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Advances in NDDS: An expansive menu of choices in the management of pandemic

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Abstract

Novel Drug Delivery System (NDDS) is a novel approach to deliver the drug that addresses the limitations of the traditional drug delivery systems with enhanced patient care and site specific drug delivery. Besides several NDDS are currently used for treating Coronavirus disease (COVID-19), nanovaccines, liposomes and nanoparticles are gaining more interest towards research and manufacturing in pharmaceutical industry. COVID-19 is an infectious disease caused by the SARS-CoV-2 virus. It has found its roots from China and has declared as a pandemic all over the world by World Health Organization (WHO). Till now, there is no ultimate cure for this outbreak. The recent developments in the domain of NDDS opened up numerous research exposures in the development of vaccines for the COVID-19. This review discusses the management of COVID-19 using NDDS like nanovaccines, the repurposing of the existing drugs using nanosystems, and the major market players of NDDS.

Keywords: NDDS; COVID-19 variants; NeoCoV; Twindemic; Repurposing

1. Introduction

Novel Drug Delivery Systems (NDDS) refers to the approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body to safely achieve its desired therapeutic effects [1]. NDDS is a system used for delivery of a drug to the targeted site other than conventional drug delivery systems for the betterment of patient [2]. NDDS have various advantages over conventional systems such as optimum dosing at the right time and right location, efficient use of expensive drugs, reduction in production cost, beneficial to patients, and improved comfort and standard of living [3].In December 2019, the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) was discovered, which then precipitated the emergence of the largest global pandemic [4]. These viruses mutate regularly and COVID-19 has undergone thousands of mutations since it first emerged. But only a small minority of those mutations are likely to be significant and change the virus meaningfully. Most mutations are just useful as a barcode to monitor outbreaks. Some of those variants of concern are Beta, Gamma, Delta and Omicron [5]. Recently, according to research NeoCoV, a type of corona virus that spreads among bats in South Africa may pose a threat to humans in future if it mutates further [6]. The variants of the COVID-19 and their month and place of origin are tabulated as follows.

To combat these viruses, novel drug delivery tools are offering great utility in the ongoing pandemic through different routes spinning from viral neutralization and detection to vaccine developments and treatment [7]. Already crippled by COVID-19, the world is now facing a Twindemic [8], a dual challenge of soaring COVID-19 cases and increasing influenza infections, causing worry for healthcare officials [9]. Until now there is no standard drug or vaccine available for the treatment, therefore the NDDS is the boon for the repurposing of the existing drugs [10].

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Table 1 COVID-19 variants and their place of origin

Variants of COVID-19	Month of outburst	Place of origin
Alpha	November 2020	United Kingdom
Beta	December 2020	South Africa
Gamma	January 2021	Brazil/Japan
Epsilon	May 2020	United States (California)
Eta	December 2020	United States (New York)/Nigeria
Iota	November 2020	United States (New York)
Kappa	October 2020	India
Delta	December 2020	India
Zeta	December 2020	Brazil
Omicron	November 2021	South Africa
NeoCoV	January 2022	South Africa

2. COVID-19 management

2.1 Nanovaccines

Nanotechnology has played an important role in response to the COVID-19 crisis, as various nanoparticles based vaccines have emerged from several companies around the world. These nanovaccination delivery systems have been developed in different forms based on their composition such as lipid, polymeric, inorganic, and virus-like nanoparticles (VLNPs). The two highly efficacious vaccines, BNT162b2 by Pfizer–BioNTech and mRNA-1273 by Moderna [11]; use nanotechnology as an essential part of their design to deliver mRNA. Once a potential antigen of an infectious pathogen has been identified, the first step involves the development of the mRNA sequence that can express this antigen and its cellular and animal testing (pre-clinical stage) to determine its efficacy. The second step involves clinical trials, a sequential four-phase process in which the vaccine candidate is tested on humans [12].

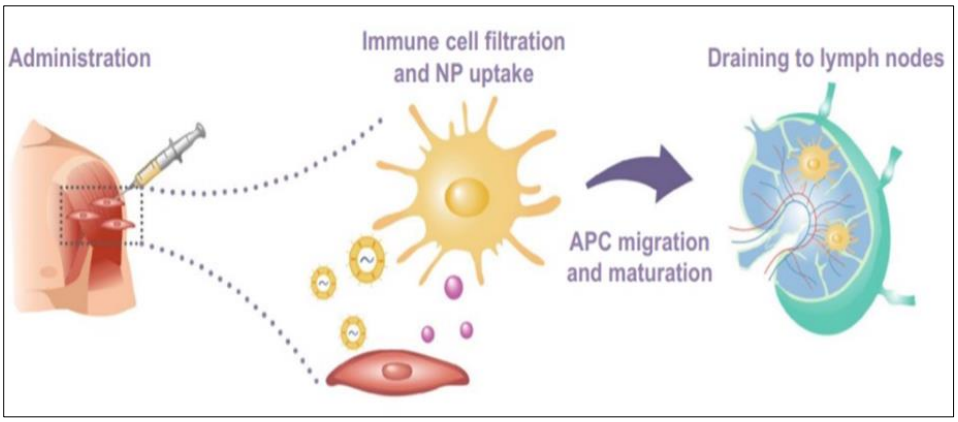

Figure 1 Schematic representation of vaccine administration, nanoparticles uptake by immature Antigen Presenting Cells (APCs), and subsequent migration to lymph nodes through the lymphatic system

Before the emergency use authorization (EUA) of Pfizer–BioNTech's and Moderna's vaccines by the FDA, mRNA-based vaccines have never been FDA-approved in humans for any disease. Novel mRNA-LNP (Lipid Nanoparticles) and protein nanoparticle vaccine platforms require specialized manufacturing facilities and highly skilled workforces, which is a major challenge in many resource-limited settings [13].

A.

B.

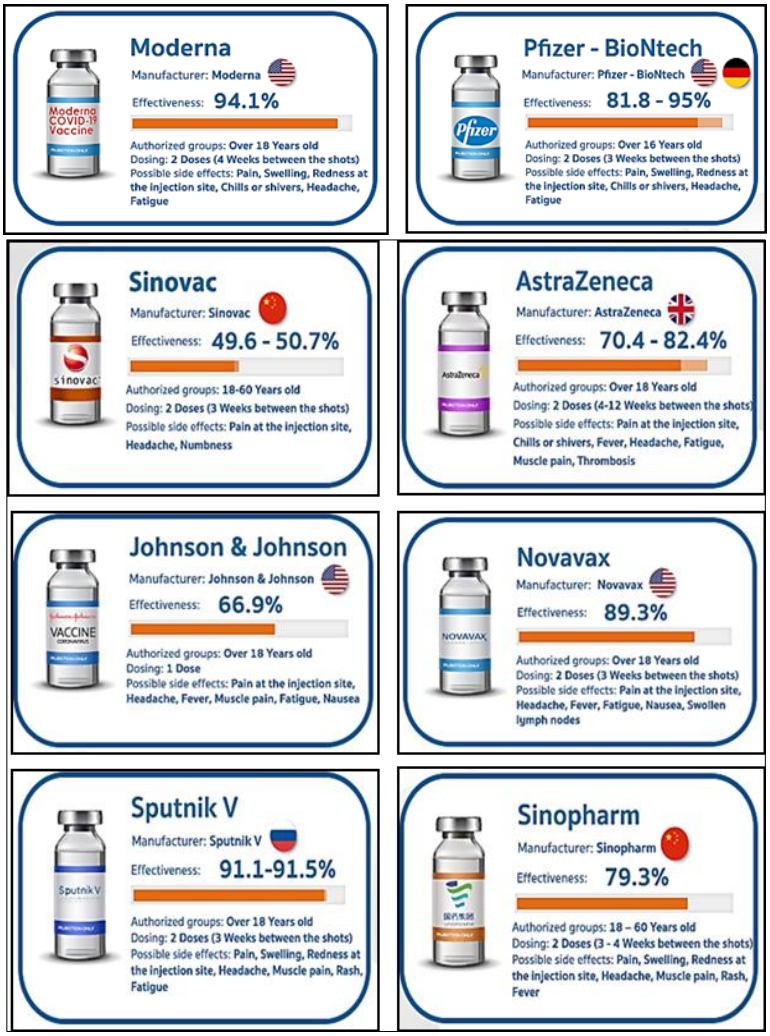

Figure 2 Comparison of effectiveness of a) Nanovaccines with b) other vaccines

Advantages of Nanovaccines over existing vaccines are as follows

- Nanovaccines have the potential to evade immune responses that would otherwise render treatment difficult [14].
- Low or no accumulation of drugs in non-target organs which reduces the toxic effects [15].
- Ability to incorporate both antigens and adjuvants within a single particle to produce maximum stimulation.
- The bio mimicking property of the nanovaccines reduces the interactions with Reticuloendothelial cells, provides longer circulations, and prevents the burst release of adjuvants from its nano-formulation [16].

2.2 NDDS in the repurposing of drugs

Along with the ongoing research towards developing an ideal and effective vaccine for the treatment of COVID-19, the scientists are repurposing the existing drugs to treat the hospitalized patients [17]. Among the various drugs screened for activity against SARS-CoV-2, some of the US FDA-approved drugs include remdesivir, dexamethasone, hydroxychloroquine and chloroquine are under vigorous investigation. Remdesivir has been explored for several indications and has currently been repurposed for COVID-19 treatment. In the case of the intravenous dosing of Remdesivir, the concentration of Remdesivir and its active metabolite in the lungs is inadequate to inhibit SARS-CoV-2.In order to address this drawback; it can be repurposed for the pulmonary drug delivery via the inhalation [18]. The main issue with delivering Remdesivir to the lungs is its poor solubility and aqueous instability [19]. By using NDDS like nanocarrier-based pulmonary drug delivery systems like liposomes possess unique properties, including small size (~100 nm) and circumvention of first-pass effect, making them suitable drug carriers for enhanced pulmonary deposition [20]. The Remdesivir liposome (Rdv-lips) aerosols, which can be supplied in the form of lyophilized liposome powder and reconstituted to liposomal suspension for pulmonary delivery. The Rdv-lips exhibited not only good drug-loading capacity and aerodynamic properties, but also improved in vivo behaviour with a much higher concentration of

Nucleoside Triphosphate (NTP) in the lungs [21]. The Rdv-lips suspension is atomized and then inhaled into lung to increase the drug accumulation. After depositing at alveoli, the Rdv-lips are taken by the alveolar epithelial cells rapidly due to the better cytocompatibility and high loading rate of Rdv-lips.

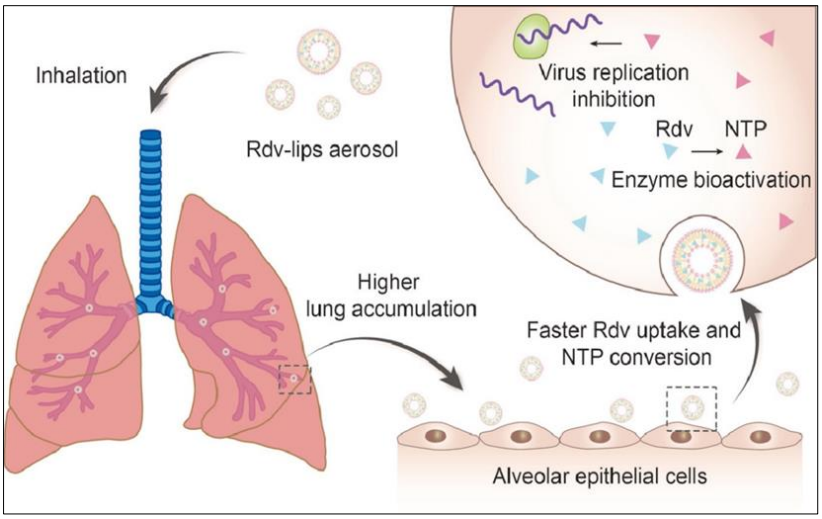

Figure 3 Schematic illustration of the Remdesivir liposome (Rdv-lips) aerosol inhaled into lung

Chloroquine, an old antimalarial agent with anti-inflammatory and immunomodulatory activities, has gained significant interest as a potential therapeutic option for the management of COVID-19 associated pneumonia [22]. Using *in silico* drug repurposing approach Chloroquine and Hydroxychloroquine have been repurposed and can be utilized as nanoparticles. The execution of artificial intelligence (AI) [23] and machine learning (ML) [24] methods may contribute to drug repurposing and development for COVID-19, possibly becoming a cornerstone of the computational approach [25][26].

3. Future Outlook

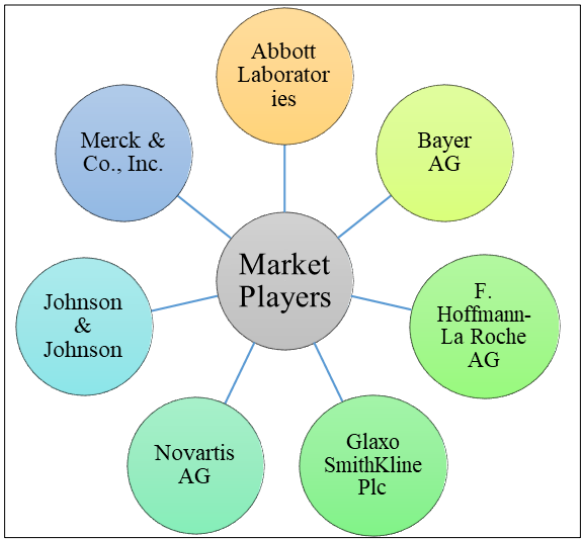

Figure 4 Major market players of NDDS

Currently, the pharmaceutical industry is preparing for widespread adoption of nanoparticles, which represents a crucial element in advanced nanotechnology-enabled delivery systems [27]. Amid the COVID-19 crisis, the global market for NDDS estimated at US$9 Billion in the year 2020, is projected to reach a revised size of US$28.1 Billion by 2026, growing at a Compound Annual Growth Rate (CAGR) of 20.8% over the analysis period [28]. The major market players of NDDS are in figure 4.

4. Conclusion

In this review, we summarized the utility of NDDS in the effective management of this threatening disease. NDDS offered great role in the transportation of the intended molecule to the targeted area in the body to safely elucidate its desired therapeutic effect. Nanotechnology has come to the force to further enhance the relevance of continuous improvisation and innovation of NDDS, especially for administering active agents. Currently, the pharmaceutical industry is preparing for widespread adoption of nanoparticles, which represents a crucial element in advanced nanotechnology-enabled delivery systems. Nanovaccines and the repurposed drugs formulated using nanosystems have achieved a benchmark which show more than 90% efficacy in preventing SARS-CoV-2 infection and symptomatic COVID-19 both in clinical trials and in real-world setups. Although many technologies are there for the formulation of nanovaccines and various nanocarrier systems there is a major pitfall regarding the structure of SARS-CoV-2 virus since it is changing and bring out new mutants frequently.

Compliance with ethical standards

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