used in the development of the vaccine, for example, lipid nanoparticles (LNPs) and proteins. The technologies used in vaccines with nanoparticles: mRNA, VLP, recombinant protein nanoparticles. Details are shown in Table 1.

Table 1 - Publications that made up the study.

Year	Authors	Nanoparticles	Type of vaccine
2020	ZHANG <i>et al.</i>	Lipid nanoparticles	mRNA
2021	SAHIN <i>et al.</i>	Lipid nanoparticles	mRNA
2021	RAUCH <i>et al.</i>	Lipid nanoparticles	mRNA
2021	JIANG <i>et al.</i>	Protein	Recombinant protein nanoparticles
2021	WANG <i>et al.</i>	Lipid nanoparticles	mRNA
2021	TAN <i>et al.</i>	Protein	VLP (Virus-like particle)
2021	NAG <i>et al.</i>	Lipid nanoparticles	mRNA
2021	HUANG <i>et al.</i>	Lipid nanoparticles /Liposomes (LPX)	mRNA
2021	CHIBA <i>et al.</i>	MS2 Protein	VLP (Virus-like particle)
2021	KARPENKO <i>et al.</i>	Lipid nanoparticles	mRNA
2021	TEIJARO e FERBER	Lipid nanoparticles	mRNA
2021	TSIAMBAS <i>et al.</i>	Lipid nanoparticles	mRNA

Table 1 Source: Author construction.

In an approach to messenger RNA-based vaccines against coronavirus disease, caused by the SARS-CoV-2 pandemic, according to Zhang *et al.* (2020), describe the creation of a vaccine (ARCoV) of mRNA encapsulated by lipid nanoparticles (mRNA-LNP), which encodes the receptor-binding domain (RBD) of SARS-CoV-2 as a target antigen. According to the author, preclinical studies have shown that mRNA-based vaccines induce potent immune responses against several pathogens in animals, with an acceptable safety profile, and have a highly scalable production capacity in a short period, which makes them attractive to fight pandemics. In this study we evaluated the immunogenicity and protection of the mRNA vaccine against SARS-CoV-2 in animal models, supporting clinical development in humans. The average size of the nanoparticles was 85.85 nm with more than 96% encapsulation. A single or two-dose ARCoV immunization elicited robust antibody and T-cell responses in mice and monkeys against multiple epidemic strains of SARS-CoV-2. The RBD antigen can induce fewer non-neutralizing antibodies, reducing the risk of increased *Antibody-Dependent Enhancement* (ADE) infection, the potential of SARS-CoV-2 infection.

According to Sahin *et al.* (2021), BNT162b2 is an mRNA vaccine, with modified nucleoside formulated in lipid nanoparticles, which encodes the spike glycoprotein of SARS-CoV-2. It was created by Pfizer and was 95% effective in preventing COVID-19. The vaccine-induced strong antibody responses when compared to individuals who had COVID-19. The serum produced by the

vaccine also neutralized 22 pseudoviruses containing the glycoprotein S from different variants of SARS-CoV-2. Some advantages of these types of vaccines are molecularly well defined and efficiently synthesized from DNA models by in vitro transcription, the production of mRNA and the formulation of lipid nanoparticles are fast and highly scalable, which makes this technology great for a scenario of need for rapid development, for example, a pandemic.

In the study by Rauch *et al.* (2021), a vaccine called CVnCoV with mRNA technology encapsulated by lipid nanoparticles, which encodes the spike protein (S) of SARS-CoV-2 stabilized in full-length pre-fusion was developed. The spike protein (S) is the main antigenic target of SARS-CoV-2 and interacts with human angiotensin 2 (*ACE2-Angiotensin-Converting Enzyme*) which allows the cellular entry of the virus (HOFFMANN *et al.*, 2020). Immunization with CVnCoV vaccine-induced humoral responses with high virus-neutralizing antibody responses and potent T cell effects. Tests were performed in animals demonstrating the absence of viral replication in the lungs and no disease problems were evidenced by the application of the vaccine, which demonstrates that is an excellent and safe candidate against SARS-CoV-2 (RAUCH *et al.*, 2021).

Jiang *et al.* (2021) developed a vaccine against SARS-CoV-2 called NVX-CoV2373 from the full-length spike protein, stable in the pre-fusion conformation. The nanoparticles have a size of 27.2 nm, are thermostable (resistant to temperature), and bind with high affinity to the ACE2 receptor. The vaccine was tested in mice with a Matrix-M adjuvant based on saponin (plant glycoside) and elicited a high-grade anti-S IgG that blocks binding to the ACE2 receptor, neutralizes the virus, and protects against SARS-CoV-2, no association of the vaccine with increased respiratory disease.

Called SW0123 a sequence-modified mRNA vaccine that encodes the Spike protein of SARS-CoV-2 and is encapsulated in lipopolyplex structured core nanoparticles (*LPP-Lipopolyplex Nanoparticles*). According to Wang *et al.* (2021), the vaccine is easy to produce on a large scale, its absorption is facilitated by the nanoparticle structured in a core-shell, it demonstrates high colloidal stability and a desirable biodistribution pattern with low targeting effect to the liver in intramuscular administration. Evaluations in animals of the vaccine demonstrated good T-cell responses, with high levels of antibodies capable of neutralizing wild-type SARS-CoV-2 and including the D614G variant. The author reports on some concerns in mRNA vaccines, regarding the unfavorable biodistribution pattern due to their unique size and composition, and problems related to production, stability, and necessary storage conditions (low temperatures). Through *Transmission Electron Microscopy* (TEM), the mean core size of the nanoparticles was identified, which was between 45 nm in diameter, through the procedure based on microfluidics, a lipid envelope layer was surrounded to the dense core, adding the nanoparticle size at 200 nm in diameter (WANG *et al.*, 2021).

Tan *et al.* (2021), describe a protein nanoparticle vaccine against SARS-CoV-2. The vaccine is based on the receptor-binding domain of the spike (S) glycoprotein of the coronavirus (RBD), on a synthetic virus-like particle. In tests performed with rats and pigs, low doses of the vaccine induced a

strong neutralizing antibody response, considered superior to convalescent human serum. According to the author, recent studies indicate that the RBD of SARS-CoV-2 induces neutralizing antibodies. Therefore, in this research, the immunogenicity of RBD, which was conjugated to a VLP, was verified. The VLP demonstrated that the protein antigen further increases immunogenicity, facilitating antigen drainage into lymph nodes, increasing uptake by cells that present the antigen, and cross-linking of the B cell receptor. The VLP platform is based on an aldolase (enzyme) engineered from thermophilic bacteria, spontaneously assembles into a hollow 36-nanometer dodecahedral cage with 60 subunits. The vaccine is highly immunogenic in animals, inducing robust SARS-CoV-2 neutralizing antibody responses.

In the study by Nag *et al.* (2021) a vaccine called GBPD060, which uses mRNA-LNP technology specific for the D614G genotype of the SARS-CoV-2 virus, was developed and is being tested in animals. According to the author, the vaccine generated specific antibodies against SARS-CoV-2 in rats. It is encapsulated in lipid nanoparticles (LNP) with a size between 60 and 140 nm, based on mRNA encoding the ‘spike’ (S) glycoprotein of SARS-CoV-2 with unmodified nucleoside (unmodified molecule), stabilized in its conformation of pre-fusion (before deformation). The coronavirus family has genetic review mechanisms, some SARS-CoV-2 sequence variations are comparatively low. However, natural selection can adopt rare but convenient mutations. Since the beginning of the pandemic outbreak in China, SARS-CoV-2 has undergone numerous mutations, one of them the alteration in the amino acid D614G in the ‘S’ protein of the Wuhan reference strain, caused by the substitution of a nucleotide (NAG *et al.*, 2021). Currently, D614G is considered the most prevalent circulating isotope of SARS-CoV-2 worldwide (KORBER *et al.*, 2020). According to Nag *et al.* (2021), bioinformatics analyzes were performed to discover the available protein (S) sequences of SARS-CoV-2, and a total of 15 sequences of variant D614G of 170 reference sequences of SARS-CoV-2 were found, which was also confirmed by (KORBER *et al.*, 2020). The ‘GBPD060’ vaccine induced a high level of specific antibodies with a single immunization, which covers the entire length of the protein peak, suggesting that a mixture of highly relevant antibodies against these domains were developed (NAG *et al.*, 2021).

According to Huang *et al.* (2021), a vaccine against SARS-CoV-2 of the mRNA type that encodes RBD, formulated in liposomes, was developed and investigated the influence of administration routes on immunogenicity. The vaccine expressed the receptor-binding domain (RBD) ‘*in vivo*’ and successfully induced specific antibodies against SARS-CoV-2 in the vaccinated mice, efficiently neutralizing the virus. According to the author, the typical morphology of liposomes was analyzed using TEM, showing nearly spherical particles in size of about 50-150 nm. The immunological tolerance of the LPX/RBD-mRNA vaccine was tested in mice inoculated through five different injection routes (iv-intravenous, im-intramuscular, ih-hypodermic, id-intradermal, ip-intraperitoneal) with 30 µg of RBD-mRNA. Alterations in eotaxin, GRO-α, IP-10, RANTES, and MCP-1 were found after 12 hours of administration and all these groups showed an increase in these indices of immune function. After the booster vaccination, all mice were sacrificed and the main organs were excised and examined, the

results showed that there was no obvious histopathological difference in the main organs of the control and treatment groups, demonstrating that the LPX/RBR-mRNA vaccine did not cause systemic toxicity (HUANG *et al.*, 2021).

According to Chiba *et al.* (2021), developed a vaccine based on a platform (VLPs) coated with the bacteriophage protein MS2 (single-stranded RNA icosahedral virus), generating nanoparticles containing multiple copies of the spike protein (S) of SARS-CoV-2. The use of these nanoparticles as vaccines generated high neutralizing and animal antibody responses against SARS-CoV-2. Nanoparticles such as pseudo viral particles (VLPs), but not infectious, are ideal structures for antigen display because they emulate or mimic many of the properties of natural viruses (SHIN *et al.*, 2020). Chiba *et al.* (2021), generated a VLP structure coated with the protein streptavidin (SA) that exhibits biotinylated (molecularly bound) antigens, such as the biotinylated SARS-CoV-2 protein (S), based on the very high affinity of the biotin-streptavidin interaction. The vaccine proved to be highly effective, protecting hamsters against SARS-CoV-2 after a single immunization, and the platform can be adapted to variant strains.

Karpenko *et al.* (2021), developed an mRNA-RBD vaccine that encodes the receptor-binding domain (RBD) of the protein 'S' of SARS-CoV-2. The vaccine uses a polycationic polyglucine conjugate with spermidine for mRNA delivery. She demonstrated increased production of antibodies with virus-neutralizing activity in mice. The use of mRNA for virus vaccines has become increasingly popular, as they present attractive features, for example, design simplicity, low production cost, low reactogenicity (adverse reaction) (PARDI *et al.*, 2018; KARPENKO *et al.*, 2021). Some ways found by researchers to increase the immune response to an mRNA vaccine is to encapsulate it in nanoparticles, using biocompatible and biodegradable materials, protecting them from degradation, and facilitating absorption by antigen-presenting cells (JASDAVE *et al.*, 2017; KARPENKO *et al.*, 2021). According to Karpenko *et al.* (2021), the choice of a cationic polymer polyglycine: spermidine conjugate (PGS - Polyglycin spermidine conjugate) is because it has been previously successful in works for the delivery of DNA vaccines (KARPENKO *et al.*, 2020). The average size of monodisperse hydrodynamic particles was between 164 and 20 nm, confirmed by electron microscopy.

Tejaro and Farber (2021), explained the significant progress in cutting-edge vaccine technology over the last decade, with the approval of two types of vaccines against SARS-CoV-2 for emergency use. Approved vaccines developed by Pfizer-BNT162b2 and Moderna-mRNA-1273 employ mRNA technology and a lipid nanoparticle (LNP) delivery system, while AstraZeneca approved formulations (ChAdox1-s-(AZD122)), Johnson & Johnson-Ad26.COV2.S, and Gam-COVID-vac (rAd26-s+rAd5-8) (Sputnik V) are delivered in a non-replicating recombinant adenovirus DNA vector system (POLACK *et al.*, 2020; BADEN *et al.*, 2021). According to Baden *et al.* (2021), mRNA and adenovirus vaccines compile the production of the protein (S) of SARS-CoV-2, which is the fundamental point for the production of neutralizing antibodies caused by natural infections and therapeutic monoclonal antibodies.

According to Tsiambas *et al.* (2021), the study demonstrated that intradermal/muscular injection of BNT162b2 and mRNA-1273 vaccines demonstrated a longer duration of mRNA compared to intravenous injection. The mRNA vaccine platform includes specific mRNA parts to encode the entire trimeric form of the protein (S) and the corresponding RBD region in the case of the BNT162b2 vaccine (Pfizer), or stable Spike protein in the mRNA-1273 vaccine. Regarding the intracellular action structure, the mRNA platform neither interacts with the host cell's DNA nor modifies the cell's DNA, because it is generally not integrated into it.

Table 2 shows data from clinical trials (available) of some vaccines used in the study, according to the screening platform and vaccine overview of the World Health Organization (WHO, 2021). The SARS-CoV-2 virus is evolving, with mutations in the receptor-binding domain (RBD) of particular concern. It is important to know how much cross-protection is offered between strains after vaccination or infection (BECKER *et al.*, 2021).

**Table 2** - Clinical trial data of some vaccines used in the study, described by the World Health Organization.

Developers	Name of vaccine	Phase I	Phase II	Phase III	Phase IV	Number of doses
Academy of Military Science (AMS), Walvax Biotechnology and Suzhou Abogen Biosciences	ARCov			X		2 Day 0 +14 or Day 0 +28
Pfizer/BioNtech + Fosun Pharma	BNT162b2				X	2 Day 0 +21
CureVac AG	CVnCoV			X		2 Day 0 +28
Novavax	NVX-CoV2373			X		2 Day 0 +21
Moderna	mRNA-1273				X	2 Day0+28

Source: Author construction.

## CONCLUSION

Different ways of using nanotechnology to create vaccines were analyzed in this work, specifically against SARS-CoV-2. Efficiency in virus neutralization was observed in all analyzed references. Some used lipid nanoparticles loaded with messenger RNA (mRNA), which have been widely used nowadays to prevent viral infections with several advantages, for example, fast manufacturing speed, potent immunogenicity, and good safety profile. Other vaccines used VLP technology and proved to be strongly immunogenic in animal tests, inducing large amounts of neutralizing antibody responses against wild-type SARS-CoV-2.

The main objective of this work was to show that nanotechnology presents a platform for vaccines development against pandemics, which need a profile of mass creation in a short period and present safety and efficiency. All results were encouraging and bring hope to the use of nanotechnology in vaccines, specifically against corona viruses.

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