

## Can Biodegradable and Biocompatible Polymeric Microneedles be Considered as a Vaccine and Drug Delivery System in the COVID-19 Pandemic?

### Biyoparçalanır ve Biyouyumlu Polimerik mikroğneler COVID-19 Pandemisinde Aşı ve İlaç Taşıyıcı Sistem Olarak Değerlendirilebilir mi?

**Short Title: Microneedle technology and COVID-19 pandemic**  
**Türkçe Kısa Başlık: Mikroğne teknolojisi ve COVID-19 pandemisi**

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#### Dear Editor;

First reported in Wuhan, China at the end of December 2019 and declared as a pandemic, COVID-19 is a disease characterized by acute respiratory failure. COVID-19 which is caused by SARS-CoV-2, a member of the *Coronaviridae* family, spread to the whole world in a short time due to its rapid transmission from person to person<sup>[1]</sup>. Increasing virus variants cause new serious mutation and fast spread of the virus and lead to questions about the efficiency of the vaccines and current treatment methods. Furthermore, the supply chain, stability, and the necessity of applying the drugs and vaccines developed/being developed for a large number of individuals in a short time brings along a series of problems on a global scale.

Microneedles (MN) are drug delivery systems designed in micron size (usually 10-2000 µm in length and 10-50 µm in diameter) and developed mainly for use in transdermal treatments. MNs can be applied without stimulating the nerve endings by crossing the *Stratum corneum*, do not cause pain and discomfort, can be used without the need for any healthcare personnel, can be designed as a controlled/extended systems and do not require cold chain for transport. MNs cross the *Stratum corneum* and carry drug molecules to the dermis layer where vascular and lymphatic vessels are concentrated<sup>[2]</sup>. Then, drug molecules penetrate lymph or blood capillaries according to their physicochemical properties and join the systemic circulation.

MN's, which were first developed in 1976 to overcome the obstacles faced by Transdermal Drug Delivery Systems, have been designed and scientifically investigated by various research groups as drug delivery systems for many drugs, vaccines, genes, and hormones. On the other hand, parallel to the developments in microfabrication technologies, studies have been carried out to increase the applicability in the pharmaceutical field by obtaining MN types with different designs and characteristics (solid MN, hollow MN, coated MN, and dissolving MN). Researchers are working to develop innovative MN systems within the framework of the target disease and target molecule to increase the potential advantages of MN, and scientific studies in this area continue intensively<sup>[3]</sup>. Oral drug administration for children is limited mainly due to the difficulty in swallowing. On the other hand, the parenteral route presents difficulties for both children and parents. The injection procedure requires a pedagogical approach by the healthcare professional. However, this is not enough to eliminate the feeling of pain and emotional trauma that will occur during the application. Therefore, MN designs for children are considered as a promising array. Nowadays, MNs are investigated as an alternative route for an efficient insulin delivery without pain for the treatment of Type 1 diabetes which appear more frequently in childhood<sup>[4]</sup>. In another study, promising results were obtained by the use of ferric pyrophosphate loaded MN developed for iron deficiency anemia in children<sup>[5]</sup>. In this context, there are clinical trials conducted on MN developed for children<sup>[6]</sup>.

In recent years, dissolving MNs have attracted more attention of research groups due to high patient compliance and not leaving biological material residue after application. MN drug delivery systems created by the use of biocompatible and biodegradable polymers as a basic principle have the potential to be used in a wide range of target disease groups. After insertion into the skin, the polymeric matrix forming MN and carrying the drug dissolves and releases the drug molecules. MN systems also allow modification in release rate and duration according to the type, structure, and molecular weight of the polymers used<sup>[7]</sup>. There is no physical wound, incision or non-biocompatible residual on the skin after dissolving MN application. Promising results have been reported on MN arrays prepared using various biodegradable and biocompatible polymers (Polylactic acid (PLA), Hyaluronic acid (HA), Poly Lactic-co-Glycolic Acid (PLGA), Polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), etc.)<sup>[8]</sup>. It is also known that MN systems are flexible systems that allow innovative approaches in terms of both release and design by developing various modifications with advanced studies and multidisciplinary approaches<sup>[3]</sup>.

Increasing studies on MN systems in recent years are considered as a harbinger that the MN systems will take place more widely in our daily lives as drug/vaccine carriers in the near future. It is known that MN vaccination method, which was developed especially for influenza immunization and evaluated clinically, is a milestone in this field and has been studied intensively over the last decade<sup>[9]</sup>. During the COVID-19 pandemic process and the pandemic conditions brought about, the necessity of fast, efficient, stable, easily applicable, result-oriented systems that do not require compelling storage conditions has again come to the fore. It should not be overlooked that one of the possible global solutions with important advantages in this sense is MN systems.

COVID-19 pandemic has brought along a large global production and logistics problem in the healthcare field. The production, stability, efficacy, and safety of many sensitive medical materials such as medicines and vaccines, as well as their rapid and large-scale application, pose serious difficulties for both health institutions and governments. Developed vaccine technologies cause more additional costs compared to drugs. The biggest problems encountered in vaccine technologies today are the need for healthcare personnel during their use, storage and transportation processes. The residues such as needles, injectors bring social, environmental and institutional problems. It is clear that soluble MN systems on a

biodegradable basis have the potential to prevent problems in this area. Being mechanically durable, not requiring any health personnel during the application, and being easy to apply without pain are among the biggest advantages of MN systems in this field. Studies suggest that it can provide a controlled/extended release without causing toxicity in the body, especially due to its biocompatible polymeric structure, and that it can maintain the immune response for a longer time in vaccine applications.

### **Conclusion**

Biocompatible and biodegradable-based drug/vaccine carrier MNs are among the most important candidates of the pharmaceutical and vaccine industry in terms of their advantages such as logistics, storage, stability and ease of use. For all these reasons, in the process of the COVID-19 pandemic affecting all humanity, the high potential and promising studies in MN technologies should be taken into consideration, developments and studies should be followed closely. Vaccine studies are the most life-saving step in the prevention of epidemic diseases. Considering the fact that we are facing an epidemic on a global scale, quick and reliable distribution is of great importance to enable widespread use of the vaccines. Based on the ongoing studies and the acquired knowledge in this field, MN-based soluble COVID-19 vaccine studies are suggested to be a promising perspective.

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