

# NANOTHERAPEUTICS: A WAY TO CURE CARDIAC COMPLICATIONS ASSOCIATED WITH COVID-19



Shreyashi Pal<sup>1,\*</sup>, Rajdeep Saha<sup>1</sup>, Shivesh Jha<sup>1</sup>, and Biswatrish Sarkar<sup>1</sup>

Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra, Ranchi, Jharkhand, India-835215

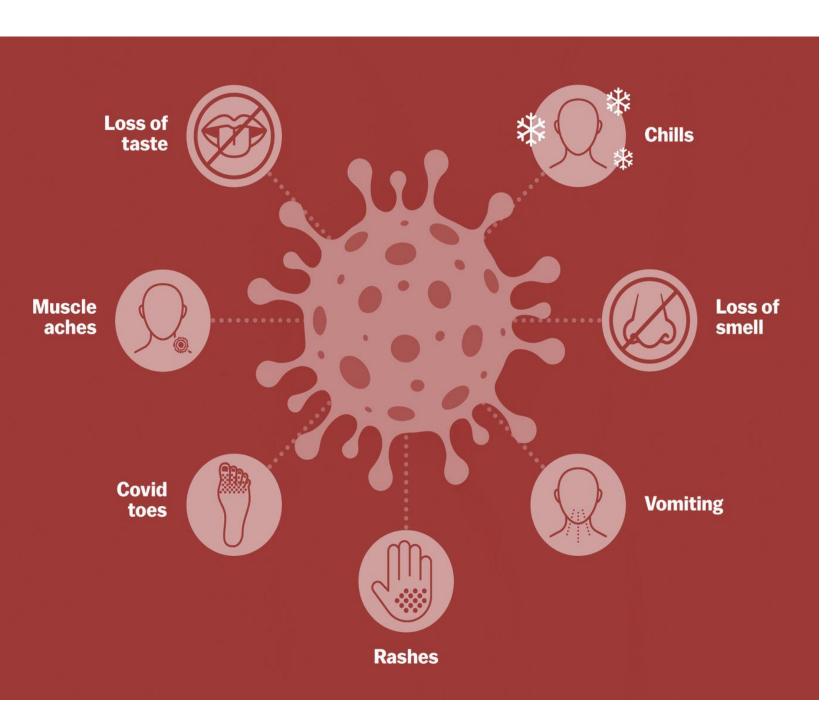
\*Corresponding author's Email ID: shreyashipal1997@gmail.com

Abstract: The outbreak of SARS-CoV-2 has caused a catastrophe in the world. With significant efforts from the medicine and scientific communities, millions of people all around the world have been vaccinated. Irrespective of that, individuals are getting infected due to mutations in the virus. Noticeable aftermath damage is seen in most of the major organs of the body. Although it is primarily a respiratory infection, the previously healthy patients have mostly developed cardiovascular diseases. Natural products through nanotechnology (nanoparticles and nanorobots) can be an efficient way to tackle this modern-day problem. This review aims to discuss the ways nanotherapeutics can be used to treat cardiac complications. Essentially, it will help to develop an idea that can be used in the future as a solution to the problem under discussion.

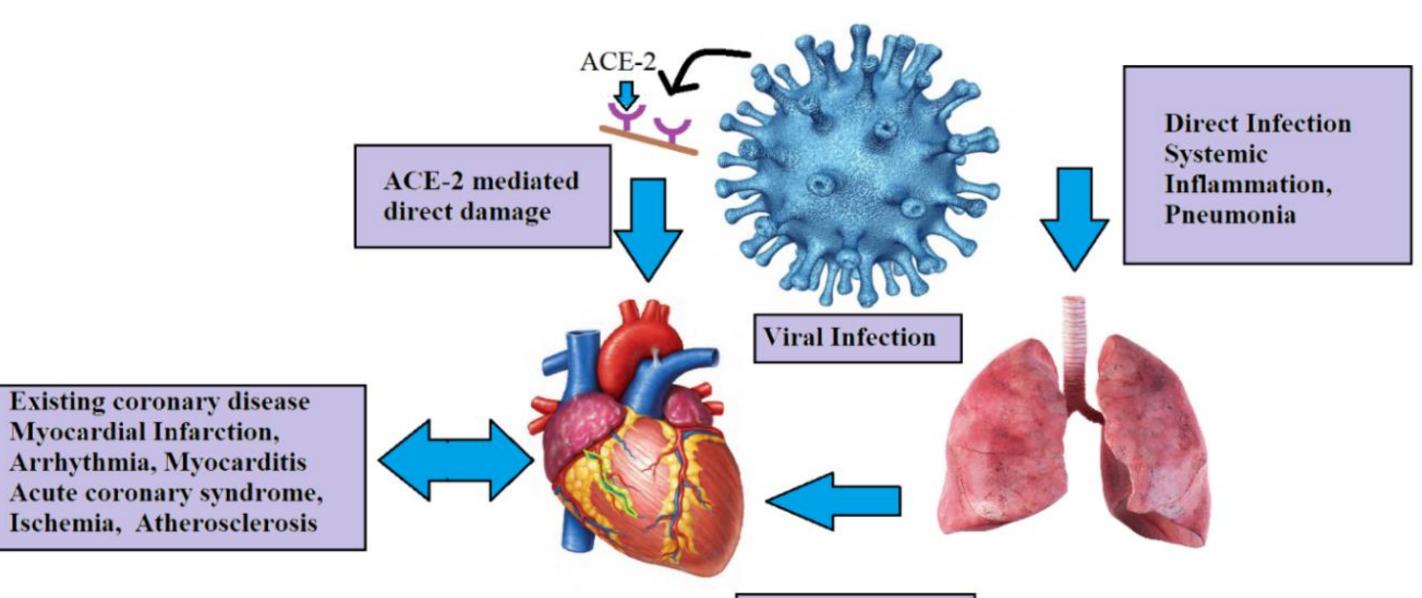
Keywords: Cardiovascular System; COVID-19; Herbal medicine; Natural Products; Nanotechnology; Nanorobots; SARS-Cov-2.

## Introduction

- The outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified as a pandemic within the year 2020 by the World Health Organisation (WHO). The infected patients often presented with symptoms like fever, fatigue, cough, shortness of breath (or dyspnea), and other symptoms identifying respiratory distress.
- Following the mode of transmission and the presented symptoms, the disease was identified as a respiratory infection.
- With the absence of any standardized treatment protocol, a call for urgency in research was felt.



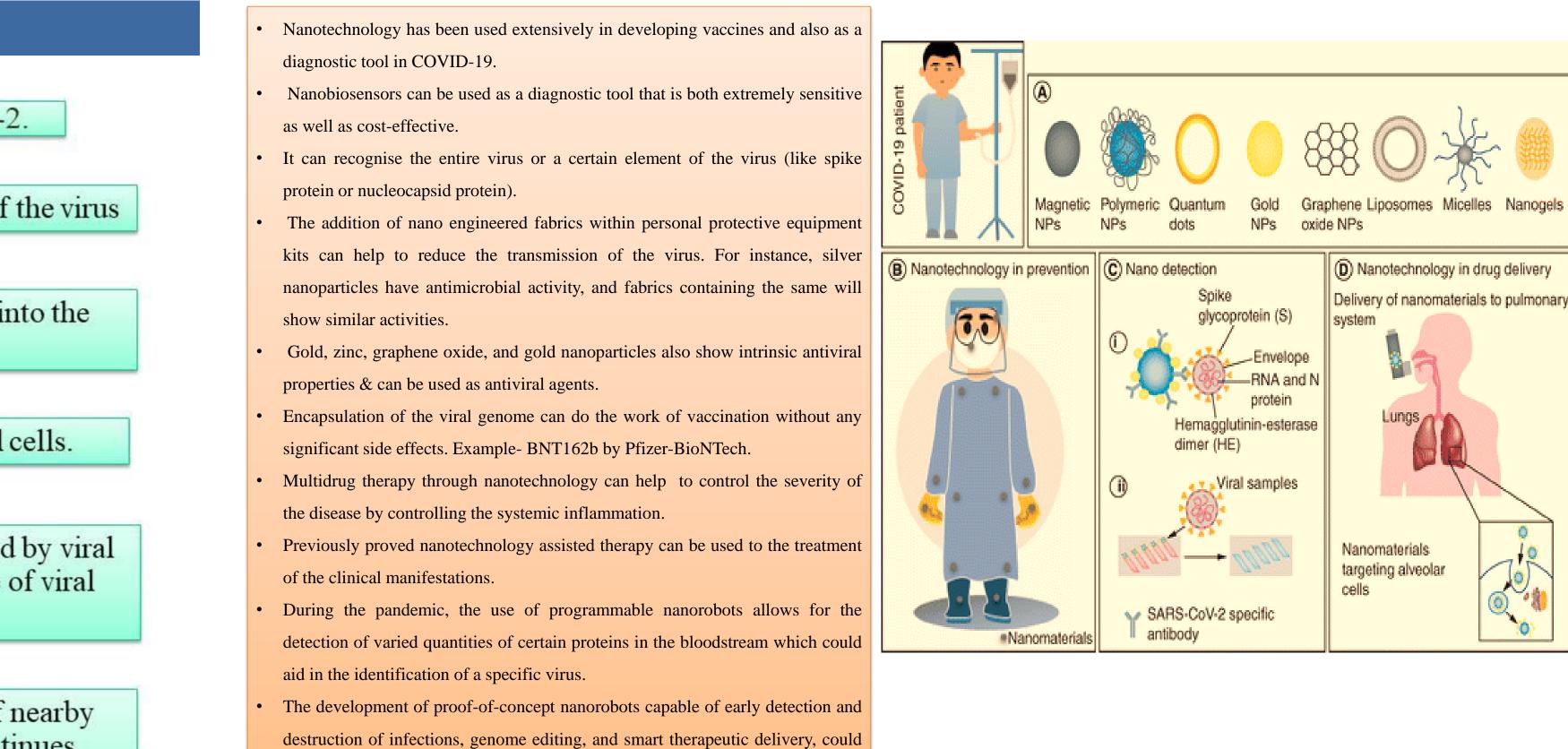
## **Probable Cardiovascular complications associated with COVID 19**



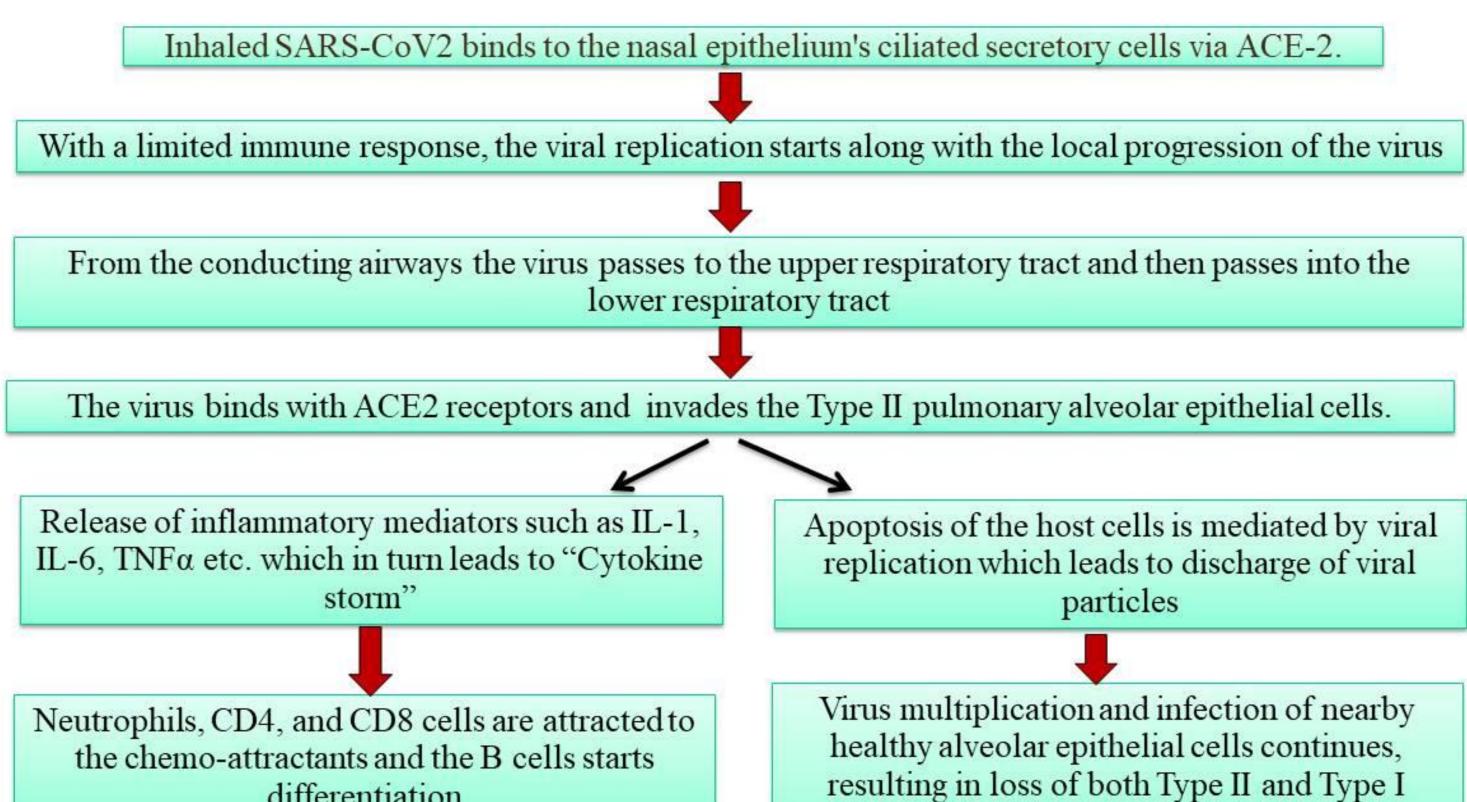
Slowly, the symptoms of the disease were studied and the effect of the virus on the various parts of the body was analysed. By 2022, this viral disease has been identified as a multi-organ disease.

Hypoxia induced **Myocardial Injury** 

## **Nanotherapeutics in COVID 19**



## **Pathophysiology of SARS-CoV-2**

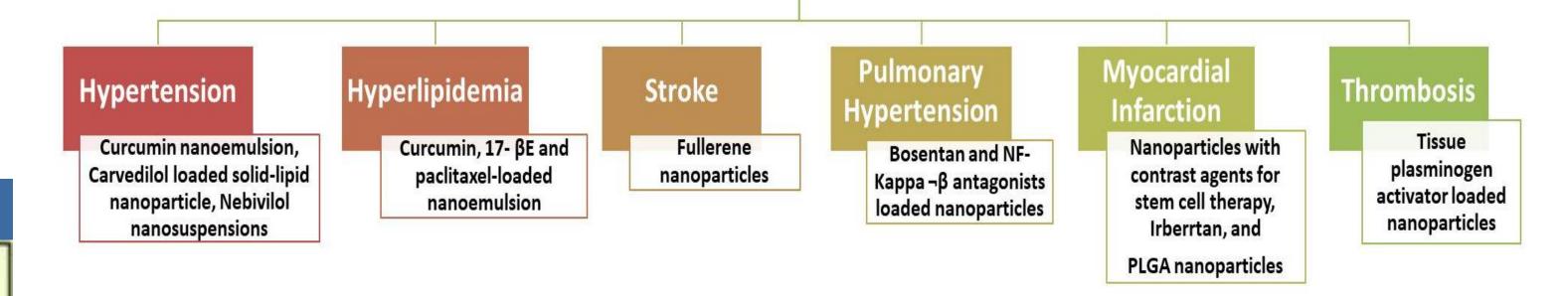


Inflammatory cells are sequestered in lung tissues, also, cytotoxicity is mediated by CD8 that causes lung damage.

differentiation

pneumocytes. Acute Respiratory Distress Syndrome as a result of diffusive alveolar damage

## Utilisation of Nanoformulations to Treat Cardiovascular Disorders



## Effect of COVID 19 on major organs of the body

#### **Pulmonary involvement**

- ACE2 receptor on type II alveolar epithelial cells → lung tropism
- SARS-CoV-2: alveolar injury and interstitial inflammation
- Proinflammatory factors, cytokine storm and immune system activation
- Diffuse pulmonary intravascular coagulopathy
- Silent hypoxia and atypical ARDS

### **Renal involvement**

- ACE2 in podocytes, mesangial cells, epithelium of the Bowman's Capsule, proximal cells brush border and collecting ducts
- inflammatory Uncontrolled systemic response → kidney injury
- Alterations in renal hemodynamics

#### Nervous system involvement

- Direct CNS invasion: hematogenously or via the retrograde neuronal route eg olfractory neurons
- Hyper-inflammatory status: cytokine-mediated brain damage
- Host immune response effects
- Cerebrovascular disease on the ground of hypercoagulation
- ACE-2 in host olfactory and gustatory pathways → anosmia, ageusia
- Direct PNS and skeletal muscle infection

#### Cardiovascular manifestations

- Heart: direct ACE2 related → acute MI,
- myocarditis, decompeansated HF, tachyarrhythias.
- Heart: indirect → inflammatory reaction leading to decompensation of underlying disease
- Endotheliopathy
- Kawasaki-like syndrome

#### Gastrointestinal and liver involvement

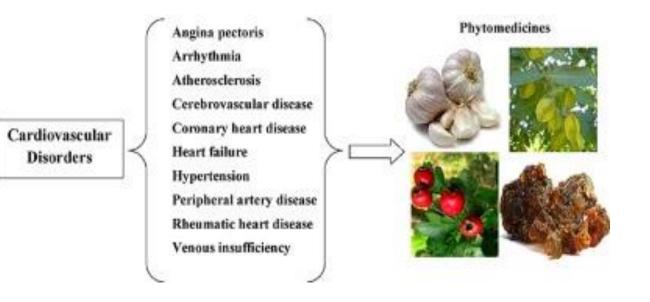
- ACE2 on enterocytes in the ileum and colon
- Direct infection and apoptosis of epithelial cells

## **Role of Natural Product in the treatment of Cardiovascular disease**

- Natural products play a significant role in the treatment of the cardiovascular disorder.
- Dietary flavonoids obtained from citrus fruits are known to lower the risk of ischaemic stroke.
- Theaflavins obtained from apples and grapes help to regulate blood pressure.

be crucial in the fight against the disease.

Thymoquinone, nicotinamide, emodin, and osthole show cardioprotective potential.



## **Potential of Natural Product Derived Nanotherapeutics in Curing Cardiovascular Complications Associated with COVID-19**

Nanotherapeutics has its application in the treatment and management of various cardiovascular alignments. Hence, the incorporation of natural products within the nanoformulation could one of the ways to achieve therapeutic potential during cardiovascular damage during COVID-19 infection.

#### Hematological manifestations

- Direct ACE2-dependent infection of lymphocytes, cytokine-induced lymphocyte apoptosis→lymphopenia
- Systemic inflammation->increased inflammatory indices
- Endothelial dysfunction and immune deregulation → blood hypercoagulability

#### Skin manifestations

- Direct virus infection
- Related to underlying vasculopathy
- Secondary to host immune response
- Treatment-related

in the GI tract → diarrhea, vomiting, nausea Liver: direct infection and apoptosis of hepatocytes, hypoxia, sepsis, drug-induced toxicity

#### **Endocrine manifestations**

- Molecular mimics to the host ACTH → cortisol insufficiency
- Direct infection → degeneration and necrosis of the adrenal gland
- ACE2 expresed on hypothalamic and pituitary tissues → direct hypothalamic damage and hypophysitis
- For example, resveratrol, is known to provide protection against vascular damages that are caused by cardiovascular diseases. But it has low oral bioavailability. Resveratrol loaded in PLGA nanoparticles have shown a significant increase in bioavailability.
- Another strategy that can be identified is the utilization of nanorobots for targeted drug delivery.
- For instance, ginsenosides can be loaded within nanoparticles that can be further loaded within the nanorobots. These nanorobots can unload the drug-containing nanoparticles near the ACE2 receptors near the myocardium. This can block the said receptors and therefore, the injury within the heart tissue can be stopped.

## Conclusion

- COVID-19 caused by SARS-CoV-2 has the potential to cause a wide array of damage within the body.
- In worst-case scenarios, it can lead to multi-organ failure and finally death.
- The number of cardiac complications associated with the disease is huge which calls for immediate actions.
- Nanotechnology can be a good alternative to the traditional therapy that is most commonly provided to patients.
- The scientific and medical communities need to find ways to incorporate nanotechnology within their repertoire and make it commonly available for people.

## **References**

- Ahmad, A.; Raish, M.; Alkharfy, K.M. The potential role of thymoquinone in preventing the cardiovascular complications of COVID-19. Curr. Vasc. Pharmacol. 2021, 141, 106899. https://doi.org/10.1016/j.vph.2021.106899
- Abubakar, M.B.; Usman, D.; Batiha, G.E.; Cruz-Martins, N.; Malami, I.; Ibrahim, K.G.; Abubakar, B.; Bello, M.B.; Muhammad, A.; Gan, S.H.; Dabai, A.I. Natural products modulating Angiotensin Converting Enzyme 2 (ACE2) as potential COVID-19 therapies. Front. Pharmacol. 2021, 12, 1-19. https://dx.doi.org/10.3389%2Ffphar.2021.629935
- Pechanova, O.; Dayar, E.; Cebova, M. Therapeutic potential of polyphenols-loaded polymeric nanoparticles in cardiovascular system. *Molecules* 2020, 25(15), 3322. https://doi.org/10.3390/molecules25153322
- Yuki, K.; Fujiogi, M.; Koutsogiannaki, S. COVID-19 pathophysiology: A review. J. Clin. Immunol. 2020, 215:108427, 1-7. https://doi.org/10.1016/j.clim.2020.108427
- Lotfi, M.; Hamblin, M.R.; Rezaei, N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. Clin. Chim. Acta 2020, 508, 254-66. https://dx.doi.org/10.1016%2Fj.cca.2020.05.044