MULTICOMPARTMENTAL MICRONEEDLE-BASED TECHNOLOGY DEVICE AS NOVEL DIAGNOSTIC TOOL

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Safe self-administration is a point of care in the modern society and everything seems to evolve in this direction. As matter of fact, point of care tests (POCT) have increased worldwide recently, due to several reasons. Firstly, they allow the patient to monitor and detect clinical relevant analytes of interest in the fastest and easiest manner. Diabetic patients can control glucose levels quickly nowadays, for instance. POCT do not keep authorized personnel away, but represent a new resource in the diagnosis and treatment field: a rapid communication is available between patient and doctor and the required care is consented [1-2].

The skin is the largest tissue of the human body and is involved in many physiological processes: it has a role in prevention of excess water loss from the body and in thermoregulation, but firstly it is a barrier from exogenous agents, protecting the human body against mechanical injures, UV-rays and micro-organisms. The skin is made up of three layers: the epidermis, the dermis and the hypodermis [3].

Diagnosis and monitoring of disease is often done by measuring biomarkers found in blood, urine, saliva, and other bodily fluids. Another rich source of biomarkers is the interstitial fluid that surrounds cells and tissues in the body, but the difficulty in accessing this fluid has limited its use in research and medicine. Dermal interstitial fluid may be used for that purpose [4].

Allergic diseases can really invalidate people quality of life and cause death by anaphylaxis rarely. They are increasing worldwide: globally, over the last 50 years or so, allergic diseases are increased to epidemic proportions maybe in connection with pollution and climate changes. [5]. More and more adolescents living in urban centres of developing countries, especially the heavily populated ones, have shown allergic disorders. There are no serious planes to face this problem because of few resources [6], thus it is necessary to have easy ways to diagnose allergic disorders. Patients self-enabled in safe conditions could implicate fast mass screening. Many patients' problems can be managed with the judicious use of medications that is why it is important to make people undergo allergic tests and discover which allergies may suffer from [7].

Epicutaneous immunotherapy is a recently rediscovered route of allergen administration via the epidermis [8]. The most common skin allergic test is the prick test: an allergen droplet is placed onto the skin which is then pricked by the use of a lancet handled by a health worker. [9]. Pricking the skin can cause blood stains and redness but the epithelial layer of the skin should be penetrated without inducing bleeding, which can lead to false-positive results. A new lancet should be utilized for each allergen to avoid cross contamination from the previous allergen tested. Wiping lancets also represents a potential risk factor for transmitting different diseases for the health care professional performing the test. [10]. The interpretation of the test is based on wheal diameter following the allergic reaction and so making this test a semiquantitative measure of allergy. Despite it is common for tipe I allergies identification, a standardized test method is not available yet [11].

Over the past decade microneedles have been developed to promote the transdermal drug delivery in a minimally invasive manner [12]. Microneedles arrays (MNs) are able to break the stratum corneum (10-20 µm length), the outer layer of the epidermis, and so accessing to intradermal and transdermal routes. They are applied to the skin surface to pierce the epidermis and create microscopic pores through which drugs may diffuse to the dermal microcirculation. MNs are long enough to penetrate to the dermis, but are short and narrow enough to avoid stimulation of dermal nerves or puncture of dermal blood vessels. They can vary from 50 to 900 µm in height, have different geometries (microblades, blunt-projections or shaped in an arrow-head), be of different materials and be produced by several microfabrication techniques. [13-14]. MNs are generally divided in five categories: solid, coated, dissolving, hollow and swellable. Dissolving MNs have gained particular interest because of polymeric materials.

This PhD project is focused on the development of a multicompartmental microneedle-based technology device as novel diagnostic tool. In principle the development of such a tool may be used to stimulate and collect biomarkers

related to other pathologies [15]. Theoretically, this class of devices allows the delivery of several drugs that might enhance the detection of specific clinical molecules monitored during a patient treatment (cancer biomarkers, ion concentration, glucose, etc). Particularly, this PhD will be focused on the development of a device overcoming the issues related to the current skin allergic tests. Microneedle-based technology might be used as painless tool to access to dermal interstitial fluid, deliver the specific allergen and then collect the fluid containing the analyte of interest, such as histamine.

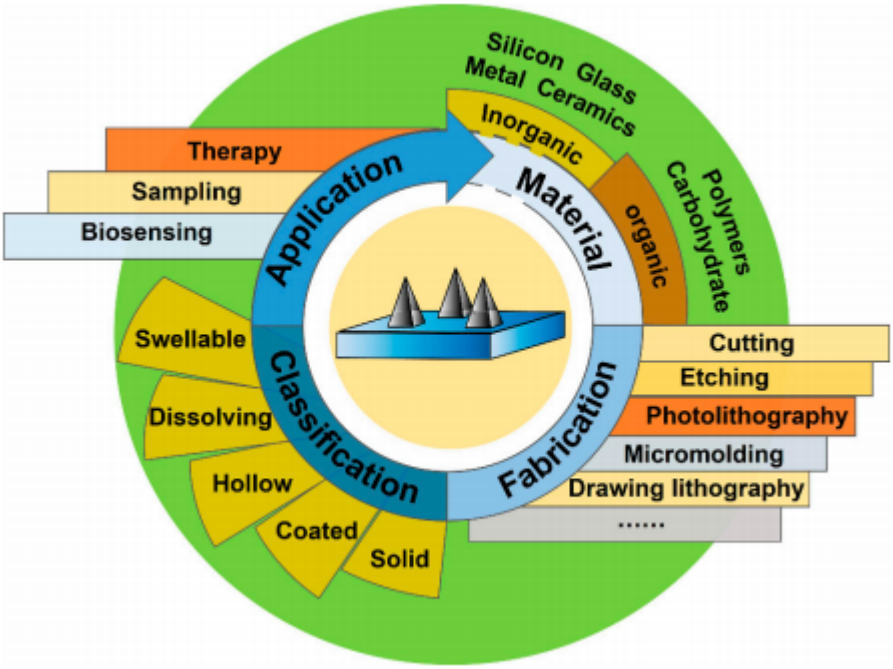

Figure 1. Schematic illustration of microneedles commonly used in biomedical diagnosis and therapy [1].

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