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MICROFLUIDICS: An Emerging Trend in Medicine

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ABSTRACT

Microfluidics is a promising field in the future of medicine and technology. It requires a minute amount of samples or reagents. This review article describes a better understanding of the emerging concept of Microfluidics and its versatility in the medical field. Organ on-chip, disease detection, drug discovery, detection of blood cells, are the main areas in which the microfluidics concept is utilized effectively. The future road map of microfluidics is also gifted in terms of new advances in technology, reliability, high resolution, faster results, etc.

Keywords: Microfluidics, Point of Care Testing, Organ On-Chip, Paper-Based Microfluidics.

INTRODUCTION

Microfluidics is a system used to processes a small number of samples, less than femtoliters with channels at a dimension of about ten to hundreds of microns [1] In 1949 a German engineer, Werner Jacobi developed the prototypes of Integrated Circuit technology (ICs) and was considered as the "father" of Microfluidics.[2] Microfluidics is a versatile field that combines the concepts from physics, chemistry, engineering, mathematics, computing, nano, and biotechnology. Microfluidics concept introduced from chromatography. [3] The very first micropumps and microvalves used to control the fluid volume were utilized in the 1980s for the manufacture of inkjet printers. In the 1990s, the department of defense in the US developed a microfluidics advancement technology to identify biological and chemical hazards [1] Microfluidics was initially introduced in the field of microbiology, as a device for analytical analysis using tiny volumes of samples and reagents. The foundation of microfluidics is based on three main different fields, microanalysis, biodefence, and microelectronics. [4].

Types of microfluidics:

Microfluidics can be categorized into continuous-flow microfluidics and droplet microfluidics.

1. Continuous-flow microfluidics: It consists of a one-phase fluid in the chip. It has got certain specialties like, less amount of sample and reagent required, intensifies the analytical speed and better reproducibility, than a conventional experiment. [5]

2. Droplet microfluidics: It deals with the formation, operation, and practices of droplets in microfluidic devices.

Its main objective is to produce discrete droplets applying non-miscible phases. [5]

Materials used for microfluidic devices:

A classical microfluidic device comprises a chain of microchannels, orifice for injecting fluids, micropumps, and microvalves for fluid administration inside the chip, exit for removing fluids, and a couple of recognition systems for analytical studies. Materials like glass, silicon, and polymers are used to fabricate microfluidic devices for many years and there won't be any ideal material, everyone has some pros and cons. [1] However, the choice is purely dependent upon the researcher's opinion, based on the application of the material.

The most frequently used materials for the manufacturing of microfluidic devices are:

Polymer:

Polymer materials are generally used in the construction of microfluidic devices due to their excellent biochemical performance and their reasonable cost.

Polydimethylsiloxane (PDMS), a mineral-organic polymer of the siloxane family is the widely used polymer material. The main peculiarities that make PDMS a unique material is:

1. Transparency: Clarity of micro-channels and their content.

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2. Elasticity: The elasticity of PDMS can be applicable for various purposes. e.g., Valve integration through channel deformation.
3. Cost: PDMS is very cheap compared to other materials used for the production of a microfluidic chip
4. Permeability: The gas absorptive nature of PDMS can be useful in cell culture, gas sensors, etc.

There are some drawbacks in using PDMS are also there, the performance of the chip is defined by the age of the material, PDMS is particularly useful in aqueous application due to their low chemical affinity with organic solvents, difficulty to setup electrodes inside the chip.Another example of a polymer is Polystyrene (PS), used in drug research.It has got properties like optically transparent, biocompatible, inert, and rigid.

Thermosets:

These polymers are connected by chemical bonds, which provides them highly cross-linked polymeric structure. Its high mechanical and physical strength are due to the cross-linked polymeric structure. The main characteristics of thermosets are insolubility, high resistance to creep, non-melting, and non-swelling in certain solvents. One of the frequently used thermosets is Thermoset Polyester. The benefits of thermosets are their reasonable price, simple and rapid chip crafting, and
their high clarity in the visible range. There are some limitations regarding thermoset are, non-elastomeric property, non-permeability to gas, require fluidic interconnectors due to their hardness.

Silicon:

Silicon was one of the primary materials used in microfluidics devices, due to its adaptability in the microelectronic industry for the production of premiere microfluidics chips. Specialties of silicon in microfluidic applications are its heat conductivity, surface constancy, and solvent affinity. The prime limitation of silicon microfluidic chips is their difficulty in optical detection due to the optical translucency present in the visible electromagnetic range.

Glass:

It has got some traits like popular surface chemistries, remarkable optical transparency, and distinctive high-pressure resistance making it the preferred one for many operations. The main drawback of glass microfluidic chips is their expensiveness as a raw material.

Paper-based:

Paper is also used as a material for microfluidic chip production due to its low cost, delicate nature, ease to handle, stack, and carry. It is an eco-friendly material for microfluidic chip fabrication due to its easily disposable property. The main defect seen in the paper-based microfluidic device is the crisis in tapping the channels on the microfluidic chip.

Hydrogel:

Hydrogel is very flexible, non-toxic to the cells, available in the market, at a reasonable rate. Agarose gel is a common hydrogel used for the production of the microfluidic chip due to its diffusible nature in most of the solutes. [4]

Microfluidics Applications in medicine:

Microfluidics is used in various fields such as microbiology, cell biology, medicine, developmental biology, genomics, diagnostic technique, organs on chips, drug discovery

In this review article, we are mainly focussing on the medical applications of microfluidics.

Diagnostics:

Point of care testing:

It is one of the cardinal applications of microfluidics in which rapid diagnosis is possible at the patient care site. [3] It will reduce the healthcare cost and increase the accessibility to many people. Paper-based microfluidic devices are fabricated on the exterior part of the paper with polymeric coating or hydrophobic materials like wax, inside this, fluid is present. [6,7] Evaluation of analytes is depending upon colorimetric, electrochemical, or chemiluminescent output. Paper-based microfluidics devices are widely available in the market for the diagnosis of various microorganisms and biochemical samples [8]. Paper-based microfluidics has peculiarities like low cost, biodegradable, and easy to handle [8,9]. PCR (Polymerized Chain Reaction) based integrated microfluidic devices are used for the rapid determination of microorganisms like Bacillus anthracis, Bordetella pertussis, Mycobacterium tuberculosis, E. coli, Salmonella typhimurium, and HIV. [10] Special biomolecules can be detected by Lateral Flow Strip Assays (LFSA). The most popular LFSA, available in the market is the home pregnancy test kit, which analyses the presence of Hcg (Human chorionic gonadotropin) hormone in the urine of a pregnant lady. LFSA is also used to detect the presence of other biomarkers, like myeloperoxidase, for the diagnosis of bronchitis as a neutrophilic bronchitis precursor. [10,11].

Detection of blood cells:

Many hematological diseases like anemia, hemophilia, etc. can be detected by Microfluidic paper-based analytical devices (µPADs) [12.13] A µPADs microfluidic device was developed by Berry et al. for evaluating the critical hematological index [12.13]. Alterations are seen in the critical hematological index used for the diagnosis of anemia. Another µPAD microfluidic device used by Hegener et al. evaluated the RBCs at the single-cell level to explain the clotting of blood in patients. which can use for the diagnosis of diseases such as hemophilia [12,13].

Cancer cell detection:

Microfluidics act as a diagnostic aid for the detection of a cancer cell. [14] Circulating Tumor cells are rarely found in the blood of cancer patients. Microfluidics imparts a special option for categorizing and detecting rare cells.

A microfluidic chip had been proposed in such a way to reproduce massive numbers of viable CTCs(circulating tumor cells standard) in a single step, which could later lead to the identification of biomarkers of cancer stem cells and elaborate the awareness about the metastasis of cancer. [15]

Organ on chip:

'Organs-on-chips' have been composed to depict the biological processes using microfluidic principles to copy the physiological status inside the living organism and coordinate all the processes needed for a bioassay. The functions of critical organs can be reproduced by using microfluidic devices with polymers. A microfluidic device was composed to recreate lung function on-chip to mirror the human inflammatory response towards microorganisms and to study the harmful effects exerted by airborne particles, chemicals, or drugs. [16] Heart-on-a-chip is another gifted option used for inquiring about the in vitro contractility and electrophysiological behaviour of heart tissue[17]. In addition to this, there are organs on a chip that have been designed to replicate the functions of the kidney, osteoblast, gastrointestinal system, etc…[18,19.20,21]

Drug Discovery:

Microfluidics emerged as an important tool in drug discovery also. Identification of a target, ie a protein or a gene troubled by a drug molecule is the first step in drug discovery. A microfluidic chip was developed by the researchers which can separate the target proteins by micellar electrokinetic chromatography (MEKC)[22], capillary zone electrophoresis[23.24], and isoelectric focusing in less than 20 min. [25]

Arising and future applications of Microfluidics:

Format Stickers are an emerging creation in microfluidics that may be mixed and matched to bring about the requirements of each reaction. A bundle of standardized stickers can be used in an instrument, everyone represents one area of the microfluidic chip. Versatile microfluidics is a spring-up idea that connects technology, gadgets, science, and drugs. [26,28] Microfluidics devices could be beneficial in pediatric patients and patients having difficulty in communication, where testing is difficult**.** An aggregate of microfluidics and ultrasounds is a novel and emerging practice, helpful in areas like pharmaceutical formulation, diagnostics, and therapeutic applications, producing combined outcomes. [27, 28]

CONCLUSION:

Microfluidics is one of the emerging fields and has got a wide range of applications in various streams such as biomedical, biotechnology, genomics, cell culture, disease detection, drug discovery, biology, etc. The new developments in microfluidics will provide a promising future to medicine as well as technology including the advancement of clinical diagnoses and testing, like bioassays for patient clinical indication, point-of-care testing, home testing, and the reformation of organs on human-on-chip systems, etc. The fusion of various technologies improves microfluidics to grow extensively in the fields of medicine and biology. We can hopefully look forward to the upcoming advances in microfluidics and their impact on the various fields.

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