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Conventional usages and innovation of microneedles

Qingshi Wang

School of Material Science and Engineering, East China University of Science and Technology, Shanghai, 201424, China

20001163@mail.ecust.edu.cn

Abstract. Nowadays, microneedle array patches (MAPs) are playing a much more role in solving medical, chemistry and biology problems and giving more incentives to these fields. This paper made a summary of traditionally practical value of MAPs since its invention and gave some vivid and realistic examples of creativity in the field of microneedle usage in order to get a fuller picture of microneedle and related newest applications. Relevant information and details are collected from the latest papers and reports, and in this way can the author draw conclusions accurately and critically. According to what is mentioned in the paper, it is time to pay more attention to the different advantages of MAPs while regarding it as a kind of effective drug-releasing tool. At the end of the paper, the author envisioned some possible usages of microneedles and enlightened readers to find new ways to make full use of different MAPs.

Keywords: microneedle array patches, drug delivery, electroporation, biomarker measurement, interstitial ion monitoring.

1. Introduction

MAPs, known as microneedle array patches, the products were invented in France 60 years ago. At that time, this kind of technology was used in the field of cosmetology and plastic surgeons to remove acne on the face. As time went by, scientists found that microneedles have the ability to carry various kinds of model drugs such as bovine serum albumin (BSA) and rhodamin B, known as classical macromolecular and micromolecular drugs in the biochemistry field. What's more, the microneedle arrays loaded with drugs may release them in different ways due to different microneedle shapes and fabrication processings. So, in the 1990s, MAPs treatment was regarded as a promising method to cure particular illnesses. From then on, microneedle patches have shown incredible potential in drug delivering and releasing and have occupied a large market share of medical devices at an unprecedented rate. Up to 2012, researchers from MIT have claimed that microneedles can be used as a tool to contain and release via skin insulin without inducing any pain, and the related outcome was reported by Nature [1]. Nowadays, traditional MAPs have been divided into four main catalogs called coated MAPs, dissolving MAPs, separable MAPs and swellable MAPs respectively. They all conventionally function as drug delivery systems. However, some innovations in usage of MAPs were announced continuously, which means this kind of product acting as medical devices has various usages in some relevant fields such as immunology or totally different fields like chemistry and instrumental analysis. That is to say, it is worth thinking about a great variety of new usages of conventional microneedles. After reading and summing up structures and details of research papers, this paper gave a new thinking pattern of

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microneedle functions ranging from drug controlling usages and other creative usages. To be more specific, this paper found that microneedles have a bright prospect in the future contributing to series of development in quantities of fields except for medicine. Therefore, it can be concluded that all scientists focusing on biology, chemistry and medicine fields need to realize that the multiusage of MAPs when making the cause of science, thus they may carry out their scientific research more efficiently.

2. History and catalogues of MAPs

2.1. Brief introduction

In modern society, there are millions of people who are suffering from rheumatoid arthritis (RA) and diabetes around the globe and medical professionals all over the world are trying their best to cure these harmful diseases [2]. Until now, injection therapy or operation has been invented to solve the problem. However, the two main treatment methods are all really devastating to human beings, which means sufferers may be treated unexpectedly inhumanely sometimes and it will take a long period of time for sufferers to recover from operation or injection. Since the 1950s, material scientists have done their part to change the situation by inventing a new kind of material or device which may substitute old treatment methods. Eventually, they invented a new type of therapy for the RA called microneedle array patches (MAPs). When it comes to the main characteristics of MAPs, they are pain-free and highly efficient. The reason why MAPs treatment is a painless therapy is that all microneedles will only pierce epidermis rather than dermis saturated with synapses which deliver signals to pallium where pain is produced. Apart from this, the reason why MAPs perform effectively is that the transdermal drug delivery system built by microneedles and skin does not influenced by the digestive system, which means that almost all the drug delivered by microneedles can reach focuses without any wastage. The two factors above contributed to the popularity of microneedle therapy for some modern diseases, such as the RA, diabetes and so on. So, the microneedle system has been regarded as one of the most effective drug delivery systems in the history of medicine. But nowadays, with the great development of different fields of scientific research, MAPs are playing different and indispensable roles in causing scientific breakthroughs.

Traditionally, MAPs are divided into four main categories according to their different drug delivery and release patterns. They are coated MAPs, dissolving MAPs, separable MAPs and swellable MAPs respectively. All of these MAPs have their own structures and properties, which is related to raw materials, material processings, drug delivering efficiency and costs [3]. Coated MAP, Dissolving MAP, Separable MAP, and Swellable MAP and their mechanics of drug releasing are shown in the figure 1. A great variety of different usages are based on these properties to a certain extent.

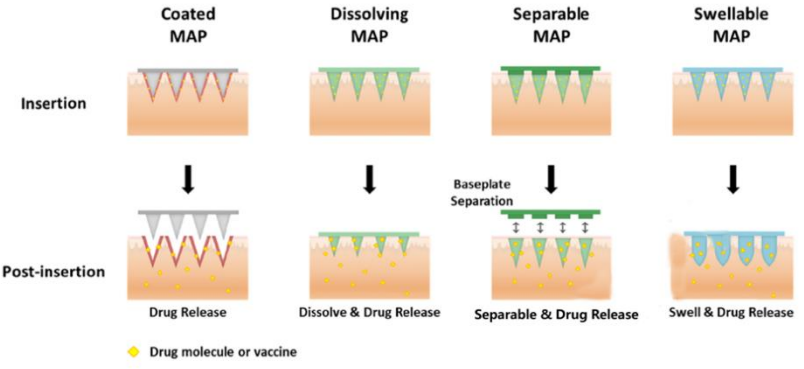

Figure 1. Different kinds of MAPs.

2.1.1. Coated MAPs. The first kind of MAP is coated microneedles. As the figure manifests (figure 1), this kind of microneedle is coated with drug on its surface and the microneedle is the first generation of

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MAPs [4]. This sort of microneedle patch can be made from many types of materials, such as metal, silicon and polymer materials under the most basic fabrication processing. Recently, this type of microneedle patch are widely used thanks to the low cost, easy materials processing. Unfortunately, the desired amount of drug carried and released by the coated MAPs is not as large as researchers expected.

2.1.2. Dissolving MAPs. The second kind of traditional MAP is dissolving MAP. The dissolving MAPs can totally dissolve in interstitial fluids. That is to say, microneedle patches which are dissoluble are made of various hydrophilic materials such as polyvinyl acid (PVA), polyacrylic acid (PAA), and hyaluronic acid (HA). What's more, almost all these hydrophilic materials are in the form of hydrogel when fabricated into microneedle patches. The main characteristics of the dissolving microneedle are biocompatibility and biodegradability. Grounded on these excellent properties, sufferers can use this kind of microneedle without the processing of removal old patches from the skin and be concerned to the negative effects from materials that induce other skin or immune disorders. Having said that, the dissolving microneedle array has its own disadvantages. For instance, this sort of microneedle can only carry a very little amount of drugs like insulin and other hormones according to a great number of research. Another drawback of the microneedle patch is that lack of enough sources of biocompatible materials leads to high costs for both producers and patients. To be more specific, conventional biocompatible and biodegradable polymer materials such as polylactic acid (PLA) and hyaluronic acid (HA) are really expensive due to complicated fabrication processings or rare sources of raw materials.

2.1.3. Separable MAPs. The third kind of MAP is separable MAPs. When it comes to the evident difference between the separable microneedle patches and the other two kinds of patches, the separable MAP contains two basic elements to form a whole microneedle patch, a solid backbone and edges. Due to the special structure, separable MAPs are endowed with excellent physical properties such as high elastic modulus and better mechanical strength. In this way can the separable MAPs insert our skin much more easily and totally so that the drug carried by the microneedle can be released to interstitial fluids, which leads to unparalleled curing performance.

2.1.4. Swellable MAPs. The fourth kind of microneedle patch is swellable MAPs. This type of microneedle array is made from hydrogel because of its swellable property. So many incredible properties have been shown thanks to the unique swellable property, such as flexibility. Furthermore, the swellable MAPs can contain the most amount of model drugs either micromoleculars or macromoleculars. But it does not mean that the swellable microneedle patch is an impeccable microneedle system. This is because researchers dispute that the time spent by this kind of MAPs in releasing drugs from the microneedle to interstitial fluids is the longest among the four traditional sorts of MAPs. Actually, low-efficiency is a main setback of the microneedle patch.

2.2. Innovated usages of MAPs nowadays

Recently, there are more and more innovative usages of MAPs to cater to different demands, which promote many fields greatly. Here this paper is going to introduce three relevant applications to demonstrate the idea.

2.2.1. MAPs for electroporation. The first application is about 3D printing microneedle patches for electroporation [5] (shown in fig.2 a). As is known to case, electroporation has functioned as a widely used method to measure the amount of particular cells and the speed of cell division since it was invented. It is regarded as one of the most effective ways to observe structure of cells and division processes. Nevertheless, there are some complicated factors affecting the accuracy and effectiveness of the method, such as the voltage value, the distance between cells and electrolodes, and shape or surface of electrodes. That's why sometimes the results of electroporation experiments are not as reliable as scientists expect. So, it is high time talents came up with strategies to overcome these problems. The 3D printing microneedle patches coated with nano Au particles can be dedicated to dealing with the problems

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mentioned above to a large extent. By coating nano particles on the surface of microneedle and making a kind of cancer cells named HCT116, which are marked by flourescent dye (EthD-1) divise on the surface of the microneedle patch, can expertise observe cancer cell division in high efficiency. This kind of application may be used to diagnose cancers at a very early stage, which means doctors can fight against the disease more effectively.

2.2.2. MAPs for ion fluctuation monitoring. Sometimes, microneedle patches are used to monitor ion fluctuations within human bodies [6] (shown in fig.2b). Introduced by Xie et al, there is a new kind of microneedle patch detecting real time ion fluctuations in interstitial fluids on the ground of 3D printing microneedle patches. With the help of microneedle arrays, main electrolytes including Na+, K+, and Ca2+ may be measured whenever and wherever. One advantage that makes the ion-monitoring microneedle stand out from other devices is that biochemical analytes can be measured directly without any secondary analysis, which improves the efficiency of biochemical analyzing and contributes to more accurate outcomes. Another outstanding advantage is that this sort of monitoring device can be made full use of by ordinary people without receiving any professional training before. That is to say, this set of facilities are likely to truly be prevailing in the future due to its convenience.

2.2.3. MAPs for biomarker extracting. Another kind of related usage for point diagnosing was introduced by Srikanth Singamaneni, et al [7]. They have invented a new method to detect and quantificate biomarkers in mouse bodies (shown in fig.2c). The microneedle patches made from polystyrene are coated with different primary antibodies which can be connected by biomarkers in interstitial fluids. After checking components on the surface of the microneedle patch, it turns out that, valuable elements including antibodies, cytokines, and matricellular proteins have been extracted without any harm to mice thanks to the microneedle patch. What's the most significant is that this kind of microneedle patch can be used to extract biomarkers contained in calvarial periosteum which function as indispensable indicators to some potential and devastating disorders in blood vessels and brain without leading to death of mice due to the painless and mild microneedle treatment method.

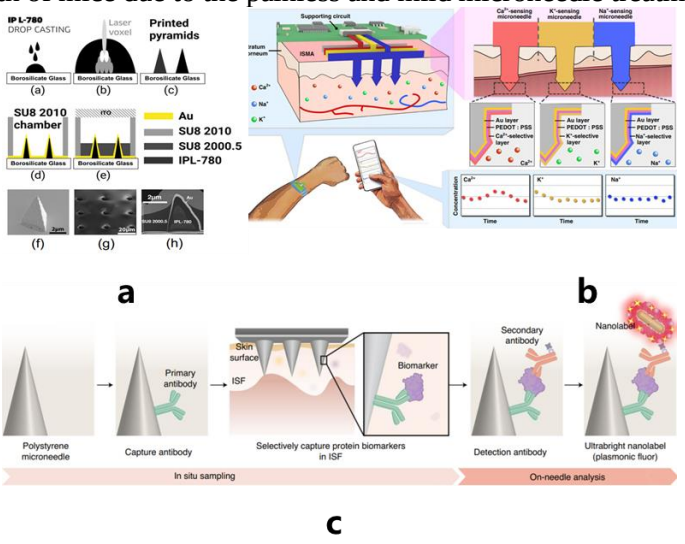

Figure 2. Three types of innovated usages of MAPs. a, MAP based on 3D printing involving nano Au particles on the surface of the patch, which greatly promote the accuracy of the electroporation. b, wearable device connected to smart facilities based on the microneedle patches monitoring ions in interstitial fluids. c, novel MAP for extracting biomarker including antiabody and other antiagents for early and accurate diagnosing particular diseases.

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3. Conclusion

Since the microneedle was invented some decades ago, it has functioned as an effective drug-controlling and releasing system in curing kinds of disorders and has won an international reputation as a painless and high-effective tool. This promotes modern drug delivery development. The paper introduced conventional MAPs and explain their discrepant characteristics and practical areas. This paper finds that MAPs, as one of the most efficient drug controlling and releasing tools can do their part in other fields like chemistry and biology due to the fact that scientists can change their internal or external design to meet different demands. This paper referred to some creative applications based on pain-free or drug-containing traits in different fields like electroporation and in vivo ion fluctuation monitoring. However, this paper did not give more examples of more creativities of microneedles and thus disclose the mechanics of advanced applications. In the future, more people would surely realize that microneedles can not only act as a drug delivery tool for disease curing or wound healing, but also can make contributions to wider fields including biology, electrochemistry and instrumental analysis for the cause of science.

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